TOWARDS A BALANCED AND ETHICALLY RESPONSIBLE APPROACH TO UNDERSTANDING DIFFERENCES IN SLEEP TIMING

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This thesis is dedicated to my parents, Te Mihikore Agnes and Cliff Paine.
With love and thanks for all of the opportunities you have given to me.

ABSTRACT

The circadian clock defines physiologically optimal times for sleeping, which vary along a continuum of circadian phenotypes from morning- to evening-type. Although different 'chronotypes' can be discriminated reliably by the Morningness/Eveningness Questionnaire (MEQ), there is little published information on their prevalence. The timing of sleep is also heavily influenced by societal norms. However, the relative contribution of circadian physiology versus psychosocial factors is unknown.

This thesis took a multidimensional approach to investigating preferred sleep timing within the general population of New Zealand (30-49 years). A New Zealand version of the MEQ was mailed to a random stratified sample of 5,000 adults living in the Wellington region (55.7% response rate). Using scoring criteria for middle-aged adults, approximately 25% of the population were morning-types and 25% were evening-types.

The sleeping patterns of 15 morning- and 16 evening-types were monitored using actiwatches and sleep diaries. Morning-types slept significantly earlier, but there were no differences in sleep duration or quality. Both chronotypes showed evidence of using the weekend to catch-up on sleep, although this was more evident among evening-types.

Differences between chronotypes were also investigated using the endogenous melatonin rhythm as a circadian phase marker. The timing of the melatonin rhythm was earlier among morning-types, with the difference being greater for melatonin onset, than offset. However, differences between weekday versus weekend sleep explained more of the variability in sleep timing that did circadian phase.

Understanding the genetic differences in the circadian clock is evolving rapidly. While this is of particular scientific interest, little consideration has been given to the ethical implications of this type of work. In the final study, a Kaupapa Māori framework was used to explore Māori hopes and concerns for genetic research in Aotearoa/New Zealand. Thematic analysis indicated that Māori are not anti-science, however there is an urgent need for ethical guidelines that uphold and respect the values of Māori society.

This thesis argues that sleep is a major public health issue for New Zealand. However, a number of challenges must be met to ensure that new scientific knowledge meets the needs and expectations of the community.

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ABBREVIATIONS & TECHNICAL TERMS

95% CI	95% confidence interval
ACC	Accident Compensation Corporation
ActSlp	Actual sleep time
ActSlpP	Actual sleep time percentage
Allele	One of the different forms of a gene that can exist at a single locus
Amplitude	The difference between the maximum and minimum points of a biological rhythm
aMT6s	6-sulfatoxymelatonin; the urinary metabolite of melatonin
ANOVA	Analysis of Variance
ANCOVA	Analysis of Covariance
ASPS	Advanced Sleep Phase Syndrome
AssSlp	Assumed sleep time
AUC	Area under the curve
Autosomal dominant	An allele that masks the expression of another allele
BMI	Body Mass Index
BT	Bed Time
CBT	Core Body Temperature
Chromosome	A linear end-to-end arrangement of genes and other DNA, sometimes with associated proteints and DNA
Chronobiology	The study of biological clocks
Chronotype	A circadian phenotype
Circadian	Latin for '*about a day'*. Refers to self-sustaining rhythms which have a periodicity of approximately 24-hours
Constant Routine	A study design used to examine endogenous rhythms free of the masking effects of sleep, posture, activity, and meals
CRS	Contact record sheet
CT	Circadian time
DASS-21	The short form of the Depression, Anxiety, and Stress Scale (DASS)
DD	Dark/Dark cycle. Refers to the use of two dark periods within one cycle and is the experimental manipulation of constant conditions
DE-type	Definitely Evening-Type
df	Degrees of freedom
Dimerise	The chemical union of two identical molecules

Diurnal	Day-active
DLMO	The Dim Light Melatonin Onset
DLMO20%	The Dim Light Melatonin Onset defined as 20% of maximum melatonin concentration for that individual
DLMO25	The Dim Light Melatonin Onset defined as 25% of maximum melatonin concentration for that individual
DLMO50	The Dim Light Melatonin Onset defined as 50% of maximum melatonin concentration for that individual
DLMOff	The Dim Light Melatonin Offset
DLMOff25	The Dim Light Melatonin Offset defined as 25% of maximum melatonin concentration for that individual
DLMOff50	The Dim Light Melatonin Offset defined as 50% of maximum melatonin concentration for that individual
DM-type	Definitely morning-type
DNA	Deoxyribose nucleic acid
ECART	The Ethics Committee on Assisted Reproductive Technology
EEG	Electroencephalogram
EMG	Electromyogram
Entrainment	The process of synchonisation of a self-sustaining rhythm to the environmental light/dark cycle
EOG	Electrooculogram
Epoch	A measure of duration of a sleep measurement
ERMA	The Environmental Management Authority
ESS	The Epworth Sleepiness Scale
ESR	The Environmental Science and Research Limited
E-type	Evening-Type
F	F-statistic
False negative	The ratio of the number of events incorrectly classified as non-events over the sum of all observations classified as non-events
FASPS	Familial Advanced Sleep Phase Syndrome
FGP	Focus Group Participants
FragIn	Movement and Fragmentation Index

Free run	The state of a circadian rhythm under constant conditions (i.e. DD); A circadian rhythm that is not entrianed to zeitgebers and therefore is running at its endogenous period length
GATT	General Agreement on Tarriff and Trade
GE	Genetic Engineering
GM	Genetic Modificaiton
GUT	Get Up Time
Heterozygous	A gene pair having different alleles in both copies e.g. AA or aa
Homozygous	A gene pair having identical alleles in both copies e.g. AA or aa
HRC	The Health Research Council of New Zealand
Heterodimer	A complex of two different proteins
HIOM	Hydroxyindole-O-methyltransferase
HTIF	The Human Time Isolation Facility
HSNO	Hazardous Substances and New Organisms
HRCEC	The Health Research Council Ethics Committee
HUGO	The Human Genome Organisation
ICSD	The International Classification of Sleep Disorders
in vitro	Latin for '*in glass'*. An experimental situation ouside the organism
IQR	Interquartile Range
IVF	*in vitro* fertilisation
KI	Key-informant
Knock-out	The process of purposely removing a particular gene or trait from an organism
KMR	Kaupapa Māori Research
KSS	Karolinska Sleepiness Scale
K-W	Kruskal-Wallis test
LD	The light/dark cycle (i.e. a fixed schedule most commonly 12 hours light and 12 hours dark)
Linkage analysis	A mathematical procedure that analyses meiotic recombination frequencies between pairs of genes to determine whether two loci are linked and, if so, how closely
Locus	The position of a gene, DNA marker or genetic marker on a chromosome
Log10	Log to base 10
LOWESS	Locally Weighted Scatterplot Smooth

Lux	The measure of light intensity which is based on the spectural sensitivity distribution of rods and cones
MActSc	The Mean Activity Score
Masking	The concealment or alteration of a self-sustaining rhythm by environmental or behavioural factors (i.e. light, posture, meals, sleep)
MelStart	Melatonin Start Time. Represents the first detectable melatonin level
MelEnd	Melatonin End Time. Represents the last detectable melatonin level
MEQ	The Horne and Ostberg Morningness/Eveningness Questionnaire
MEQ1	MEQ scoring criteria developed by Horne and Ostberg (1976)
MEQ2	MEQ scoring criteria developed by Taillard and colleagues (2004)
Metazoan	An animal whose body consists of cells that are separated into different parts such as tissues and organs. All animals except for sponges and protozoans are classified as metazoans.
MOU	Memorandum of Understanding
mRNA	An RNA molecule transcribed from the DNA of a gene, and from which a protein is translated by the action of ribosomes. The basic funtion of the nucleotide sequence of mRNA is to determine the amino acid sequence
MSlpEff	Mean Sleep Efficiency
Mutation	The process producing a gene or a chromosome differing from the wild-type
NAT	*n*-acetyltransferase
NEAC	The National Ethics Advisory Committee
Night work	A pattern of work which involves working for at least 3 hours between midnight and 5am
NKTT	Nga Kaihautu Tikanga Taiao (The Māori Advisory Committee of ERMA)
non-REM	non-Rapid Eye Movement
Nucleotide	A subunit that polymerises into nucleic acids (DNA or RNA). Each nucleotide consists of a nitrogenous base, a sugar and one to three phosphate groups

Null allele	An allele whose effect is either an absence of normal gene product at the molecular level or an absence of normal function at the phenotypic level
NZDep	The New Zealand Deprivation Index
OR	Odds Ratio
Orthologous	Genes that have evolved directly from an ancestral gene
OSA	Obstructive Sleep Apnoea
OSAS	Obstructive Sleep Apnoea Syndrome
Period	The time interval between recurrances of a defined phase of a rhythm
pg/ml	picograms per millilitre
Phase	The position of the circadian clock in its cycle
Phase angle	The difference in time or degrees between the phase of one rhythm and the phase of another rhythm or environmental cycle
Phase advance	An earlier relative phase position
Phase delay	A later relative phase position
Phase marker	Any identifiable point in the cycle of a rhythm (e.g. maximum or minimum)
Phase shift	The process of moving the phase position of the circadian clock to an earlier (phase advance) or later (phase delay) clock time
Phenotype	The detectable outward manifestation of a specific genotype; the observable attributes of an organism
Phosphorylate	To add phosphate e.g. to a protein to alter its function
Photoperiod	The duration of light in a light/dark cycle
pM	picomolar units
Polymorphism	The occurance in a population (or among populations) of several phenotypic forms associated with alleles of one gene or homologues of one chromosome
Prevalence	The number of instances of a given disease or occurrence in a given population at a specific point in time
PRC	Phase Response Curve
PSG	Polysomnography, the gold standard measure of sleep consisting of EEG, EOG and EMG channels
PSQI	The Pittsburgh Sleep Quality Index

***p*-value**	A statement of the probability that the difference observed could have occurred by chance, reflecting the statistical significance of the result
PVT	The Psychomotor Vigilance Task
r	Correlation coefficient
REM	Rapid Eye Movement
RCoGM	The Royal Commission on Genetic Modification
RNA	Ribonucleic acid
RR	Response Rate
REML	Residual Maximum Likelihood estimation
RIA	Radioimmunoassay
SBC	Schwarz-Bayesian Criteria
SCN	Suprachiasmatic Nucleus
SD	Standard Deviation
Shift work	Any work that forces sleep to be displaced
SlpEff	Sleep Efficiency
SlpEnd	Sleep End Time
SlpSt	Sleep Start Time
SNP	Single Nucleotide Polymorphism; DNA sequce variation that occurs when a single nucleotide (A, T, C, or G) in the genome sequence is altered
SQRT	Square Root Transformation
Subjective day	The light portion of the LD cycle for diurnal species and the dark portion of the LD cycle for nocturnal species
Subjective night	The dark portion of the LD cycle for diurnal species and the light portion of the LD cycle for nocturnal species
S-W	Shapiro-Wilk Test
SWA	Slow Wave Activity
SWRC	The Sleep/Wake Research Centre
SWS	Slow Wave Sleep
TActSlp	Total Actual Sleep Time
TAssSlp	Total Assumed Sleep Time
TIB	Time in Bed
TMActSc	Total Mean Activity Score
TMFragIn	Total Movement and Fragmentation Indec
t	The *t*-statistic
$\mathbf{T_{min}}$	The minimum of the core body temperture rhythm
Transactivation	The stimulation of transcription by a transcription factor binding to DNA and activating adjacent proteins

Transcription	The process whereby RNA is synthesised from a DNA template
Transcription factor	A protein that binds to a cis-regulatory elements and thereby, directly or indirectly, affects the initiation of transcription
Translation	The process of protein synthesis whereby the primary structure of the protein is determined by the nucleotide sequence in mRNA
The Treaty of Waitangi	The founding document of New Zealand signed in 1840 by some Māori chiefs and representatives of the Crown
TTiB	Total Time in Bed
Wild-type	A strain or characteristic which prevails in natural conditions, as distinct from an atypical mutant
WTO	The World Trade Organisation
x^2	Chi-square
Y=a+b*X	The regression equation. The Y variable can be expressed in terms of a constant (a) and a slope (b) times the X variable. The constant is also referred to as the intercept, and the slope as the regression coefficient or B coefficient.
Zeitgeber	German for *time giver*. External stimuli that provide time cues for the synchronisation of the circadian clock
ZT	Zeitgeber Time

MĀORI TERMS

Aotearoa	New Zealand; the land of the long white cloud
Aroha	Love
Atua	Gods, deity
Ea	The successful restoration of relationships
Hapū	Sub-tribe
Hawaaiki	Ancestral homeland
Hinengaro	Psyche; the mental state
Hine-nui-te-Pō	Originally named Hinetītama; in Māori mythology she is the great woman of the place of the departed spirits
Hui	Gathering
Iwi	Tribe
Ira tangata	Human element; gene
Kai	Food
Kanohi kitea	The face seen
Kainga	Home
Kaitiaki	Guardian
Kaitiakitanga	Guardianship
Kaupapa	Foundation; base; philosophy
Kaumatua	Elder
Kawa	Protocol
Mana	Authority; presitge; power
Manaakitanga	Hospitality; an expected state of behaviour
Mana motuhake	Separate authority; effective outcomes and evidence of benefit
Mana tangata	Dignity; safety; mutuality
Mana whakahaere	Collaboration; control
Mana whenua	The tribe who hold the authority of the area
Manuhiri	Guests
Marae	A complex of buildings and the surrounding land; a focal point for a sub-tribe
Mataatua	Māori for *'the face of god'*; one of the canoe which brought Māori to Aotearoa/New Zealand
Mātauranga	Knowledge
Maui	A special force within Māori mythology who was responsible for many great feats including the fishing up of the North Island of Aotearoa/New Zealand
Mauri	Life essence
Mihimihi	Greeting

Ngā Wahine Tiaki o te Ao	Guardians of our world; a group of Māori women concerned with genetic engineering and the future of our world
Ngāti Kahungunu	The tribe located in Hawkes Bay to Wairarapa
Nga Kaihautu Tikanga Taiao	The Māori Advisory Committee of the Environmental Risk Management Authority
Ngāti Porou	The tribe located on the East Coast of the North Island
Ngāti Rongo	A sub-tribe of Tūhoe
Ngai Tahu	The tribe located in the South Island
Noa	The restoration of balance
Pākehā	Person of predominately European descent; not Māori
Pono	True; genuine
Powhiri	The traditional practice of welcoming guests
Rangatahi	Youth
Rangatira	Chief; noble status
Ranginui	The sky father; a god personified in the sky
Rongoa Māori	Traditional medicine and healing practices
Rongokarae	The ancestor of the Ngāti Rongo hapū of Tūhoe
Ruatoki	Settlement in Te Urewera
Tangata whenua	People of the land; indigenous people
Tane	Man
Tāne	Men
Taonga	A treasured possession
Tapu	Sacred
Tauarau	The marae belonging to the Ngāti Rongo hapū of Tūhoe
Tauranga-Moana	Tauranga, Bay of Plenty
Te ao marama	Māori for *'the world of light'*
Te ao Māori	The Māori world
Te ao turoa	The natural world
Te hohonutanga	In depth
Te Kopere	The Māori Caucus of the Constructive Conversations Project
Te Mahurehure	A sub-tribe of Tūhoe
Te maramatanga	Understanding; enlightenment
Te reo	The Māori language
Te Pumanawa Hauora	The Māori Health Research Centre at Massey University
Te Rōpū Rangahau Hauora a Eru Pōmare	The Eru Pōmare Māori Health Research Centre at the Wellington School of Medicine and Health Sciences

Te Runanga o Ngai Tahu	The Ngai Tahu tribal authority
Te Ture Whenua Act	The Māori Land Act
Te Urewera	Lands belonging to the Tūhoe people
Te Whakatane	A sub-tribe of Tūhoe
Te whanuitanga	Outwards
Tiaki	Guard; protect
Tika	Right; correct
Tikanga	Cultural practices
Tinana	Body
Tino rangatiratanga	Self-determination; sovereignty; absolute chieftenship
Tipuna	Ancestor
Tūhoe	The tribe of Te Urewera
Wahine	Woman
Wāhine	Women
Waikaremoana	Māori for *'the sea of rippling waters'*; a lake in Te Urewera
Wairoa	Town, Hawkes Bay
Wānanga	Schools of learning; discussions
Waka	Canoe
Whāngai	Foster child
Wairua	Spiritual essence
Whakapapa	Genealogy
Whakatane	City, Bay of Plenty. Landing place of the Mataatua waka
Whānau	Family; extended family
Whānaungatanga	Expressions of support; love within a family
Utu	Compensation; revenge; reciprocity

CHAPTER 1
BACKGROUND

Being diurnal (i.e. day-active) is not simply a matter of culture or social convention. We are effectively programmed for sleep at night by an internal timekeeping system, or 'circadian clock'. Circadian clocks are a very ancient and fundamental property of life on Earth, found in all classes of plants and animals. However, human society has begun placing unprecedented demands on our diurnal nature, with the advent of 24-hour operations and jet air travel across time zones (Gander, 2003).

The circadian clock co-ordinates daily cycles in a multitude of biological processes, keeping them in step with the environmental day/night cycle. Of primary importance is its key role in the timing and quality of sleep. This is the source of many of the occupational safety and health problems that arise when people try to work against the circadian clock's programming for sleep at night.

This chapter begins with a brief overview of some of the key concepts in current understanding of the physiological processes that underlie our diurnal functioning. A number of theoretical and mathematical models have been proposed to explain the role of the endogenous mechanisms that regulate sleep timing, some of which will also be described in this section. Several recent studies have elucidated the genetic and molecular components of the mammalian circadian system, so this section includes a detailed description of the core genes that drive circadian rhythmicity. Experimental studies have provided a wealth of information and knowledge about the physiological processes that regulate sleep/wake cycles. However in daily life, the timing of sleep and wakefulness is also heavily influenced by societal factors such as work/school patterns, family commitments and social expectations. Therefore this section ends with a consideration of the psychosocial factors that influence sleep in our 24-hour society.

The subsequent section focuses on individual variability in the preferred timing for sleep and waking activity, known as morningness/eveningness. This section will introduce the literature which now convincingly demonstrates that morningness/eveningness is a characteristic of the endogenous circadian clock, including genetic studies linking polymorphisms in circadian genes to extreme sleep timing preference and circadian sleep disorders.

Sleepiness and inattention because of insufficient or disrupted sleep can have serious consequences for the individual, and for society (Walsh, Dement, & Dinges, 2005). Furthermore, there is a rapidly growing body of evidence implicating habitual short sleep as an independent risk factor for the development of obesity, diabetes and cardiovascular illness

(Knutson & Turek, 2006). Thus, the final section in this chapter addresses the relevance of circadian physiology to public health in Aotearoa/New Zealand.

1.1 Key Concepts in Sleep and Circadian Physiology

1.1.1 A Brief Definition of Human Sleep

Cycling between sleep and wakefulness is one of the most prominent and profound rhythms in life (Zee & Turek, 1999). Normal human sleep is comprised of two distinct states correlated with characteristic changes in brain activity, muscle tone and autonomic activity (Zee & Turek, 1999), non-Rapid Eye Movement (non-REM) and Rapid Eye Movement (REM) (Carskadon & Dement, 2005). Non-REM sleep is divided into four arbitrarily defined stages which are associated with depth of sleep, with arousal thresholds generally lowest in Stage 1 (i.e. 'light' sleep) and highest in Stage 4 (i.e. 'deep sleep'). On the other hand, REM sleep is characterised by high levels of brain activity, bursts of rapid eye movements and muscle paralysis. Thus, Carskadon and Dement (2005) describe non-REM sleep as '…a relatively inactive yet actively regulating brain in a movable body' while REM sleep is '…a highly activated brain in a paralyzed [sic] body (p. 14 in (Carskadon & Dement, 2005)).

Normal nocturnal sleep in young adults includes four to six alternating cycles of non-REM and REM sleep (Zee & Turek, 1999), each cycle lasting approximately 90 minutes, with REM sleep episodes becoming longer across the night (Carskadon & Dement, 2005). Although it is commonly believed that we should all have 8 hours of sleep each night, there is considerable inter-individual and night-to-night variability in sleep duration. A recent nationwide survey of 10,000 New Zealand adults aged 30-60 years (71% response rate) found that the average self-reported sleep duration was 7.41 hrs (*SD* ± 1.42 hrs) (Harris, 2003), with the majority of individuals reporting between 7-9 hours of sleep per night (Gander, 2003).

Changes in sleep consolidation and sleep architecture are an intrinsic characteristic of the ageing process in healthy individuals (Dijk et al., 1999). In later life sleep becomes shorter (i.e. early morning waking) and more fragmented (Bliwise, 1993, 2005). Insomnia is a common sleep complaint among older adults and a recent national survey of insomnia symptoms and risk factors among New Zealand adults found that older age (increasing years from 20-59yrs) was a significant independent predictor of reporting waking 3 or more times per night, having difficulty falling back to sleep, often or always waking too early, never or rarely waking refreshed, having a current sleep problem and having a chronic sleep problem lasting more than six months (Paine et al., 2004).

1.1.2 Concepts in Chronobiology

Our daily functioning varies systematically across the 24-hour day. Although oscillations in numerous physiological, endocrine and behavioural variables occur in step with the earth's rotation, they are not a passive response to the environmental day/night cycle. Rather, the timing of these regular rhythms arises from an internal time keeping system that is ubiquitous across most species including humans (Pittendrigh, 1960). This time keeping system allows organisms to anticipate and prepare for changes in the physical environment that are associated with day and night (Merrow, Spoelstra, & Roenneberg, 2005) and provides internal temporal organisation of a multitude of physiological and biochemical processes (Vitaterna, Takahashi, & Turek, 2001). The system responsible for the coordination of these daily rhythms is described in this thesis as the 'circadian clock'. Using the metaphor of a clock, the intrinsic workings of the circadian timing system represents the *mechanism* of the clock, while the rhythmic expression of this system is described as the *hands* of the clock. If the hands of the clock are interrupted so that the rhythm is disturbed, the internal clock mechanism continues to 'tick'. However, if the mechanism itself is interrupted, then the hands of the clock no longer function.

The term *circadian* is derived from the Latin words *circa* and *dies* meaning 'about a day', illustrating the approximately 24-hour rhythms that are endogenously driven in an organism (Moore-Ede, Sulzman, & Fuller, 1982). The circadian clock drives oscillations of a number of behavioural, physiological and endocrine rhythms including hormone secretion (e.g. melatonin, cortisol and growth hormone), core body temperature, alertness, cognitive and physical performance and sleep/wake cycles (Czeisler, Buxton, & Khalsa, 2005). This thesis focuses on the *phase* of a circadian rhythm, which can be any easily identified point of a circadian rhythm (i.e. minimum or maximum). Circadian phase is used in chronobiology to describe where the rhythm is up to in its cycle.

For a circadian clock to be of any use to an organism, it must first be synchronised with the day/night cycle. The process of synchronisation is called *entrainment*. Endogenous circadian rhythms are synchronised by *zeitgebers* (German for 'time givers') which provide cues to the underlying clock. The strongest of these cues is the light/dark (LD) cycle, however other zeitgebers include the sleep/wake cycle, physical activity and social interaction. Zeitgebers can also *mask* an endogenous rhythm. For instance, if light is given to nocturnal rodents at night, there is a loss of locomotor activity and sleep is promoted. In this case light has masked the true phase of the circadian clock by concealing the normal circadian behaviour in these animals (Mistlberger & Rusak, 2005).

1.2 The Timing of Human Sleep

The timing, duration and quality of human sleep is considered to be regulated by the interaction of a circadian process (process C), which promotes wakefulness during the day, and a homeostatic process (process S) which regulates the increasing need or pressure for sleep that accumulates with prolonged wakefulness and dissipates during sustained sleep (Dijk et al., 1999). In addition to these two endogenous factors, sleep timing is also controlled by a number of exogenous factors such as work schedules, family commitments, light, noise and other components of the modern 24-hour society. In order to understand the cyclic alternation between sleep and wake it is necessary to consider the mechanisms driving this oscillation.

1.2.1 The Circadian Clock

There is overwhelming evidence (Weaver, 1998) to support the suprachiasmatic nuclei (SCN), a small bilateral pair of nuclei located in the anterior hypothalamus of the brain (Moore-Ede et al., 1982), as the site of the master circadian clock in mammals. Early tract tracing studies (Moore and Lenn, 1972; Hendrikson, Wagoner, and Cowan, 1972 cited in (Moore-Ede et al., 1982)) identified the retinohypothalamic tract (RHT) as a visual pathway terminating specifically in the SCN of the hypothalamus, thus confirming observations that circadian rhythms were synchronised by the environmental LD cycle. Although it was originally thought that the endogenous clock mechanism was located in the general area of the ventral hypothalamus, subsequent studies demonstrated that lesions of the SCN specifically resulted in the complete loss of multiple circadian rhythms (Moore and Eichler, 1972; Stephan and Zucker, 1972 cited in (Moore-Ede et al., 1982)). More recently it has been reported that regulatory feedback loops of gene expression within the SCN are responsible for the generation of 24-hour rhythmicity (see section 1.3 for more details). While the SCN is considered the master circadian clock, it is now known that the circadian timing system consists of multiple peripheral oscillators in individual tissues and cells (see (Rossenwasser & Turek, 2005)).

Pittendrigh (1960) listed a number of generalisations which described the inherent and pervasive nature of circadian rhythms in organisms, and reinforced that they are considered fundamental features of living systems.

The most critical feature of a circadian rhythm is its ability to oscillate with a self-sustained amplitude under constant conditions (Roenneberg, Daan, & Merrow, 2003a). This characteristic was clearly demonstrated with the discovery of a mutant form of the Syrian hamster where heterozygous and homozygous mutant animals have a period of 22 hours and 20 hours respectively, as compared to wild-types who have a free-running period of 24 hours. Transplantation of SCN tissue between genotypes showed that the period of restored rhythmicity was characteristic of the donor animal rather than the host, indicating that circadian

rhythms are indeed endogenous (reviewed by (Weaver, 1998)). A series of *in vitro* studies have also demonstrated the endogenous nature of circadian rhythmicity, as cultured mammalian SCN cells are capable of generating circadian activity (see (Roenneberg & Merrow, 2005)).

Another important property of circadian rhythmicity is the ability to cycle with a period close to the earth's rotation (Pittendrigh, 1960). Early studies proposed that the endogenous free-running period in humans was more than 25 hours. However, these studies were confounded by factors which can cause phase shifts or alter circadian period in humans (e.g. light and activity) In comparison, Czeisler and colleagues (1999) investigated the intrinsic free-running period of 24 young (mean age 23.7yrs) and old (mean age 67.4yrs) adults using the highly controlled forced desynchrony protocol[1]. The authors reported that the average free-running period of core body temperature, plasma melatonin and plasma cortisol was 24.20 hours in both groups (Czeisler et al., 1999). This was confirmed in a similar study where a weak zeitgeber (i.e. very dim light during wakefulness) was found to synchronise the free-running period of participants entrained to a 24.0hr day but not a 23.5hr or 24.6hr day (Wright et al., 2005). Although seemingly imprecise, the approximately 24-hour free-running period of circadian rhythmicity actually allows greater precision by the internal time keeping system, as rhythms are only able to drift a little before adjustment by the LD cycle.

The process of entrainment is the third fundamental characteristic of circadian rhythmicity, whereby the period and phase of the circadian clock is synchronised to the period and phase of the external stimuli, or zeitgeber (Czeisler & Wright, 1999; Mistlberger & Rusak, 2005). It has been demonstrated that circadian rhythms persist in the absence of external time cues, however in daily life there are very few opportunities for rhythms to free-run. Instead, circadian rhythms express a cycling pattern that is said to be entrained to the environment. Roenneberg and colleagues (2003) explained that entrainment refers to an oscillatory system that responds discriminately to specific external stimuli that can reset it. This contrasts with simple synchronisation whereby any system can passively respond to changes in light and/or temperature (Roenneberg et al., 2003a). Stable entrainment of the circadian clock to the LD cycle is achieved when the light exposure offsets the drift due to the longer than 24-hour intrinsic period of the clock (Czeisler & Wright, 1999).

The range of entrainment refers to the limited range of periods to which the circadian clock can be synchronised by zeitgebers. If the LD cycle is too long or too short for entrainment then the circadian rhythm will free-run with a period close to 24-hours. The range of entrainment is dependant on: (1) the free-running period of the oscillator (τ); (2) the proportion of light and

[1] Forced desynchrony protocols place participants in artificial 'days' that are either too long (e.g. 28 hours) or too short (e.g. 20 hours) for the circadian clock to follow. This results in participants sleeping across all phases of the circadian cycle.

darkness (photoperiod); (3) the strength of the zeitgeber (i.e. the maximum light intensity); and (4) the amplitude of the zeitgeber (Roenneberg et al., 2003a).

The primary synchronising agent for circadian rhythms across a wide array of species, including humans, is the light/dark cycle (Czeisler et al., 2005; Czeisler & Wright, 1999). Light synchronises the SCN by way of direct input from the retina via the RHT, however this process does not involve rods or cones. Instead, the SCN is directly innervated by specialised retinal ganglion cells that contain the photopigment melanopsin which is responsible for the intrinsic sensitivity of these cells to light (Berson, Dunn, & Takao, 2002).

Light will induce a phase advance, phase delay or no phase shift at all depending on when in the circadian cycle the stimuli is presented (Moore-Ede et al., 1982). In chronobiology the phase response curve (PRC) provides the best quantification of the phase dependence of light-induced phase shifts (Khalsa et al., 2003). To construct a PRC, light pulses are systematically applied across the entire circadian cycle and the magnitude and direction of the resultant phase shifts are plotted as a function of the phase at which the organism is exposed to the stimuli (Czeisler et al., 2005).

The PRC for light shares a number of characteristic features across all species (Duffy & Wright, 2005). Firstly, the largest phase-shifts are induced by light that is applied during the subjective night of the circadian cycle (Czeisler et al., 2005). In some species, light applied during the subjective day has no phase-shifting effect on the circadian system (a so-called 'dead zone') and thus has little if any influence on the entrainment process (Mistlberger & Rusak, 2005; Moore-Ede et al., 1982). However, there is increasing evidence to suggest that the human circadian clock is sensitive to light during the subjective day (e.g. (Jewett et al., 1997; Khalsa et al., 2003)).

Secondly, the light PRC demonstrates that photic exposure during the late subjective day or early subjective night results in phase delays, while light applied during the early subjective day or late subjective night causes a phase advance of the circadian clock. In effect, the LD cycle 'constantly nudges' the circadian clock forward in the morning and backwards in the evening with each 24-hour day (Moore-Ede et al., 1982) producing an overall daily shift that is equal to the difference between τ of the circadian clock and T of the LD cycle (Mistlberger & Rusak, 2005).

The phase shifting effects of light also depends on the intensity of the light stimuli and the number of consecutive days of exposure. This relationship can be described by a dose response curve (also referred to as an illuminance response curve (Zeitzer et al., 2000)) whereby three consecutive daily pulses elicit a larger phase shift than a single light pulse. Moreover the dose response curve predicts an increased response to the phase resetting effects of light by the circadian clock at an intensity of 50 lux with an inflection point at approximately 120 lux and

reaching saturation at approximately 550 lux (Czeisler et al., 2005; Zeitzer et al., 2000). This was a very important finding as it was originally thought that only very bright light could phase shift the circadian clock.

It is important to differentiate between the masking and entraining effects of light on the circadian system. While specifically timed light exposure shifts the phase and the period of the underlying circadian clock, light can also mask or conceal the expression of the overt circadian rhythm. For example, the pineal hormone melatonin has a distinctive circadian rhythm of secretion, with very low levels during the subjective day, and high levels at night (see Chapter 5 for a detailed description of this hormone). However, light exposure at night has an immediate masking effect on the melatonin rhythm, significantly damping the apparent amplitude of the rhythm.

In addition to the photic entrainment of the circadian system, Mistlberger and Rusak (2005) reviewed a number of non-photic stimuli which have been shown to entrain, and not mask, the endogenous circadian clock in mammals including scheduled feeding, temperature, activity and arousal states and social cues. For humans there is growing evidence to suggest that appropriately timed exercise can cause phase shifts, however Czeisler and colleagues (2005) explained that this may be due to an interaction between exercise and the homeostatic control of sleep rather than exercise *per se* (i.e. exercise at night = staying awake during the normal sleep episode).

Common circadian marker rhythms

There is a wide array of human behavioural, physiological and endocrine variables that show a distinct circadian rhythm (see (Czeisler et al., 2005)). The two most commonly measured as markers of circadian phase are core body temperature (CBT) and melatonin levels. The circadian rhythm of CBT exhibits a highly regular sinusoidal shape, reaching a maximum in the evening prior to the onset of darkness and minimum during sleep at night (Cagnacci, Elliott, & Yen, 1992). The pineal hormone melatonin also has a distinct 24-hour pattern of secretion, but unlike CBT, melatonin levels peak during the night and are very low during the day.

The circadian rhythms of melatonin secretion and core body temperature exhibit a tight temporal relationship (Cagnacci et al., 1992), which have been confirmed in blind individuals, sighted individuals who suffer from the circadian sleep disorder non 24-hour sleep wake cycle syndrome, and in forced desynchrony experiments where the circadian and sleep homeostat systems are separated out from each other (see (Cajochen, Krauchi, & Wirz-Justice, 2003) for a review)

Cagnacci et al. (1992) demonstrated that under entrained conditions, the nocturnal decline in CBT is temporally associated with the rise in melatonin levels. Experimental studies have also shown that these relationships exist independently of the sleep wake cycle. For example, using a

20-hour desynchrony protocol, Wyatt and colleagues (1999) demonstrated a stable phase relationship between the circadian rhythms of melatonin and core body temperature with the nocturnal onset of melatonin secretion and decline in CBT occurring at a phase normally encountered a few hours before habitual bed time, while peak levels of melatonin were achieved just prior to the T_{min} which normally occurs a few hours before wake time (Wyatt et al., 1999).

The ease in which an individual is able to fall asleep also varies across the 24-hour day. The circadian rhythm of sleep propensity has several distinctive features. Firstly sleep propensity is greatest during the night and lowest during the day, although there is a small mid-afternoon peak in sleepiness ('siesta time'). There is also a nocturnal 'sleep gate' which correlates with a steep rise in sleepiness in the late evening. The 'forbidden zone' (Lavie, 1986) or 'wake maintenance zone' (Strogatz, Kronauer, & Czeisler, 1986) is characterised by a 2-3 hour period of very low sleep propensity in the early evening which terminates at the opening of the sleep gate (Lavie, 1986).

There is also a close correspondence between the circadian phase of T_{min}, peak melatonin levels and maximal sleep propensity (Wyatt et al., 1999). Sleep propensity is lowest during the wake maintenance zone (Strogatz et al., 1986), which occurs just prior to the onset of melatonin secretion (Rajaratnam et al., 2004). Lavie (1997) suggested that the nocturnal rise in melatonin levels opens the 'sleep gate' marking the transition from low to high sleep propensity which continues throughout the night. The onset of melatonin secretion has been described as the best physiological predictor of sleep onset, as the normal thermoregulatory processes which lead to the decrease in CBT begin with the nocturnal rise in melatonin. Cagnacci et al. (1992) proposed that the relationship between sleep and the rhythm of melatonin secretion may result in an additive hyperthermic effect, possibly providing neuroendocrine cues regulating the nocturnal temperature decrease in the rhythm of CBT. Another interpretation of this relationship is that melatonin weakens the signal from the SCN, promoting heat loss which induces sleepiness (Cajochen et al., 2003), however this is unresolved as some individuals with no observable melatonin secretion are still able to sleep normally (Wehr, Aeschbach, & Duncan, 2001).

1.2.2 The Sleep Homeostat

Borbély (2005) describes sleep homeostasis as the sleep/wake balance of sleep regulation. While the circadian mechanisms are responsible for maintaining the appropriate phase relationship between sleep/wake and the environmental light/dark cycles, the homeostatic mechanisms are those that respond to changes in the timing or history of sleep, by altering the duration and architecture of the following sleep episode (Dijk & Franken, 2005).

The intensity of the homeostatic sleep drive is dependent on the duration of prior wakefulness, such that maximum sleepiness (i.e. greatest sleep propensity) is reached after only 30 hours of continuous wakefulness (Dijk & Edgar, 1999). The sleep homeostatic process is considered to

be marked by changes in slow-wave sleep (SWS, non-REM stages 3 and 4) and in particular slow-wave activity (SWA, 0.5-4.5 Hz in EEG) during non-REM sleep (Dijk & Lockley, 2002). Slow-wave activity declines exponentially during sleep, from an initial level largely determined by the duration of prior wakefulness (Borbely & Acherman, 2005).

1.2.3 Models of Sleep Regulation

The classical two-process model of sleep regulation described by Borbély and colleagues posits that sleep and wakefulness are regulated by the interaction of two processes. The circadian process (process C) is a sinusoidal function that represents the circadian component of sleep propensity which is independent of the sleep/wake cycle and modulates sleep timing, propensity and architecture as a function of the circadian clock cycle. The homeostatic process (process S) is a physiologically determined drive for sleep which increases in an exponentially saturating manner during wakefulness and exponentially declines during sleep.

Although it is conceptually elegant, there is evidence that the two-process model may be somewhat simplistic. For example, studies utilising the forced desynchrony protocol have provided compelling evidence that the circadian timing system provides an alerting signal or 'wake drive' which increases over the subjective day and is greatest just before bed time and lowest in the hours preceding habitual wake-up time (Dijk & Czeisler, 1994, , 1995). The signal promoting wakefulness rises steeply approximately 6 hours after T_{min} and becomes stronger on the rising limb of the CBT rhythm, reaching a maximum at a time which approximates the timing of the forbidden- or wake maintenance zone, when sleep initiation is rare (Dijk & Czeisler, 1995). Data from the forced desynchrony studies of Dijk and Czeisler also indicate how the circadian clock may contribute to the consolidation of sleep at night. A circadian 'sleep drive' peaks near the core body temperature minimum, close to habitual wake time, and reaches a trough close to habitual bed time (Dijk & Czeisler, 1995).

This antagonistic interaction between the circadian and homeostat mechanisms was brought together by Edgar and colleagues in their opponent-process model (see Figure 1.1) which proposed that the circadian clock actively promotes wakefulness and opposes accumulating homeostatic sleep drive across the waking day and into early night (Edgar, 1996). Under entrained conditions the circadian clock provides a waking signal that becomes progressively stronger during the subjective day, reaching a peak at approximately 22:00 hours and declining rapidly after the onset of melatonin secretion. This waking signal opposes the homeostatic increase in sleep propensity across the subjective day (reviewed in (Dijk et al., 1999)). The homeostatic sleep drive contributes to sleep onset and maintains sleep during the first half of the night. As the homeostat sleep drive declines during the second half of the night the circadian drive for sleep increases reaching a peak shortly before habitual wake time (i.e. around the time of the temperature minimum, approximately 3-6 am) thus promoting the maintenance of sleep

through to the end of the sleep episode. The process begins again with the circadian drive for wakefulness rising steeply approximately six hours after T_{min}

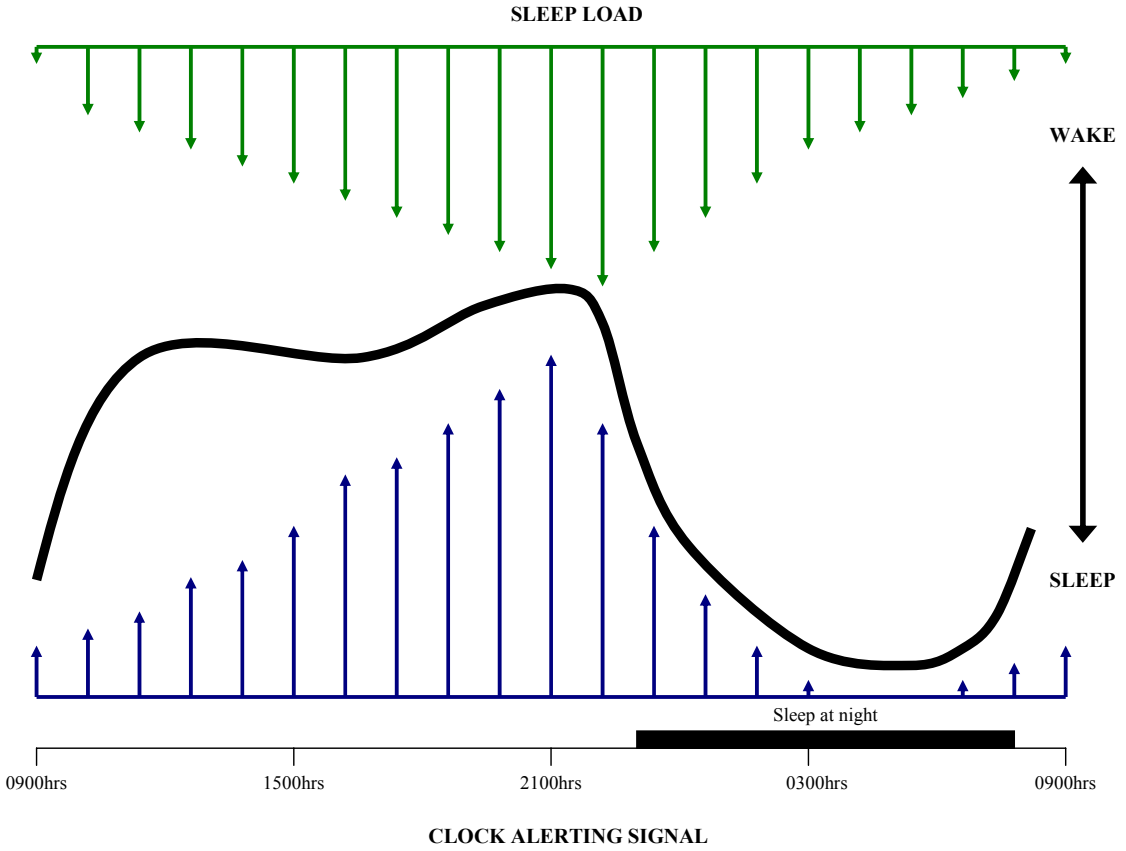


Figure 1.1 A schematic representation of the 'opponent process' model.

Physiological sleepiness (black line) is mediated as a function of time of day. The homeostatic sleep drive (green arrows) increases with prolonged wakefulness across the day. This is actively opposed by an alerting signal derived from the SCN (blue arrows) which maintains wakefulness until sleep at night (after (Edgar, 1996) and (Dijk & Edgar, 1999)).

1.2.4 Societal Factors Influencing Sleep

With the advent of artificial lighting, humans have been able to freely determine their sleep/wake scheduling despite the signals coming from the circadian and homeostat systems. In everyday life, our decisions about the timing of sleep are influenced by external factors such as work/school patterns, family commitments and societal expectations. To accommodate these external forces, many individuals shift the phase of the sleep/wake cycle by a few hours either earlier or later than desired. In this instance, the sleep/wake and LD cycles remain relatively in step with each other, and so the effects often go unnoticed. However, societal pressures to work more and sleep less have drastically altered the timing and amount of sleep we achieve each day (Dement & Vaughan, 1999). Of these influences, shift work and transmeridian flight cause the most significant disruptions to the homeostatic and circadian mechanisms driving sleep and wakefulness.

Transmeridian flight

International travel, in particular that including multiple time-zone crossings, is a growing cause of circadian and sleep/wake misalignment. Rapidly changing time-zones causes zeitgebers to be displaced relative to an individual's current circadian cycle. Because the circadian clock is responsible for co-ordinating oscillations in numerous behavioural and physiological processes, it must re-entrain to ensure that these variables regain the appropriate phase relationships with each other and with the various external time cues.

Often after flying to a new time zone, individuals complain of symptoms such as daytime sleepiness, difficulty sleeping, impaired performance and gastrointestinal complaints (Arendt, Stone, & Skene, 2005). These symptoms are known as jet-lag and are thought to be partly due to the desynchronisation of the circadian clock from the new LD cycle during the process of adaptation to the new time zone. Another factor thought to contribute to jet-lag is the desynchronisation of the various rhythms from each other, as each system adjusts to the new time zone at a slightly different rate (Arendt et al., 2005).

The rate of circadian re-entrainment after transmeridian flight differs depending on the direction of travel. Shifting circadian rhythmicity is slower during eastward travel (phase advance) compared to westward travel (phase delay) (Haus & Smolensky, 2006).

Shift work

The most striking example of self-selected sleep timing is shift work. In the context of this thesis, shift work is considered to be any work that forces sleep to be displaced (Signal, 2002). For the period 1998-1999 it was estimated that at least 25% of employment contracts in New Zealand had provisions for shift work, however from this data it is not possible to extrapolate the numbers of people actually involved in shift work at that time. In 2001, the prevalence of

night work in New Zealand was estimated as part of a nationwide survey of insomnia symptoms and risk factors (Paine et al., 2004). In this study, the prevalence of night work was higher among Māori (indigenous New Zealanders) compared with non-Māori (15.8% vs. 10.5%, p =0.0005) and men compared with women (15.2% vs. 9.7%, p =0.0002).

Shift work, and in particular night work results in significant disruption of the mechanisms driving sleep and wakefulness. Under entrained conditions, consolidated sleep is maintained when the sleep episode is initiated at the end of the evening wake maintenance zone (Czeisler et al., 2005). However, night workers often attempt to sleep in the early subjective day when sleep propensity is low and the circadian wake drive is rapidly increasing. Thus for these workers, the effect of the work pattern on sleep/wake scheduling is that sleep is truncated.

When changing to a new shift schedule (i.e. working at night and sleeping during the day) there are several non-photic zeitgebers that encourage the circadian clock to shift to a new pattern of work and rest (i.e. activity, meals and social contact). The circadian clock seldom fully re-entrains to altered work patterns because it is sensitive to the unchanged day/night cycle and activities of the rest of day-active society. These environmental cues draw the circadian clock back to its preferred orientation (Gander et al., 1998). Moreover, studies suggest that it can take up to a week for entrainment to occur however as Monk (2005) points out this would mean becoming synchronised to a work pattern just in time for the next off-duty break and another change in the diurnal patterns of sleep and wakefulness.

Shift workers commonly report symptomatology similar to that experienced with jet-lag, and for similar reasons. However, circadian realignment takes longer for shift workers than for international travellers. Monk (2005) explains that when crossing time zones, the circadian clock is encouraged to re-entrain by both physical (e.g. daylight and darkness) and social zeitgebers (e.g. meal times and traffic noise). However, re-entrainment for the shift worker is hampered because the physical time cues oppose adaptation to nocturnal activity, as do many of the social time cues (Monk, 2005).

1.3 Recent Advances in Understanding the Circadian Clock

One of the areas in chronobiology that has developed most rapidly is the identification of the genetic mechanisms underlying the regulation of sleep and circadian rhythms. While this thesis does not include any genetic studies it is important to review and consider the growing literature in this area because it is directly relevant to the consideration of an interaction between biological circadian rhythms and the psychosocial factors determining sleep timing.

The identification of the *period* locus in *Drosophila melanogaster* (the fruit fly) more than 30 years ago marked a defining moment in chronobiology, as the presumption that a single gene could control complex behaviour was at that time considered ‘radical’ (Takahashi, 2004;

Vitaterna, Pinto, & Turek, 2005). However, since then a number of genes have been identified with essential roles in the maintenance of daily rhythms in physiology and behaviour.

The molecular 'clockworks' consists of a core set of 'clock' genes which encode the molecular components that alternatively drive or inhibit the expression of specific subsets of these genes. The timing of this system is crucial to the provision of near 24-hour rhythms. Clock genes are expressed at different phases and there is also a lag between accumulating levels of mRNA transcripts and the subsequent translation of their proteins.

Two fundamental ideas have emerged from the work focused on the molecular genetic basis of circadian rhythmicity (King & Takahashi, 2000):

(1) For all organisms in which molecular components have been identified and analysed, circadian transcription/translation feedback loops are conserved, probably as a result of convergent evolution.

(2) Among metazoans, circadian rhythms arise from a conserved (homologous) set of genes.

Although the clock works of the *Drosophila* is better understood because of its relative simplicity, this section will focus primarily on the mammalian system which has been largely modelled in the mouse genome. According to standard nomenclature, genes and the proteins they encode share the same name, however for differentiation genes will appear in *lower case italics*, while proteins will be presented using NORMAL UPPERCASE typeset. Moreover, murine genes will be identified by a lower case m in front of the gene name (*mPer*) while a lower case h will identify those genes which have been identified in humans (*hPer*).

1.3.1 The Mammalian Clock Genes

Period (*per*)

The *period* gene in *Drosophila* has 3 alleles which are responsible for the circadian rhythms of locomotion and eclosion (hatching). Mutations in these alleles either lengthen (approx. 29hrs), shorten (approx. 19hrs), or completely abolish the endogenous free-running period (Van Gelder, 2004; Vitaterna et al., 2005). The role of *per* as a central clock component was confirmed following observations that when wild type alleles were introduced into the mutant gene, levels of *per* mRNA oscillated in a circadian manner and the levels of PER lagged *per* mRNA levels (Vitaterna et al., 2005).

Three mammalian orthologues of *period* (*per1*, *per2* and *per3*) have been identified in mice and humans. Single *mPer1* knockouts result in a shortening of the period length which is eventually followed by a loss of rhythmicity (arrythmicity) under constant darkness (DD). A single *mPer2* knockout produces a similar result, however the effect is more dramatic with a 1.5hr shortening of period length followed by arrhythmicity in DD conditions (Takahashi, 2004).

The importance of *per3* within the clockworks remains in doubt. For example, the *per1*/*per2* double knockout has a strong effect of arrythmicity in DD conditions, while *per1*/*per3* and *per2*/*per3* knockouts share the phenotype of *per1* and *per2* respectively (Albrecht, 2002). In addition, a single *per3* knockout shows only a very mild effect on period length (Takahashi, 2004). Taken together these findings suggest that the expression of *per3* is less important than *per1* and *per2* in the regulation of circadian rhythms.

The transcription of *per* within the SCN shows high levels of mRNA during the subjective day and low levels of mRNA across the subjective night. This creates a challenge for explaining why the circadian clock is more sensitive to light exposure during the subjective night (Takahashi, 2004). To investigate this further, Albrecht and colleagues (2001) measured the phase shifting effects of light on the wheel running behaviours among wild type, *mPer1* and *mPer2* mutant mice. In this experiment, 500 lux light pulses were applied for 15 minutes at the two times which reflect the phase delay and phase advance portions of the PRC: zeitgeber time 14 (ZT14 or 14 hours after the onset of the light cycle) and zeitgeber time 22 (ZT22 or 22 hours after the onset of the light cycle) respectively. When a light pulse was given at ZT14 the wild type and *mPer1* mutant mice were phase delayed while there was no phase shifting effect observed in the *mPer2* mutants. On the other hand a light pulse given at ZT22 had no effect on *mPer1* mutants while both the wild type and the *mPer2* mutants became phase advanced, furthermore the phase shift of the *mPer2* mutants (113 min ± 16 min) was significantly larger than in the wild type mice (35 min ± 5 min, $p < 0.001$). These results suggested that the *mPer1* gene is necessary for phase advance, while *mPer2* is needed for a phase delay. The implications of this phase relationship to the overall functioning of the mammalian clockworks will be discussed later.

Cryptochrome (*cry*)

The two mammalian *cryptochrome* genes, *cry1* and *cry2* have been identified in the inner nuclear layer and ganglion cells of the retina and in the SCN (Vitaterna et al., 2005). Like the *per* genes, *cry1* and *cry2* appear to have distinct and compensatory roles. While *cry1* knockout mice display a shortening of their period by approximately one hour relative to the wild type animals, the free running period of *cry2* knockouts is one hour longer than wild types (King & Takahashi, 2000). In addition when *mCry2* knockouts are exposed to a 6-hour light pulse beginning at circadian time 17 (CT17, or 17hrs after the beginning of the subjective day), they exhibit a high amplitude phase shift which is several hours greater than in the wild type control animals (King & Takahashi, 2000).

Although it was originally speculated that the cryptochrome proteins may represent the photoreceptors for the mammalian circadian clock, the current suggestion is that the *cryptochromes* have a light independent role in the negative feedback of the mammalian clock

works (Griffin, Staknis, & Weitz, 1999). The finding that *cry1*/*cry2* double knockouts are arrhythmic in DD conditions suggested that the *cryptochrome* genes may be important for the oscillation of the clock, otherwise it would be expected that the double knockout animals might express free-running rhythms regardless of the light conditions (King & Takahashi, 2000). In addition, *cry1*/*cry2* double knockout mice result in arrhythmic *mPer1* mRNA levels which are elevated in both LD and DD conditions suggesting that the cry genes have a negative inhibitory role on *per1* expression. In contrast, *mPer2* mRNA levels are rhythmic in LD but arrhythmic in DD conditions in these mice (King & Takahashi, 2000).

Clock (*clk*) and *Bmal1*

The circadian gene *clock* (*clk*) was the first to be discovered in mammals (King & Takahashi, 2000). Although wild type animals showed a robust entrainment to the light/dark cycle with a free running period of 23.7hrs, mutations at this gene resulted in a slowing down of the free-running period in DD conditions with an eventual loss of circadian rhythmicity (heterozygous *clk* mutants τ =24.8hrs; homozygous mutants τ =28hrs) (King & Takahashi, 2000; Vitaterna et al., 2005). The *clk* gene encodes a CLOCK protein which belongs to the bHLH/PAS family of transcription factors. The bHLH (basic Helix-Loop-Helix) region permits binding with DNA sequences while PAS (PER-ARNT-SIM) is necessary for transactivation of mRNA. Vitaterna et al. (2005) explain that the identification of the PAS domain on CLOCK led to the search for possible binding partners.

The *Bmal1* (brain and muscle ARNT-like 1) gene encodes the transcription factor BMAL1 which also belongs to the bHLH/PAS family, suggesting that BMAL1 could be the normal binding partner of CLOCK (Vitaterna et al., 2005). Mice with a null allele of *Bmal1* (also known as *MOP3*) display normal differential responses to the LD cycle, however under DD conditions there is an extreme and immediate loss of rhythmicity (King & Takahashi, 2000; Vitaterna et al., 2005) indicating that it may be the only non-redundant gene in the clock works (Albrecht, 2002). Daily oscillations of *Bmal1* mRNA are anti-phase to that of *cry* and *per* mRNA levels, reaching peak levels between CT12 to CT21 (Shearman et al., 2000).

The significant role of *clk* within the molecular framework was revealed using a mutant form of CLOCK (CLOCKΔ19) which was found to be missing the PAS domain. Although CLOCKΔ19 was able to dimerise with BMAL1 and interact with the DNA sequences of *per,* there was a loss of transactivation. Moreover, *clk* mutations result in alterations to the oscillatory patterns of *per* and *cry* mRNA which supports the proposition that CLOCK plays a critical role in the transactivation of the *per* and *cry* genes (Reppert & Weaver, 2001; Shearman et al., 2000; Vitaterna et al., 2005). Although *clk* mRNA levels do not oscillate, the nuclear localisation of CLOCK does, and this is dependent on the formation of the CLOCK:BMAL1 complex (Vitaterna et al., 2005).

Non-essential clock genes

While mutations in the core clock genes result in extreme phenotypes, there exist a number of additional genes which when altered have a more subtle effect, and as such they are believed to have a 'non-essential' role in the overall clockworks (Takahashi, 2004). For example, *rev-erb alpha* (*rev-erbα*) expression is promoted by CLOCK:BMAL1 and suppressed by the PER:CRY complex (Vitaterna et al., 2005). It has been proposed that the *rev-erbα* may regulate the anti-phase relationship between *Bmal1* and *per* as the gene product REV-ERBα promotes *Bmal1*. Similarly phase differences in *cry* mRNA rhythms relative to other clock genes may be the result of REV-ERBα inhibition of *cry1* expression (Vitaterna et al., 2005). However circadian rhythms are still generated in the absence of REV-ERBα with only subtle effects on the period and stability of the rhythms (Takahashi, 2004).

1.3.2 An Overview of the Mammalian Clock Works

As mentioned earlier, the basic molecular clockworks involves both positive and negative transcription/translation feed back loops. However, the regulation of the mammalian system is in fact more complex, given the additional number of *per* and *cry* genes and the different phase relationships. This section will outline a current working model of the SCN clock works which is based on the findings of Shearman and colleagues (2001). This is also illustrated in Figure 1.2. A brief summary of the morning- and evening- oscillator model proposed by Daan and colleagues (2002) is then given.

In the positive or regulatory arm of the mammalian clock works, the transcription factors CLOCK and BMAL1 dimerise via the bHLH/PAS domain to form a CLOCK:BMAL1 heterodimer (Vitaterna et al., 2005). This complex is translocated back into the nucleus where levels of CLOCK:BMAL1 accumulate at the start of the circadian day (CT 0) (Reppert & Weaver, 2001). Once in the nucleus, CLOCK:BMAL1 binds with *per* and *cry* at the regulatory regions containing the E-box elements (nucleotide sequence CACGTG) which are necessary for the positive regulation of mRNA transcription (Albrecht, 2002; Albrecht & Eichele, 2003) (Vitaterna et al., 2005). Oscillations of *per* and *cry* mRNA exhibit similar yet temporally distinct profiles; *per1* mRNA rhythms peak from CT4 through CT6, *per3* from CT4 to CT8, *per2* at CT8, and *cry1* at CT10 (Reppert & Weaver, 2001).

Once in the cytoplasm, PER proteins are phosphorylated by the enzyme Casein Kinase 1 epsilon (CKIε) which leads to a loss of protein stability and prevents PER levels from accumulating. Interestingly, the tau mutation in hamsters, which manifests as a long free-running period, was identified as a mutation at the level of CKIε. As CRY levels build, they form dimeric complexes with PER binding at their common PAS regions. This is thought to be necessary to protect PER from further phosphorylation by CKIε and to assist translocation back into the nucleus (Albrecht & Eichele, 2003).

By CT12, the PER and CRY proteins are synchronously expressed in the nucleus where the CRY proteins shut off transcription by antagonising the CLOCK:BMAL1 heterodimer (Reppert & Weaver, 2001; Shearman et al., 2000). This framework of autoregulation ensures that the system does not move into a state of equilibrium and loss of oscillation.

Evidence from *mPer2* mutant studies indicates that PER2 is involved in positive, rather than negative transcriptional regulation (Reppert & Weaver, 2001). It was proposed that at CT12, PER2 either shuttles a transcriptional activator into the nucleus or co-activates a transcription complex to enhance *Bmal1* transcription, leading to peak *Bmal1* mRNA rhythms from CT15 through CT18 (Reppert & Weaver, 2001). It is then presumed that the *Bmal1* mRNA rhythm drives a BMAL1 protein rhythm after a 4- to 6-hr delay. The renewal of BMAL1 levels at the end of the night presumably increases CLOCK:BMAL1 heterodimers at the appropriate circadian time to drive *per*/*cry* transcription, thereby restarting the cycle. It appears that BMAL1 availability is rate limiting for heterodimer formation and is critical for restarting the loops at the start of a new circadian day (Reppert & Weaver, 2001).

Daan and colleagues (2002) have extended the molecular clockwork model to suggest that the mammalian clockworks consist of a morning (M) and evening (E) oscillator, based on the photic entrainment of the circadian clock via the release of glutamate from retinal projections to the SCN (not indicated in Figure 1.2). The phase setting response is dependent on the timing of exposure, light during the early night phase delays the clock, while light in the late night causes a phase advance. Thus in the Daan et al. (2002) model, the M oscillator is accelerated by light and decelerated by dark, while the E oscillator is decelerated by light and accelerated by dark. In addition *per* and *cry* form gene sets within each oscillator: *per1 cry1* within the M-oscillator and *per2 cry2* within the E-oscillator. This is consistent with reports that *per1* expression peaks in the early subjective day and *per2* expression peaks in the late subjective day (Daan et al., 2001) and that *cry1* and *cry2* have opposite effects on period length (Albrecht, 2002).

In the M oscillator, which tracks dawn, CRY2 blocks CLOCK:BMAL1 activated transcription of *per2* and *cry2* while PER2 regulates *Bmal1* expression which is important for the maintenance of the appropriate phase relationships of the genes and their products as well as the overall synchronisation of the M and E oscillatory systems (Albrecht, 2002).

In the E oscillator which tracks dusk, the PER1:CRY1 complex inhibits gene expression of *per1* and *cry1*. However, PER1 also interacts directly with PER2 in a negative feedback loop which influences the amount of PER2 which is able to enter the nucleus subsequently altering *Bmal1* expression (Albrecht, 2002).

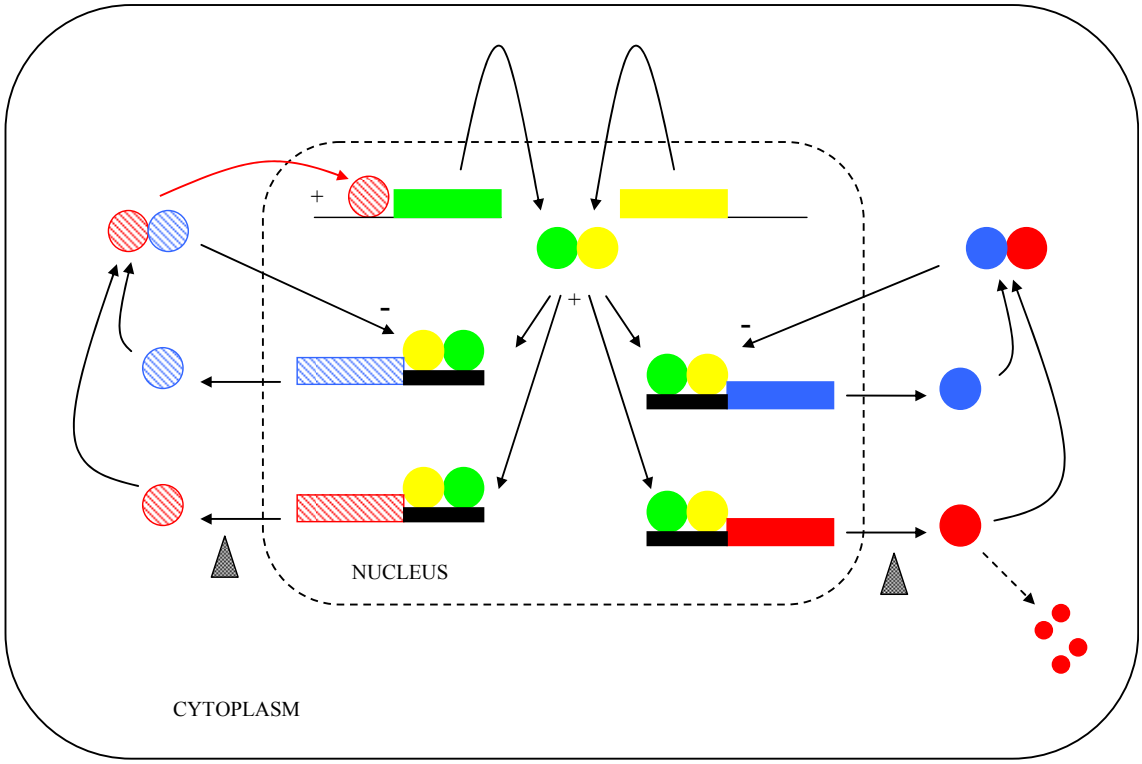


Figure 1.2 A schematic diagram of the molecular clock works regulating circadian rhythms in mammals.

In the nucleus the CLOCK (yellow) and BMAL1 (green) heterodimer complex interacts with per1 (solid red rectangle), per2 (shaded red rectangle), cry1 (solid blue rectangle) and cry2 (shaded blue rectangle) via the E-box motifs (black rectangle) at their regulatory regions. This interaction represents the positive transcription/translation feedback loop. Once in the cytoplasm, the PER proteins (solid and shaded red circles) are phosphorylated by CKIε (shaded black triangle) which results in their degradation by other enzymes. In the negative feedback loop of this model, CRY proteins (blue solid and shaded circles) dimerise with the PER proteins and these complexes are translocated back into the nucleus where CRY1 and CRY2 inhibit expression by blocking the CLOCK:BMAL1 complex while PER2 (red shaded circle) promotes the expression of Bmal1 via a second positive feedback loop (after (Albrecht, 2002))

1.4 Individual Differences in Preferred Sleep Timing

While numerous physiological, endocrine and behavioural variables demonstrate near 24-hour rhythmicity, there are considerable inter-individual differences in the temporal organisation of these circadian rhythms. The most important source of this variance is described as morningness/eveningness and is most obvious as individual differences in the preferred timing for sleep and waking activities. The first descriptions of a diurnal phenotype, or *chronotype*, were provided by the pre-eminent sleep researcher Dr. Nathaniel Kleitman in his pioneering work *Sleep and Wakefulness* where he described the existence of "morning" and "evening" types who showed two distinct body temperature curves and differed in their preference for the timing of sleep and study (Kleitman, 1963). Since then it has been established that a morning-type person prefers to go to bed early, wake-up early, and feels more alert and active in the morning, while the opposite is true for evening-types. However, it is commonly accepted that morning- and evening-types exist toward the ends of a continuum which is largely occupied by individuals who are no more morning- than they are evening-type (i.e. neither-type) (Kerkhof, 1985).

There is considerable interest in the linkages between sleep timing preference and an individuals' ability to cope with shift work and jet-lag. Several lines of evidence suggest that morningness/eveningness is directly controlled by the endogenous circadian clock as measured by differences in circadian phase and the intrinsic free-running period between chronotypes (e.g. (Baehr et al., 2003; Duffy et al., 1999; Duffy, Rimmer, & Czeisler, 2001; Lack & Bailey, 1994; Mongrain et al., 2004)). Similarly, it has been shown that mutations in, or specific alterations of some of the core circadian genes may determine extreme morning- or evening-type preference, which can manifest as the circadian sleep disorders advanced sleep phase syndrome and delayed sleep phase syndrome. Thus the ability to determine an individual's circadian phase using a simple subjective tool would be advantageous for the design of treatments for adaptation to jet-lag and shift work, and in the diagnosis and treatment of sleep disorders (Arendt et al., 2005). The importance of the accurate classification of chronotypes is evident when considering the increasing knowledge of the genetic control of the circadian system. In spite of these advances, very little is known about the variability of clock genes in the general population.

1.4.1 The Epidemiological Evidence

Of all the self-report questionnaires, the Horne and Östberg Morningness/Eveningness Questionnaire (MEQ) is the most widely used subjective tool for identifying different chronotypes. Total scores on the MEQ are used to categorise people as definitely morning-type,

moderately morning-type, neither (or intermediate)-type, moderately evening-type, or, definitely evening-type (Horne & Östberg, 1976).

Despite the widespread availability of the MEQ (Chelminski et al., 2000), epidemiological data for the general population are lacking. Apparently, no study has examined the influence of ethnicity on MEQ scores. The only data available compared students attending university in Spain (Adan & Natale, 2002), where Spanish students (n=879) were found to be more evening-type than Italian students (n=1,256).

In his review of individual differences in human circadian rhythms, Kerkhof described the relationship between circadian rhythmicity and sex as "scanty and inconsistent" (Kerkhof, 1985). Adan and Natale (2002) found male students (n=1041) scored as more evening-type than female students (n=1094). Chelminski et al. (1997) also reported a significant difference in the proportions of morning- and evening-types between men and women (N=1617 college students) but an insignificant difference in average scores on the MEQ by sex in this population. In contrast, several studies have suggested that scores on circadian rhythm questionnaires are independent of gender (reviewed in (Tankova, Adan, & Buela-Casa, 1994)).

It has been well established that higher morningness scores are related to advancing age (Carrier et al., 1997; Kerkhof, 1985; Taillard, Philip, & Bioulac, 1999; Tankova et al., 1994) (Adan, 1992; Chelminski et al., 1997; Gander et al., 1993). There is growing evidence to suggest that morningness/eveningness is influenced by developmental changes and ageing. The delayed sleep times common among teenagers are thought to be attributable, at least in part, to changes in the mechanisms regulating sleep timing (Dahl & Carskadon, 1995). Conversely, there is a trend for people to become more morning-type in later adulthood (Carrier et al., 1997, , 1998; Gander et al., 1993; Ishihara et al., 1988; Taillard et al., 1999; Taillard et al., 2001) and it has been proposed that this change typically begins to be manifested around age 50 years (Bliwise, 2005; Tankova et al., 1994).

Confounding this relationship is the strong synchronising effect of societal demands, in particular work schedules, in modifying the natural morningness/eveningness preference (Adan & Natale, 2002; Meccaci & Zani, 1983; Tankova et al., 1994). Most studies on morningness/eveningness have been carried out in young adult populations (e.g. (Adan & Natale, 2002; Chelminski et al., 1997; Chelminski et al., 2000; Hidalgo et al., 2003; Natale & Cicogna, 2002; Smith, Reilly, & Midkiff, 1989), because they are more able to follow their natural preference for the timing of sleep and waking activity (Natale & Cicogna, 2002). Indeed, the MEQ itself was developed and validated in a sample of college students aged 18-32 years. Moreover, Horne and Östberg (1976) wrote this of their sample:

> …these subjects are not typical of a normal population, particularly in respect of life style….The arising time for these students, particularly the Morning types, would seem to be later than an

> arising time which could be expected from an older population having to start a regular job…with various family commitments prior to work. Needless to say, the questionnaire has to be further assessed with a greater variety of subjects (p.108).

Similarly, Adan and Amirall (1990) questioned the relevance of data collected from students, to the rest of the population. Studies on students have shown a distribution of scores that is weighted towards eveningness (Adan & Natale, 2002; Chelminski et al., 1997; Hidalgo et al., 2003), whereas similar research among older, working individuals presents a distribution that is weighted towards morningness (Ishihara et al., 1988; Taillard et al., 1999; Taillard et al., 2001), possibly demonstrating an exogenous influence of strict work schedules on sleep timing .

1.4.2 Differences in Sleep Timing between Morning- and Evening-Type

Central to the morningness/eveningness paradigm is the understanding that individuals differ in their preferred timing of behavioural rhythms, in particular the rhythm of sleep and wake (Kerkhof, 1985). Actigraphy and sleep diaries have been used extensively to investigate differences in the patterns of sleep among self-identified morning- and evening-types and it has been consistently shown that their preferred and habitual sleep timing is correlated, with earlier bed times and rising times among M-types (e.g. (Horne & Östberg, 1976; Ishihara et al., 1988; Ishihara et al., 1987; Lavie & Segal, 1989; Mongrain et al., 2004)).

Morning- and evening-types also differ in their perceived experience of sleep. Evening-types report needing sleep more than morning- or neither-types (Gianotti et al., 2002; Taillard et al., 1999; Taillard et al., 2004). Similarly on waking, morning-types report being more alert (Carrier et al., 1997) and in a better mood (Ishihara et al., 1988; Ishihara et al., 1987), while E-types report finding it easier to return to sleep in the morning (Taillard et al., 2004).

Significant changes to the sleep/wake pattern also occur in later adulthood as part of the normal ageing process, with night time sleep becoming lighter, shorter and more fragmented (Bliwise, 2005; Gander et al., 1993). The influence of age on sleep/wake scheduling was investigated in a comprehensive study of 110 healthy individuals aged 20-59yrs taking part in the 'Pittsburgh Study of Normal Sleep' (Carrier et al., 1997). Advancing age was significantly associated with earlier bed times and rising times, a shortening in the length of time spent in bed, and with a number of polysomnographic (PSG) characteristics of sleep such as less time spent asleep, an increased number of awakenings and decreased sleep efficiency. However, when morningness/eveningness was taken into account, many of the reported age effects disappeared, indicating that age-related changes in sleep may be mediated by simultaneous changes in the morningness/eveningness dimension during the middle-years of life (Carrier et al., 1997).

Differences between men and women with regards to sleeping patterns are less clear. Objective measurement tools have shown that men experience greater changes to their sleep with age,

however women more frequently report worse sleep (Armitage, Baker, & Parry, 2005). Yoon (2003) reported a significant interaction between sex and chronotype, with younger men sleeping later than younger women (but not for the older aged group). Similarly, an interaction between sex and chronotype was found by Mongrain (2005) who suggested that morningness/eveningness influences sleep in a sex-specific manner, with males more affected by their chronotype. Kerkhof (1985) speculated that sex differences in the timing of circadian rhythms may be related to a differential in the response to external disturbances of the clock mechanisms.

The timing of human sleep is heavily influenced by social cues (Roenneberg, Wirz-Justice, & Merrow, 2003b), the most significant perhaps being the somewhat restrictive schedules of school and work commitments (Ishihara et al., 1988; Ishihara et al., 1987). The burden of these schedules may affect evening-types more, as during the week they are often required to get up earlier in the morning than they would prefer in order to meet their work demands. If it is accepted that these social schedules force changes to their rising time, whilst bed times remain the same, then a shortening in the duration of sleep would be expected. The evidence however remains unclear. Studies in younger student populations (e.g. (Ishihara et al., 1987; Lavie & Segal, 1989; Touchette et al., 2001)) including the original publication by Horne and Östberg (1976), found no significant difference in sleep durations between morning- and evening-types, possibly due to the reasonably homogenous nature of the student population who may share similar study schedules. In contrast, both Ishihara (1988) and Roenneberg (2003) investigated the sleeping patterns of working individuals and found that sleep durations are longer in morning-types.

There is growing concern that contemporary society is "chronically short changed on sleep" (Monk et al., 2000) and considerable research effort has been devoted to understanding the long-term and often deleterious effects of chronic sleep debt to the community (Walsh et al., 2005). Individuals require different amounts of sleep in order to feel fully rested and refreshed upon waking. However, when less than this fundamental amount of sleep is achieved and deficits to waking function manifest over several days, then an individual is said to be accumulating a sleep debt (Dinges, Rogers, & Baynard, 2005). Likened to a bank balance being "in the red", sleep debt can only be reversed by having at least two full nights of recovery sleep (Belenky et al., 2003; Signal, 2002; Van Dongen et al., 2003). Free of restrictive work schedules, weekends provide the only opportunity for most individuals to catch up on their sleep.

Differences between weekday and weekend sleep, and their relationship to sleep debt, were investigated in a study of 266 normal healthy individuals aged 20-50 years using the Pittsburgh Sleep Diary (Monk et al., 2000). The authors found that adults spent approximately 27 minutes

longer in bed on the weekend compared to during the week and that sleep started and finished later on the weekend (26 minutes longer and 53 minutes later respectively). It was proposed that the difference between weekday and weekend time in bed (TIBdiff) provided a means of measuring the size of the week day sleep debt that needs to be dissipated on the weekend. Indeed, the authors found that TIBdiff was associated with general measures of sleep debt, such as decreased weekday time in bed, decreased weekday alertness and an increase in the use of an alarm clock (Monk et al., 2000).

Differences in weekday and weekend (or work days vs. free days) sleep patterns are an important consideration within the framework of morningness/eveningness. Recently, Roenneberg and colleagues (2003) presented the initial findings from a pilot study using a new questionnaire designed to quantitatively asses sleep timing within the 24-hour day (the Munich Chronotype Questionnaire, MCTQ). Although work schedules heavily influenced the timing of sleep and wakefulness, sleep onset times were more strongly determined by chronotype indicating that the social zeitgebers were not sufficiently strong to advance either the circadian clock or sleep phase among late chronotypes (~ evening-types). Accordingly, later chronotypes accumulated a significant sleep debt on work days, as they were required to get up earlier than preferred and this debt was compensated for on free days. In contrast, early chronotypes accumulated a sleep debt on free days due to social pressures to stay up late (Roenneberg et al., 2003b).

1.4.3 Circadian Phase Differences between Morning- and Evening-Type

There is considerable interest in the potential to use self-identified morningness/eveningness preferences as a subjective marker of circadian phase. The daily rhythms of core body temperature and melatonin secretion have been widely used to confirm differences in the circadian timing system between morning- and evening-types. For example, raw scores on the Horne and Östberg (1976) MEQ consistently show an inverse relationship with the timing of the temperature nadir (T_{min}) such that higher MEQ scores are associated with an earlier temperature rhythm (Baehr, Revelle, & Eastman, 2000; Duffy et al., 1999; Hall et al., 1997; Horne & Östberg, 1976). Similarly, when questionnaire scores are used to categorise chronotypes, morning- and evening-types differ in terms of the timing of the core body temperature with M-types exhibiting an earlier T_{min} (Baehr et al., 2000; Duffy et al., 1999; Griefhan, 2002; Hall et al., 1997; Lack & Bailey, 1994; Mongrain et al., 2004; Taillard et al., 2003), and temperature acrophase (or peak), compared with E-types (Bailey & Heitkemper, 2001).

Two recent studies argued that the temporal parameters of the dim light melatonin profile are better markers of the circadian clock than the temperature nadir (Benloucif et al., 2005; Griefhan, 2002). The timing of the dim light melatonin onset (DLMO) occurs approximately 2 to 3 hours earlier among M-types compared to E-types (Griefhan, 2002; Lack & Bailey, 1994;

Mongrain et al., 2004). Similarly, Hall et al. (1997) reported an earlier midpoint of melatonin secretion among M-types, while Liu et al. (2000) reported a significant inverse relationship between scores on the MEQ and the time of the melatonin peak.

Although morning-types sleep earlier and have earlier circadian phase with respect to the 24-hour day, this does not necessarily mean that their circadian clocks are fundamentally different from those of evening-types. At least part of the phase angle difference could be due to self-selected sleep/wake patterns and light exposure (Duffy et al., 1999). The phase angle describes the difference in timing between circadian phase markers of interest (e.g. T_{min} or the DLMO) and the rhythm of the sleep/wake cycle, most commonly marked by the parameter sleep end time, or wake time. Several studies have reported that morning-types have a longer phase angle between T_{min} and sleep end (Duffy et al., 1999; Hall et al., 1997; Mongrain et al., 2004; Taillard et al., 2003). This would suggest that despite going to bed at an earlier clock hour, morning-types wake at a later circadian hour compared with evening-types. However, this relationship is complicated by the effects of age. Duffy and colleagues (1999) found that older M-types (n=40, 68.2yrs ± 3.8yrs) had an earlier circadian phase with respect to the 24-hour day compared with young morning-types (n=68, 23.5yrs ± 3.4yrs). However they also had a significantly shorter phase angle (T_{min} to wake time) than young M-types (p <0.01). Thus, in that study older M-types went to bed at an earlier clock hour but they also woke at an earlier circadian hour, with an internal phase angle which was more like that of young evening-types (old M-types 1.53 ±1.89hrs ; young E-types 2.26 ± 0.97hrs) (Duffy et al., 1999).

1.4.4 The Role of Clock Genes in the Timing of Human Sleep

The molecular clock works model illustrates how the co-ordinated interaction of the core clock genes and their products ensure that daily biological rhythms oscillate with a period of approximately 24 hours. Many of the clock genes are conserved across species and thus the mechanisms that underlie the circadian rhythmicity in mice are likely to play an important role in regulating human circadian rhythms. Animal studies have demonstrated that mutations in the core clock genes can produce phenotypes with significantly altered period lengths, so it is feasible that even subtle changes to the DNA sequence of the human clock genes, such as naturally occurring polymorphisms could result in a phenotype which displays an altered period length in circadian rhythms.

In 2001, Duffy and colleagues demonstrated a significant inverse correlation between self-reported sleep timing preference and the endogenous free-running period, such that shorter periods were associated with more morning-type preferences while longer periods were associated with more evening-type preferences. Furthermore, shorter circadian periods were significantly correlated with earlier wake times and an earlier circadian phase. Several groups have since focused on the possibility that alterations to the clock genes could form the

biological basis to morningness/eveningness and in particular the pathogenesis of the circadian rhythm sleep disorders, advanced sleep phase syndrome and delayed sleep phase syndrome.

Clock genes and morningness/eveningness

The first evidence of a relationship between preferred sleep timing and the circadian clock genes was reported in a random sample of normal healthy adults (n=410, mean age 50.0 ± 7.9yrs) taking part in the Wisconsin Sleep Cohort Study. The investigators undertook a systematic screen of all known human circadian genes and detected a single nucleotide polymorphism (SNP) located in the 3` flanking region of the human *clock* gene (locus 3111, C to T substitution) (Katzenberg et al., 1998). After adjusting for age, sex and heritage, there was a significant difference in mean MEQ scores between the 3111C and 3111T allele carriers (58.8 ± 0.8 vs. 61.7 ± 0.8, p <0.005) indicating that C allele carriers were more evening-type and the T allele carriers were more morning-type, even though the mean scores lie close to the boundary between neither- and moderately morning-type categories. Although there was no significant difference in the average MEQ scores between homozygous (C/C) and heterozygous (C/T) groups (60.1 ± 2.0 vs. 58.5 ± 0.9 respectively), Katzenberg et al. argued that factor analysis and individual item comparisons of the responses on the MEQ showed that C allele carriers had an increased tendency for eveningness and a decreased tendency for morningness, and that the lack of significance was probably due to the small numbers of homozygous carriers analysed (n=28).

Robilliard and colleagues (2002) investigated whether the small but significant difference in MEQ scores between the 3111C and the 3111T allele carriers reported by Katzenberg et al. (1998) could be enhanced by comparing individuals with extreme self-reported morning- or evening-type preference. It was predicted that the 3111C allele would be present at a higher frequency among individuals categorised as extreme evening-type, compared to others, however, there was no significant difference in the frequency of the 3111C allele by chronotype (M-type 0.37; N-type 0.37 and E-type 0.34). In addition the frequency of the 3111C allele for the whole control group (n=105) was not significantly different from the frequency of the allele among patients with a clinical diagnosis of delayed sleep phase syndrome (DSPS), who by definition exhibit significantly later sleep timing compared to normal individuals (Reid & Zee, 2005).

Robilliard et al. (2002) also proposed that the 3111C allele should be associated with a longer free-running period (τ) given the significant association between morningness/eveningness and τ (Duffy et al., 2001). However there was no significant difference in the average τ measured in a group of free-running blind individuals categorised as C/C (n=1), C/T (n=9) or T/T genotype (n=16). This finding also conflicted with Katzenberg et al. (1998), who had concluded that a preference for eveningness required only one 3111C allele.

Both Katzenberg et al. and Robilliard et al. indicated that polymorphisms in the 3' flanking region of the *clock* gene may have an effect on the stability of mRNA which would modify the levels of CLOCK protein that are eventually produced, and influence the expression of *per* gene, which has an important role in the phase resetting of the circadian clock. This possibility was investigated by Robilliard et al. (2002), however there was no significant difference in mRNA translatability between either variant, although the results were not conclusive (Robilliard et al., 2002).

The Katzenberg group also investigated the effect of polymorphisms at the level of *hPer1* (locus 2548, A to G substitution) (Katzenberg et al., 1999) and *hTim* (locus 2634, A to G substitution) (Pedrazzoli et al., 2000) on morningness/eveningness preference in the general population, however in both studies MEQ scores were not significantly different across genotypes.

Clock genes and circadian rhythm sleep disorders

At the extreme ends of the morningness/eveningness distribution there are people who have sleep/wake patterns that are at odds with societal norms. Advanced sleep phase syndrome (ASPS) is a disorder in which the major sleep episode is advanced in relation to the desired clock-time. This results in symptoms such as compelling evening sleepiness, early sleep onset times and waking in the morning at an earlier time than is preferred (American Academy of Sleep Medicine, 2001). The International Classification of Sleep Disorders (ICSD) lists typical sleep onset times between 1800hrs and 2000hrs and no later than 2100hrs while wake times typically occur between 0100hrs and 0300hrs and no later than 0500hrs (American Academy of Sleep Medicine, 2001). There is very little epidemiological evidence available describing the distribution of ASPS. The ICSD describes the prevalence as 'apparently rare' (American Academy of Sleep Medicine, 2001) while a small survey of 417 middle-aged adults estimated the prevalence at only 1% (Ando, Kripke, & Ancoli-Israel, 1995).

At the other extreme, Delayed Sleep Phase Syndrome (DSPS) is a disorder in which the major sleep episode is delayed in relation to the desired clock time. This results in symptoms of sleep-onset insomnia (i.e. difficulty initiating sleep) or difficulty awakening at the desired clock hour (American Academy of Sleep Medicine, 2001). DSPS patients generally have a sleep onset time between 0200hrs and 0600hrs, sleeping until late morning or early afternoon, although this is usually not possible because of work, school or social demands (American Academy of Sleep Medicine, 2001; Ancoli-Israel et al., 2001). Again, the exact prevalence of DSPS is unknown. It is estimated that 5% to 10% of patients presenting with a complaint of insomnia in fact have DSPS. Ando and colleagues (1995) estimated that the prevalence was 0.7% in middle-aged adults, while a survey of adolescents suggested a 7% prevalence in this age-group (American Academy of Sleep Medicine, 2001). Ancoli-Israel and colleagues (2001) described a familial form of DSPS in one pedigree where 6/27 adults (12/51 total family members, including

children and adolescents) had a preference for eveningness. However there were no objective sleep measurements taken from the family members, nor did they undergo a clinical interview or circadian phase assessment to confirm this.

A number of studies have focused on the involvement of *hPer1*, *hPer2* and *hPer3* within the pathophysiology of these circadian sleep disorders.

Jones and colleagues (1999) identified a familial pattern for ASPS (FASPS) in three separate families which segregates as a highly penetrant autosomal dominant trait. Affected family members scored as extremely morning-type on the MEQ (n=14, mean MEQ score 76.2 ± 5.6) while the average MEQ score from the unaffected members was in the range of moderate morning-type (n=12, 60.5 ± 6.8, p <0.0005). Overnight polysomnography showed that the sleep onset, sleep offset, the first slow wave sleep and the first REM period were advanced by approximately 4 hours in affected family members (n=6) compared to age- and gender-matched controls (all p <0.001). The FASPS members had a significantly earlier circadian phase compared to controls (difference in DLMO =3.83hrs, p <0.0005 and difference in T_{min} =4.22hrs, p =00002) and three weeks of actigraphy confirmed a significant phase advance in sleep timing in this group. In addition the authors reported that one family member had an extremely short free-running period (τ =23.3hrs) compared to a single control (τ = 24.2hrs).

The genetic basis of FASPS was investigated further in one of the families described by Jones et al. 1999 segregating an FASPS allele (kindred K2174) (Toh et al., 2001). Linkage analysis identified a single marker on chromosome 2qter (i.e. at the terminal end on the q arm of chromosome 2) that was linked to FASPS in this kindred. Moreover it was confirmed that the *hPer2* gene was also located on chromosome 2qter. A base change at *hPer2* (locus 2106, A to G substitution) predicted a serine to glycine substitution at amino acid 662 (S662G). This missense mutation was found in all affected and genetically linked members of K2174 but not in 92 control chromosomes. In addition, the S662G cosegregated with ASPS in this family except for one branch where the FASPS-associated marker alleles were unlinked. It was then demonstrated that the S662G mutation was located in the CKIε binding region of *hPer2* and *in vitro* investigation found that the mutation leads to hypophosphorylation by CKIε. Although the functional consequences of this decreased phosphorylation are not fully understood, it was suggested that it may impair the degradation of *hPer2* and/or accelerate transportation back into the nucleus, speeding its accumulation. This could cause a phase advance in the rhythm of *hper2* which may shorten the free-running period and lead to an earlier sleep/wake rhythm (Toh et al., 2001).

Reid and colleagues (2001) also identified a large family (n=32) with at least one member in every generation affected by ASPS, all of whom were phase advanced in terms of their sleep/wake schedule and endogenous melatonin rhythm. However, further investigation found

that the affected family members did not have any mutations of *hPer1*, *hPer2* or *hPer3* ((Chang et al., 2002) cited in (Satoh et al., 2003)), suggesting that polymorphisms in the *hPer* genes alone cannot account for the development of ASPS.

The likelihood of genetic heterogeneity of the FASPS phenotype was further supported in a study of two families, where a systematic survey of 28 relatives in these two families identified nine affected individuals who met the ICSD criteria for ASPS (Satoh et al., 2003). The affected family members had a higher average MEQ score compared to unaffected members (77.3 ± 4.8 vs. 57.5 ± 7.6, p <0.001) and a significantly earlier sleep/wake rhythm (difference between mean onset times = 2.5hrs; wake times =1.3hrs, both p <0.05) and a phase advance in the rhythm of melatonin secretion (difference between mean DLMO =2.2hrs, p <0.02). However the size of the difference between the groups was smaller than expected, and there was an overlap in the sleep phase between some affected and non-affected members. This highlighted some of the difficulties in the diagnosis of ASPS, particularly if some individuals modify their sleep schedule according to other family members. Mapping the chromosome 2qter region of *hPer2* in seven affected and seven unaffected individuals found no significant linkage with *hPer2*, and an absence of the A/G mutation in both groups. The authors concluded that the argument for heterogeneity in the genetics of FASPS is well-supported, given that mutations or SNPs of other clock genes can also result in alterations to the translation/transcription rate of the feedback loops regulating the circadian timing system (Satoh et al., 2003).

More recently, Carpen and colleagues (2005) screened the *hPer2* gene for novel polymorphisms and investigated the association between three SNPs (C-1128T, C111G and C3853A) and preferred sleep timing in 35 extreme morning- and 35 extreme evening-types. Although the allele frequencies for these polymorphisms were not significantly different between extreme M- and extreme E-types, the frequency of the 111G allele was significantly higher in extreme morning-types (G =0.14, C =0.86) compared to extreme evening-types (G =0.03, C =0.97, p =0.031) suggesting that it may be a possible candidate allele for ASPS (Carpen et al., 2005).

Several investigators have examined *hPer3* as a possible candidate gene involved in the pathogenesis of DSPS. For example, a screen of the genomic DNA from patients with DSPS and non-24-hour sleep/wake syndrome (i.e. daily delay of sleep phase resulting in cyclic episodes of insomnia) identified 20 sequence variations in *hPer3* of which six predicted amino acid changes. Five of these polymorphisms occurred in four haplotypes (H1-H4) and further analyses indicated that the frequency of the H4 haplotype was substantially higher in DSPS patients compared with controls (odds ratio = 7.79 85% CI 1.59-38.3, Bonferroni's p =0.037) (Ebisawa et al., 2001). It was speculated that one polymorphism (G647) in the H4 haplotype may alter the CKIε-dependent phosphorylation of *hPer3*, however there were several limitations to this proposal, as outlined by the investigators. Firstly, it was indicated that an additional

unknown polymorphism may be needed to alter phosphorylation and thus result in DSPS. In addition, the exact functional role of *Per3* in the circadian clock works is still not clearly understood, thus the authors were uncertain as to how an alteration in *hPer3* phosphorylation could cause an increased susceptibility to DSPS.

In a subsequent study, Archer and colleagues (2003) investigated a length polymorphism in *hPer3* (4- and 5-repeat allele) that was described but not specifically analysed by Ebisawa et al. (1999). There was a significant trend for higher frequencies of the 5-repeat allele with increasing morningness (E-types =0.24, N-types =0.32 and M-types =0.42) and higher frequencies of the 4-repeat allele with increasing eveningness (E-types =0.76, N-types =0.68 and M-types =0.58). Moreover, the frequency of the 4-repeat allele was significantly greater in a small group of DSPS patients (n=16) compared to the combined group of M- N- and E-types (n=105; 0.88 vs. 0.68 respectively, OR=3.352 p =0.02). Among the DSPS group, 75% were homozygous for the 4-repeat allele. It was suggested that the length of the *hPer3* repeat region may provide a genetic marker for extreme sleep timing preference, and in addition the authors argued that these findings presented evidence for a functional role of *hPer3* in the development of DSPS, similar to that of *hPer2* in ASPS. The authors suggested that the 4-repeat allele may have fewer amino acids available as phosphorylation substrates for CKIε, which would lead to hypophosphorylation of *hPer3* and stabilisation of its products.

The correlation between the *hPer3* length polymorphism and sleep timing preference was confirmed by Pereira and colleagues (2005), with increasing frequency of the 5-repeat allele with morningness. Comparing a small group of DSPS patients (n=17) to a larger group of individuals from the general population (n=110) indicated a lower frequency of the 4-repeat allele and a higher frequency of the 5-repeat allele in the patient group (χ^2 =4.85, p =0.028). Similarly, compared with a group of E-types (n=40), the DSPS patients had a lower frequency of the short allele and a higher frequency of the long allele (χ^2 =5.82, p =0.016). The authors suggested that the incongruent findings could be explained by differences in latitude (Archer et al. 2003 London, 51˚ 30'N; Pereira et al. 2005 Sao Paolo, 23˚ 32'S) which would result in differences in exposure to day length and temperature variations between the study populations. The synchronisation of the circadian clock to the external environment by light depends on the timing of the exposure, while the phase of entrainment depends on the strength of the zeitgeber and the free-running period of the individual. Thus, it was posited that at different latitudes the same genotypes would be exposed to different photoperiods and zeitgeber strengths which could result in different phenotypes. Although the mechanism by which *hPer3* could influence the phase of entrainment and/or the intrinsic free-running period in different latitudes was not speculated, Pereira et al. (2005) cited a study whereby the *mPer3* gene showed marked changes in the amplitude of mRNA expression and a large phase advance when exposed to a short photoperiod. In addition, Vitaterna et al. (2005) suggest that the association with latitude raises

the possibility that evolutionary changes may have involved subtle alterations to the clock genes which allowed humans to fine tune their temporal relationship with their new environments.

Pereira et al. (2005) also reported an unexpected association between DSPS and morningness, based on their finding that the frequencies of the 4- and 5- alleles were not significantly different between these two groups (M-types n=58, 4-repeat =0.60, 5-repeat =0.40; DSPS n=17, 4-repeat =0.44, 5-repeat =0.56, χ^2 =2.95 p=0.086). The authors suggested that this may reflect similarities in the mechanisms underlying these conditions, given reports of a longer phase angle between the T_{min} and wake time between DSPS patients and controls (Ozaki et al., 1996) and morning- vs. evening-types (Duffy et al., 1999). However, given that both groups showed allele frequencies in the appropriate directions according to their phenotype, it is likely that the small number of DSPS patients included in the analyses affected the ability to detect statistically significant differences.

It was concluded that *hPer3* has an important role in the development of DSPS and sleep timing preference, which possibly includes the tracking of day length as opposed to a direct effect on the regulation of the circadian period. This would lend support to the morning- and evening-oscillator model for the circadian clock works presented by Daan and colleagues (2001), with the *per3* gene responsible for maintaining the phase relationship between the two oscillators rather than as a non-essential clock controlled gene.

1.5 The Relevance of Morningness/Eveningness to Public Health in Aotearoa/New Zealand

Adequate sleep is vital to effective waking function and health. Many aspects of our society challenge our ability to obtain adequate sleep, including time pressures, the prevalent notion of getting more out of life by cutting back on sleep, and the move of increasing numbers of enterprises to 24-hour operations and shift work (Gander, 2003). The national survey of sleep habits and sleep apnoea risk factors found that 36% of New Zealanders aged 30-60 years report never or rarely getting enough sleep (Harris, 2003). Moreover, the national insomnia survey found that 29% of Māori and 25% of non-Māori aged 20-59 years report a chronic sleep problem lasting more than 6 months (Paine et al., 2005). Inadequate sleep is clearly a major public health issue in New Zealand.

Very little is known about natural variability in sleep timing, or about the relative importance of the genetic versus environmental factors determining sleep timing. If the presence of specific polymorphisms is reliably linked to abnormal sleep timing, then they may serve as a valuable diagnostic indicator for differential diagnosis of patients with sleep disorders, leading to improved treatment. It may also be possible to make recommendations about more suitable work patterns for people with extreme phenotypes, to reduce their risk of deleterious health and

safety effects from shift work. The circadian phase-related sleep disorders (ASPS and DSPS) are likely to be a factor in only a small fraction of the total burden of sleep problems affecting the health and well being of New Zealanders. A much larger contribution might be expected from chronic sleep restriction as a result of long and/or irregular work patterns.

Theoretical arguments, and a limited number of field studies, suggest that different chronotypes may adapt better to different sorts of shift work, and to time zone crossings (Gander et al., 1993; Harma, 1993). For example, evening-types may cope better with night shift, while morning-types would be expected to have less difficulty with early shift start times. The available evidence is limited and the magnitude of the measured differences is small. Nevertheless, this is an area of particular interest to New Zealand, since at least 25% of our workforce have employment contracts with shift work provisions (Gander, Le Quesne, & Armstrong, 2002), and our geographical isolation requires us, and foreign visitors to this country, to be long-distance international travellers. There is also evidence that people become more morning-type across adulthood, which may be relevant to the sleep and health of our ageing population.

When individuals are unable to sleep at their (biologically) preferred time because of societal demands (e.g. shift work, international travel) or endogenous alterations to their circadian timing system (e.g. circadian sleep disorders) then it is likely that the sleep they do achieve will be restricted.

Experimental studies have clearly demonstrated that chronic sleep restriction causes dose-dependent progressive impairment in psychomotor vigilance performance, subjective sleepiness, fatigue, and mood (Belenky et al., 2003; Dinges et al., 1997; Van Dongen et al., 2003). These studies raise the issue of chronic sleep restriction as a potential risk factor in occupational and driving safety. Recent studies have also revealed biologically plausible links to longer-term health problems. Several consecutive nights of sleep restricted to 4 hours have been shown to impair immune responses (Spiegel, Sheridan, & Van Cauter, 2002), decrease glucose tolerance, elevate evening cortisol levels, and increase sympathetic activity (Van Cauter & Spiegel, 1999) in healthy young adults. The authors of the latter study concluded that ongoing sleep restriction may facilitate the development of chronic conditions such as obesity, diabetes, and hypertension. It is noteworthy that these conditions all affect Māori disproportionately, and recent national survey data indicate that sleep problems also affect Māori disproportionately (Harris, 2003; Paine et al., 2005). A recent epidemiological study found that being involved in night work increased the risk of reporting often or always having difficulty falling asleep (OR=1.36, p <0.05), having a current sleep problem (OR=1.64, p <0.001) and having a chronic sleep problem lasting longer than 6 months (OR=1.61, p <0.01) (Paine et al., 2004).

Sleeping out of phase with the environmental LD cycle causes significant disruption to an array of physiological and endocrine variables and desynchronisation of the internal architecture of

the sleep episode. There is also increasing evidence to suggest that circadian disruption, such as that experienced during shift work and transmeridian travel, may significantly increase the risk of developing cancer. For example, several recent studies have indicated that there may be a relationship between prolonged exposure to shift work (graveyard and rotating shifts) and an increase in the incidence of breast cancer (reviewed in (Davis & Mirick, 2006)). Similarly there is evidence to suggest an increased risk of colorectal cancer among women working rotating night shifts (Davis & Mirick, 2006). Interestingly, the relative risk of breast cancer among female flight attendants and cancer patients with a first-degree family history of the disease are said to be of comparable magnitude, however studies to date are confounded by the differing definition of shift work in this occupational group and possible interactions with other exposures (Moser et al., 2006).

One possible mechanism driving these relationships may be the suppression of melatonin secretion due to light exposure during night time work (melatonin protects against the proliferation of breast and colonic tissue and cancer cells) (Haus & Smolensky, 2006; Moser et al., 2006). Another possible mechanism driving the increase in cancer risk is the disruption of circadian clock gene functionality. Davis and Mirick (2006) described new evidence from animal studies that a polymorphism in the circadian gene *per3* may be associated with the development of breast cancer, and that changes in *per2* may affect tumour suppression and the response to DNA damage, possibly suggesting a genetic component that affects the ability of an individual to adapt to circadian disruption such as shift work.

1.5.1 Challenges for Sleep and Circadian Rhythm Research in Aotearoa/New Zealand

> If future basic work in [circadian sleep disorders] solidifies a biologic or genetic basis for the disorder, then the public and healthcare professionals must be made aware. To do otherwise would be to risk continued misperception of patients simply being 'lazy', unmotivated, or eccentric in choosing to live on a schedule incompatible with that of much of diurnal society. (Wyatt, 2004)

As in many other areas of science, the field of sleep and circadian research is increasingly focused on identifying the molecular genetic substrates that are responsible for generating 24-hour rhythms in humans. Vitaterna and colleagues (2005) suggest that clarifying the genetic basis of human circadian rhythmicity may provide a deeper understanding of human health and disease and holds promise for new therapeutic approaches for both the voluntary and involuntary disruption of normal circadian function. Individual differences in the characteristics of the circadian timing system may play a role in determining an individuals' innate ability to cope with shift work (Monk, 2005), thus the ability to tolerate night shift work, time zone transitions, and artificial time cues in our 24-hour society is likely to depend upon the presence of specific clock gene variants (Archer et al., 2003). However, there has been little

consideration in the scientific literature of the ethical implications of screening for clock gene polymorphisms and the social and political consequences of determining an individual's ability to cope with different work patterns based on genetic information alone.

Many sleep and circadian researchers are intensely aware of our social responsibilities to improve public understanding about the importance of the circadian and homeostatic processes for health and safety. A significant challenge is developing methods to translate the rapidly increasing knowledge in these areas to positively influence public health and policy (Walsh et al., 2005). However, with an increasing focus on the elucidation of those genetic mechanisms driving sleep timing, we also face a number of challenges in order to meet our ethical responsibilities to the public. In the context of health research in New Zealand, this includes an ethical responsibility to recognise and respect the values of the Māori community.

Māori are tangata whenua, the indigenous people of Aotearoa/New Zealand. The 1840 Treaty of Waitangi (the Treaty) facilitates the relationship between Māori and the Crown and provides a legal and ethical framework for ensuring that Māori values and aspirations are upheld (Human Genome Project., 2006). The Health Research Council of New Zealand (HRC) is the Crown agency responsible for the management of the Government's investment in public good health research. The HRC vision for Māori health reads that "All health research in Aotearoa New Zealand benefits the hauora (health and well-being) of tangata whenua" (Health Research Council of New Zealand, 2004). In particular there is a commitment to recognise the Treaty as the founding document of Aotearoa/New Zealand and to incorporate processes that affirm the Treaty Articles that articulate and guarantee Māori rights to rangatiratanga (sovereignty or self-determination) and to a fair share of the (good health) benefits afforded to other members of society. The Royal Society of New Zealand also reminds scientists and technologists in New Zealand of their responsibility under the Treaty of Waitangi in their code of ethics, particularly when the research investigation involves individuals, groups of people, the natural environment, customs, objects or place which hold special cultural significance (Royal Society of New Zealand., 2003).

While research on human subjects is governed by a number of well established moral and scientific principles, it is believed that genetic research may involve some unique challenges for the researcher. In anticipation of these, the HRC produced a series of "points to consider" for researchers in the field of human genetics (Winship & Marbrook, 1998), which indicated the responsibilities of the researcher to maintain privacy and confidentiality, to minimise harm, and to protect and support those taking part in the research by ensuring that the full spectrum of possible adverse events is considered at an early stage and incorporated into the development of the study. The document also points out that conflict may arise because multiple groups (e.g.

researchers, participants, regional genetic services and society) will have their own expectations of the proposed genetic study.

The ethical implications of genetic research and new biotechnologies have received significant attention and sparked serious debate among many sections of New Zealand society, the most significant of which occurred during the Royal Commission on Genetic Modification (RCoGM). Although the discussions were framed within a particular application of genomic sciences, the conversations broached issues that spoke to the fundamental principles of humanity and indeed New Zealand society. While the public is aware of the benefits of genetic research, particularly in terms of human health and medicine, it is also aware of the dangers inherent in this science, which include the control of genetic information by scientists and commercial enterprises. Moreover, the public are reluctant to trust these groups to consistently act in the best interest of humanity (Royal Society of New Zealand., 2003). In their guidelines, Winship and Marbrook (1998) consider the potential for the misuse of genetic information which may harm participants via stigmatisation, discrimination, the invasion of privacy, and confidentiality of the information. Molina (2005) cites a recent report from the Organisation for Economic Cooperation and Development (OECD) which states that "Both the indigenous Māori and European populations in New Zealand agree that the collection of genetic information may threaten individual autonomy, dignity and privacy and raise concerns of discrimination" (OECD, 2004 cited in (Molina, 2004)). The significance of privacy, misuse, and discrimination, within genetic research is derived from the perception that genetic information is deterministic and that our history and relationships held within our genetic code are fixed and unchangeable (Molina, 2005).

From these conversations and others since, it is clear that a second challenge for genetic research, and those investing in this knowledge area, is confronting the publics' resistance to new biotechnologies (Battye, Blair, & Mellor, 1999) and the information contained therein. In a report to the Ministry of Research, Science and Technology, Battye and colleagues (1999) explain that increasing public distrust of scientists is attributable to a poor understanding of the science, ethics, and risk evaluation, together with a growing focus on individuality as compared to community orientation. However, this supposed naivety around genetic issues may not be limited to the public. A recent study investigating the social implications of genetic testing in the areas of employment and ACC found no evidence of policy development to manage the issues raised by genetic testing for the areas of employment and insurance for work-related injury (Govern, 2005). Moreover there appeared to be an assumption that current legislation provided the necessary protection, despite comments to the contrary by the Human Rights Commission. While public approval requires improved public education on 'scientific matters', it must be coupled with direct consultation between the public and scientists, funding providers and government agencies (Battye et al., 1999).

Māori have serious and valid concerns that genetic research and new biotechnologies confront the traditional Māori intellect (mātauranga Māori) and principles which regulate Māori society (tikanga Māori). Although Māori concerns for genetic research in Aotearoa/New Zealand are derived from a specific body of knowledge and history of research, the values held by Māori add special emphasis to the ethical and cultural objections of many people to gene research and technology (Eichelbaum et al., 2002). Several documents and guidelines have been produced (e.g. (Health Research Council of New Zealand, 1998; Ministry of Health, 2004a, , 2006)) in an effort to meet some of these concerns, addressing issues such as the access to and control of genetic information, appropriate storage and use of human tissues and fluids, methods of consultation with Māori groups, and the collective nature of informed consent, which are incorporated within an ethical framework for genetic research in Aotearoa/New Zealand. However, a deeper understanding of the discourse on genetic research which comes from the Māori community speaks to broader social and political issues about the treatment and perception of Māori in this country, including racism, colonisation, and marginalisation. Thus, the final challenge for genetic research in Aotearoa/New Zealand is to develop research processes that affirm Māori rights to sovereignty in research, which value traditional knowledges and practices, and that will negotiate and ultimately reduce the physical and theoretical space between Māori and scientific communities.

1.6 Thesis Organisation

At the time of designing this research programme there was a strong focus on the isolation of the human clock genes and their role in the development of extreme sleep timing preference. However there was little known about the variability of the clock genes in the general population. While this was of particular scientific interest, there were several unresolved issues particularly with regards to the distribution of chronotypes in the general population, which needed to be addressed before a genetic study of clock gene polymorphisms in the general population could reasonably be attempted. Similarly, while it is recognised that the circadian clock defines physiologically optimal times for sleeping, increasing pressures from our 24hr society mean that the timing of sleep is also heavily influenced by societal norms. However, little attention was being paid to understanding the contribution of psychosocial factors to the timing of sleep in daily life.

The first section of this thesis presents three studies which were designed to provide new insights on the relative contribution of circadian physiology versus psychosocial factors in determining sleep timing. It represents the first population-based study of the natural variability in circadian phenotypes and it also presents an innovative study of sleep/wake schedules and circadian phase in morning- and evening-types in daily life. Consistent with established practice in the discipline, quantitative research methods were used throughout this section.

The first study undertaken (Chapter 2) used the MEQ to measure the prevalence of different chronotypes in a structured random sample of adults aged 30-49yrs, drawn from the electoral role in the Wellington region. The sample was designed to recruit equal numbers of Māori and non-Māori participants and equal numbers in each decade of age. This study aimed to investigate the prevalence of different chronotypes comparing Māori and non-Māori, men and women. Moreover the study design allowed the investigation of the possible age-related changes in sleep timing and the possible relationships between socio-economic position and work status.

The second study (Chapter 4) recruited a subset of 31 morning- and evening-types from the survey population and used wrist activity monitors and sleep diaries to document their sleep patterns in daily life, across a two-week period (the specific methods used are described in Chapter 3). This study contrasts with much of the previous literature, which has related MEQ scores to sleep in controlled laboratory conditions, or following strict sleep/wake schedules. The specific aim of this study was to compare the timing, duration and quality of sleep between the two groups and to investigate differences in weekday versus weekend sleep patterns.

In the third study (Chapter 5), the participants in study 2 were brought into the time isolation facility for a 17-hour constant routine protocol, to assess the timing of their nocturnal melatonin profile, under controlled conditions. This study aimed to investigate the relationship between circadian phase and self-identified morningness/eveningness. Moreover, it aimed to examine the contribution of circadian phase versus other psychosocial factors to the variability in sleep timing.

At the inception of this research programme there was growing public debate around the ethical implications of conducting genetic research in New Zealand. However, there had been no discussion in the scientific literature around the consequences of screening for clock genes from an ethical, political or social point of view. In addition, through our consultation process it was brought to our attention that there was an urgent need to develop ethical frameworks for genetic research in New Zealand, which centred and prioritised Māori needs within health research as part of our indigenous rights. While elucidating the genetic basis to morningness/eveningness has the potential to clarify the role of the circadian timing system in an individual's ability to cope with physiological and societal challenges to sleep and waking performance, this approach will not be sufficient, and we had significant concerns about the ability of genetic research to improve and advance Māori health and development in Aotearoa/New Zealand.

In the second section of this thesis the ethical implications of conducting genetic research in New Zealand are explored with Māori, with the aim of developing some ethical guidelines for health researchers working with Māori genetic material and information (Chapter 6). While this study does not focus on circadian genetics specifically, it provides valuable information

regarding the perceived utility of genetic research by the public which will have a significant impact on the social, political and economic investment in this type of research in the future.

A significant feature of this thesis is the use of Kaupapa Māori research as the underlying methodology, or process of inquiry, in Chapters Two and Six. As a point of clarification, a distinction is made between the terms methodology and method. Methodology denotes the epistemological stance that informs the research strategy (McKinley, 1990 cited in (Harris, 2003)) and it reflects the underlying theory and analysis on which the research is based (Smith, 1999). Method, on the other hand, refers to the practical techniques for gathering evidence (Smith, 1999).

There is no one universal definition of Kaupapa Māori research (Harris, 2003), and many of the explanations offered by writers and theorists of Kaupapa Māori research are explored in Chapter 6. However in the context of this thesis, Kaupapa Māori research is viewed as an approach to research that brings Māori from the margins to the centre, and views Māori as 'the norm'. By prioritising Māori needs within the research endeavour, and focusing on providing useful outcomes for Māori (Smith, 1999) Kaupapa Māori research helps to define the issues that are explored, the questions that are asked, the methods that are used and the interpretation that is given. In the framework used in this thesis, Kaupapa Māori focuses first on getting the approach right, and is not prescriptive with regard to the choice of methods that are used for any given type of research (Smith, 1999).

Indeed, this thesis exemplifies how Kaupapa Māori research can achieve these goals using multiple methods. Qualitative methods have been seen by some as particularly well suited to Māori (Moewaka Barnes, 2000) and in Chapter Six of this thesis focus groups and key-informant interviews were deemed to be the most appropriate method of understanding Māori views around genetic research. However, Kaupapa Māori research is not limited to qualitative methods and is expanding in scope to include quantitative methods. In health research a number of Māori researchers are now applying Kaupapa Māori methodologies within the framework of epidemiology (e.g. (Harris, 2003; Mihaere, 2004; Paine et al., 2005; Robson, 2002)). The study presented in Chapter Two has utilised a number of important concepts for the use of quantitative methods in Kaupapa Māori research.

CHAPTER 2
AN EPIDEMIOLOGICAL SURVEY OF MORNINGNESS/EVENINGNESS IN THE GENERAL POPULATION

2.1 Introduction

The development and evaluation of subjective tools for discriminating chronotypes has commanded significant attention within the fields of sleep research, chronobiology and human factors. The potential to use a questionnaire to identify those individuals who may be better suited to shift work, or to better understand why some individuals are more able to adjust to the acute effects of jet-lag, is of interest to many. Similarly, self-report measures could provide a simple clinical screening tool for the identification and diagnosis of those who suffer sleep problems due to a misalignment and/or disorganisation of the timing of their internal circadian clock.

Subjective measurement tools, such as questionnaires, are often used in epidemiology to collect information on the health status of a population at a particular point in time (Ahrens, Krickeberg, & Pigeot, 2005). Although laboratory based studies may provide information about the biological reasons for differences in the timing of sleep, large-scale surveys can provide critical information about the prevalence of sleep problems in the population and the potential social influences which may force some individuals to sleep at unusual or unwanted times of the day.

Of all the self-report questionnaires available, the Horne and Östberg Morningness/Eveningness Questionnaire (Horne & Östberg, 1976) is the most well known and widely used, but despite this there is very little epidemiological evidence available about the distribution of chronotypes in the general population. This chapter presents the findings of an epidemiological survey designed to estimate the population prevalence of chronotypes among New Zealand adults as well as investigate the possible influence of demographic and/or socioeconomic factors on sleep timing preference.

2.1.1 Morningness/Eveningness Questionnaires

In 1976 Horne and Östberg published a 19-item morningness/eveningness questionnaire (MEQ) which purported to be able to distinguish morning- and evening-type individuals based on their self-reported preference for arising and bedtimes, their preferred times for peak physical and mental performance, as well as subjective ratings of appetite and alertness at different times of the day. The authors also provided scoring criteria and cut-offs for the differentiation of five

chronotypes based on the total MEQ score (in ascending order): definitely evening-types (DE-types), moderately evening-types (ME-types), neither-types (N-types), moderately morning-types (MM-types) and definitely morning-types (DM-types). Neither the descriptive statistics or the frequency distribution of the chronotypes in the total sample were presented in this paper, however Posey and Ford (1981) later administered the MEQ to a similar sample (259 college students, 62 men and 187 women, no ages given) and found that the distribution of scores was not significantly different from a normal distribution (median 51, range 19-82).

Since then, the MEQ has been translated into many languages (Adan & Amirall, 1990) (Griefhan, 2002; Van Dongen, 1998) and remains the most commonly used subjective tool for differentiating chronotypes (Adan & Natale, 2002; Smith et al., 1989; Tankova et al., 1994). Psychometric evaluation confirms that the MEQ is comprised of a fairly homogeneous set of items, with good internal consistency (coefficient alpha 0.82), that is valid and reliable among those who work daytime schedules (Smith et al., 1989).

Despite this, the MEQ has been widely criticised for measuring inter-individual differences other than morningness (Adan & Amirall, 1991; Larsen, 1985; Monk & Folkard, 1985; Torsvall & Akerstedt, 1980) and for being insensitive to changes in sleep associated with shift work (Adan & Amirall, 1991; Roberts & Kyollonen, 1999). Other questionnaires were developed for use among shift-workers (Folkard, Monk, & Lobban, 1979; Torsvall & Akerstedt, 1980) however they were found to have poor psychometric properties (Smith et al., 1989) and as a result they have not been as popular. The MEQ has also been criticised for its length and therefore impracticability as a field tool or pre-screening questionnaire. Smith et al. (1989) developed a 13-item Composite Scale (CS) and Adan and Amirall (1991) reduced the MEQ to the five items which were found to be the most important (and therefore discriminatory) for the definition of morningness/eveningness (rMEQ). Both tools were found to possess good psychometric properties (Chelminski et al., 2000; Diaz Morales & Sanchez-Lopez, 2004; Smith et al., 1989) but again neither have attained the popularity of the MEQ.

In 2001, Taillard and colleagues presented the findings from a study of French adults (mean age 51.3 ± 3.3yrs) enrolled in the GAZEL cohort, who completed the MEQ as one of several questionnaires. The investigators identified a "good sleepers' subgroup" (mean age 51.2 ± 3.2yrs) who, according to the original MEQ score cut-offs, fell into the following distribution: 0.1% DE-type, 2.1% ME-type, 36.6% N-type, 52.9% MM-type, and 9.2% DM-type.

Subsequently, Taillard and colleagues (2004) predicted that the observed reduction in the numbers of evening-type individuals in this population was due to inaccurate classification, rather than reflecting any age-associated changes in the sleep and circadian systems. Without changing the original instructions or scoring of the MEQ, these investigators proposed new cut-offs to more accurately identify chronotypes in middle-aged working adults. The application of

these new cut-offs resulted in 28.1% of the sample being classified as morning-type (9.0% DM-type), 51.7% neither-type and 20.2% evening-type (7.5% DE-type). Validation of these cut-offs against daily sleep logs confirmed significant differences between evening- and morning-types on a number of sleep parameters including bedtimes and rising times, sleep debt and sleep quality.

2.1.2 Rationale

As mentioned previously, there is little information about the prevalence and distribution of different chronotypes in the general population. Also, given the increasing interest in the isolation of human genes related to extreme sleep timing, there was an urgent need to understand the phenotypic variability in the general population.

Undertaking a large-scale survey of morningness/eveningness preference in Aotearoa/New Zealand offered several advantages over those studies reported in the literature. Firstly, given our geographical size, it would be possible to randomly select a large sample of adults who would more accurately reflect the diversity of the general population, compared to those studies that had limited their sample to college students or gathered information from employment records.

Secondly, the study would be undertaken within a Treaty of Waitangi framework in accordance with the HRC vision for Māori health (Health Research Council of New Zealand, 2004). In this way, the study would have a particular strength compared to other international sleep research which has neglected the importance of developing research partnerships and examining inter-ethnic differences (Gander, 2003).

2.1.3 Objectives and Hypotheses

The specific objectives of this study were:

1. *To develop a circadian-type questionnaire adapted for New Zealanders, including the Horne and Östberg Morningness/Eveningness Questionnaire.*

2. *To achieve a 70% response rate from 5,000 adults selected at random from the electoral rolls in the Wellington region.*

3. *To estimate the prevalence of different circadian phenotypes, comparing Māori and non-Māori, men and women.*

4. *To investigate possible age-related changes in self-reported sleep timing.*

5. *To investigate possible relationships between socioeconomic position and extreme circadian phenotypes.*

6. *To investigate possible relationships between circadian phenotypes and self-reported sleep habits, employment status and general health.*

7. *To identify potential participants for recruitment into subsequent studies.*

The research hypotheses were:

1. *That approximately 25% of the population has a measurable tendency towards morningness or eveningness, as defined by the MEQ.*

2. *That the prevalence of different chronotypes is independent of ethnicity, sex and socioeconomic position.*

3. *That older people are more morning-type.*

4. *That evening-types will report greater levels of daytime sleepiness and shorter sleep durations than morning-types.*

5. *That evening-types will report poorer general health, as a result of their weekday sleep restriction, compared to morning-types*

6. *That there will be a significant relationship between current employment status (particularly night work) and self-reported sleep timing preference.*

2.2 Methods

The following section provides a detailed overview of the methods used in this study. It is noteworthy that this process was carefully developed within the context of a longstanding research partnership between the Sleep/Wake Research Centre and Te Rōpū Rangahau Hauora a Eru Pōmare (TRRHaEP, Otago University at the Wellington School of Medicine and Health Sciences). Together, these research centres have conducted a series of epidemiological surveys designed to investigate the prevalence of, and risk factors for sleeping problems and disorders in Aotearoa/New Zealand (e.g. (Harris, 2003; Mihaere, 2004; Paine et al., 2004; Paine et al., 2005)). This research partnership ensured that each study has achieved the research goals and objectives (i.e. random sampling, adequate response rates) whilst also meeting the needs of Māori (i.e. development and training of Māori researchers and providing outcomes that are useful and beneficial for Māori) in accordance with our indigenous rights.

The study was approved by the Wellington Campus Massey University Human Ethics Committee (03/126, see Appendix 1).

2.2.1 Sampling Strategy

Target population

The target population for this study was defined as Māori and non-Māori men and women aged 30-49 years living in the Wellington region.

As mentioned, a key objective of this study was to ensure that the research outcomes were relevant to Māori, and in line with a Kaupapa Māori philosophy, centered Māori development and aspirations. Te Rōpū Rangahau Hauora a Eru Pōmare (2002) and Harris (2003) have shown that in epidemiology these goals can be achieved by ensuring that ethnicity data is collected appropriately, and that the study design is conducive to the principles of equal explanatory and analytical power. According to the Kaupapa Māori framework used in this thesis, equal explanatory and analytical power ensures Māori participation and control of research, such that the analysis of Māori and non-Māori data occurs with a similar level of precision while also allowing Māori and non-Māori comparisons to be made (Robson, 2002). To achieve this, a sampling method must allow for similar numbers of Māori and non-Māori responders to the survey.

Understanding the influence of age and sex on morningness/eveningness preference was also an important feature of the present study. To permit comparisons by sex in this population, it was hoped that the sampling process would include equal numbers of men and women, whilst to minimise confounding by age-related changes in sleep it was decided that the target population would be restricted to the range of 30-49 years.

Finally, the target population was also limited geographically. Although the present study was primarily designed to investigate the prevalence of different chronotypes in the general population, it also served to identify extreme chronotypes for further study and investigation. Therefore, only adults living in the Wellington region were included in the sampling frame.

Sampling frame and sample size

The New Zealand electoral roll was the sampling frame used in this study, therefore only those who were enrolled at the time of drawing the sample had a chance of being selected. In New Zealand, at the time of first enrolment, all adults who indicate that they are of Māori descent have the option to enrol on either the general roll or the Māori roll. This decision influences whether an individual votes in a Māori electorate or a general electorate and determines the number of Māori electorates in Parliament. For the purposes of health research, an electronic version of the electoral roll may be purchased, which contains electors on both the general roll and the Māori roll and for the remainder of this chapter, the use of the term electoral roll will refer to the combination of both.

A Māori descent field (yes/no) is included in the electoral roll and in the context of health research provides a convenient frame for selecting a random sample of Māori. In this study, the Māori sample was selected from those who answered yes to being of Māori descent, and the non-Māori sample was selected from those who answered no, or left the Māori descent field blank. In order to achieve equal numbers of Māori and non-Māori participants people of Māori descent were oversampled (Harris, 2003).

The electoral roll does not provide information on sex, so the sample could not be stratified by sex, however it was expected to include approximately equal numbers of men and women.

The electoral roll provides information on the year of birth and so the sample was also stratified by age in 10-year age groups (30-39yrs and 40-49yrs). This provided more power for age-group comparisons and it controlled for differences in the age structure between the Māori and non-Māori populations.

The electoral roll also includes a Postal Address Type field. All electors listed as living overseas are indicated by an 'O' in this field, and therefore can be excluded from the sampling frame. Similarly, all electors whose postcode associated with their mailing address did not match those belonging to the Wellington region were excluded.

The final sample

A final stratified random sample was selected from the New Zealand electoral rolls that consisted of 5,000 New Zealand adults (2,674 Māori descent and 2,326 non-Māori), aged 30-49 years living in the Wellington region.

2.2.2 Questionnaire Design

In addition to the 19-items of the MEQ, the questionnaire used in this study also asked for demographic information as well as general sleep habits and self-reported general health using validated questions where possible.

Given the differences between the original sample of Horne and Östberg (1976) used to develop and validate the MEQ and our target population, careful attention was paid to the language used in the MEQ, as the present sample was expected to include people with varying levels of literacy, and some having English as a second language.

A modified version of the MEQ was pretested at a local shopping mall in August 2003. Those who completed the questionnaire were asked to comment on the language and terms used, the length of the questionnaire, as well as its overall appearance. Minor changes were made following the pretest and incorporated into the final version (see Appendix 2).

Sex (Question 1)

As mentioned earlier, the electoral rolls do not provide information on sex, so to enable comparisons between men and women, participants were asked to identify their sex.

Date of birth (Question 2)

Although the electoral roll provided information on the year of birth, each participant was asked to give their date of birth (day/month/year) to enable accurate calculation of participant age at the time of completing the survey. This question also provided an opportunity to check that the questionnaire had been completed by the intended person.

Ethnicity (Question 3)

The appropriate classification of ethnicity is crucial for the monitoring of disparities in health between Māori and non-Māori (Harris, 2003; Robson & Reid, 2001). It is important to note that not all people of Māori descent identify their ethnicity as Māori (Harris, 2003; Statistics New Zealand, 1997), however, self-identified ethnicity has been recommended as the standard for study and commentary in health, and is usual practice in New Zealand (Te Rōpū Rangahau Hauora a Eru Pōmare, 2000). The 2001 census question was used to determine participant ethnicity in the present study and allowed the data collected to be weighted back to the appropriate general population proportions. Any participant who identified themselves as Māori, either alone or as one of multiple ethnicities, was classified as Māori for the analyses.

Current work status (Question 4 and 5)

Participants were asked if they currently worked for pay, profit or income (yes 1 paid job/yes, more than 1 paid job/no) (Statistics New Zealand, 2002). If yes, they were then asked if, in the last 4 weeks, they had worked for pay, profit or income for at least 3 hours between midnight and 5am (yes/no) (International Labour Organization, 1990; Council of the European Union, 1993). The combination of answers to these questions allowed respondents to be categorised as currently unemployed, currently employed but not working any nights, or currently working nights.

Sleep habits (Questions 6 and 7)

To be able to investigate the relationship between chronotype and sleep quantity, question six asked "How many hours sleep do you usually get in 24 hours?"(Harris, 2003; Paine et al., 2004). Asking participants to disclose their sleep in a 24-hour period, rather than across the traditional nocturnal period, permits the inclusion of shorter daytime sleep periods in the overall estimation. This may be an important consideration for shift-workers who are unable to sleep at night and those who top up their sleep by using naps.

Daytime sleepiness was measured using the Epworth Sleepiness Scale (ESS)(Gander et al., 2005a; Johns, 1991, , 1992). The ESS is one of the most frequently used self-report tools for assessing sleepiness, asking individuals to rate their likelihood of falling asleep in eight commonly encountered situations on a four-point scale. Each answer is assigned a value from 0-3, which together provides an overall sleepiness score ranging from 0-24. ESS scores > 10 are indicative of excessive daytime sleepiness.

General health (Question 8)

We have previously reported a significant relationship between self-reported general health and insomnia symptoms and chronic sleeping problems among New Zealand adults (Paine et al., 2005) and there is reasonable evidence to suggest that self-rated health is correlated to actual health and/or mortality (Idler & Angel, 1990; Idler & Benyamini, 1997). In order to investigate the possible relationship between self-reported morningness/eveningness and health, participants were asked to rate their general health as either excellent, very good, good, fair or poor (Ministry of Health, 1999b).

Socioeconomic deprivation

In New Zealand, Māori are more likely to be disadvantaged in terms of socioeconomic measures such as education, housing, income, employment, and deprivation(Howden-Chapman & Wilson, 2000; National Health Committee, 1998; Pōmare et al., 1995). As in other countries, socioeconomic factors have been identified as primary determinants of health that contribute to persisting health inequalities in New Zealand (National Health Committee, 1998; Wilson, 2000). Socioeconomic position, therefore, has traditionally been seen as a major driver of health disparities between Māori and non-Māori. However, an increasing amount of evidence suggests that the interaction with ethnicity is complex and disparities remain even when socioeconomic position has been taken into account (Howden-Chapman & Tobias, 2000).

Recently, a validated deprivation index (NZDep) was developed based on small areas (census meshblocks) that includes nine variables taken from the New Zealand census relating to material deprivation namely, having no access to a telephone; receiving a means tested benefit; being unemployed; low household income; no access to a car; single parent family; no educational qualifications; not living in own home; overcrowded home (Salmond and Crampton, 2002). NZDep2001 provides a deprivation score for each meshblock (geographical units containing a median of 90 people) in New Zealand, ranging from 1 (least deprived) to 10 (most deprived). Increasing deprivation on this index has shown to be related to a number of health outcomes (Ministry of Health, 2004b) including an increased risk of hypertension, diabetes and smoking (Salmond & Crampton, 2002). Our previous national survey of insomnia symptoms and sleeping problems found that socioeconomic deprivation, as measured using

NZDep2001, was a more significant independent risk factor for chronic sleeping problems (self-reported, lasting longer than 6 months) than either ethnicity or sex (Paine et al., 2004).

It is important to note that NZDep provides a geographical measure of deprivation and therefore provides an indication as to the level of deprivation of the area in which a person lives rather than a measure of their individual level of deprivation, which is equally important when attempting to understand health inequalities. Care must also be taken when inferences are made about individuals on the basis of aggregated data, as errors can occur during interpretation (Salmond & Crampton, 2002).

The Morningness/Eveningness Questionnaire

The Horne and Östberg Morningness/Eveningness Questionnaire was used to identify chronotypes in the present study. Following the original instructions by Horne and Östberg, the New Zealand version of the morningness/eveningness questionnaire asked that each question be answered in numerical order and that participants not go back and check or change their answers. In addition, the questionnaire asked the participants to "Imagine that you are completely free to plan your day. Think only about what feels best for you."

2.2.3 Data Collection

Consistent with other national surveys of sleep habits in New Zealand conducted by SWRC and TRRHaEP, data collection in the present study was a staged process of mailing questionnaires to participants and the subsequent intensive follow-up of non-respondents.

All participants were allocated a unique identifier that was stamped on the bottom corner of the front page of the questionnaire, the accompanying covering letter and reminder post-card. To ensure participant confidentiality, ID numbers and participant details were linked in a dataset available only to the research team

The first mailout was sent to all participants on 01st October 2003. This study package included a covering letter explaining the purpose of the study and contact information for members of the research team; a questionnaire (2 double-sided A4 pages); an information sheet describing future studies (2 double-sided A4 pages); a consent form (indicating whether the participant was willing to be contacted regarding the future studies); and a prepaid return envelope (Appendix 3).

A toll-free telephone number was available throughout the data collection period for participants to ask questions and to respond by telephone, if they so wished.

At approximately three-weekly intervals, all non-responders were mailed a reminder post-card (mailout 2; lodged at New Zealand Post on 15th October 2003) and then a complete new study package (mailout 3; lodged with New Zealand Post on 20th November 2003). Similar surveys

have found that this follow-up process is important for achieving a high response rate, particularly from Māori (Harris, 2003; Mihaere, 2004; Paine et al., 2004).

Telephone follow-up was then attempted for those people for whom telephone numbers could be found (calling began on 25th January 2004). The process used to search for telephone numbers has been described in detail by Harris (2003). Briefly, initial searching for the entire sample was undertaken before the first mailout using a service provided by Telecom (telematching), with the internet Whitepages (http://www.whitepages.co.nz) providing a secondary source of telephone numbers. Phone follow-up was conducted by a team of callers, hired to facilitate the process, and continued to the extent of the available resources (approximately 4 weeks).

At the conclusion of the phone follow-up process, it was decided that a fourth and final mailout would be organised for the remaining non-responders from the Māori sample, to increase the response rate from this group (Lodged with New Zealand Post 29th April 2004). In contrast to previous mailouts, the study package for mailout 4 consisted of only a questionnaire, a cover letter and a prepaid return envelope as the number of items and therefore the amount of information included in the study packages may have been a deterrent to response[2].

Significant attempts were made to find alternative contact details for those participants whose mail was 'return to sender' including searching the electoral roll for alternative addresses such as residential addresses (postal addresses include private bags, rural addresses, PO Box numbers and street addresses) and using the information provided in the telematched file by Telecom. As with the phone follow-up process, searching for alternative addresses continued to the extent of the available resources.

To facilitate the tracking of responders and the subsequent follow-up of non-responders, a response database was set-up and response codes were developed at the time of drawing the sample (see Appendix 4). This process was critical for the overall management of the data collection process as well as the calculation of response rates. Reasons for non-response were coded where possible and the major categories included: (1) no longer in the sampling region (including those participants who were deceased or living outside of the Wellington region at the time of mailing); (2) Ineligible (including those participants who could not complete the questionnaire due to language difficulties, physical and/or psychological illness); and (3) returned to sender (those participants whose questionnaires were returned to sender and therefore deemed to no longer reside at the address(s) provided by the electoral roll).

[2] Because the information sheet and consent form were not included in this study package it was decided that those who responded to the 4th mailout would not be eligible for participation in the future studies.

2.2.4 Data Entry and Cleaning

All data were double-entered to minimise error using EpiInfo version 6.04 (World Health Organisation). A conservative set of data entry rules were developed by the research team to allow for consistency of coding answers, particularly outliers and anomalous responses that did not correspond to the provisions of the questionnaire (see Appendix 5). EpiInfo provides basic frequency checking for each question and this was used to identify any ineligible codes, outliers and missing data, all of which were checked manually against the questionnaire. Data were then exported to an Excel spreadsheet for final checking and development of a database to be used for analysis.

In the MEQ, 16 questions are tick-box format and three questions require individuals to indicate their preference along a timeline. The formats of items on the questionnaire are as follows:

- Items 1, 2 and 10: Respondents are required to place a single cross on a timeline that matches their preferred time of day for the activity supplied. Timelines are divided into 15 minute epochs.
- Items 3-9, 11-16 and 19: Respondents are required to tick one box that best reflects their answer.
- Items 17 and 18: These items present a series of boxes in 60-minute bins along a continuum from midnight to midnight. Item 17 requires respondents to indicate which five consecutive hours best represent their preference for the named activity. Item 18 requires respondents to indicate one hour that best represents their preference.

In their original paper, Horne and Östberg provided scores for each possible answer, with maximum scores ranging from 4 to 6.

Because participants were not supervised when completing the questionnaire, a small proportion of respondents did not complete all of the questions in the MEQ. Participants who answered items incorrectly by ticking two boxes or ticking between boxes were assigned a half-score for that item (Prof. J. Horne, personal communication, August 08 2004). Only those participants who completed 15 or more items on the MEQ were eligible for analysis. MEQ scores for those participants who missed between one and four items were derived by weighting the remaining questions accordingly.

2.2.5 Data Analysis

Analyses in the present study were performed using SAS v8 (SAS Institute Inc., Cary, NC) and STATA v.8.2 (STATA co; Texas, USA). Data were analysed by ethnicity and sex throughout, and statistical significance was accepted at the level of $p < 0.05$. Correction factors such as Bonferroni adjustments are often used when multiple comparisons have been made to avoid the possibility of Type I errors, or false negatives. Such corrections were not employed in the

present study, instead, all findings were considered based on the plausibility of the findings within the context of the available *a priori* evidence (Perneger, 1998).

Response rates

Response rates were calculated for each sample (Māori and non-Māori) and Cochran-Armitage trend tests were used to test for significant trends in response rates by age and socioeconomic deprivation. Logistic regression models were used to test for independent associations between response rates and Māori and non-Māori descent, and deprivation.

Univariate analyses

The Kruskal-Wallis test (K-W) was used to examine the age distribution of the analytical sample by ethnicity and sex.

In the univariate analyses, the data was broken down by ethnicity and sex to provide four categories: Māori men, Māori women, non-Māori men and non-Māori women. Proportions and 95% confidence intervals (95% CI) are reported for categorical variables and chi-square tests are used to compare Māori and non-Māori within each sex.

For continuous data, ANOVA was used to test for differences in the mean when data were normally distributed. Wilcoxon's rank sum tests were used to tests for differences in medians in non-normal data.

Description of MEQ scores

The internal consistency of the MEQ was analysed using Cronbach's alpha correlation coefficient, and although there is apparently no absolute criterion (Anastasi, 1990 cited in (Henry & Crawford, 2005)) values between 0.7 and 0.9 are considered to be very good (Nunnally & Bernstein, 1994). Given the sample size, the frequency distribution of scores on the MEQ was visually analysed for normality. One-way ANOVA analyses were used to test for differences in mean scores by ethnicity, sex, and 5-year age-group.

MEQ scores were grouped into five categories: definitely evening-type (DE); moderately evening-type (ME); neither-type (N); moderately morning-type (MM); and definitely morning-type (DM), according to two sets of criteria (See Table 2.1). MEQ1 used the criteria proposed by Horne & Östberg (1976), while MEQ2 followed the criteria of Taillard and colleagues (2004).

Table 2.1 MEQ score cut-offs for the determination of five categories of chronotypes

	MEQ score cut-offs				
	DE-type	ME-type	N-type	MM-type	DM-type
MEQ1	16-30	31-41	42-58	59-69	70-86
MEQ2	16-46	47-52	53-64	65-69	70-86

Note: MEQ1 chronotypes defined using the Horne and Östberg (1976) score cut-offs. MEQ2 chronotypes defined using the Taillard et al. (2004) score cut-offs

Population prevalence estimates

Population prevalence estimates for each chronotype were derived by weighting the data by the population proportions of age, sex and ethnicity. The prevalence estimates for Māori and non-Māori, men and women and each age-group were compared using chi-square tests.

Multivariate analyses

All multivariate analyses were conducted using MEQ2 chronotypes as there were insufficient numbers in some chronotypes using the MEQ1 criteria. All variables found to be associated with the outcome (p-value ≤ 0.10) in the univariate analyses were included in the multivariate models. Logistic regression modeling was employed in those analyses where the outcome variable (also known as the dependent variable) was a categorical variable with 2-levels (e.g. ESS > 10 vs. ESS $\leq$ 10). In contrast, if the outcome variable had more than 2-levels (e.g. chronotype) then a multinomial logistic regression model was necessary.

2.3 Results

2.3.1 Response Rates

Table 2.1 presents the numbers of questionnaires received at each phase of data collection. At the end of the data collection period, a total of 2,584 questionnaires were received. Table 2.3 presents the equations used to calculate response rates to the questionnaire, which were based on the original study inclusion criteria. The initial overall response rate of 51.68% is based on the proportion of responses from the original sample of 5,000 (RR1). However, if the denominator is adjusted to exclude those participants who were no longer living in the Wellington region (n=79), the response rate is 52.51% (RR2). When return to senders (n=264) are excluded from the denominator, the response rate increases further to 55.49%. Finally, 15 participants were excluded because they were unable to complete the survey due to language difficulties, physical or psychological impairments, giving a final adjusted response rate of 55.67% (RR3).

The Kaupapa Māori positioning of this study determined that the primary breakdown of the data was by ethnicity, allowing Māori and non-Māori comparisons to be made. However, given that the electoral did not provide information on ethnicity, comparisons of response rates presented here are based on Māori descent, and therefore compare the Māori and non-Māori samples (Table 2.4). The greatest response to the questionnaire followed the first mail-out. However, phone-follow-up was extremely important for increasing the number of responses from both populations. The addition of a 4th mailout following the phone follow-up period to the remaining non-responders from the Māori sample provided an additional 123 questionnaires increasing the response rate to 49.14% for this population.

Table 2.2 The number of responses received at each mailout

	Number (*n*)	Percent of 5,000 (%)	Cumulative percent (%)
Mailout 1	980	19.60	19.60
Mailout 2	451	9.02	28.62
Mailout 3	433	8.66	37.28
Phone follow-up	597	11.94	49.22
Mailout 4	123	2.46	51.68
Total	**2584**	**51.68**	**51.68**
No longer resident	79	1.58	
Return to senders	264	5.28	
Ineligible	15	0.30	

Table 2.3 The calculation of response rates

	Equations	RR calculations	RR (%)
RR1	(number of responders/number in original sample)*100	2584/5000	51.68
RR2	(2584/(5000-no longer in sampling region))*100	2584/4921	52.51
RR3	(2584/(4921- RTS))*100	2584/4657	55.49
RR4	(2584/(4657 - ineligibles))*100	2584/4642	55.67

Note. RR= response rate

Table 2.4 A comparison of responses between the Māori and non-Māori samples

	Māori sample			non-Māori sample		
	(*n*)	% of 2674	Cumulative percent (%)	(*n*)	% of 2326	Cumulative percent (%)
Mailout 1	432	16.16	16.16	548	23.56	23.56
Mailout 2	242	9.05	25.21	209	8.99	32.55
Mailout 3	222	8.30	33.51	211	9.07	41.62
Phone follow-up	295	11.03	44.54	302	12.98	54.60
Mailout 4	123	4.60	49.14			
Total	**1314**	**49.14**	**49.14**	**1270**	**54.60**	**54.60**
No longer resident	29	1.08		50	2.15	
Return to senders	180	6.73		84	3.61	
Ineligible	5	0.19		10	0.43	

Table 2.5 shows the calculation of the final adjusted response rates for the Māori and non-Māori samples (RR4= 53.41% and 58.20% respectively). As reported in a recent national survey of obstructive sleep apnoea risk factors among New Zealand adults, the use of multiple mailouts and follow-up of non-responders was important in terms of ensuring equal response rates between Māori and non-Māori (Harris, 2003).

The use of the electoral rolls as a sampling frame also allowed the comparison of respondents by age (according to year of birth) and socioeconomic deprivation (NZDep2001) which is also important for understanding the context of subsequent analyses. Table 2.6 presents the responses for the Māori and non-Māori samples by 10yr age-groups. Cochrane-Armitage trend tests identified a significant trend for increasing response rate for each decade increase in age for the non-Māori sample (p <0.0001) but not the Māori sample.

Table 2.5 The calculation of response rates for the Māori and non-Māori samples

	RR calculations Māori sample	**RR (%)**	**RR calculations non-Māori sample**	**RR (%)**
RR1	1314/2674	49.14	1270/2326	54.60
RR2	1314/2645	49.68	1270/2276	55.80
RR3	1314/2465	53.31	1270/2192	57.94
RR4	1314/2460	53.41	1270/2182	58.20

Table 2.6 Responses by age for the Māori and non-Māori sample

	Māori sample			**non-Māori sample**		
Age (yrs)	(*n*)	sample size	RR1	(*n*)	sample size	RR1
30-39	647	1337	48.39	580	1163	49.87
40-49	667	1337	49.89	690	1163	59.33
Total	**1314**	**2674**	**49.14**	**1270**	**2326**	**54.60**
p-value			NS			<0.0001

Note. Cochrane-Armitage trend test for significant trends in response rates by 10-yr age groups

To investigate the possible influence of socioeconomic deprivation on the likelihood of responding, the proportions of responses within each NZDep2001 decile were analysed. For both the Māori and non-Māori samples, the likelihood of responding decreased with each decile increase in deprivation (p <0.0001 for both samples). This trend is illustrated in Figure 2.1. Logistic regression models were used to investigate whether differences in response between the Māori and non-Māori samples were due to differences in the deprivation profiles of each sample and the response gradient found by level of deprivation. At the univariate level, participants from the Māori sample were less likely to respond than non-Māori (OR=0.80, 95% CI 0.72-0.90, p <0.01). However, when socioeconomic deprivation was included in the model, Māori descent and response rate were no longer significantly associated (OR=0.98, 95% CI 0.87-1.10, p =0.750). This suggests that differences in response rates observed between Māori and non-Māori were mainly due to differences in socioeconomic deprivation (OR=0.89, 95% CI 0.88-0.91, p <0.0001).

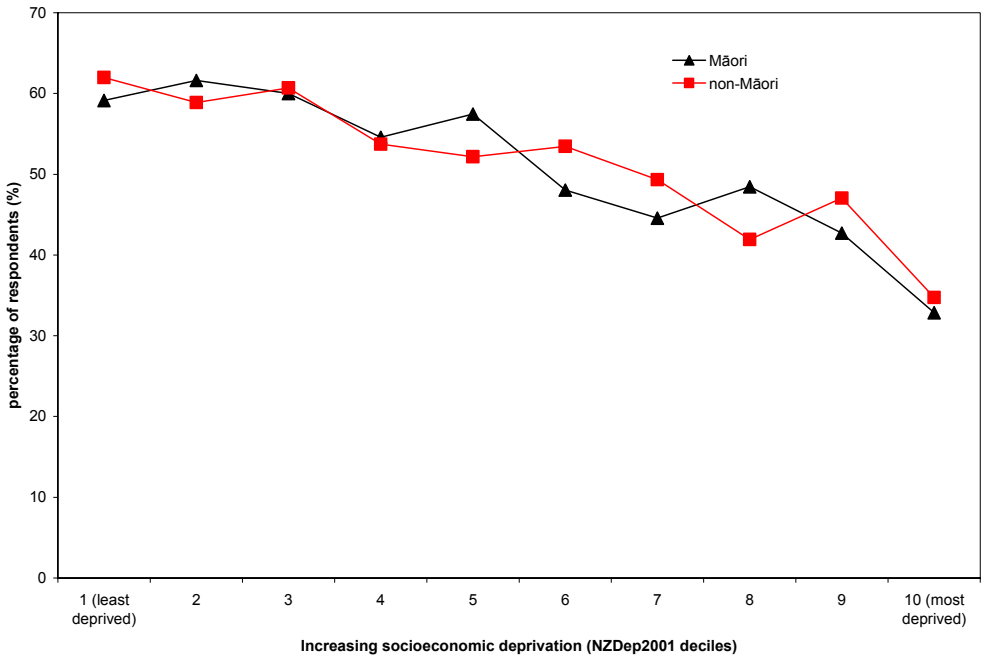


Figure 2.1 The socioeconomic deprivation profile of the Māori and non-Māori samples

2.3.2 The Characteristics of the Analytical Sample

The analyses presented here are based on data from the 2,526 participants who provided complete information on the demographic variables of ethnicity[3], sex and age in 5-year age groups.

Table 2.7 shows the proportion of Māori and non-Māori, men and women in the analytical sample. Chi-square tests were used to compare Māori and non-Māori by sex and age (in 5-year age groups). There were significantly more women (χ^2 =4.89, *df* =1, *p* =0.03) and older participants (χ^2 =8.44, *df* =3, *p* =0.04) in both the Māori and non-Māori samples. There was also a small but significant difference in the mean age of Māori and non-Māori, men and women in the present study (Table 2.8). Examination of the deprivation profiles of the Māori and non-Māori ethnic groups highlights clear differences between the two, with Māori under-represented in the least deprived deciles and over-represented in the most deprived deciles (Figure 2.2). Compared to a recent national survey of a representative sample of 30-59 year-olds (Harris, 2003), both Māori and non-Māori in the present study were less deprived than the general population.

Table 2.7 The demographics of the analytical sample

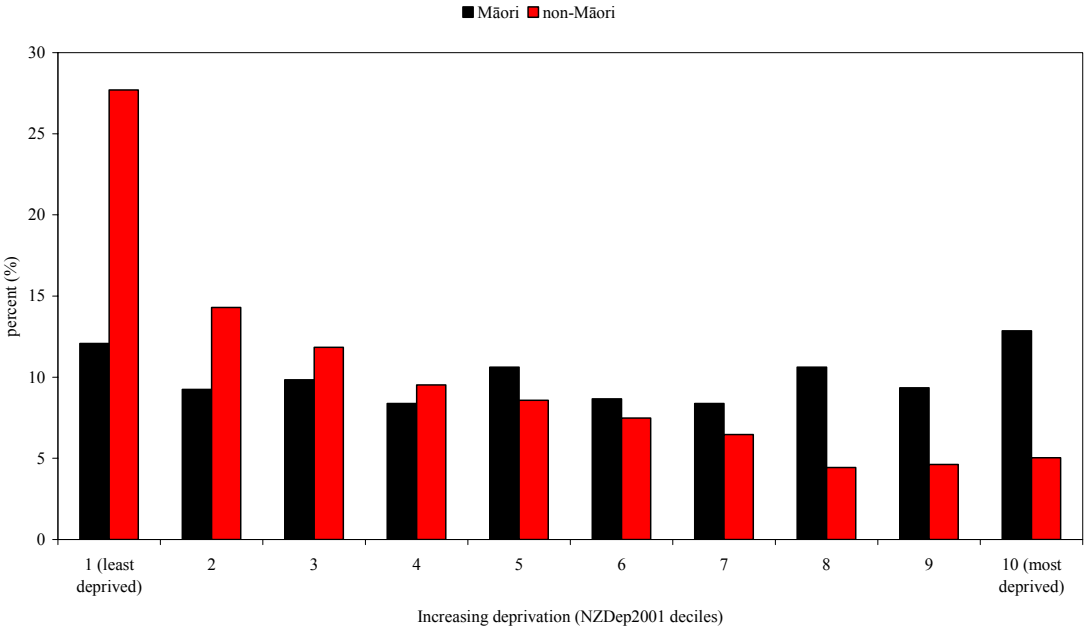
	Total	**Māori**	**non-Māori**		
	n (% of sample)	*n* (% of sample)	*n* (% of sample)	χ^2	*p*-value
Men	1060 (41.96)	409 (16.19)	651 (25.77)	4.89	0.03
Women	1466 (58.04)	630 (24.94)	836 (33.10)		
Total	**2526 (100.00)**	**1039 (41.13)**	**1487 (58.87)**		
30-34yrs	563 (22.29)	248 (9.82)	315 (12.47)	8.43	0.04
35-39yrs	604 (23.91)	253 (10.02)	351 (13.90)		
40-44yrs	755 (29.89)	319 (12.63)	436 (17.26)		
45-49yrs	604 (23.91)	219 (8.67)	385 (15.24)		
Total	**2526 (100.00)**	**1039 (41.13)**	**1487 (58.87)**		

[3] As mentioned previously, not all individuals of Māori descent identify with the Māori ethnic group. In the present study 80.22% of respondents (n=1,289) from the Māori descent sample self-identified as Māori, while only 0.40% of the non-Māori sample identified as Māori (n=5).

Table 2.8 The average age of Māori and non-Māori, men and women

	n	mean age (yrs)	SD	χ^2	*df*	*p*-value
Māori males	409	39.51	5.32	8.34	3	0.04
Māori females	630	39.43	5.33			
non-Māori males	651	40.22	5.58			
non-Māori females	836	39.81	5.40			

Figure 2.2 The socioeconomic deprivation profile of Māori and non-Māori adults aged 30-49 years in the study sample.



Given that work schedules are likely to influence sleep timing, the classification of current work status was an important consideration in this study. Table 2.9 examines the self-reported work status of the analytical sample by ethnicity, sex, 5-year age group and socioeconomic deprivation (in quintiles). In the present study, Māori were more likely than non-Māori to be unemployed (16.51% vs. 14.33%) and to work nights (13.03% vs. 8.32%). Women were more likely than men to unemployed (20.64% vs. 7.76%) but were less likely to work nights (7.68% vs. 13.81%). Chi-square tests found a significant difference in work status by age-group (p <0.05) and by socioeconomic deprivation (p <0.0001).

Table 2.9 Current work status by ethnicity, sex, age and socioeconomic deprivation

	Unemployed	**Employed, no nights**	**Night work**	**Total**			
	n (%)	*n (%)*	*n (%)*	*n*	$\chi 2$	*df*	*p*-value
Ethnicity							
Māori	171 (16.51)	730 (70.46)	135 (13.03)	1036	18.96	2	<0.0001
non-Māori	212 (14.33)	1144 (77.35)	123 (8.32)	1479			
Sex							
Men	82 (7.76)	829 (78.43)	146 (13.81)	1057	93.03	2	<0.0001
Women	301 (20.64)	1045 (71.67)	112 (7.68)	1458			
Age (yrs)							
30-34	110 (19.57)	402 (71.53)	50 (8.90)	562	15.29	6	0.02
35-39	86 (14.31)	452 (75.21)	63 (10.48)	601			
40-44	111 (14.78)	551 (73.37)	89 (11.85)	751			
45-49	76 (12.65)	469 (78.04)	56 (9.32)	601			
NZDep2001							
Quin1	106 (12.71)	663 (79.50)	65 (7.79)	834	59.71	8	<0.0001
Quin2	64 (12.80)	392 (78.40)	44 (8.80)	500			
Quin3	57 (13.16)	318 (73.44)	58 (13.39)	433			
Quin4	60 (17.05)	254 (72.16)	38 (10.80)	352			
Quin5	93 (25.41)	223 (60.93)	50 (13.66)	366			

Note. Ethnicity, sex and 5-year age group comparisons have 11 missing data. NZDep2001 missing 45 data points. NZDep2001 deciles have been collapsed into quintiles as follows: Quin1 = Dec1-2; Quin2 = Dec3-4; Quint3 = Dec5-6; Quin4 = Dec7-8; Quin5 = Dec 9-10.

2.3.3 The Distribution of Morningness/Eveningness in the General Population

Figure 2.3 illustrates the frequency distribution of MEQ scores in the present study. The full scale Cronbach alpha-coefficient of the MEQ for the total sample was 0.83 (Māori 0.80; non-Māori 0.85), and MEQ scores ranged from 23-81 (mean= 58.08, standard deviation = 9.38; median = 59, interquartile range 52-64; mode = 63). The distribution of MEQ scores was slightly skewed to the right (skewness -0.39, kurtosis 0.15), but closely resembled a normal distribution. There were no significant differences in mean scores by ethnicity or sex, however, average MEQ scores increased significantly with age, in 5-yr age groups (p <0.0001) for the whole group (Table 2.10), and among Māori and non-Māori, men and women (Table 2.11).

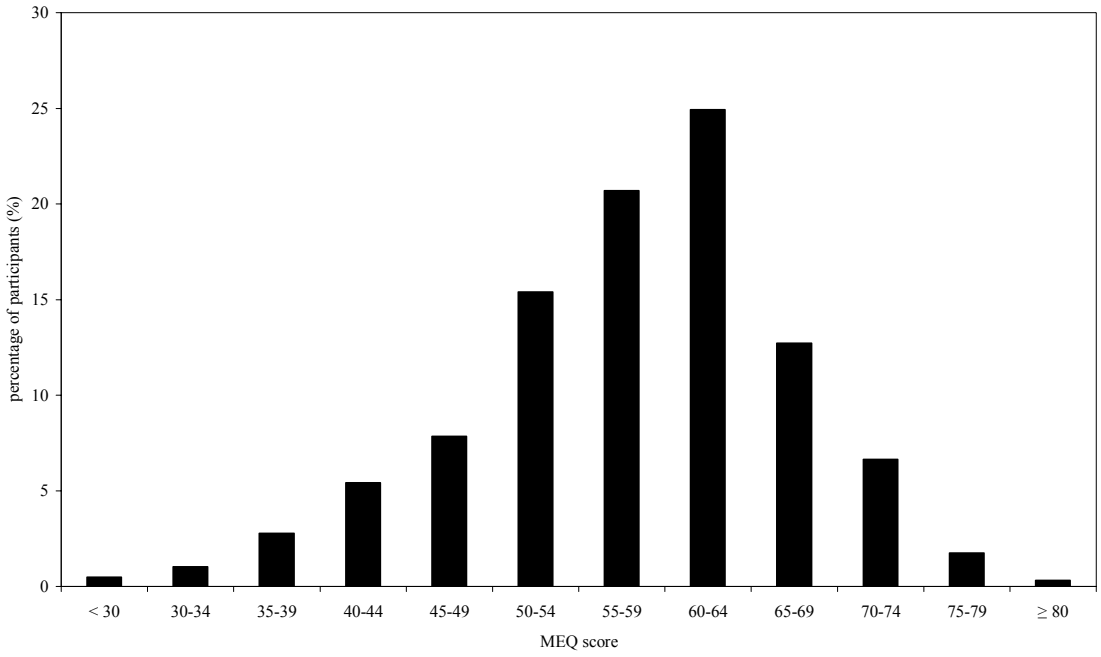


Figure 2.3 The frequency distribution of MEQ scores in the study sample

Table 2.10 Morningness/eveningness scores by ethnicity, sex and age

	MEQ score				
	Mean	*SD*	*F*	*df* (between, within)	*p*-value
Ethnicity					
Māori	58.32	9.08	1.15	1, 2524	0.2835
non-Māori	57.92	9.59			
Sex					
Men	58.36	9.15	1.53	1, 2524	0.2167
Women	57.89	9.54			
Age					
30-34yrs	56.36	9.67	14.10	3, 2522	<0.0001
35-39 yrs	57.95	9.01			
40-44 yrs	58.03	9.28			
45-49 yrs	59.89	9.29			

Note. ANOVA used to test for differences in mean scores by ethnicity, sex and 5-yr age group

Table 2.11 Average MEQ scores by age among Māori and non-Māori, men and women

	Māori men		**non-Māori men**		**Māori women**		**non-Māori women**	
Age (yrs)	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
30-34	56.46	9.15	56.54	10.09	55.92	9.31	56.54	10
35-39	58.20	8.39	58.15	8.83	57.71	9.19	57.87	9.36
40-44	59.99	8.74	57.24	9.27	58.22	8.95	57.52	9.7
45-49	61.07	9.14	59.65	8.72	60.05	8.71	59.50	10.23
Total	58.94	8.97	57.99	9.25	57.92	9.13	57.86	9.85
ANOVA	*F*	*p*-value	*F*	*p*-value	*F*	*p*-value	*F*	*p*-value
	5.07	0.002	3.55	0.014	4.97	0.002	3.03	0.0286

General population prevalence estimates

Population prevalence estimates were weighted according to the different age-structures of the Māori and non-Māori populations. Five categories of chronotypes are presented for MEQ1 (after (Horne & Östberg, 1976)) and MEQ2 (after (Taillard et al., 2004)).

Table 2.12 and Table 2.13 presents the weighted population prevalence estimates for MEQ1 and MEQ2 chronotypes for the total population, and also among Māori and non-Māori, men and women. There were no significant differences in the prevalence of different chronotypes by ethnicity or sex.

The differences in the distribution of chronotypes within the general population between MEQ1 and MEQ2 chronotypes are clearly illustrated in Figure 2.4. Using the MEQ1 criteria, morning-

types predominated, whereas the MEQ2 criteria provided a more balanced population distribution of chronotypes.

Table 2.12 Weighted population prevalence estimates of chronotypes categorised using the MEQ scoring criteria of Horne and Östberg (1976) among New Zealand adults (30-49yrs)

	Total	Māori males	Māori females	non-Māori males	non-Māori females
	% (95% CI)	*% (95% CI)*	*% (95% CI)*	*% (95% CI)*	*% (95% CI)*
DE	0.67	0.29	0.19	0.54	0.91
	(0.28-1.06)	(0.00-0.84)	(0.00-0.56)	(0.00-1.14)	(0.28-1.54)
ME	4.95	3.1	5.12	5.28	4.85
	(3.94-5.96)	(1.36-4.85)	(3.33-6.90)	(3.56-7.00)	(3.36-6.34)
N	44.62	44.78	45.35	43.43	45.61
	(42.35-46.90)	(39.93-49.64)	(41.41-49.29)	(39.59-47.27)	(42.22-49.01)
MM	39.56	42.22	39.6	41.17	37.71
	(37.32-47.19)	(37.39-47.05)	(35.76-43.44)	(37.37-44.98)	(34.40-41.01)
DM	10.2	9.6	9.74	9.58	10.92
	(8.82-11.57)	(6.38-12.38)	(7.41-12.07)	(7.30-11.85)	(8.81-13.02)

Note. Estimates weighted to reflect the gender and age structures of the Māori and non-Māori populations.

Table 2.13 Weighted population prevalence estimates of chronotypes categorised using the MEQ scoring criteria of Taillard and colleagues (2004) among New Zealand adults (30-49yrs)

	Total	Māori males	Māori females	non-Māori males	non-Māori females
	% (95% CI)	*% (95% CI)*	*% (95% CI)*	*% (95% CI)*	*% (95% CI)*
DE	11.5	8.51	12.08	11.77	11.53
	(10.02-12.97)	(5.74-11.27)	(9.46-14.71)	(9.26-14.29)	(9.35-13.71)
ME	14.94	14.92	15.1	14.19	15.63
	(13.31-16.58)	(11.39-18.45)	(12.23-17.97)	(11.48-16.90)	(13.14-18.12)
N	48.91	49.55	49.95	49.96	47.71
	(46.62-51.20)	(44.65-54.46)	(45.98-83.92)	(46.07-53.84)	(44.30-51.11)
MM	14.46	17.41	13.25	14.5	14.21
	(12.85-16.06)	(13.73-21.09)	(10.56-15.95)	(11.77-17.23)	(11.83-16.59)
DM	10.19	9.6	9.61	9.58	10.92
	(8.81-11.56)	(6.83-12.38)	(7.29-11.93)	(7.30-11.85)	(8.81-13.02)

Note. Estimates weighted to reflect the gender and age structures of the Māori and non-Māori populations.

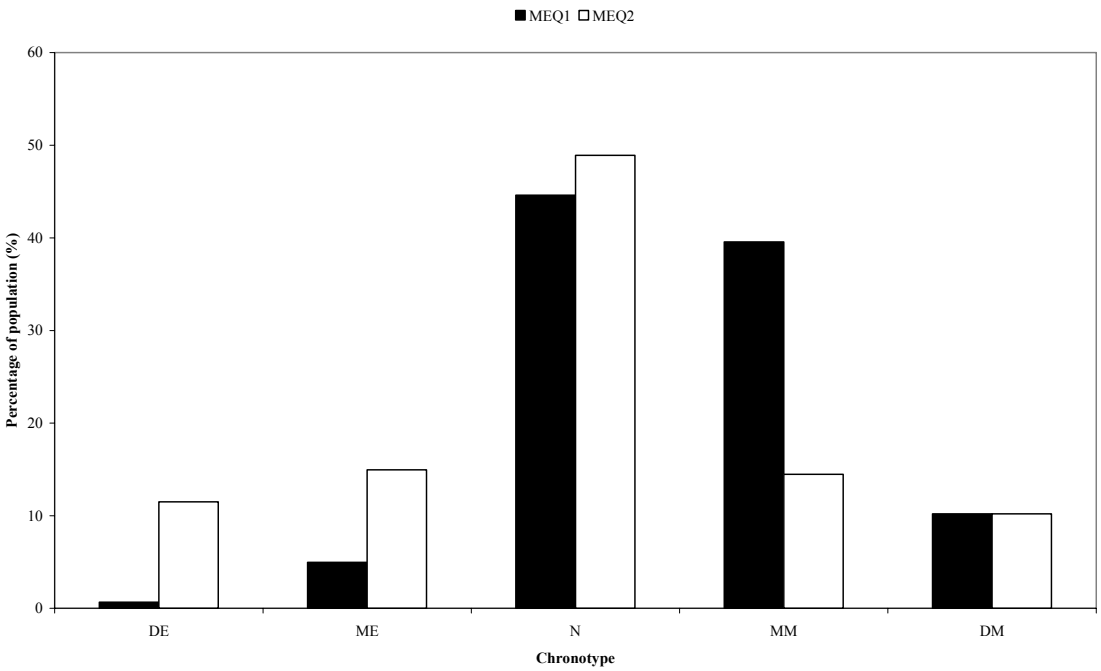


Figure 2.4 The prevalence of morningness/eveningness in the general population

Two sets of MEQ scoring criteria were used to compare the population prevalence estimates of chronotypes in adults aged 30-49yrs. MEQ1 chronotypes were identified using the scoring criteria of Horne and Ostberg (1976), while MEQ2 chronotypes were identified using the scoring criteria of Taillard et al. (2004).

2.3.4 What Factors Independently Predict Morningness/Eveningness Preference?

This section presents the findings of a series of univariate and multivariate analyses which were used to identify significant independent predictors of self-reported morningness/eveningness. These analyses were performed using MEQ2 chronotypes only, due to insufficient numbers in some chronotypes using MEQ1 criteria.

Proportions and 95% confidence intervals were calculated for each chronotype (DE, ME, N, MM and DM) by ethnicity, sex, age (5-year age groups), socioeconomic deprivation (NZDep2001 quintiles) and employment status (Table 2.14). Chi-square tests identified significant differences in proportions by 5-year age group (χ^2 =43.77, *df* =12, *p* <0.0001) and employment status (χ^2 =19.59, *df* =8, *p* =0.01).

Table 2.14 Univariate relationships between chronotype and demographic factors

	DE	ME	N	MM	DM
	% (95%CI)	*% (95%CI)*	*% (95%CI)*	*% (95%CI)*	*% (95%CI)*
Ethnicity					
Māori	10.30	14.63	49.95	15.11	10.01
	(8.52-12.31)	12.54-16.93	(46.87-53.04)	(12.99-17.44)	(8.25-12.00)
non-Māori	11.57	14.86	48.69	14.39	10.49
	(9.98-13.30)	(13.09-16.77)	(46.12-51.26)	(12.65-16.28)	(8.98-12.16)
Sex					
Men	10.38	14.25	49.62	15.85	9.91
	(8.61-12.37)	(12.20-16.50)	(46.57-52.68)	(13.70-18.19)	(8.17-11.64)
Women	11.53	15.14	48.91	13.85	10.57
	(9.94-13.27)	(13.35-17.08)	(46.32-51.50)	(12.12-15.72)	(9.04-12.26)
Age group (yrs)					
30-34	14.74	17.05	48.85	11.37	7.99
	(11.92-17.94)	(14.04-20.42)	(44.64-53.06)	(8.87-14.28)	(5.89-10.55)
35-39	9.93	16.06	49.01	16.23	8.77
	(7.67-12.60)	(13.22-19.24)	(44.95-53.07)	(13.37-19.41)	(6.64-11.32)
40-44	10.86	14.83	51.13	12.85	10.33
	(8.73-13.03)	(12.37-17.57)	(47.50-54.75)	(10.54-15.45)	(8.25-12.73)
45-49	8.94	11.26	47.35	18.54	13.91
	(6.79-11.50)	(8.85-14.05)	(43.31-51.42)	(15.52-21.88)	(11.25-16.93)
NZDep2001					
quintile 1	11.12	14.35	48.33	15.55	10.65
	(9.07-13.45)	(12.05-16.92)	(44.89-51.77)	(13.16-18.19)	(8.64-12.94)
quintile 2	9.78	15.97	49.90	15.57	8.78
	(7.32-12.72)	(12.87-19.47)	(45.43-54.37)	(12.51-19.05)	(6.45-11.61)
quintile 3	12.21	16.36	48.39	12.67	10.37
	(9.28-15.67)	(13.00-20.18)	(43.60-53.20)	(9.69-16.17)	(7.66-13.63)
quintile 4	12.39	11.83	48.45	14.93	12.39
	(9.15-16.28)	(8.66-15.65)	(43.14-53.78)	(11.39-19.07)	(9.15-16.28)
quintile 5	10.81	14.86	51.08	14.05	9.19
	(7.84-14.43)	(11.40-18.91)	(45.86-56.28)	(10.68-18.02)	(6.45-12.60)
Work status					
unemployed	12.53	17.23	51.96	10.18	8.09
	(9.39-16.27)	(13.59-21.39)	(46.83-57.06)	(7.34-13.66)	(5.57-11.29)
employed, no nights	10.25	14.30	48.56	15.96	10.94
	(8.91-11.71)	(12.75-15.97)	(46.27-50.85)	(14.32-17.69)	(9.56-12.44)
nights	14.73	15.12	49.61	12.02	8.53
	(10.64-19.65)	(10.98-20.08)	(43.35-55.88)	(8.31-16.62)	(5.42-12.63)

Note. 30 missing data for NZDep2001 and 11 missing data for work variables

In order to assess the independent associations between a range of demographic and socioeconomic factors on preferred sleep timing, a multivariate analytical method was employed. In addition, because the outcome variable (i.e. chronotype) consisted of more than 2-levels, a multinomial logistic regression model was necessary. The variables included in the models are described in Table 2.15. Although there were no significant associations between ethnicity, sex, and socioeconomic deprivation at the univariate level, a specific objective of the present study was to examine the possible associations between demographic and socioeconomic factors and self-reported sleep timing. Therefore, all of the demographic variables were included in the final model. Significant relationships are highlighted in Table 2.16.

After controlling for ethnicity, sex and socioeconomic deprivation, participants aged 30-34yrs were more likely to be DE-type (p <0.05) and less likely to be morning-type (MM-type, p <0.01 or DM-type, p <0.05) compared to those aged 45-49yrs. Work schedules were also important independent predictors of chronotype. Night workers were almost 1.5 times more likely to be DE (p =0.05) while those who were unemployed were significantly less likely to be MM-type (p <0.05).

Table 2.15 Multinomial logistic regression model construction: Independent predictors of chronotype

Variable	Type	Reference category
Dependent		
MEQ2	Categorical	N-type
Independent		
Ethnicity	Dichotomous	non-Māori
Sex	Dichotomous	male
Age	Categorical	45-49 years
Socioeconomic Deprivation	Categorical	Quintile 1
Employment status	Categorical	Employed, no night work

Table 2.16 Independent predictors of morningness/eveningness in the general population (30-49yrs)

	DE-type	**ME-type**	**MM-type**	**DM-type**
	OR (95% CI)	*OR (95% CI)*	*OR (95% CI)*	*OR (95% CI)*
Māori	0.82 (0.62-1.08)	0.97 (0.76-1.24)	1.09 (0.85-1.40)	0.93 (0.70-1.25)
Women	1.16 (0.88-1.53)	1.08 (0.84-1.37)	0.92 (0.72-1.17)	1.10 (0.83-1.46)
Age (yrs) [a]				
30-34	1.59* (1.09-2.34)	1.42 (1.00-2.03)	0.59** (0.42-0.85)	0.59* (0.39-0.88)
35-39	1.06 (0.71-1.59)	1.38 (0.97-1.96)	0.83 (0.60-1.14)	0.64* (0.43-0.94)
40-44	1.11 (0.76-1.62)	1.23 (0.88-1.73)	0.64** (0.46-0.87)	0.71 (0.50-1.01)
Increasing deprivation [b]				
quintile 2	0.88 (0.60-1.29)	1.09 (0.78-1.50)	0.96 (0.69-1.33)	0.81 (0.55-1.21)
quintile 3	1.11 (0.76-1.63)	1.14 (0.81-1.60)	0.82 (0.57-1.18)	1.01 (0.68-1.51)
quintile 4	1.15 (0.77-1.74)	0.83 (0.55-1.23)	0.99 (0.68-1.43)	1.19 (0.79-1.81)
quintile 5	0.96 (0.63-1.47)	0.98 (0.67-1.43)	0.88 (0.60-1.29)	0.86 (0.55-1.35)
Work status [c]				
Night work	1.49 (1.00-2.22)	1.08 (0.73-1.59)	0.76 (0.50-1.16)	0.81 (0.50-1.31)
Unemployed	1.09 (0.76-1.56)	1.13 (0.82-1.56)	0.64* (0.44-0.93)	0.72 (0.47-1.09)

Note. Reference category for the outcome variable is N-type. a = 45-49yrs; b =Quintile 1; c =currently employed, but no night work * $p<0.05$ ** $p<0.01$

A second model was used to assess the significant independent predictors of work status. Table 2.17 describes the multinomial model used in this analysis and Table 2.18 presents the model findings. After controlling for age, Māori were more likely than non-Māori to be involved in night work (p <0.01) whilst women were less likely than men to be night workers (p <0.001). Individuals living in the most deprived deciles (quintile 5) were twice as likely to be night workers (p =0.001), whereas evening-types were 1.6 times more likely than morning-types to report night work. After controlling for ethnicity, the significant independent predictors of unemployment were being female (p <0.0001), younger age (30-34yrs, p =0.01), living in a more deprived decile (quintile 5, p =0.001), and chronotype (E-types and N-types both p <0.01).

Table 2.17 Multinomial logistic regression model: Unemployment and night work.

Variable	Type	Reference category
Dependent		
Work status	Categorical	Employed, not night work
Independent		
Ethnicity	Dichotomous	non-Māori
Sex	Dichotomous	male
Age	Categorical	45-49 years
Socioeconomic Deprivation	Categorical	Quintile 1

Table 2.18 Independent predictors of work status

	Night work	**Unemployment**
	OR (95% CI)	*OR (95% CI)*
Māori	1.56 **(1.18-2.05)	0.99 (0.78-1.26)
Women	0.59** (0.45-0.77)	2.84** (2.18-3.70)
Age (yrs) [a]		
30-34	0.97 (0.64-1.46)	1.55* (1.11-2.16)
35-39	1.12 (0.76-1.66)	1.11 (0.78-1.56)
40-44	1.32 (0.92-1.91)	1.15 (0.83-1.60)
Increasing deprivation[b]		
quintile 2	1.07 (0.71-1.61)	1.06 (0.75-1.49)
quintile 3	1.68** (1.15-2.48)	1.11 (0.78-1.59)
quintile 4	1.41 (0.91-2.17)	1.42 (0.99-2.03)
quintile 5	2.00** (1.32-3.02)	2.58** (1.84-3.61)
Chronotype [c]		
E	1.62* (1.11-2.37)	1.65** (1.18-2.30)
N	1.29 (0.92-1.82)	1.49** (1.10-2.01)

Note. Reference category for the outcome variable is employed but not working nights. Reference categories for the independent variables [a] = 45-49yrs; [b] =Quintile 1; [c] =morning-types.
* p <0.05 ** p <0.01

2.3.5 Is There a Relationship between Morningness/Eveningness and Self-Rated General Health?

Participants were asked to rate their overall general health in order to investigate whether or not morningness/eveningness influences perceived general health. Possible answers were grouped as poor/fair vs. excellent/very good/good. Fifteen participants did not answer this question.

Overall, only 6.7% of participants (n=168) said that their general health was poor or fair. Māori were more likely to report poor/fair health than non-Māori (8.99% vs. 5.08%, χ^2=14.94, *df* =1, *p* <0.001) and there was a highly significant association between perceived general health and level of deprivation (χ^2=64.96, *df* =4, *p* <0.0001). Approximately 14% of participants who were unemployed and 9% of those who worked nights reported poor/fair general health (χ^2=42.96, *df* =2, *p* <0.000.1) (full tables are presented in Appendix 6).

To evaluate the association between morningness/eveningness and perceived general health, MEQ2 chronotypes were collapsed into three groups: E-types (DE- and ME-types combined), N-types, and M-types (DM- and MM-types combined). Almost 11% of evening-type individuals reported poor/fair general health, compared with 5.7% of neither-types and 4.5% of morning-types (χ^2=24.59, *df*=2, *p* <0.0001).

A multivariate logistic regression model was used to evaluate the independent contributions of morningness/eveningness and demographic factors on perceived general health (see Table 2.19 for model construction).

Table 2.19 Logistic regression model construction: Poor/fair self-reported general health

Variable	Type	Reference category
Dependent		
General Health	Categorical	Excellent/very good/good general health
Independent		
Ethnicity	Dichotomous	non-Māori
Socioeconomic deprivation	Categorical	Quintile 1
Employment status	Categorical	Employed, but no nights
Chronotype	Categorical	M-type

After controlling for ethnicity, participants living in more deprived areas (represented by quintiles 3, 4, and 5) were between 3 and 5 times more likely to report that their general health was only poor or fair (all p <0.0001) compared to those participants in quintile 1 (Table 2.20). After controlling for ethnicity, those who were unemployed were significantly more likely to say that their general health was only poor or fair (OR=2.58, p <0.0001) compared to those who were currently employed, but not working any night shifts. In this study, working nights was not a significant independent predictor of poor/fair general health. After controlling for ethnicity, evening-types were almost 2.5 times more likely to report that their general health was poor or fair, compared to morning-types (p <0.0001).

Table 2.20 Independent predictors of poor/fair self-reported general health

Variable	*OR*	*95% CI*	*p*-value
Māori	1.33	0.95-1.87	0.09
Socioeconomic deprivation [a]			
Quintile 2	1.72	0.93-3.17	0.09
Quintile 3	3.87	2.24-6.67	<0.0001
Quintile 4	3.08	1.71-5.56	<0.0001
Quintile 5	4.80	2.77-8.30	<0.0001
Work status [b]			
Unemployed	2.58	1.77-3.75	<0.0001
Night work	1.61	0.99-2.60	0.06
Chronotype [c]			
E	2.46	1.54-3.94	<0.0001
N	1.18	0.74-1.87	0.49

Note. Reference category for the outcome variable is excellent/very good/good general health. [a] ref = quintile 1 [b] ref = employed, but not nights [c] ref = M-types

2.3.6 Is There a Relationship Between Morningness/Eveningness and Self-Report Sleep Habits?

The extent to which self-reported morningness/eveningness preference was associated with self-reported sleep habits was evaluated for self-reported sleep quantity and daytime sleepiness.

In order to estimate sleep quantity, each participant was asked "How many hours sleep do you usually get in 24 hours". Eight hundred and forty five participants did not complete this question and were excluded from the analyses.

Graphs illustrating the distribution of usual hours sleep for Māori and non-Māori men and women are presented in Figure 2.5. Visualisation of the frequency distributions showed that the data were peaked with long tails and therefore not normally distributed.

Differences in the median sleep durations between groups were calculated by ethnicity and sex (Table 2.21). There were no significant differences between Māori and non-Māori amongst either men (p =0.13) or women (p =0.73). However, there was a marginal difference in the median hours of sleep comparing men and women in the non-Māori ethnic group (p =0.05) and a highly significant difference comparing men and women in the Māori ethnic group (p <0.001).

Table 2.21 Self-reported usual sleep quantity in a 24hr period among Māori and non-Māori men and women

	n	***mean* (hrs)**	***SD* (hrs)**	***median* (hrs)**	***IQR* (hrs)**
Māori men	396	7.17	1.21	7.00	5.5-8.5
Māori women	604	7.44	1.37	7.50	6.0-9.0
non-Māori men	300	7.23	0.95	7.50	6.5-8.5
non-Māori women	381	7.38	1.02	7.50	6.0-9.0
Total	**1681**	**7.32**	**1.19**	**7.51**	**6.0-9.0**

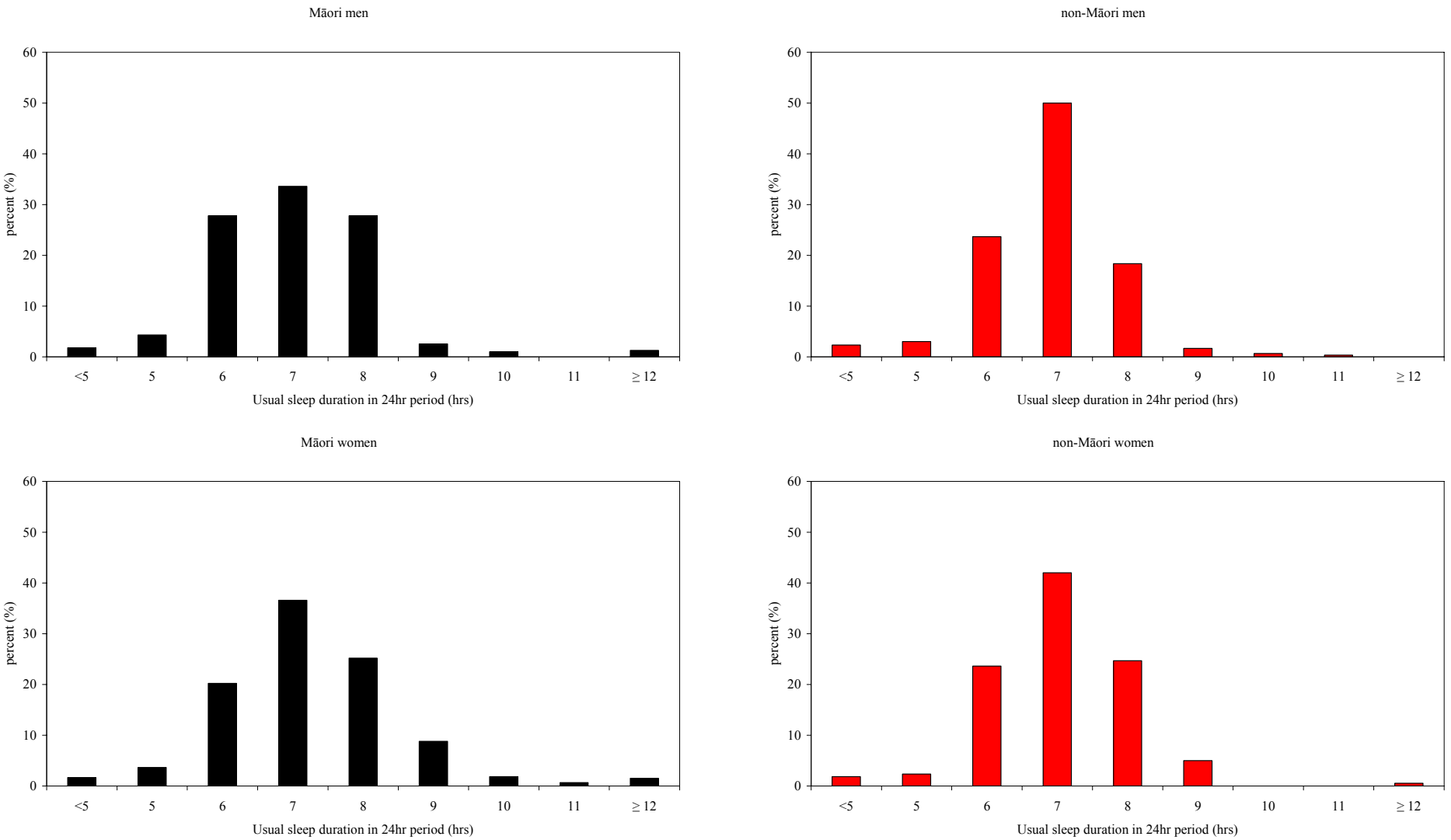


Figure 2.5 The frequency distribution of self-reported usual sleep duration among Māori and non-Māori, men and women in the study sample

To examine whether abnormal sleep duration was associated with morningness/eveningness, the data on usual hours sleep was grouped as follows: short sleep (<6.5hrs); normal sleep (6.5-7.5hrs); and long sleep (>7.5hrs). According to these definitions, 15.23% of participants were short sleepers (n=256), 52.89% were normal sleepers (n=889) and 31.89% were long sleepers (n=536). When chronotypes were considered, 16.80% of E-types were short sleepers, compared with 31.15% of M-types. Conversely, 40.80% of E-types and 30.60% of M-types were long sleepers.

Chi-square tests identified significant differences in the proportions of short-, normal- and long-sleepers by ethnicity (χ^2 =66.44, *df* =2, *p* <0.0001); sex (χ^2 =12.32, *df* =2, *p* <0.001); 5-year age groups (χ^2 =23.27, *df* =6, *p* <0.001); level of deprivation (χ^2 =33.59, *df* =8, *p* <0.0001) and current work status (χ^2 =61.61, *df* =4, *p* <0.0001). There were no significant differences by chronotype (categorised as E-type, N-type or M-type). Full tables are presented in Appendix 7.

Table 2.22 summarises the variables which were included in a multinomial logistic regression model used to identify the independent predictors of abnormal sleep duration while Table 2.23 presents the model findings.

After controlling for ethnicity, sex and chronotype, those participants aged 30-34yrs were less likely to be a short sleeper compared to those aged 45-49yrs (*p* <0.02). People living in quintile 2 were more likely to report being a short sleeper, compared to those living the least deprived areas of quintile 1 (*p* <0.05). Night workers were 2.7 times more likely to be short sleepers (*p* <0.001).

On the other hand, after controlling for sex, socioeconomic deprivation, and chronotype, significant independent predictors of long sleep (>7.5hrs in 24hrs) were: ethnicity (being Māori, *p* <0.0001); advancing age (all 5-year age groups, *p* <0.05); unemployment (*p* <0.01); and night work (*p* <0.05).

Table 2.22 Multinomial logistic regression model construction: Abnormal sleep duration

Variable	Type	Reference category
Dependent		
Abnormal sleep duration	Categorical	6.5hrs-7.5hrs
Independent		
Ethnicity	Dichotomous	non-Māori
Sex	Dichotomous	men
Age	Dichotomous	45-49 years
Socioeconomic deprivation	Categorical	Quintile 1
Employment status	Categorical	Employed, but no nights
Chronotype	Categorical	M-type

Table 2.23 Independent predictors of abnormal sleep duration.

	Short sleepers (<6.5hrs)			Long sleepers (>7.5hrs)		
Variable	*OR*	*95% CI*	*p*-value	*OR*	*95% CI*	*p*-value
Māori	1.20	0.94-1.55	0.15	1.67	1.31-2.14	<0.001
Women	0.87	0.68-1.12	0.27	1.26	0.99-1.61	0.06
Age (yrs) [a]						
30-34	0.64	0.45-0.92	0.02	1.56	1.09-2.22	0.01
35-39	0.73	0.52-1.04	0.08	1.53	1.07-2.19	0.02
40-44	0.84	0.61-1.16	0.28	1.44	1.02-2.02	0.04
Socioeconomic deprivation [b]						
quintile 2	1.45	1.02-2.07	0.04	1.15	0.81-1.63	0.43
quintile 3	1.06	0.74-1.53	0.75	1.07	0.76-1.52	0.69
quintile 4	1.24	0.85-1.82	0.27	1.10	0.76-1.58	0.62
quintile 5	1.41	0.97-2.05	0.08	1.11	0.77-1.60	0.59
Work status [c]						
Unemployed	1.31	0.90-1.88	0.16	1.68	1.20-2.34	0.002
Night work	2.70	1.82-4.00	<0.001	1.64	1.08-2.50	0.02
Chronotype [d]						
E	1.34	0.95-1.90	0.10	0.75	0.54-1.04	0.08
N	1.21	0.89-1.64	0.23	0.77	0.58-1.02	0.07

Note. The reference category for the outcome variable is 6.5-7.5hrs sleep in 24hrs. [a] ref=45-49yrs [b] ref=Quin1 [c] ref=employed, but no nights [d] ref=M-types

The Epworth Sleepiness Scale (ESS) was used to assess levels of daytime sleepiness among the participants. Seventy participants did not answer this question and were excluded from the analyses.

ESS scores for the entire sample ranged from 0-23 (mean= 6.17, S.D. = 3.83; median = 6, interquartile range 3-9; mode = 4) and the frequency histogram illustrated that the score distribution was skewed to the right (skewness = 0.75; kurtosis = 0.63). Figure 2.6 illustrates the distribution of ESS scores and the relevant descriptive statistics for Māori and non-Māori men and women.

Scores on the ESS were also grouped as ESS $\leq$ 10 and ESS > 10, with scores greater than 10 indicative of excessive levels of daytime sleepiness. Univariate analyses found that Māori were more likely to report excessive levels of daytime sleepiness, compared to non-Māori (16.83% vs. 10.70% respectively, χ^2 =19.47, *df* =1, *p* <0.0001). There was also a significant univariate association between current work status and daytime sleepiness, with night workers more likely to report excessive levels of daytime sleepiness than either unemployed or those who were employed but not working nights (χ^2 =23.45, *df* =2, *p* <0.0001). Approximately 14% of E-types and 12% of M-types reported excessive daytime sleepiness. There was no significant univariate relationship between chronotype and daytime sleepiness (see Appendix 8 for full tables).

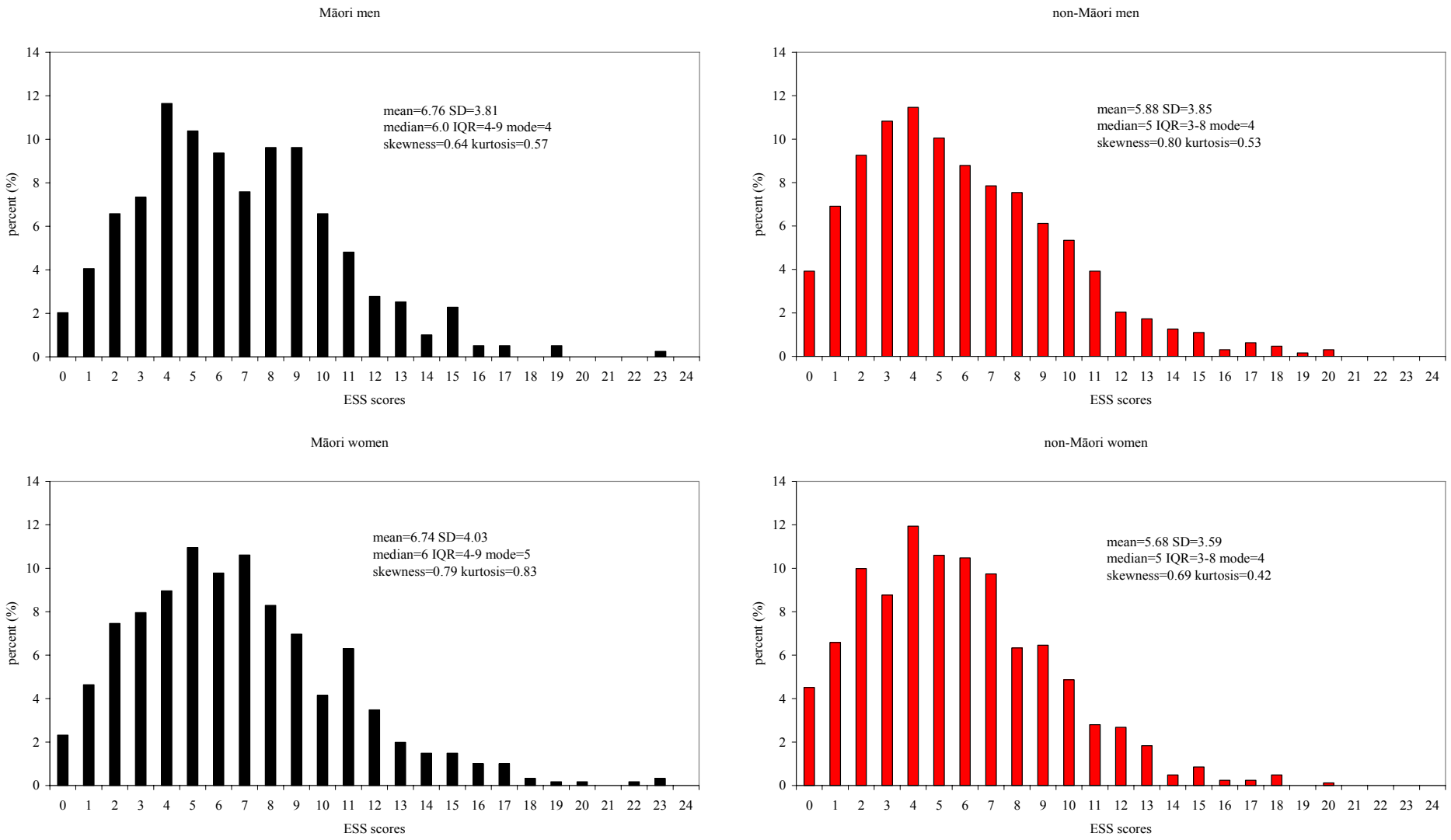


Figure 2.6 The frequency distribution of ESS scores among Māori and non-Māori, men and women in the study sample

A multivariate logistic regression model was constructed that included ethnicity, work and chronotype as independent variables (Table 2.24). As shown in Table 2.25 after controlling for morningness/eveningness preference, Māori were more likely than non-Māori to report excessive daytime sleepiness (p <0.0001). Similarly, those who were working nights were twice as likely to have an ESS score >10, than those whose work did not involve night shifts (p <0.0001).

Table 2.24 Logistic regression model construction: Excessive daytime sleepiness

Variable	Type	Reference category
Dependent		
Excessive daytime sleepiness	Dichotomous	ESS ≤ 10
Independent		
Ethnicity	Dichotomous	non-Māori
Employment status	Categorical	Employed, but no nights
Chronotype	Categorical	M-type

Table 2.25 The independent predictors of excessive daytime sleepiness (ESS >10)

	Excessive daytime sleepiness		
Variable	*OR*	*95% CI*	*p*-value
Māori	1.60	1.26-2.03	<0.0001
Work status [a]			
Unemployed	0.99	0.70-1.39	0.94
Night work	1.99	1.44-2.77	<0.0001
Chronotype [b]			
E	1.20	0.86-1.67	0.29
N	1.08	0.80-1.45	0.63

Note. Reference category for the outcome variable = ESS <10 [a] ref= working, but no nights. [b] ref=M-types

2.4 General Summary

This chapter presents the results from the first large survey of morningness/eveningness using the MEQ (Horne and Östberg, 1976) in New Zealand adults aged 30-49 years (55.7% response rate). It is unique in being able to simultaneously examine the influence of ethnicity, sex, age, socioeconomic deprivation and employment, on preferred sleep-timing.

Objective 1: To develop a circadian-type questionnaire adapted for New Zealanders, including the Horne and Östberg Morningness/Eveningness Questionnaire.

The questionnaire developed through pre-testing showed good psychometric properties in the main survey (Cronbach-α for the total sample 0.83; for the Māori sample 0.80; and for the non-Māori sample 0.85). In the future it would be useful to factor analyse the questionnaire to see if it could be reduced in length without significant loss of information.

Objective 2: To achieve a 70% response rate from 5,000 adults selected at random from the electoral rolls in the Wellington region.

This study was designed to recruit a stratified random sample from the New Zealand electoral rolls, with approximately equal numbers of Māori and non-Māori participants and in each decade of age, with the expectation that random electoral roll sampling would also give approximately equal numbers of men and women.

The overall response rate was 55.7% (53.4% Māori and 58.2% non-Māori). Reasons for the modest response are unknown. However possible deterrents to response may have included the length of the questionnaire; the number of items included in the study packages; and misinterpretation of the purpose of the study. Although Māori were less likely to respond than non-Māori, logistic regression showed that the differences in response rate which were observed were mainly due to differences in the socioeconomic deprivation profile of the Māori and non-Māori populations, rather than ethnicity *per se*.

The first possible reason for the low response rate may be the length of the questionnaire. As noted by Harris (2003), when designing a questionnaire it is important to consider the length and the readability of questions so as not to jeopardise the response rate. Careful attention was paid to the overall design of the questionnaire, which included pre-testing a draft at a local shopping mall. The final questionnaire design (4-pages consisting of 29-items) was significantly longer than the OSAS questionnaire (Harris, 2003) and the insomnia questionnaire (Paine et al., 2004) both of which achieved a greater than 70% response rate. The inclusion of items asking about demographic information, current employment, sleep habits and general health, in addition to the MEQ, was considered to be important as these are possible predictive factors and also possible outcomes of morningness/eveningness.

The present study also differs to that of Harris (2003) and Paine (2004) with regards to the content of the study packages. Firstly, the study packages used in the present study consisted of five inserts. A key study objective was to identify potential participants (particularly extreme chronotypes) for subsequent studies. The study package therefore included an information sheet (2 double-sided A4 pages) detailing the other study protocols, the inclusion criteria, potential sources of risk and benefit to the participants, as well as contact information for members of the research team and the local ethics committee. The study packages also included a consent form which gave the participants an opportunity to indicate their permission to be contacted by a research team member about subsequent studies. It is possible that some of the non-responders in the present study may have been overwhelmed by the amount of information included in each package, and therefore chose not to complete the questionnaire.

It is also possible that the information included in the study packages lead to some misunderstanding as to the purpose of the survey study. There may have been a number of participants who were not interested in taking part in the subsequent studies and who therefore did not complete the questionnaire, thinking that they had to participate in all or nothing.

Similarly, a small number of participants had returned their unanswered questionnaires to the research team and commented that they were ineligible to take part in the survey because they were currently involved in shift work. This was a misunderstanding, because being a shiftworker was only an exclusion criterion for the subsequent studies, not the questionnaire survey.

These factors were taken into consideration for the final mail-out to the Māori sample, and as a result the study package for the fourth mail-out excluded the information and consent form for the subsequent studies.

Given the response rate, it is important to examine whether the responders and the non-responders were systematically different. Using the electoral rolls as a sampling frame allowed the comparison of responders and non-responders for the demographic variables of Māori descent, age and socioeconomic deprivation. Harris (2003) cautioned about the comparison of response rates between Māori and non-Māori, particularly when the proportion of return-to-senders from the Māori sample is much larger than the proportion for the non-Māori sample.

The most conservative response rate from the Māori sample was lower than that for the non-Māori sample (RR1 49.14% vs. 54.60 respectively). However, there was also a significant trend for decreasing response with increasing deprivation for both samples (i.e. responders were less deprived than non-responders). A logistic regression model including both Māori descent and socioeconomic deprivation indicated that differences in response between the two samples were mainly explained by the differences in the deprivation profiles of Māori and non-Māori. Compared to a recent national survey of a representative sample of 30-59 year-olds (Harris,

2003), both Māori and non-Māori in the present study were less deprived than the general population.

Approximately 54% of respondents in the present study were aged 40-49 years. A significant trend for increasing response with advancing age was detected for the non-Māori sample, indicating the respondents were older than non-respondents in this sample. However, this trend was not significant for the Māori sample. Given that the response gradient by age was significant for non-Māori, this response bias may have caused an overestimation of prevalence estimates of morningness/eveningness among non-Māori.

An additional source of response bias may have been limited English literacy, although all potential participants were given the opportunity of responding by telephone, and the questionnaire was carefully designed for ease of readability and comprehension. Similarly, it is possible that not owning a telephone or having an unlisted number introduced non-response bias because potential participants could not respond, or be followed up, by phone.

Objective 3: To estimate the prevalence of different circadian phenotypes comparing Māori and non-Māori, men and women.

Univariate and multivariate analyses were based on the 2,526 participants who provided complete information on all demographic variables. Scores on the MEQ ranged from 23-81 with a frequency distribution that was slightly skewed to the left but closely resembled normal. Average scores on the MEQ were significantly different among 5-year age groups.

Using the criteria of Horne and Östberg (1976) 49.8% of the total population were M-types (10.2% DM-type) while only 5.6% had an evening-type preference (0.7% DE-type). Other large surveys of morningness/eveningness have reported a similar pattern of distribution (Taillard et al., 1999; Taillard et al., 2001). Using the new score cut-offs of Taillard et al. (2004) our prevalence estimates suggest that approximately one-quarter of the population aged 30-49 years report either a morning- (24.7%) or an evening-type (26.4%) preference. Taillard and colleagues (2004) also proposed cut-offs for the identification of extreme chronotypes. In the present study we found that 11.50% were DE-type and 10.19% were DM-type signalling that ‘owls’ and ‘larks’ are not rare in a middle-aged population. There were no significant differences in the prevalence of any of the chronotypes (MEQ1 or MEQ2) by ethnicity or sex.

Objective 4: To investigate possible age-related changes in sleep timing.

The present study supports the reported trend for increasing morningness with age, after controlling for demographic and socioeconomic factors. Univariate analyses suggested that scores on the MEQ increased significantly with advancing age and there was also a significant association between the proportions of each chronotype and 5-year age group. After controlling

for ethnicity, sex and socioeconomic deprivation, participants aged 30-34yrs were more likely to be DE-type and less likely to be MM- or DM-type than those aged 45-49yrs.

Objective 5: To investigate possible relationships between socioeconomic position and extreme circadian phenotypes.

Socioeconomic deprivation was determined using a validated small-area index, NZDep2001. This is a composite index of nine variables taken from the 2001 census which provides a deprivation score for each meshblock in New Zealand, ranging from 1 (least deprived) to 10 (most deprived).

Chi-square tests found no significant association between chronotype and socioeconomic deprivation. Similarly, in multivariate analyses, socioeconomic deprivation was not a significant independent predictor of morningness/eveningness preference.

Objective 6: To investigate possible relationships between circadian phenotypes and self-reported sleep habits, employment status and general health.

It has been suggested that age and work schedules are greatly influential with regards to morningness/eveningness preference (Adan & Amirall, 1991; Chelminski et al., 2000), and if taken into consideration, may eliminate any sex differences (Adan, 1992). Our results confirm this, with multivariate analyses establishing that ethnicity, sex, and socioeconomic deprivation are not important determinants of morningness/eveningness preference.

After controlling for demographic and socioeconomic factors, E-types were more likely to be involved in night work or be unemployed compared to M-types. However, chronotype was not significantly associated with abnormal sleep duration (<6.5hrs or >7.5hrs in a 24-hour period) or with excessive daytime sleepiness (ESS >10).

In the present study, evening-types were 2.5 times more likely than morning-types to report poor or fair general health ($p<0.05$), but the chronotypes did not differ in their self-reported sleep durations.

Objective 7: To identify potential participants for recruitment into subsequent studies

Of the 2,584 respondents to the survey questionnaire, 937 individuals indicated their willingness to participate in subsequent studies. Of these, 12.70% scored as DM-, 14.19% as MM-, 44.18% as N-, 16.01% as ME- and 12.91% as DE-type, based on the scoring criteria of Taillard et al. (2004). Since ethnicity and sex were not found to be independent predictors of morningness/eveningness these groups were not subdivided further.

CHAPTER 3
METHODS USED TO MONITOR SLEEP AND CIRCADIAN PHASE

3.1 Background

This chapter describes the procedures which were developed for the objective measurement of sleeping patterns and circadian phase position among self-identified morning- and evening-type individuals. It outlines the study protocols, measures and decision-making processes used to manage any challenges which arose in the course of the studies.

3.2 Participants

3.2.1 Recruitment

Participants were selected from those who took part in the questionnaire survey and who returned a consent form indicating their willingness to be contacted regarding participation in these studies and who provided contact telephone numbers. In November 2004 a database was created in *Excel*™ that included the names of all respondents who provided complete questionnaires along with the following information gathered from their survey answers:

- ID number: a unique identifier assigned to each participant at the time of drawing the random sample from the electoral roll.
- Name: according to the information provided by the electoral roll.
- Sex
- Ethnicity
- Age
- MEQ score
- Chronotype: Categorised according to the score cut-offs proposed by Taillard and colleagues (2004).

The initial study inclusion criteria were (1) scoring as either a morning- or an evening-type on the MEQ; (2) aged 30-49yrs; and (3) not currently involved in shift work, particularly night work.

Each respondent was ranked according to their MEQ score in ascending order and only those respondents who met the study inclusion criteria were included in the final database. All consent forms received were then manually searched to identify potential participants and the name provided on the consent form was cross-checked against the name on the database for accuracy. A total of 358 eligible respondents (134 evening-types and 224 morning-types) agreed to being contacted and their telephone details were added to the database.

Telephone recruitment

A research assistant (RA) was hired to contact potential participants by phone, with support and guidance from the research leader. The RA had considerable experience recruiting participants for research projects, and her style of engagement by establishing common links and relationships was a crucial factor in the success of this process. Telephone recruitment and screening began on the 28th February 2005 and continued until November 30th 2005.

The RA was responsible for communicating the purpose of the study, the proposed methods and measures, and what was required if the individual was to take part. A contact record sheet (CRS) and a set of response codes was developed to assist with the management of the recruitment process (see Appendix 9). Potential participants were able to put questions about the study to the RA, and telephone numbers for the research leader were available if further explanation and discussion was sought.

The first telephone call also served as an initial screening process, with the RA checking that the respondents still met the study inclusion criteria for age and shift work involvement. Finally, the RA explained to the respondents that participation in the study required short-term abstinence from caffeine, alcohol, certain drugs/medications and tobacco. If respondents were satisfied with the information given to them and they were interested in taking part, then arrangements were made for them to come to the Sleep/Wake Research Centre (SWRC) to take part in the full screening process.

3.2.2 Screening

The final stages of the recruitment and screening process were carried out on Saturday mornings at the SWRC and considerable effort was made to coordinate an appointment that was compatible with the respondents' personal and family responsibilities. Transport to and from the appointment was offered and respondents were invited to bring friends or family members with them. They were advised that the appointment would involve filling out a screening questionnaire about their general health and lifestyle as well as undergoing a medical examination with a registered medical practitioner. Appointments were scheduled to last 30 minutes, however they sometimes ran longer than this. Morning tea and refreshments were provided during each session and the RA and/or the research leader were available to the respondents throughout the morning. Each respondent who attended the screening session was presented with a small koha[4] in appreciation of their time.

The screening questionnaire

[4] The koha for this phase of the study consisted of a box of herbal 'sleep' tea, stationary items (pens, notepads) and information brochures about other sleep research conducted by the SWRC and TRRHaEP

To assess the suitability of each respondent to take part in the study a 15-page screening questionnaire (Appendix 10) was developed by the research team which was based on a similar tool used by the Centre for Sleep Research (CFSR) at the University of South Australia, in combination with the advice of professional colleagues. A draft version of the screening questionnaire was informally piloted with professional colleagues and through personal networks, and recommendations were incorporated into the final version. The questionnaire was divided into nine sections and was composed of previously used or validated questions were possible.

(1) Demographic information. Sex, date of birth, height and weight.

(2) Work and home life. This section addressed: household composition and care giving responsibilities (Gander et al., 2005b); overseas travel; current employment status (International Labour Organization, 1990; Statistics New Zealand, 2002) and the self-perceived impact of work schedules on sleep and social life[5] (Baker, Ferguson, & Dawson, 2003; Ribet & Derriennic, 1999);

(3) General health. In this section each respondent was asked about their caffeine, smoking and alcohol usage (Harris, 2003); stress (CFSR questionnaire); general health and quality of life (Paine et al., 2005).

(4) Sleep. Respondents were asked whether they take naps and the frequency and perceived reasons for these naps and whether they had even been diagnosed with a sleeping problem (yes/no). These questions were taken from the CFSR questionnaire. Daytime sleepiness was measured using the Epworth Sleepiness Scale (Gander et al., 2005a; Johns, 1991, , 1992).

(5) Personal and family medical history. Respondents were asked to indicate (yes/no) whether they had a personal or family history of epilepsy and/or other neurological disorders, respiratory problems and mental illness. Respondents were also asked if they had a current physical illness or were taking any medications (prescription or over-the-counter).

(6) Sleep quality. The Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) was used to assess sleep quality and frequency of sleep disturbances during the previous month. The full-PSQI contains 19 self-report items and five items which are completed by a bed partner or room mate, however as a research tool only the self-report items are relevant (Buysse et al., 1989). Responses to these items are grouped into seven component scores which reflect: subjective sleep quality; sleep latency; sleep duration;

[5] During the screening session several participants complained that this question was difficult to answer, and so it was decided to remove it from the screening questionnaire

habitual sleep efficiency; sleep disturbances; sleeping medication use; and daytime dysfunction. According to the original scoring criteria of Buysse et al. (1989), the component scores are summed to provide a global score which ranges from 0-21, with a PSQI score greater than five indicative of poor sleep quality and high sleep disturbance. The PSQI has a high degree of internal homogeneity (Cronbach's α 0.83) and good test-retest reliability among a group of depressed patients considered to have 'poor' sleep (Buysse et al., 1989). In the present study, individuals with PSQI scores between five and eight (Carpenter & Andrykowski, 1998) were followed up individually to determine whether there were unusual circumstances that had contributed to their recent poor sleep (Dr. D. Bartlett, personal communication, April 14 2005; and Dr. N. Rodgers, personal communication, March 17 2005).

(7) Depression, Anxiety and Stress. Following consultation with a local psychologist and communication with international colleagues, it was decided that the short form of the Depression Anxiety Stress Scales (DASS-21) (Lovibond & Lovibond, 1995) would provide a sufficient indication of the psychological suitability of a respondent for the study. Each dimension is comprised of seven self-report questions where respondents are required to indicate how much the previous statement applied over the past week. Possible answers ranged from 0 (did not apply to me at all) to 3 (applied to me very much, or most of the time). The DASS-21 is purchased from the School of Psychology at the University of New South Wales and a scoring template is provided. Overall scores are generated for each dimension, which are converted into z-scores and categorised as normal, mild, moderate, severe, and extremely severe. The DASS-21 has been shown to have adequate validity and internal reliability in a non-clinical population (Henry & Crawford, 2005).

(8) Morningness/Eveningness. Respondents were required to complete the MEQ a second time to verify that they were morning- or evening-types (according to the score cut-offs of (Taillard et al., 2004)).

(9) Availability. The final section of the screening questionnaire asked respondents to indicate preferred dates for undergoing an overnight laboratory protocol if invited to take part in the full study. The research team went to great efforts to ensure that personal, work and family commitments were catered to the extent possible.

If respondents were unable to attend a Saturday morning session due to work or family commitments, arrangements were made to have the questionnaire mailed to them at home to be completed in their own time. These packages included a copy of the questionnaire, a cover letter

from the research team and a pre-paid reply envelope. Respondents were requested to complete the screening questionnaire as soon as possible, with a follow-up telephone call from the RA approximately 2-weeks after mailing. If a respondent was unable to attend a screening session, an appointment for a medical examination was made at a suitable time only if the questionnaire information indicated that the respondent met the study inclusion criteria.

The medical examination

The primary purpose of the medical examinations was to screen all potential participants for any health complaints, psychological conditions or medications that could adversely affect the study outcomes and conversely, to ensure that the overnight laboratory protocol would not pose undue risks for a potential participant due to any existing medical conditions.

Each medical consultation commenced with a detailed medical history and then progressed to a rudimentary examination of the respiratory, cardiovascular, gastrointestinal, and neurological systems. Any specific issues raised in the history taking were examined in more detail. To ensure consistency between consultations, a detailed format was developed by the research team under the advice of medical colleagues (Appendix 11).

All consultations were conducted by doctors registered with the Medical Council of New Zealand who were employed by the research team, and were carried out at the Sleep/Wake Research Centre. Chaperones were available at all times. The doctors were responsible for obtaining consent from the respondents for the release of any medical information to other health professionals as deemed necessary. During this appointment, respondents had the opportunity to raise medical issues outside of the requirements for the study.

Any medical notes taken during this appointment were sealed in an envelope and labelled with the participant ID number. These notes were held in confidentiality and stored by the research team in a secure location at the Sleep/Wake Research Centre. All personal information will be returned to the respondent or destroyed following the completion of this study.

Urinary drug testing

The final screening procedure was urine analysis for the presence of cannabinoids, amphetamines, benzodiazepines, opiates and propoxyphines. Because of the limited resources available for the study, only those individuals who took part in the full protocol were required to undergo this test. Urine sample kits and instructional training was provided by Environmental Sciences and Research (ESR, located in Kenepuru, Wellington) who are responsible for workplace drug testing throughout New Zealand. All urine samples were collected by the research team leader, using standard procedures, prior to participants entering the overnight laboratory protocol. All participants were instructed to avoid taking any over the counter medications in the 48-hours preceding their sample. Similarly, participants were requested to

restrict their fluid intake to 1 glass per half hour for three hours prior to their sample. All samples and documentation were labelled using the participants' unique ID number. Urine samples were split into two containers to allow for a second test to be conducted if necessary. All samples were sealed at the time of collection and stored in a -20˚C freezer until being sent to ESR for analysis. Initial analysis was qualitative testing to detect target substances. If this test was positive, subsequent quantitative analysis was available. The research team leader was advised of the results in writing by ESR.

3.2.3 Study Inclusion Criteria

The final study inclusion criteria were:

(1) Scoring as either morning- or evening-type on the MEQ according to the criteria of Taillard and colleagues (2004).

(2) Aged between 30 and 49 years

(3) Not involved in night work.

(4) Having an ESS score ≤ 10, indicating normal levels of daytime sleepiness

(5) Having a PSQI global score less than five

(6) Having a z-score within the 'normal' range for each of the three dimensions of the DASS-21

(7) Meeting all of the requirements of the medical examination and having a positive recommendation for selection from the examining physician

Any respondents who had an ESS > 10 or a PSQI between 5 and 8 whilst meeting the other inclusion criteria were also selected to take part in the study protocol. All respondents who met the study inclusion criteria detailed above were telephoned by the research leader and invited to take part in the full study protocol.

The selection of participants to be invited to take part in the full study protocol was the responsibility of the research leader; however advice was sought from the research team and other professional colleagues when necessary. The results of the screening process can be found in Appendix 12.

3.3 Measures

The measures used are described separately for the two phases of data collection: (1) monitoring of sleep patterns for two weeks at home prior to the overnight laboratory protocol; and (2) the overnight laboratory protocol.

3.3.1 Actigraphy and Sleep Diaries

In order to objectively measure the sleeping patterns of self-identified morning- and evening-type individuals, each participant who was invited to take part in the full study wore a small activity monitor known as an *Actiwatch*™ (Mini-Mitter, Oregon, USA) which is about the same size as a wrist watch (see Figure 3.1). The underlying principle of actigraphy is that movement is reduced during sleep compared to wake, so sleep-wake patterns can be discriminated by evaluating periods of activity and inactivity (Littner et al., 2003). Actigraphy is a valid and reliable method of measuring sleep in healthy, adult populations (Littner et al., 2003; Signal, Gale, & Gander, 2004a).

The *Actiwatch*™ uses an accelerometer to detect the occurrence and degree of motion which is digitally integrated to produce a voltage. The accelerometer is omnidirectional but the shape of the sensor makes it more sensitive to movement in certain directions. In order to account for this sensitivity, and because no two *Actiwatches*™ produce identical readings for the same motion, it is important that the location and positioning of the watch is standardised. To maximise standardisation each participant was shown how to wear and use the watch and provided with instructional information by the research team leader (see Appendix 13).

Voltages are sampled at 32Hz and converted into 'activity counts' which can be summed across a set timeframe ranging from 15 seconds to 15 minutes (1 minute epochs were used in the present study). The activity counts are stored onto a 64KB memory chip in the *Actiwatch*™ which can collect data continuously for 45 days with the epoch length set to 1 minute.

While wearing the actiwatch, each participant was also required to keep a sleep diary which was developed by the SWRC, based on other diaries which have been used successfully in studies of international flight crew (Signal, Gander, & van den Berg, 2003; Signal et al., 2004b), air-traffic controllers (Signal, 2002), hospital-based anaesthetists (Garden, 2006; Miller, 2001), skippers and crew on fishing vessels (Gander, van den Berg, & Signal, 2005c) and women during pregnancy (Signal et al., 2007).

The sleep diary consisted of a series of 24-hour time lines on which participants were asked to record the times they went to bed, the times they got up, any disturbances during the night and whenever they had taken the actiwatch off. The research team leader showed each participant how to complete the diary and provided written instructions to be taken with them (see Appendix 14 for a copy of the sleep diary).

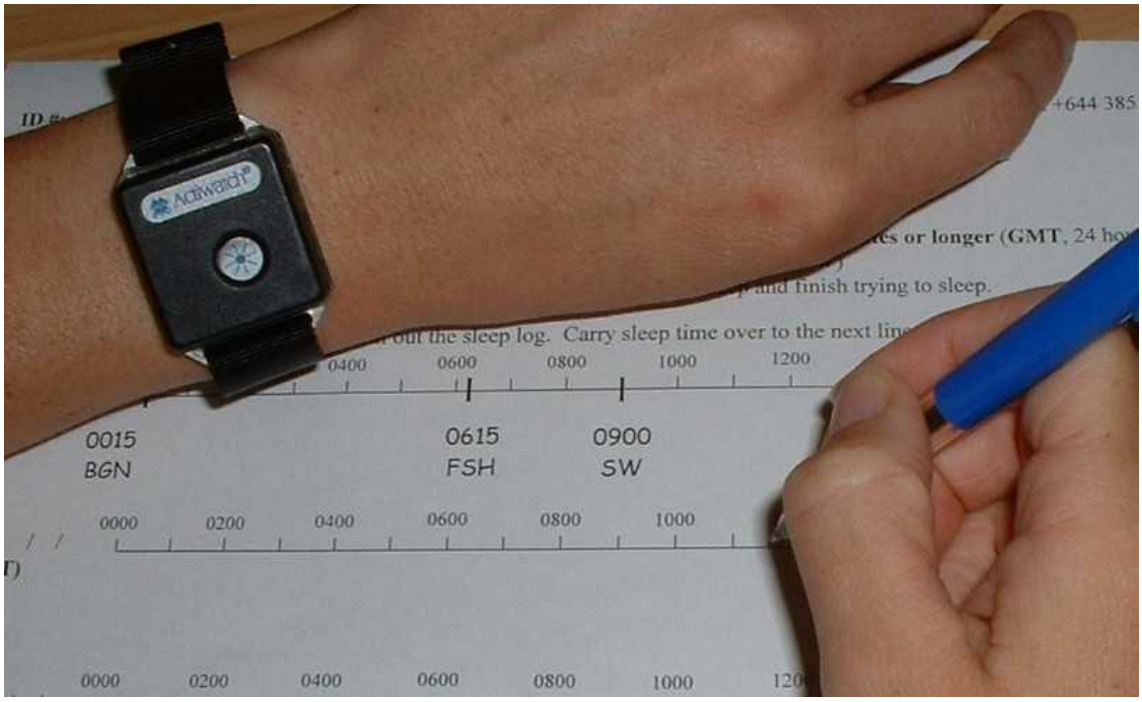


Figure 3.1 An actiwatch and sleep diary

At the end of the overnight laboratory protocol, the actiwatches and sleep diaries were collected by the research leader and data were downloaded via a serial port connection to a PC. The actigraphy data were analysed with reference to the sleep diary information using software provided by the actiwatch manufacturer (*Actiware*™-Sleep, MiniMitter, Oregon, USA).

The software algorithm scores each one miniute epoch between bed-time and get-up time as either sleep or wake. To be identified as a wake epoch the activity count for that particular epoch, as well as weighted contributions from the epochs immediately prior to and after it, are compared to a pre-set sensitivity value. If the activity count exceeds the threshold value, the epoch is scored as wake. The contributions of epochs adjacent to the scored epoch are one fifth of their activity count. Epochs two minutes from the scored epoch contribute one twenty fifth of their counts.

Using the software, the sensitivity threshold can be set at a high (80 counts), medium (40 counts) or low (20 counts) value. A high sensitivity, or low activity count, requires relatively little movement before wake is scored, while a low sensitivity, or high activity count, has the opposite effect of only scoring wake when much larger amounts of movement occur. In the present study a medium sensitivity setting was used since this has been shown to provide the most accurate relationship with polysomnographically scored sleep (Signal et al., 2004a).

The software was used in conjunction with the sleep diaries to generate a number of measures of sleep timing, duration, and quality (see Chapter 4).

3.3.2 Salivary Melatonin

The main measure in the overnight laboratory protocol was the collection of saliva for the detection of melatonin. The collection of salivary melatonin is relatively non-invasive and allows an indirect measurement of the levels of circulating melatonin which can be used to estimate an individual's circadian phase.

Procedures for collecting saliva samples were developed in consultation with Prof. Dave Kennaway from the University of Adelaide. Saliva samples were collected using plain *Salivettes*® (Sarstedt, Germany), which consist of four parts: a cap, cotton swab, inner chamber and outer vessel. Each salivette was labelled using a water-proof marker with the participants' unique ID number, the local date and the sample number which it represented (ranging from 1-34).

To collect a sample, participants removed the cap and placed the cotton swab in their mouth. They were instructed to gently chew and move the swab around in their mouth for two minutes, which was timed by a member of the research team. If, at the end of the two minute period, the participant believed they had not completely soaked the cotton swab, they were requested to chew on the swab for a further minute before putting the swab back inside the salivette and replacing the cap. All salivettes were stored immediately in a -20˚C freezer.

Figure 3.2 A Salivette

Saliva samples were spun in batches by the research leader using the facilities provided by the laboratory at the Centre for Public Health Research. After 15 minutes of defrosting, the saliva was recovered following centrifugation for 10 minutes at 1000 x *g* in a Heraeus Labofuge 400. Approximately 2ml of the resulting saliva was pipetted into Eppendorf micro test tubes which were labelled with the participant ID number and sample number. The Eppendorf tubes were stored in plastic boxes and refrozen (-20˚C) to await transportation in dry-ice to the University of Adelaide, Australia. Any remaining saliva was retained in the salivette and kept frozen at the SWRC.

All saliva samples were assayed in batches by the staff at the Circadian Physiology Laboratory, Department of Obstetrics and Gynaecology, University of Adelaide, Australia using validated protocols and reagents (Voultsios, Kennaway, & Dawson, 1997) (see Appendix 15 for the assay protocol).

3.3.3 Additional Measures

The Psychomotor Vigilance Task (PVT) and the Karolinska Sleepiness Scale were used as additional markers of circadian phase during the overnight laboratory protocol, although data from these measures are not presented here.

Changes in alertness and performance between morning- and evening-types across night were assessed using the Psychomotor Vigilance Task (PVT) (Dinges et al., 1998). The PVT is widely used in studies of fatigue, sleep deprivation, and performance and has been shown to be sensitive to changes in alertness associated with circadian phase (Dinges et al., 1997; Wyatt et al., 1997). The PVT is a simple reaction time test, in that it does not involve choice between responses, but does provide feedback on performance via the numerals of the LED display, which are the time in milliseconds taken to react. After a random time interval, the stimulus reappears and the participant is required to respond again.

Changes in subjective sleepiness across the night were measured using the Karolinska Sleepiness Scale (KSS) (Akerstedt & Gillberg, 1990). The KSS is a nine-point likert-scale with semantic anchors at the following steps: 1=extremely alert; 3=alert; 5=neither alert nor sleepy; 7=sleepy but no difficulty remaining awake; and 9=extremely sleepy, fighting sleep (see Appendix 16). The KSS has relatively strong positive intra-individual correlations with alpha and theta EEG activity (i.e. drowsiness) (Akerstedt & Gillberg, 1990) and was recently shown to have high positive correlations with most PVT measures (Kaida et al., 2006).

Participants completed the KSS and PVT every hour, in that order.

Figure 3.3 The Psychomotor Vigilance Task (PVT) device

3.4 Procedure

A study design was developed in consultation with members of the Sleep/Wake Research Centre and international research colleagues which incorporated two distinct periods of data collection, each seeking to answer independent, but interrelated, research questions. Ethics approval for the study design was granted by the Wellington Campus Massey University Human Ethics Committee (Protocol numbers 03/126 and 04/31). As a Māori researcher leading and conducting this work I was also informed by my own understandings of ethics and tikanga. The present programme also presented the first opportunity to conduct an overnight protocol in the Sleep/Wake Research Centre human time isolation facility. Therefore the research team was guided by the literature and advice from professional colleagues during the protocol development. It was also important that a dimension of flexibility was incorporated into the process to ensure not only the success of the study but to accommodate all of those who were involved.

3.4.1 Phase One – Sleep Monitoring at Home

Individual meetings were arranged between the research leader and the participants at a time and location that was determined by the participant and compatible with their work and family commitments. During this meeting, the research leader explained the purpose of the study as well as the methods and measures to be used, the potential benefits and risks of participation, and the expected study outcomes. Participants were encouraged to ask questions during this meeting and information sheets were given to each participant for their own review. Participants were also given consent forms to complete either at the meeting or in their own time. Copies of these forms can be found in Appendix 16.

Participation in Phase One of the study involved wearing an *Actiwatch*™ and completing a sleep diary for two weeks. The researcher described the basic functioning of the *Actiwatch*™ and gave the participant instructions on how to wear and use the device. Similarly, the purpose of the sleep diary, and instructions on how and when to complete it were also explained. An instruction sheet summarising this information was given to each participant to take home.

The *Actiwatch*™ was programmed to begin collecting data on Saturday at 1200hrs however participants were asked to begin wearing the watch the night before. Participants wore the watch on the wrist of their non-dominant hand throughout the study. Although the *Actiwatch*™ is water-resistant, it is not water proof, therefore participants were reminded to remove the watch when showering, bathing or taking a swim and indicate this on their sleep diary. Participants were not required to follow a strict sleep schedule during this phase of the study.

Finally, the night before Phase two began (a Friday night), each participant was asked to call the SWRC and record their bed time on the telephone answering system. The participants were

instructed to go to bed when they felt tired, and if possible, to wake without an alarm clock. The participants were also asked to call the SWRC and record their wake time on the Saturday morning.

3.4.2 Phase Two – Overnight Laboratory Study

The overnight laboratory protocol was based on the constant routine paradigm (Czeisler et al., 1985). Endogenous circadian rhythms, such as melatonin secretion, are driven by the internal circadian clock. However, exogenous factors, such as the light/dark cycle, act to keep the circadian mechanism in synchrony with the environment. Circadian rhythms are also susceptible to the masking effects of external variables such as light, sound and activity, which are able to alter the behavioural or physiological marker rhythms without affecting the internal pacemaker. Czeisler et al. (1985) developed a modified version of an experimental procedure first introduced by Mills et al. (cited in (Czeisler et al., 1985)) whereby participants were subjected to 40-hours of enforced wakefulness in a supine position, in constant indoor light and with regimented intake of food and fluids. Under these conditions, the masking effects of the light/dark cycle, postural changes, meals and sleep/wake activity were minimised so that the phase of the underlying circadian oscillator was revealed. Since this first report, constant routine protocols have been used extensively, and typically consist of 24-48 hours of continual wakefulness in a semi-recumbent position under temporal isolation, although variations have been reported (Dawson et al., 1992; Duffy & Dijk, 2002; Herman, 2005). Arendt (2005) lists a number of factors that are reported to influence the human melatonin rhythm including antidepressant (e.g. 5HT and MAOA) and antihypertensive medications (β-blockers), pain relief (asprin, ibuprofen), hard exercise, alcohol, smoking, and caffeine. Deacon and Arendt (1994) found that changes in posture from sitting to standing caused a rapid redistribution of fluid which decreased melatonin concentration, however this finding is not consistently reported (Arendt, 2005; Voultsios et al., 1997).

The Sleep/Wake Research Centre human time isolation facility (HTIF) is a 3-bed unit in which light intensity, temperature, and humidity can be closely controlled and exterior sound is highly attenuated. Each cubicle contains a hospital-style bed with adjustable head, bedside table, cupboards for the storage of personal effects and research related items, portable meal tray, office chair, and entertainment unit which includes a 14" television, and *Xbox*™ console for playing games and watching DVDs. Cubicles are separated by custom-made removable partitioning walls, and curtains are provided at the entrance of the cubicle for additional comfort and privacy. The HTIF is serviced by a single exit through a double-door. Lighting in the isolation facility is provided by a series of overhead and wall lights which are controlled using dimming switches.

The indoor lighting of the isolation facility was set at <20 lux throughout the protocol. Measurement of the ambient light intensity in each cubicle was taken from three positions (eye-level with the TV on, directly above the head, and to the side of the head) and ranged from 2.75-15.51 lux (IDEAL® Digital Lightmeter, Ideal Industries, Inc., Illinois, U.S.A.). The temperature was adjusted and maintained at 18˚C until the conclusion of the protocol. During the protocol participants were allowed to leave the isolation facility to use the toilet facilities in an adjacent room. To maintain the dim light conditions, a custom made floor to ceiling black out curtain was drawn to create a corridor between the two areas and similar curtains were used to cover all windows. Participants were provided with small hand torches to guide their way to the bathroom and light intensity measurements taken in the bathroom areas ranged between 0.01-0.5 lux.

Figure 3.4 A cubicle in the Human Time Isolation Facility (HTIF) at the Sleep/Wake Research Centre

In the week leading up to Phase two of data collection, each participant was contacted by the research leader to make travel arrangements and to discuss any challenges or issues which may have arisen during Phase one. All participants were reminded to refrain from caffeine and alcohol for 48hrs prior to the laboratory study.

All participants were requested to arrive at the SWRC between 1530-1600hrs. Due to the minor levels of sleep deprivation which were involved in the study, all participants were forbidden

from driving a motor vehicle. Instead each participant was transported to the SWRC by taxi unless a friend or family member was available to bring them. On arrival at the SWRC, the participants were introduced to the researchers who would be involved in the overnight study, shown around the facilities, and provided with afternoon tea. Following a brief presentation by the research leader, each participant was asked to provide a urine sample prior to entering the HTIF. If participants were unable to provide a sample before 1700hrs, they were required to do this at the conclusion of the protocol on Sunday morning before leaving the facility.

The study protocol formally began at 1700hr, at which time all participants were required to be lying on their beds in their own cubicles. All participants were asked to remain in a near supine position for the entire protocol. When participants needed to use the bathroom, they were asked to do so during those times when they were not performing a task required of them by the protocol and not during the 10 minutes before collecting a saliva sample.

Samples were collected at 30 minute intervals from 1730hr until 1000hrs (see Appendix 18 for an overview of the full study protocol). Ten minutes prior to sample collection, a researcher entered the facility and asked each participant to brush their teeth without toothpaste using the toothbrushes provided, and to rinse their mouths with water. This was to ensure that the mouth was clear of any residual food or drink which may contaminate the sample.

Water, juice and herbal decaffeinated drinks were available *ad libitum* except in the 10-minute period before a saliva sample was collected. Small meals were provided at two-hourly intervals between 1800hr and 1000hr, and any remaining food was removed after 15 minutes. After consultation with our international colleagues, each meal was designed to ensure that the food provided did not contain any bananas, cheese, caffeine, chocolate or red food colourings. To ensure consistency, each meal was replicated across each laboratory protocol. Vegetarian and vegan options were available on request.

Participants were required to remain awake throughout the entire protocol and they were permitted to undertake quiet activities such as watching movies, reading, listening to music, playing games, using a personal laptop, or talking to a researcher or another participant. Because a research team member was unable to be present in the isolation facility at all times, some participants dozed in between tasks. If this was observed, a researcher would quietly wake the participant at the first opportunity and encourage them to try to stay awake. Because of the timing and frequency of tasks during the protocol, the maximum period during which a participant may have dozed would be 10 minutes.

The protocol formally concluded at 1000hr on Sunday morning. Participants were invited to use the shower facilities if they wished, and to stay for morning-tea and informal conversation with the research team. Participants were also invited to stay and sleep at the SWRC before going home. All participants were transported home by taxi unless prior arrangements had been made,

and on their departure each participant was presented with a small koha[6] on behalf of the research team, in appreciation of their time and commitment to the study.

3.5 Data Management

All databases that were generated from the various measures were cross-checked against the original raw data files to ensure that data had been correctly entered. Descriptive statistics were generated for each variable in each database and checked for plausible values. Statistical and graphical methods were used to screen data for normality according to the grouping that was required for the analysis. In the present study the Shapiro-Wilk statistic was considered appropriate given the moderate size of the sample. Histograms, box plots, normal probability plots and detrended normal probability plots were also generated and assessed to determine normality if necessary. Any departures from normality were dealt with in ungrouped data and any necessary data transformations are specified in the relevant chapters. Any suspect values which were identified using these techniques were cross-checked against the raw data files and retained in the database if valid.

Similarly, each database was inspected to evaluate the amount and pattern of missing data for each individual. Out of 461 at home sleep recordings, 93.28% of entries had actigraphy data and 3.9% had only sleep diary data available. The amount of missing data was considered minimal (2.8%) and in subsequent analyses any cases with missing data were excluded.

With regard to the melatonin data, out of the 493 saliva samples that were collected, two participants each had two missing samples (0.8%). It is noted that for one participant the missing samples were not noticed until centrifugation of the *Salivettes*™ failed to produce any saliva, and the second participant requested that he leave the protocol one hour prior to the end of the overnight study (i.e. at 0900 hours). Radioimmunoassay of the samples from the latter participant found that melatonin offset had occurred prior his leaving the protocol.

Because of the repeated measures nature of the actigraphy and sleep diary data the statistical procedure utilised most for data analysis was mixed linear modelling performed in the SAS system for Windows (version 9.0). The mixed linear model is an extension of the general linear model and is so called because it allows the modelling of both fixed and random effects. Fixed effects are the "traditional" predictor variables, while random effects are additional variables also assumed to impact on the variability of data. The strength of mixed modelling is that data are permitted to exhibit correlation and non-constant variability, which can be modeled and controlled for.

[6] The koha consisted of a mens or womens gift pack provided by Living Nature.

The assumptions of the mixed model are that data are normally distributed, the expected relationships are linear, and the variances and covariances exhibit a structure matching one of those available in the modelling procedure. The assumptions of normality, linearity and homoscedascity can be checked by analysing the residuals (Tabachnick & Fidell, 2001) and with each model a histogram, normal probability plot and the Shapiro-Wilk statistic (S-W) were generated to asses the structure of the residuals. Where outlying residual values were identified, the model was re-run without the value(s). Residual plots were then re-checked to evaluate the effect of removing the outlier(s). In all instances the process used was to determine if removing the outlying value(s) altered the residuals and the findings of the model. Transformations were also applied (square root, log10 and reciprocal) to improve normality if necessary. If normality was not achieved then the outlying residual values were systematically removed and transformations applied until the S-W statistic indicated normality of the residuals.

In specifying the covariance structure, the procedure applied was to run a general covariance structure, known as "unstructured", which makes no assumptions regarding equal variances or covariances. Because of the computational capacity required in calculating such a structure this is not always possible to achieve (Littell, Henry, & Ammerman, 1998), however this was not an issue in the present study. Diagonal values from the covariance matrix and the values from the correlation matrix were plotted against time to see if there was a pattern that fitted the available covariance structures. This structure was then applied and compared to alternative structures to confirm it was the best fit.

Schwarz Bayesian Criteria (represented by the BIC value in output obtained from SAS v. 9 for Windows) was used to objectively assess the fit of a covariance structure, with the smallest value computed by the SAS system indicating the most suitable structure. This approach is considered the most conservative and adjusts the REML log likelihood value by imposing a penalty according to the number of parameters estimated (Littell et al., 1998).

When main and interaction effects were statistically significant, post-hoc *t*-tests were used to investigate comparisons of interest. As mentioned previously, corrections to the significance level are commonly applied when multiple comparisons are made in order to avoid Type I errors. However, the analyses presented in this thesis were driven by the hypotheses relevant to that study which were based on available *a priori* knowledge. Therefore, it was deemed appropriate to present unadjusted significance levels and consider any significant findings based on whether the result is biologically plausible.

CHAPTER 4
THE SLEEPING PATTERNS OF SELF-IDENTIFIED MORNING AND EVENING-TYPE ADULTS

4.1 Introduction

Subjective measurement tools such as questionnaires and sleep diaries provide a simple and cost-effective way of documenting an individuals' perception of their sleep. Investigators such as Horne and Östberg (1976) and Taillard et al. (2004) have used sleep diaries to validate the assignment of chronotypes based on questionnaires, with morning-types consistently indicating a preference for an earlier sleep/wake schedule compared to neither- (also called intermediate-types) or evening-types.

However, our ability to reliably and accurately recall certain characteristics of the sleep we obtain is questionable (Carskadon et al., 1976; Gander et al., 1993). In the context of this thesis, further investigation was required to examine the extent to which the MEQ categories defined by Taillard and colleagues (2004) reflected habitual sleep/wake behaviour.

This chapter presents the findings of a study that was designed to measure and compare the timing, length and quality of sleep among self-identified morning- and evening-type individuals using actigraphy and sleep diaries.

4.1.1 Subjective versus Objective Measures of Sleep

Sleep can be measured using a number of different subjective and objective techniques, however, it is widely accepted that polysomnography (PSG) provides the definitive measure of sleep (Carskadon & Rechtschaffen, 2005). Polysomnography involves attaching small electrodes to the face and scalp to record the physiological signals of brain activity, (electroencephalogram or EEG), eye movements (electrooculogram or EOG) and muscle tone (electromyogram or EMG) which are necessary to accurately determine the onset, offset, different types (non-REM vs. REM) and stages of human sleep (non-REM stages 1-4) (Carskadon & Rechtschaffen, 2005). Although PSG provides a depth of information pertaining to changes in sleep, it requires significant financial and human resources, and can also be invasive and cumbersome to the individual(s) involved in the study. The combination of these factors limits the collection of data and as such impacts on the utility of this tool when one is interested in the patterns of sleep and wakefulness across a 24-hour period or longer.

Actigraphy provides an alternative technique for the collection of objective sleep information. The underlying principle of actigraphy is that movement is reduced during sleep compared to wake, therefore using a portable device, such as an *Actiwatch*™, sleep-wake patterns can be

discriminated by evaluating periods of activity and inactivity (Littner et al., 2003). Actigraphy is a valid and reliable method of measuring sleep in healthy, adult populations (Littner et al., 2003) and a recent review by Ancoli-Israel and colleagues (2003) (under the auspices of the American Academy of Sleep Medicine) reported that actigraphy was highly correlated with PSG for the differentiation of sleep from wake, and that the most reliable actigraphic sleep measure was total sleep time. The accuracy of the actigraph decreases as sleep becomes more fragmented (i.e. in sleep disordered patients) (Ancoli-Israel et al., 2003; Signal et al., 2004a). In addition, actigraphy may be less accurate than PSG for determining some sleep measurements (i.e. sleep latency, and sleep efficiency) (Signal et al., 2004a). However, any expectation that actigraphy should perform to the same level as PSG has been said to be unreasonable given that actigraphy is only able to take into account 'activity' in the estimation of sleep parameters, compared to PSG which incorporates EEG, EMG and EOG (Ancoli-Israel et al., 2003; Signal et al., 2004a; Tryon, 2004). Actigraphy has several advantages over PSG, the major benefit being the ability to continuously collect 24-hr recordings of sleep over multiple nights (Ancoli-Israel et al., 2003). In addition, actigraphy is cost-effective and easy to use, making it a highly effective research tool.

Sleep diaries (also known as sleep logs) and questionnaires are frequently used in the study of sleeping patterns. Diaries typically record the times at which participants go to bed, first attempt to sleep, wake up, and get out of bed. The perceived quality of sleep can be assessed by asking individuals to report the number of awakenings during the night as well as their alertness and mood on final awakening, using visual analogue or likert scales. Subjective tools provide a cost-effective and non-invasive means of estimating the timing, quantity or quality of sleep. However a major criticism of self-report methods is their reliance on the individual to accurately recall their previous sleep episode (Ancoli-Israel et al., 2003).

In both the clinical and research setting, sleep diaries are a particularly useful adjunct to actigraphy, as the reporting of parameters such as bed time and rising time can be used as reference markers which aid the interpretation of actigraphic measurements (Signal et al., 2004a). Both tools require little supervision and can be easily maintained, which is advantageous in a naturalistic setting. Together, actigraphy and sleep diaries provide a valid and reliable methodology for the investigation of sleep patterns.

4.1.2 Research Objectives and Hypotheses

The purpose of the present study was to objectively compare the timing, length, and quality of sleep among self-identified morning- and evening-type individuals across a two week period.

The specific objectives were:

1. *To collect 14 consecutive days of sleep diary and continuous wrist actigraphy data from 16 people who score as M-types on the MEQ and 15 people who score as E-types on the MEQ.*

2. *To compare sleep duration, timing, quality and weekend versus weekday sleep, between the two groups, using mixed model analysis of variance*

The research hypotheses were:

1. *That sleep onsets and offsets will be earlier among M-types than E-types*

2. *That M-types will get more total sleep than E-types, who will experience chronic sleep restriction on work days*

3. *That E-types will show greater differences in weekend versus weekday sleep duration than M-types, due to their restricted weekday sleep and extended recovery sleep on weekends.*

4. *That women will show less evidence of recovery sleep on non-work days, due to ongoing domestic and care-giving responsibilities*

4.2 Method

To determine whether the timing, length and quality of sleep differed between self-identified morning and evening-type individuals, variables were generated from the actigraphy and sleep diary data. The following section focuses on the specific measures which were used in the analyses, as well as the main statistical techniques that were employed to analyse the data.

A total of 32 participants collected actigraphy and sleep diary data as part of the present study. However, due to a failed urine screen for one individual, the findings presented in this chapter are based on the analysis of data from 31 participants.

4.2.1 Measures

The following variables were generated from the *Actiwatch*™ software (Actiware™-Sleep v.3.14) and accompanying sleep diaries in order to estimate the differences in the timing, length and quality of sleep between self-identified morning- and evening-type individuals. The variable descriptions presented here were adapted from the *Actiwatch*™ manual by Dr. T.L. Signal (2002).

Sleep Timing Variables.

Bedtime**:** A time based on an event marker in the actigraphy data (cross-checked against the sleep diary entry). Participants were asked to press the event marker on the *Actiwatch*™ when they began trying to sleep. This was to ensure that the time spent in bed, but not trying to sleep (such as reading a book) was not included in the actigraphy calculations. In the software this was set manually. For actigraphy outputs that had no event markers, consistent guidelines were

followed in the interpretation of data to determine bedtime (see Appendix 19). Bedtime was the time at which the software programme began to sample epochs of data to determine if the participant was asleep or awake.

Get up time**:** Also a time based on an even marker in the actigraphy data (cross-checked against the sleep diary entry). Participants were asked to press the event marker again on the *Actiwatch*™ when they finished trying to sleep, for identical reasons as described above. In the software, get up time was set manually, and when no event makers were available, the guidelines in Appendix 19 were followed. Get up time marked the last epoch used by the software algorithm to determine if the participant was asleep or awake.

Sleep start**:** This parameter may either be set manually or derived automatically via the software algorithm and represents time of sleep onset. It has been demonstrated that subjective reports of sleep are discrepant from physiological measures of sleep (Gander et al., 1998; Signal, Gale, & Gander, 2005), with the trend being an over estimation of time taken to fall asleep (Rosekind & Schwartz, 1988a, , 1988b). Therefore it was decided to use the automated option to calculate sleep start. The software searches for the first period of 20 consecutive epochs from the bedtime mark, in which a maximum of one epoch contains a non-zero value. This procedure is carried out in a stepwise manner. The first epoch in the group of 20 meeting the criterion is set as sleep start time. On this basis, it is possible for sleep start to be the same as bedtime. In the instances where actigraphy data were not available, but a subjective estimate of sleep start was recorded in the sleep diary, then this time was entered into the main database as sleep start.

Sleep end**:** This parameter represents the time of sleep termination and can either be set manually or derived automatically. As with sleep onset, individuals may be poor at judging exactly when they woke up and how long they have been awake for (Rosekind & Schwartz, 1988a), so to ensure accuracy and consistency, this value was also calculated by the software algorithm. The algorithm examines the ten minutes immediately prior to get up time and scores the last epoch with no movement as sleep end. Because very little movement is required to set sleep end, the logbook entry was cross-checked for accuracy. Sleep end can be identical to get up time. As with sleep start, when actigraphy data were unavailable but a subjective estimate of sleep end was recorded in the logbook, this time was entered in the database as sleep end.

Sleep length variables.

Time in bed**:** The length of time in hours and minutes between bedtime and get up time is known as time in bed and represents the amount of time spent attempting to sleep. This variable was of interest because it indicates the length of time participants had, or made available, for sleeping.

Assumed sleep**:** Is the difference between sleep start and sleep end times in hours and minutes, and may include short periods of wakefulness.

Actual sleep time: This is the amount of time activity levels are below the threshold sensitivity value for wakefulness, and is calculated by subtracting actigraphically determined wake time from assumed sleep time. In the present study the medium sensitivity threshold was used as it has been shown to have the least amount of bias and optimal accuracy (Signal et al., 2004a). If actigraphy data are not available, this variable cannot be calculated.

Sleep Quality Variables.

Actual sleep time percentage**:** This variable is the percentage of assumed sleep that was actigraphically scored as sleep, and is calculated by dividing actual sleep time by assumed sleep time and multiplying by 100.

Sleep efficiency**:** This variable represents the amount of time in bed (TIB) spent sleeping and is determined by dividing "actual sleep time" by "TIB" and multiplying by 100.

Movement and fragmentation index**:** This variable was considered an index of the restfulness of sleep and therefore provides an insight into the quality of sleep obtained. It was comprised of the "number of minutes spent moving percentage" added to the "immobility phases of one minute percentage".

The first component of the movement and fragmentation index "number of minutes spent moving percentage" was determined by dividing the "number of minutes moving" during assumed sleep time by "assumed sleep" and expressing this as a percentage. "Immobility phases of one minute percentage" was calculated by dividing the number of phases during which an individual was immobile for exactly a minute (no more or no less) by the total number of immobile phases. This is expressed as a percentage. As the resulting index value increases, the quality of the sleep is considered poorer, due to greater fragmentation and more movement.

Mean activity score: This is calculated by dividing the sum of all activity counts between sleep start and sleep end times by the number of epochs during the assumed sleep period, indicating the average amount of activity per epoch of sleep.

All of these variables were generated for each participant and then copied directly from the software programme into individual Excel files. A combined file was created at the end of data collection and imported into SPSS and SAS for data management and statistical analyses.

Actigraphy and sleep diary data was available for every study participant. However, there was some variability in when the recording started, due to difficulties in recruiting the participants at least 14-days before their overnight laboratory study. Of the 31 participants included in the analyses, the complete data collection period was not available for six participants.

Main night sleep episodes

In order to determine whether the pattern of sleep observed among morning- and evening-type individuals changed across the week, it was necessary to focus on main night sleep episodes. The nature of the study design meant that participants were not required to follow a strict sleep schedule therefore a system of rules for defining main night sleep was developed to take into account the normal variability in sleep which was seen among participants.

A main night sleep episode was defined as any sleep episode that started between 2000hrs and 1200hrs. This rule for main night sleep accounted for 94.16% of all recorded sleep.

If more than one sleep episode was recorded between 2000hrs and 1200hrs, it was necessary to determine whether the sleep episodes warranted merging together to create a single sleep period or whether they were in fact distinct periods of sleep. To determine this, the amount of waking time in between episodes was evaluated using the raw data and the following rules were created:

Rule 1: If the first Bedtime and the final Get Up Time for the two sleep periods were within the normal range for that individual *and* the waking period separating the two sleep periods was less than 60 minutes *then* the data were merged

Rule 2: If the Bedtime for the first sleep period and the Get Up Time for the final sleep period were within the normal range for that individual *and* the waking period separating the two sleep periods was greater than 60 minutes *but* the waking period occurred during the middle of the normal night time period, *then* the data were merged.

Rule 3: If the participant clearly identified two separate sleep periods in the sleep diary *and* there was a lot of activity (as recorded by the *Actiwatch*™) in between the sleep periods *and* the waking period separating the two sleep periods was greater than 60 minutes *then* the data were not merged.

Finally, a database was created in Excel which included demographic information along with the sleep variables of interest. In addition a variable was created that distinguished a main night sleep period from any other sleep period. This database was then exported to SPSS and SAS for the analysis of the sleep timing, sleep duration and sleep quality variables

A total of 416 main sleep episodes were included in this database, and of these four main sleep episodes had only sleep diary information available. Approximately 3.26% of actigraphy and/or logbook data were missing entirely from this database. Because the amount of missing data was minimal, subsequent analyses excluded those cases with missing data.

The total amount of sleep across a 24hr period

In addition to the main night sleep episode, it was useful to take into account the total amount of sleep taken in a 24-hour period in order to determine whether the total amount and quality of sleep differed between chronotypes.

If more than one sleep episode occurred in 24-hours, the total amount of sleep obtained was summed using a purpose-built *LabVIEW*™ programme. The start and end times of the 24hr periods were set at midday. This summed data was then exported to Excel, SPSS and SAS for analysis of the sleep length and sleep quality variables.

The actiwatch software cannot be used to calculate variables for periods of sleep shorter than 60 minutes because the accuracy of the algorithm is reduced for such short time frames. As the participants had still used the event marker and sleep diary to record these short sleep periods the variables Bed Time, Get Up Time and Time in Bed can still be deduced. A variable was included in the final database to indicate whether a sleep period was calculated using full actigraphy or limited actigraphy in combination with sleep diary data (and in some instances diary data alone).

A total of 419 sleep episodes were included in this database and of this 6.19% included one or more sleep diary recordings in the summed information. The amount and pattern of missing data in this database was not considered to be problematic with only 3.23% of actigraphy and/or logbook data missing, therefore all analyses excluded those cases with missing data.

4.2.2 Statistical Analyses

Data management

Inspection of the raw data files for each individual was also necessary to identify any unusual sleep periods. One participant noted in their sleep diary that they had three nights across a public holiday weekend where they had atypical sleep patterns and, on inspection of the raw data files, this was illustrated by the presence of three sleep periods with Bed Times and Get Up Times that were extremely late in comparison to the other recorded sleep periods. Taking this information into account, it was decided that these sleep periods would be excluded from the analyses of main night sleep episodes because they did not accurately represent the sleeping patterns of that individual.

It was also discovered that a second participant had recorded one extremely short sleep period (Bed Time = 0146hrs and Get Up Time = 0308hrs). Because the sleep parameters of Bedtime and Get Up Time are used by the Actiware algorithm to generate other sleep parameters used in this study, it was decided that this sleep period would be excluded from the analyses of main night sleep episodes because of the potential to skew the distribution of the other values.

Data transformations

An important assumption of the mixed model procedure is that the residuals follow a normal distribution. Prior to running each of the mixed model ANCOVAs, the distributions of the residuals from the dependent variables were evaluated using statistical and graphical methods. If the data did not meet the requirements of the mixed model, a system of checking for outliers, applying common transformations on the dependent variable and systematically removing outliers was followed until normality of the residuals were achieved.

Descriptive statistics

All participants are described using the information provided in the screening questionnaire which was completed during the recruitment phase of this study.

Descriptive analyses are presented in order to understand the overall pattern of data for different variables. Given the variability in sleeping patterns observed in these participants, the data rarely followed a normal distribution. Therefore the mean, standard deviation, median and inter-quartile range are consistently presented throughout this chapter.

Univariate analyses

Relationships between the sleep parameters and the variables of interest were investigated using non-parametric tests because they do not require the data to be normally distributed.

The Kruskal-Wallis test was used throughout this chapter to test for significant associations between the sleep parameters and morningness/eveningness (M- vs. E-types), age group (30-39yrs vs. 40-49yrs), and caring for dependants (any dependants vs. none). Grouping the sample according to sex (male vs. female) and work status (employed vs. unemployed) resulted in insufficient numbers in some cells and therefore univariate tests were not conducted for these groupings.

Multivariate analyses

In all mixed model ANCOVAs used in this chapter, the covariance of values was modelled most appropriately by the compound symmetric structure, which assumes that multiple measures have the same variance and that all pairs of measures for an individual have the same covariance. Such a structure implies that the only aspect of covariance between repeated measures is due to the contribution of the individual, and is independent of the relationship of measures to each other over time.

Individual models were run for each sleep timing, duration and quality variable and in each case the independent variables were chronotype (M- vs. E-type), age group (30-39yrs vs. 40-49yrs), caring for dependents (any vs. none) and an interaction effect of chronotype by weekday (weekdays vs. weekends).

In the present study, post hoc *t*-tests were used to investigate comparisons of interest when interaction effects were determined to be statistically significant. Based on the study hypotheses, the specific comparisons of interest were (1) differences between weekday (Sunday-Thursday night) and weekend (Friday and Saturday night) sleep periods within each chronotype; and (2) differences between chronotype (M- and E-types) within weekday or weekend sleep periods.

4.3 Results

4.3.1 Characteristics of the Study Participants

Table 4.1 presents the characteristics of the participants in the present study. Twenty participants were female and 11 participants were male and the mean age was 41.2 years (*SD* = 4.77, *Range* = 31-48, *N* = 31). Four women reported using oral contraceptives, and one woman reported using an intrauterine contraceptive device. The average Body Mass Index (BMI) for these participants was 28.04 (*SD* = 4.72, *Range* = 20.28 – 39.69). BMI categories (normal, overweight and obese) were also created in the present study. It is important to note that the thresholds used for these categories differed between Māori and non-Māori participants as it has been reported that standard BMI benchmarks are inappropriate for Māori (Mihaere, 2004). Self-identified ethnicity for each participant was available from the data collected as part of the questionnaire survey presented in Chapter 2.

Only three participants in the present study reported being unemployed, whilst one participant reported having more than one job. Fifteen participants had one or more dependants living in their household. Four participants reported being a regular or occasional smoker. Participants were asked to list the average amount of caffeine consumed each day (including coffee, tea, chocolate bars and energy drinks). Twenty-one participants reported consuming more than two servings of caffeine per day. Only four participants reported never drinking alcohol, while 15 participants reported having two or more standard drinks on a typical drinking occasion. All of the study participants reported that their general health was, good, very good or excellent (versus poor or fair).

In the present study, 16 participants were morning-type (10 Definitely M-type and 6 Moderately M-type) and 15 participants were evening-type (13 Definitely E-type and 2 Moderately E-type). The mean age of morning-types was 42.85yrs (*SD* = 4.25, *Range* = 35-48) while for the evening-type participants it was 39.45yrs (*SD* = 4.80, *Range* = 31-47) (Table 4.2).

Although 12 participants were considered “poor sleepers” (global Pittsburgh Sleep Quality Index score > 5), all of the participants had normal levels of self-reported daytime sleepiness (ESS score ≤ 10). Only one participant reported that they normally took a daytime nap.

Table 4.1 Characteristics of the study participants

	Whole group	Morning-type	Evening-type
	n (% of sample)	*n* (% of sample)	*n* (% of sample)
Men	11 (35.48)	7 (22.58)	4 (12.90)
Women	20 (64.52)	9 (29.03)	11 (35.48)
30-39yrs	12 (37.81)	5 (16.13)	7 (22.58)
40-49yrs	19 (61.29)	11 (35.48)	8 (25.81)
BMI1[a]	9 (29.03)	4 (12.90)	5 (16.13)
BMI2[b]	14 (45.16)	9 (29.03)	5 (16.13)
BMI3[c]	8 (25.81)	3 (9.68)	5 (16.13)
No Dependants	16 (51.61)	7 (22.58)	9 (29.03)
Any Dependants	15 (49.39)	9 (29.03)	6 (19.36)
Employed	28 (90.32)	15 (48.39)	13 (41.94)
Unemployed	3 (9.68)	1 (3.23)	2 (6.45)
DM-type	10 (32.3)		
MM-type	6 (19.4)		
ME-type	2 (6.5)		
DE-type	13 (41.9)		

Note. [a] BMI1 = normal range (Māori <26 kg/m^2; non-Māori <25 kg/m^2); [b] BMI2 = overweight range (Māori 26-32 kg/m^2; non-Māori 25-30 kg/m^2); [c] BMI3 = obese range (Māori >32 kg/m^2; non-Māori >30 kg/m^2)

Table 4.2 Average age and MEQ scores of the study participants

	Whole group	M-types		E-types	
	Age (yrs)	Age (yrs)	MEQ score	Age (yrs)	MEQ score
Mean	41.20	42.85	70.31	39.45	38.57
SD	4.77	4.25	3.22	4.80	6.91
Range	31-48	35-48	65-77	31-47	30-49

4.3.2 The Timing of the Main Night Sleep Episode, Comparing Self-Identified Morning- and Evening-Types

The specific sleep parameters of interest were bedtime (BT), get up time (GUT), sleep start time (SlpSt) and sleep end time (SlpEnd). A total of 416 main sleep episodes were analysed for BT and GUT, and 412 main night sleep episodes were analysed for SlpSt and SlpEnd (four main sleep periods had diary data but not actigraphy).

Figure 4.1 plots the cumulative percentage of participants who were in bed by time of day for weekdays and weekends separately. Similarly, Figure 4.2 illustrates the cumulative percentage of participants who were asleep by time of day for weekdays and weekends. In both figures, the later sleep timing of E-types, compared to M-types, is clear. Moreover, there appears to be a greater range of sleep times on weekends, compared to weekdays, for both groups. The difference in average BT and SlpSt between chronotypes was 1.09hrs and 1.20hrs respectively whilst differences in average GUT and SlpEnd between chronotypes were 2.36hrs and 1.63hrs respectively (Table 4.3).

Table 4.4 shows the differences in the timing of the main sleep episode between weekdays (Sunday-Thursday night) and weekends (Friday and Saturday night) for both chronotypes. The range of sleep start times, comparing weekday and weekend main night sleep episodes, showed the greatest variability (M-types difference = 1.08hrs; E-types difference = 2.56hrs).

The Kruskal-Wallis test identified significant univariate relationships between bed time and chronotype (M- vs. E-type, p <0.0001), age group (30-39yrs vs. 40-49yrs, p <0.0001), dependants (any vs. none, p =0.0043) and day of the week (weekdays vs. weekends, p =0.0016) (Table 4.5). Similarly, significant univariate relationships were found for sleep start times and chronotype (p <0.0001), age group (p <0.0001), dependants (p =0.0055) and weekday/weekend (p =0.0079) (Table 4.6).

Get up time (Table 4.7) and sleep end time (Table 4.8) were both significantly associated with chronotype, age group and weekday/weekend (all p <0.0001).

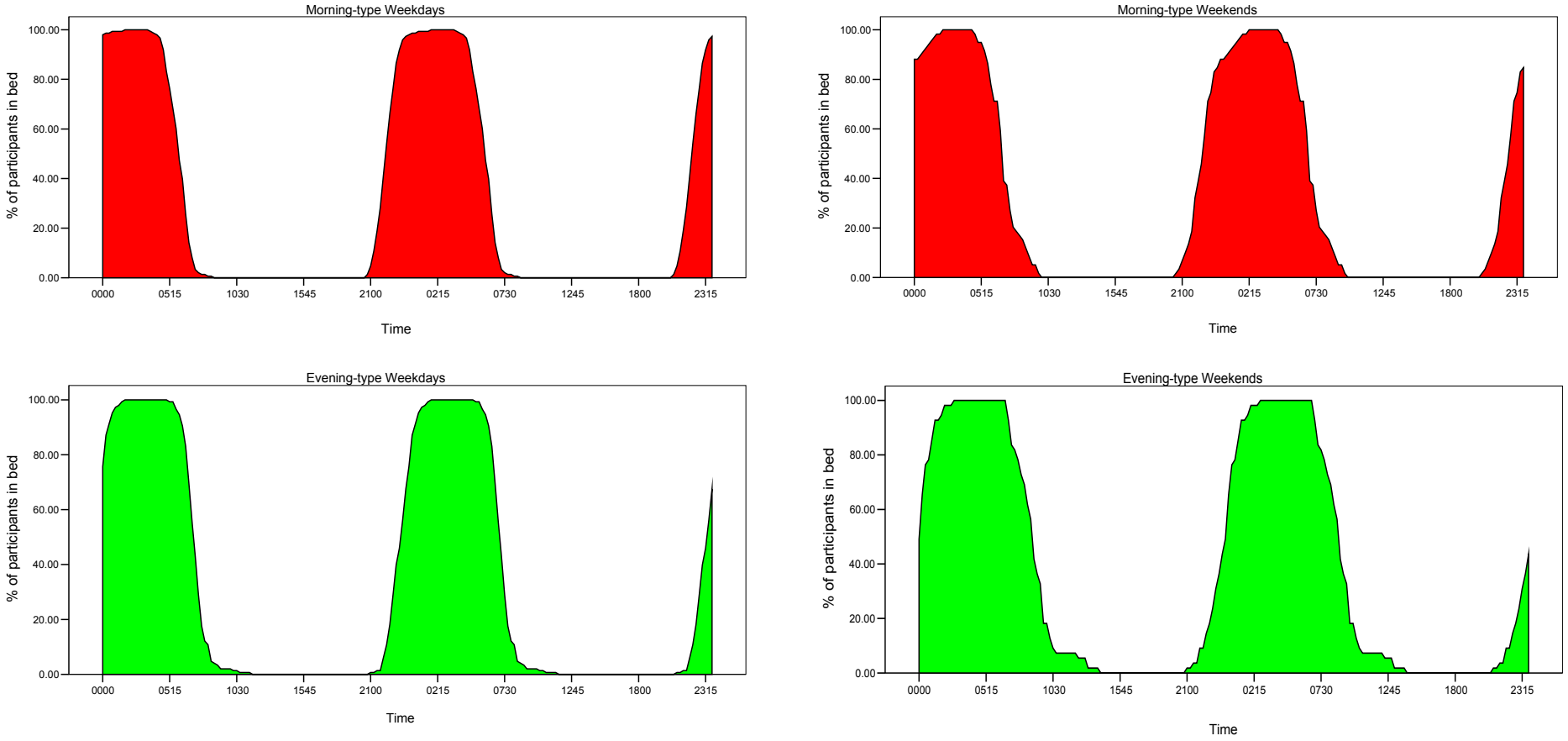


Figure 4.1 Who's in bed?

Overall cumulative percentage of morning- (in red) and evening-types (in green) in bed attempting to sleep on weekdays (left panel) and weekends (right panel).

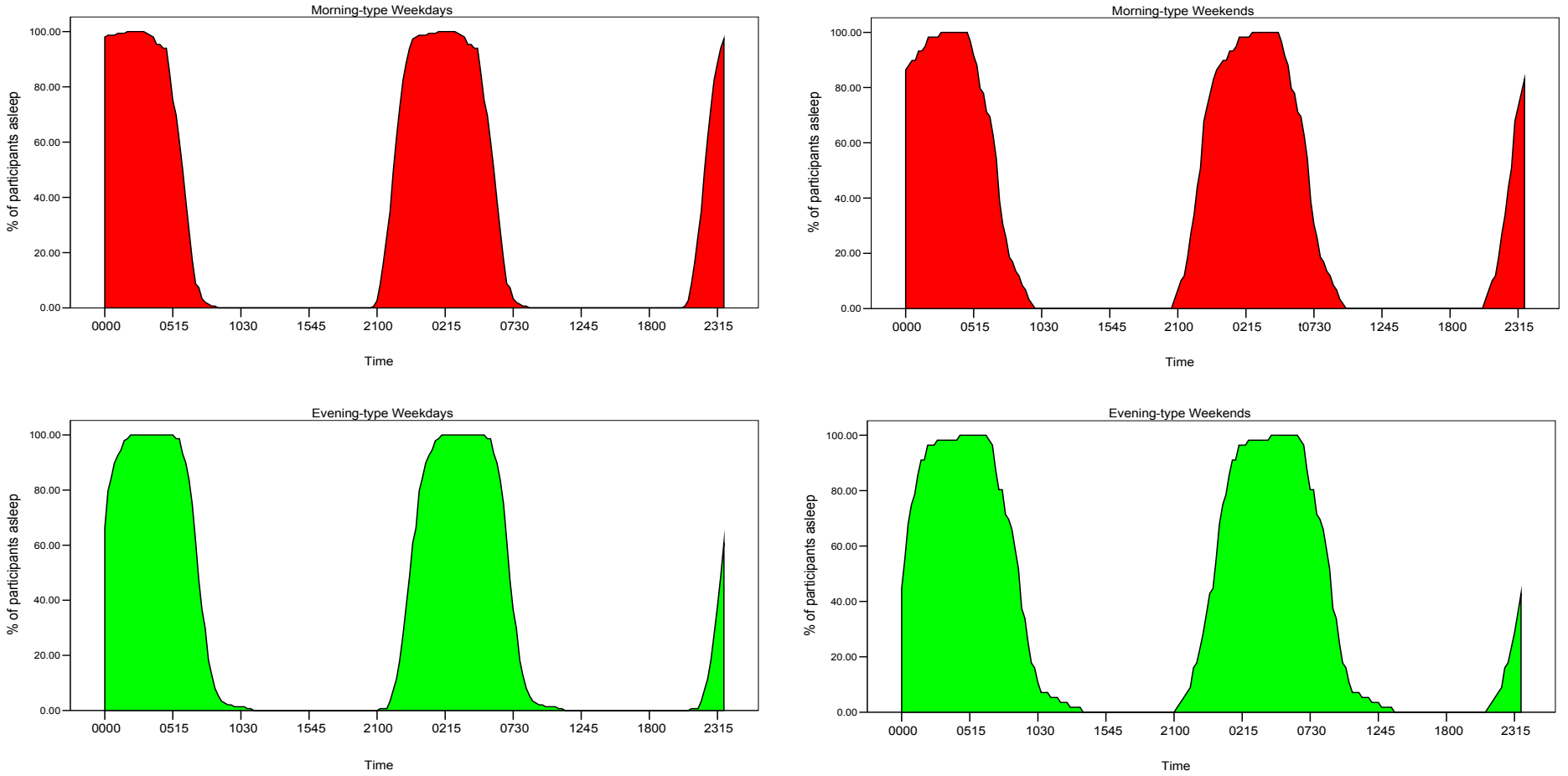


Figure 4.2 Who's asleep?

Overall cumulative percentage of morning- (red) and evening-types (green) asleep on weekdays (left panel) and weekends (right panel)

Table 4.3 Descriptive statistics for the sleep timing variables for morning- and evening-types

Sleep parameter	Chronotype	Descriptive Statistics				
		Mean (hrs:mins)	*SD*	*Median (hrs:mins)*	*Range*	*n*
Bedtime	M	22:35	0.953	22:30	20:41-02:26	212
	E	23:40	1.001	23:42	21:04-02:46	204
Sleep Start Time	M	22:41	0.966	22:35	20:53-02:55	208
	E	23:55	1.068	23:54	21:20-04:34	204
Get Up Time	M	6:27	1.080	6:24	03:45-10:07	212
	E	7:54	1.342	7:35	05:24-14:08	204
Sleep End Time	M	6:16	1.134	6:15	03:00-09:52	208
	E	7:47	1.344	7:27	05:24-13:54	204

Table 4.4 Descriptive statistics for the sleep timing variables on weekdays and weekends for morning- and evening-types

Sleep parameter	**Chronotype**	**Weekdays**					**Weekends**				
		Mean (hrs:mins)	*SD*	*Median (hrs:mins)*	*Range*	*n*	*Mean (hrs:mins)*	*SD*	*Median (hrs:mins)*	*Range*	*n*
Bedtime	M	22:27	0.795	22:26	20:47-01:50	152	22:55	1.210	22:53	20:41-02:26	60
	E	23:33	0.879	23:35	21:04-0200	148	0:00	1.219	0:14	21:08-02:46	56
Get Up Time	M	6:09	0.84	6:06	03:45-08:45	152	7:15	1.210	7:09	04:52-10:07	60
	E	7:26	0.868	7:23	05:24-11:34	148	9:11	1.541	9:08	07:00-14:08	56
Sleep Start Time	M	22:33	0.798	22:30	20:59-01:56	149	23:02	1.241	22:58	20:53-02:55	59
	E	23:49	0.913	23:49	21:25-02:05	148	0:13	1.364	0:27	21:20-04:34	56
Sleep End Time	M	5:57	0.930	6:01	03:00-08:42	149	7:03	1.240	7:02	04:52-09:52	59
	E	7:19	1.480	7:09	05:24:11:16	148	9:02	1.480	9:03	06:41-13:54	56

Table 4.5 Bed Time: univariate associations with chronotype, age group, caring for dependents and weekday versus weekends.

	Bed Time		Kruskal-Wallis Test		
	Median (hrs:mins)	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	22:18	1.15			
E	23:25	1.42	110.68	1	<0.0001
Age group (yrs)					
30-39	23:18	1.63			
40-49	22:52	5.75	17.43	1	<0.0001
Caring for dependents					
Any	22:52	1.53			
None	23:11	1.55	8.15	1	0.0043
Weekday/Weekends					
Weekdays	22:54	1.42			
Weekends	23:16	1.96	10.01	1	0.0016

Table 4.6 Sleep Start Time: univariate associations with chronotype, age group, caring for dependants and weekdays versus weekends

	Sleep Start Time		Kruskal-Wallis Test		
	Median (hrs:mins)	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	22:35	1.17			
E	23:54	1.42	127.33	1	<0.0001
Age group (yrs)					
30-39	23:28	1.69			
40-49	23:03	1.55	15.20	1	<0.0001
Caring for dependents					
Any	23:02	1.59			
None	23:18	1.75	7.71	1	0.0055
Weekday/Weekends					
Weekdays	23:07	1.57			
Weekends	23:23	2.00	7.07	1	0.0079

Table 4.7 Get Up Time: univariate associations with chronotype, age group, caring for dependants and weekdays versus weekends

	Get Up Time		Kruskal-Wallis Test		
	Median (hrs:mins)	*IQR*	*χ2*	*df*	*p*-value
Chronotype					
M	6:24	1.33			
E	7:35	1.43	134.821	1	<0.0001
Age group (yrs)					
30-39	7:23	1.55			
40-49	6:45	1.65	45.153	1	<0.0001
Caring for dependents					
Any	7:03	1.13			
None	7:02	1.95			NS
Weekday/Weekends					
Weekdays	6:48	1.42			
Weekends	7:54	2.15	67.32	1	<0.0001

Table 4.8 Sleep End Time: univariate associations with chronotype, age group, caring for dependants and weekdays versus weekends

	Sleep End Time		Kruskal-Wallis Test		
	Median (hrs:mins)	*IQR*	*χ2*	*df*	*p*-value
Chronotype					
M	6:15	1.37			
E	7:27	1.57	129.704	1	<0.0001
Age group (yrs)					
30-39	7:12	1.48			
40-49	6:36	1.98	37.548	1	<0.0001
Caring for dependents					
Any	6:53	1.26			
None	6:53	1.93			NS
Weekday/Weekends					
Weekdays	6:40	1.39			
Weekends	7:46	2.13	62.795	1	<0.0001

A series of mixed model ANCOVAs were used to determine whether the timing of the main night sleep episodes differed significantly by chronotype (M- vs. E-type), age group (30-39yrs vs. 40-49yrs), caring for dependants (any vs. none) or weekdays versus weekends. The steps used to improve the normality of the data are indicated in Table 4.9 (i.e. applying common transformations or removing outliers).

Table 4.9 Data transformations: Sleep timing variables

Dependent Variable	Data Transformations	Number of Outliers Removed
Bed Time	SQRT	1
Sleep Start Time	SQRT	2
Get Up Time	Log10	2
Sleep End Time	SQRT	2

The results of the mixed model ANCOVAs indicated that bed times differed significantly between chronotypes, with E-types going to bed 1.08hrs later than M-types (p <0.0001). Similarly, evening-types also had significantly later sleep start times (difference between E- and M-types = 1.22hrs) (Table 4.10).

The mixed model analyses also identified a significant interaction effect between chronotype (morning- vs. evening-types) and weekdays vs. weekends. Post-hoc tests indicated that all combinations of the interaction effect were significant. Thus, using the appropriate data from the coefficient matrix for least squares means, separate *t*-tests were calculated for the appropriate comparisons (see Appendix 20).

Figure 4.3 illustrates that bed times and sleep start times were significantly later on weekends than on weekdays for both morning- and evening-type individuals (p < 0.001 for both). When weekday main night sleep episodes were considered, E-types went to bed 1.07hrs later than M-types, while on weekends E-types went to bed 1.10hrs later than M-types. Similarly, compared to M-types, E-types had a later sleep start time on weekdays and weekends (1.25hr and 1.19hrs respectively, p <0.0001 for both).

The results of the mixed model also indicated that sleep end times were significantly later among E-types compared to M-types (estimated difference=1.60hrs, p <0.0001), as were get up times (estimated difference=1.49hrs, p <0.0001). There was also a significant main effect of age group identified in these analyses, with SlpEnd (estimated difference=0.76hrs, p =0.0043) and GUT (estimated difference=0.83hrs, p =0.001) significantly later among participants aged 30-39yrs (Table 4.10).

Again, mixed model ANCOVAs identified a significant interaction effect of chronotype and weekday/weekend sleep for GUT and SlpEnd (Appendix 20). Both chronotypes had later rising

and sleep offset times on the weekend, compared to the weekday. However, on the weekend evening-types finished sleep and got out of bed significantly later than morning-types.

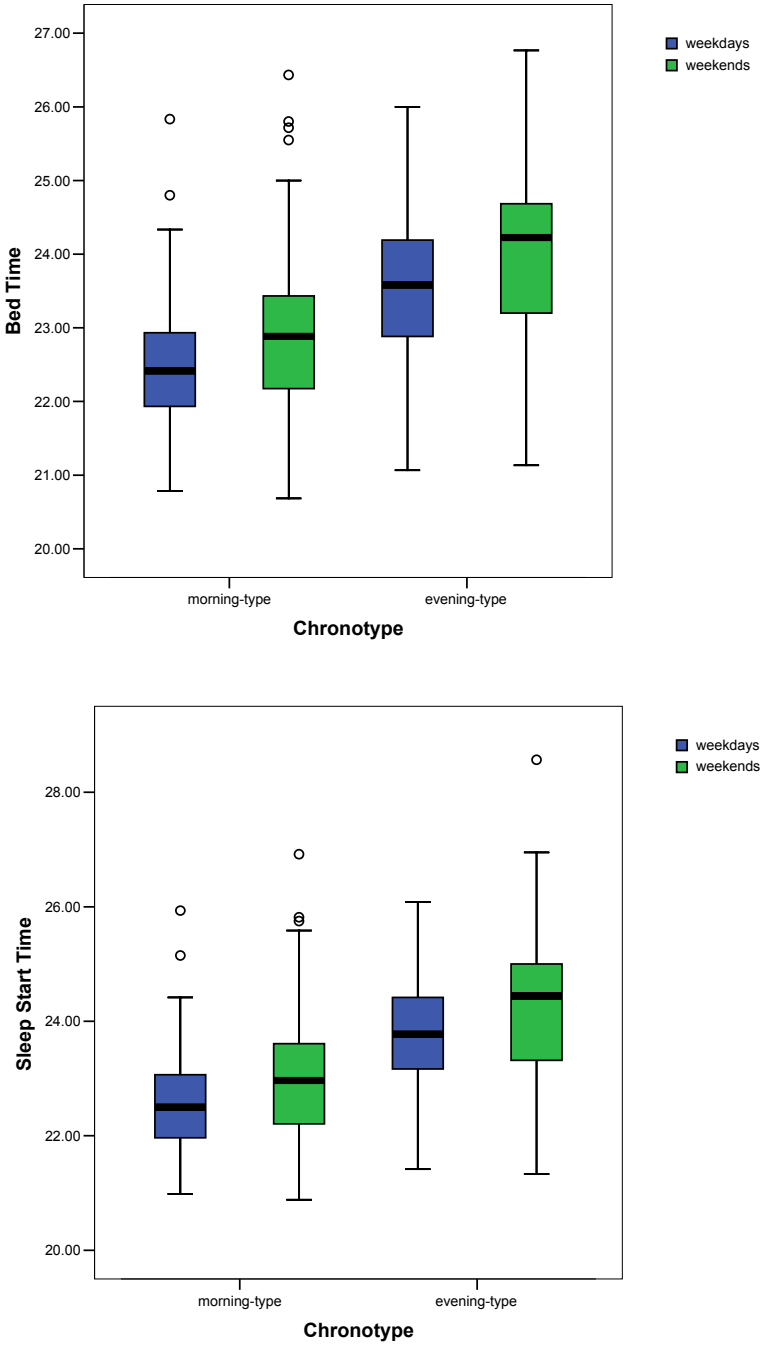


Figure 4.3 Median bed times and sleep start times among morning- and evening-types

The median, inter-quartile range and range of bed times (top panel) and sleep start times (bottom panel) on weekdays (blue) and weekends (green) are presented for morning- and evening-types.

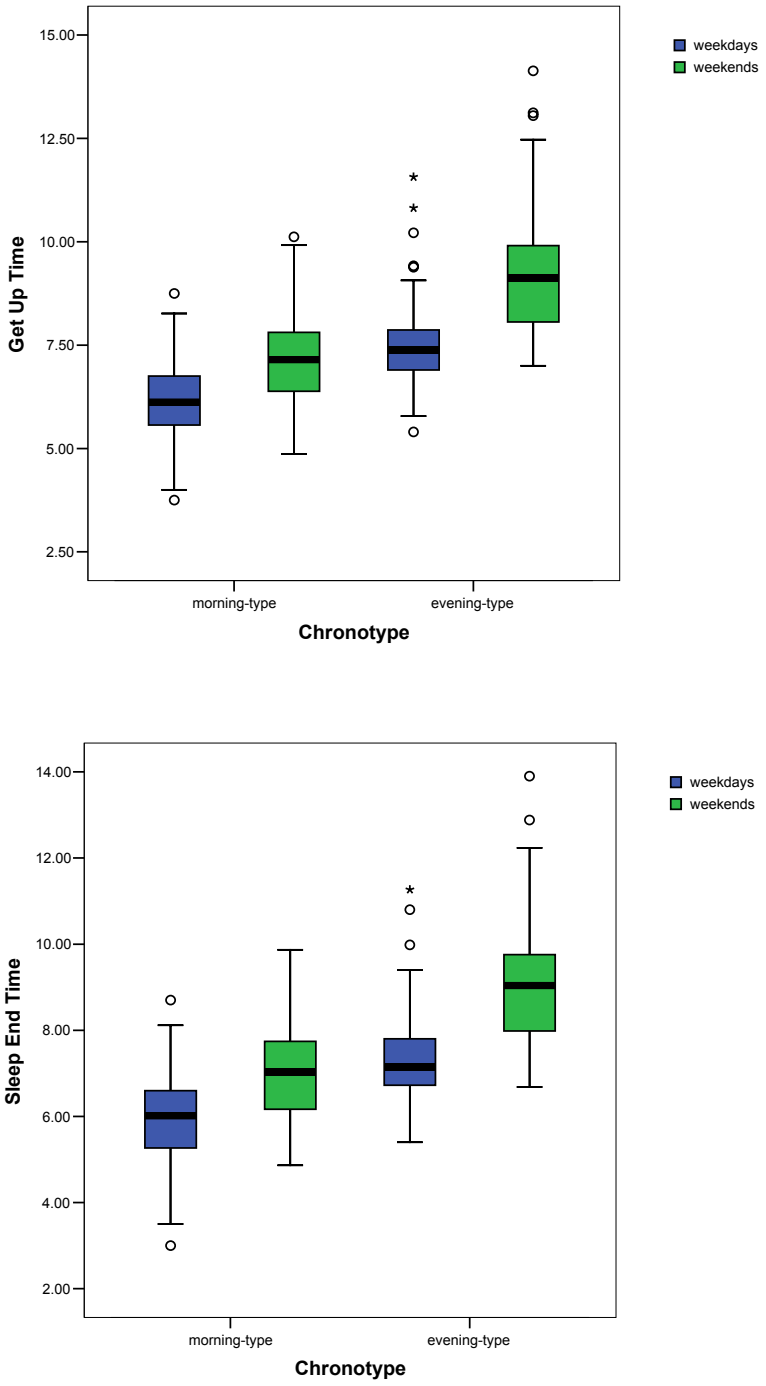


Figure 4.4 Median get up times and sleep end times among morning- and evening-types

The median, inter-quartile range and range of get up times (top panel) and sleep end times (bottom panel) on weekdays (blue) and weekends (green) are presented for morning- and evening-types.

Table 4.10 Details and results of mixed model ANCOVAs for the sleep timing parameters of main night sleep episodes

Dependent variable	Fixed and Interaction Effects in the Mixed Model[a]	Significant Main Effects		Significant Interaction Effects	
Bed Time	ME, Age group, Dependents, ME*Weekday	ME	$F_{(1, 28.9)} = 26.56$, $p < 0.0001$	ME*Weekday	$F_{(2, 382)} = 11.93$, $p < 0.0001$
Sleep Start Time	As above	ME	$F_{(1, 28.6)} = 29.32$, $p < 0.0001$	ME*Weekday	$F_{(2, 377)} = 8.99$, $p = 0.0002$
Get Up Time	As above	ME	$F_{(1, 28.3)} = 43.83$, $p < 0.0001$		
		Age group	$F_{(1, 26.7)} = 13.54$, $p = 0.0010$	ME*Weekday	$F_{(2, 381)} = 131.64$, $p < 0.0001$
Sleep End Time	As above	ME	$F_{(1, 28.2)} = 43.18$, $p < 0.0001$		
		Age group	$F_{(1, 26.6)} = 9.77$, $p = 0.0043$	ME*Weekday	$F_{(2, 377)} = 124.98$, $p < 0.0001$

Note. [a] ME = M- vs. E-types. Age group = 30-39yrs. vs. 40-49yrs. Dependants = any dependants vs. none. Weekday = weekdays (Sun-Thurs nights) vs. weekends (Fri and Sat nights)

4.3.3 The Duration of the Main Night Sleep Episode, Comparing Self-Identified Morning- and Evening-Types

The specific sleep parameters of interest were Time in Bed (TIB), Assumed Sleep Time (AssSlp), and Actual Sleep Time (ActSlp). There were four missing cases in the analyses of assumed sleep time and actual sleep time because only sleep dairy information was available for those main night sleep periods. Therefore, 416 main sleep episodes were analysed for time in bed and 412 main sleep episodes were analysed for assumed sleep and actual sleep variables.

Descriptive statistics for each sleep duration parameter by chronotype can be found in Table 4.11, while Table 4.12 presents descriptive information for the sleep duration parameters comparing weekday and weekend main night sleep episodes.

Univariate relationships between the sleep duration parameters on main night sleep episodes and chronotype, age group, caring for dependants and weekday/weekends are presented in Table 4.13 (TIB), Table 4.14 (AssSlp) and Table 4.15 (ActSlp). The median length of time in bed was associated with chronotype (K-W p =0.0264), age group (K-W p <0.0001) and day of the week (K-W p <0.0001), while both assumed sleep and actual sleep time were associated with age group (K-W p =0.0005 and p =0.01 respectively), caring for dependants (K-W p =0.0585 and p =0.0023 respectively) and day of the week (K-W p <0.0001 for both).

Table 4.11 Descriptive statistics for the sleep duration variables for morning- and evening-types

Sleep parameter	**Chronotype**	**Descriptive Statistics**				
		Mean (hrs)	*SD*	*Median (hrs)*	*Range*	*n*
Time in Bed	M	7.87	1.19	7.86	4.67-11.10	212
	E	8.24	1.68	7.98	6.03-13.50	204
Assumed Sleep Time	M	7.58	1.25	7.57	4.33-10.88	208
	E	7.86	1.27	7.65	5.53-13.27	204
Actual Sleep Time	M	6.69	1.09	6.72	3.43-9.72	208
	E	6.91	1.20	6.85	4.78-11.00	204

Table 4.12 Descriptive statistics for the sleep duration variables on weekdays and weekends for morning- and evening-types

Sleep parameter	Chronotype	Weekdays					Weekends				
		Mean (hrs)	*SD*	*Median (hrs)*	*Range*	*n*	*Mean (hrs)*	*SD*	*Median (hrs)*	*Range*	*n*
Time in Bed	M	7.69	1.08	7.76	4.67-9.82	152	8.32	1.34	8.17	5.58-11.10	60
	E	7.88	1.02	7.84	6.03-12.23	148	9.18	1.47	9.09	6.27-13.50	56
Assumed Sleep Time	M	7.40	1.14	7.48	4.33-9.78	149	8.02	1.42	7.78	5.20-10.88	59
	E	7.50	1.01	7.40	5.53-11.73	148	8.81	1.41	8.63	6.17-13.27	56
Actual Sleep Time	M	6.57	1.04	6.70	3.43-9.72	149	6.99	1.17	6.77	4.55-9.38	59
	E	6.62	0.99	6.52	4.78-9.93	148	7.69	1.38	7.83	5.08-11.00	56

Table 4.13 Time in Bed: univariate associations with chronotype, age group, caring for dependents and weekdays versus weekends

	Time in Bed (hrs)		Kruskal-Wallis Test		
	Median (hrs)	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	7.85	1.59			
E	7.98	1.66	4.927	1	0.0264
Age group (yrs)					
30-39	8.28	1.69			
40-49	7.80	1.53	15.629	1	<0.0001
Caring for dependents					
Any	7.93	0.173			
None	7.95	1.63			NS
Weekdays/Weekends					
Weekdays	7.80	1.48			
Weekends	7.63	2.36	36.951	1	<0.0001

Table 4.14 Assumed Sleep Time: univariate associations with chronotype, age group, caring for dependents and weekdays versus weekends

	Assumed Sleep Time (hrs)		Kruskal-Wallis Test		
	Median (hrs)	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	7.65	1.61			
E	7.57	1.61			NS
Age group (yrs)					
30-39	7.87	1.54			
40-49	7.40	1.53	12.176	1	0.0005
Caring for dependents					
Any	7.55	1.67			
None	7.70	1.48	3.582	1	0.0585
Weekdays/Weekends					
Weekdays	7.32	2.30			
Weekends	7.45	1.42	37.081	1	<0.0001

Table 4.15 Actual Sleep Time: univariate association with chronotype, age group, caring for dependents and weekdays versus weekends

	Actual Sleep Time (hrs)		Kruskal-Wallis Test		
	Median (hrs)	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	6.85	1.75			
E	6.72	1.36			NS
Age group (yrs)					
30-39	6.98	1.57			
40-49	6.62	1.45	6.559	1	0.0104
Caring for dependents					
Any	6.50	1.77			
None	6.93	1.23	9.281	1	0.0023
Weekdays/Weekends					
Weekdays	6.62	1.52			
Weekends	7.20	1.90	25.544	1	<0.0001

Differences in the duration of the main night sleep episode by chronotype, age group, caring for dependents and weekday/weekends were investigated using mixed model ANCOVAs. A recent study using the activity monitors described here found that actigraphic measures of assumed sleep significantly overestimated sleep duration compared to PSG measures of sleep duration (Signal et al., 2004a). Thus, it was decided that mixed model analyses would only be carried out using the sleep duration parameters of time in bed and actual sleep time (see Table 4.16 for details of data transformations). The results of these models are presented in Table 4.17.

Table 4.16 Data transformations: Sleep duration variables

Dependent Variable	Data Transformations	Number of Outliers Removed
Time in Bed	SQRT	Nil
Actual Sleep Time	Nil	Nil

The length of time in bed was significantly different between younger and older aged adults in this study, with participants aged 30-39yrs spending 31 minutes longer in bed than those aged 40-49yrs. There were no significant main effects of chronotype, or caring for dependents. In addition, mean actual sleep times did not differ significantly by chronotype, age group, or caring for dependents.

The mixed model analyses identified a significant interaction between chronotype and weekday/weekend main night sleep episodes for both sleep duration parameters. Post-hoc tests were carried out to identify which combinations of factors were significantly different from each other and the full details of these tests are presented in Appendix 21.

Figure 4.5 illustrates the differences in sleep duration on weekdays vs. weekends comparing M- and E-types. The pattern for longer sleep durations on Friday and Saturday nights is clear, particularly among the evening-type participants. However, when chronotypes were compared, there was a significant difference of sleep durations on weekends, but not on weekdays.

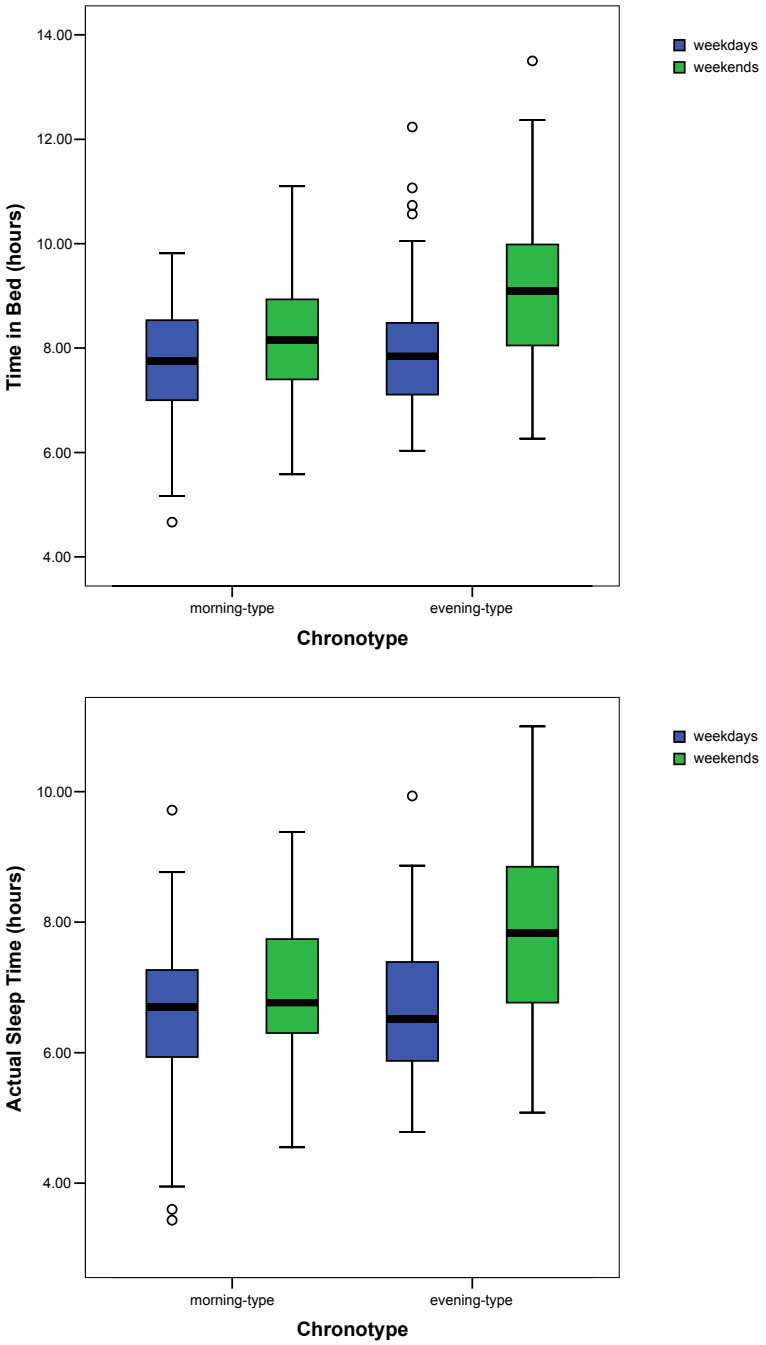


Figure 4.5 Median time in bed and actual sleep times among morning- and evening-types

The median, inter-quartile range and range for time in bed (top panel) and actual sleep times (bottom panel) on weekdays (blue) and weekends (green) are presented for morning- and evening-types.

Table 4.17 Details and results of mixed model ANCOVAs for the sleep duraiton parameters of main night sleep episodes

Dependent variable	Fixed and Interaction Effects in the Mixed Model[a]	Significant Main Effects		Significant Interaction Effects	
Time in Bed	ME, Age group, Dependents, ME*Weekday	Age group	$F_{(1, 26.8)} = 4.58$, $p = 0.0417$	ME*Weekday	$F_{(2, 383)} = 39.76$, $p < 0.0001$
Actual Sleep Time	As above			ME*Weekday	$F_{(2, 379)} = 37.87$, $p < 0.0001$

Note. [a] ME = M- vs. E-types. Age group = 30-39yrs. vs. 40-49yrs. Dependants = any dependants vs. none. Weekday = weekdays (Sun-Thurs nights) vs. weekends (Fri and Sat nights)

4.3.4 The Quality of the Main Night Sleep Episode, Comparing Self-Identified Morning- and Evening-Types

In these analyses the specific sleep parameters of interest were Actual Sleep Time Percentage (ActSlpP), Sleep Efficiency (SlpEff), and Mean Activity Score (MActSc) and the Movement and Fragmentation Index (FragIn). There were four missing cases in the analyses because only sleep dairy information was available for those main night sleep periods, so a total of 412 main sleep episodes were analysed in this section.

Descriptive data for the sleep quality variables are presented in Table 4.18 while Table 4.19 compares the data by weekday vs. weekends.

Each of the sleep quality measures showed significant univariate relationships with age group and caring for dependants (all K-W p <0.05). In addition there was a small but significant relationship between mean activity score and day of the week (K-W p =0.006).

Table 4.18 Descriptive statistics for the sleep quality variables for morning- and evening-types

Sleep parameter	Chronotype	Descriptive Statistics				
		Mean	*SD*	*Median*	*Range*	*n*
Actual Sleep Time Percentage	M	88.38	4.59	89.10	72.40-99.50	208
	E	87.98	6.32	89.05	61.00-97.90	204
Sleep Efficiency	M	85.08	6.13	86.40	63.00-99.50	208
	E	84.05	7.92	84.55	53.40-97.00	204
Mean Activity Score	M	14.02	7.72	12.23	0.56-53.24	208
	E	14.50	9.94	11.59	2.19-70.61	204
Movement and Fragmentation Index	M	28.24	12.14	26.30	5.00-71.00	208
	E	27.34	12.52	25.65	5.00-71.50	204

Table 4.19 Descriptive statistics for the sleep quality variables on weekdays and weekends for morning- and evening-types

Sleep parameter	**Chronotype**	**Weekdays**					**Weekends**				
		Mean	*SD*	*Median*	*Range*	*n*	*Mean*	*SD*	*Median*	*Range*	*n*
Actual Sleep Time Percentage	M	88.72	4.29	89.10	75.40-99.50	149	87.82	5.22	88.90	72.40-94.90	59
	E	88.29	5.95	89.60	71.50-97.80	148	87.18	7.19	88.35	61.00-97.90	56
Sleep Efficiency	M	85.42	6.20	86.60	63.00-99.50	149	84.22	5.92	85.70	65.30-92.90	59
	E	84.09	7.37	84.15	61.50-95.90	148	83.97	9.30	85.55	56.40-97.00	56
Mean Activity Score	M	13.15	6.54	11.85	0.56-39.62	149	16.20	9.82	13.09	04.52-53.24	59
	E	13.85	8.38	11.42	2.19-44.43	148	16.23	13.15	12.93	2.51-70.61	56
Movement and Fragmentation Index	M	27.20	11.10	25.70	5.00-57.80	149	30.86	14.20	27.20	11.40-71.00	59
	E	26.81	12.33	25.85	5.00-71.50	148	28.75	13.03	25.15	5.20-66.90	56

Table 4.20 Actual sleep time percentage: univariate associations with chronotype, age group, caring for dependents and weekdays versus weekends

	Actual Sleep Time Percentage		Kruskal-Wallis Test		
	Median	*IQR*	*χ2*	*df*	*p*-value
Chronotype					
M	89.10	5.20			
E	89.05	9.70			NS
Age group (yrs)					
30-39	88.40	7.80			
40-49	89.40	7.30	7.72	1.00	0.0055
Caring for dependents					
Any	90.00	5.10			
None	87.70	8.90	12.01	1.00	0.0005
Weekday/Weekends					
Weekdays	89.40	6.90			
Weekends	88.70	7.80			NS

Table 4.21 Sleep efficiency: univariate associations with chronotype, age group, caring for dependents and weekdays versus weekends

	Sleep Efficiency		Kruskal-Wallis Test		
	Median	*IQR*	*χ2*	*df*	*p*-value
Chronotype					
M	86.40	6.50			
E	84.55	11.40			NS
Age group (yrs)					
30-39	84.40	9.40			
40-49	86.60	8.90	6.19	1.00	0.0128
Caring for dependents					
Any	87.10	6.35			
None	83.70	11.60	19.74	1.00	<0.0001
Weekday/Weekends					
Weekdays	85.70	8.90			
Weekends	85.80	8.85			NS

Table 4.22 Mean activity score: univariate associations with chronotype, age group, caring for dependents and weekdays versus weekends

	Mean Activity Score		Kruskal-Wallis Test		
	Median	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	12.23	7.87			
E	11.59	12.18			NS
Age group (yrs)					
30-39	13.41	11.03			
40-49	11.31	9.38	4.80	1.00	0.0285
Caring for dependents					
Any	10.92	6.74			
None	14.31	12.43	10.18	1.00	0.0014
Weekday/Weekends					
Weekdays	13.09	12.20			
Weekends	11.60	9.33	3.66	1.00	0.01

Table 4.23 Movement and fragmentation index: univariate associations with chronotype, age group, caring for dependents and weekdays versus weekends

	Movement and Fragmentation Index		Kruskal-Wallis Test		
	Median	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	26.65	16.50			
E	26.30	14.60			NS
Age group (yrs)					
30-39	28.00	15.80			
40-49	24.70	16.30	9.17	1.00	0.002
Caring for dependents					
Any	23.90	11.70			
None	29.50	18.20	28.93	1.00	<0.0001
Weekday/Weekends					
Weekdays	26.40	16.80			
Weekends	25.80	15.70			NS

Table 4.25 presents the details and results of a series mixed model analyses which were used to investigate whether actigraphically determined sleep quality differed by chronotype, age, caring for dependants or weekday/weekend sleep. The construction of the models is described in Table 4.24.

Table 4.24 Data transformations: Sleep quality variables

Dependent Variable	Data Transformations	Number of Outliers Removed
Actual Sleep Percentage	Reflect SQRT	Nil
Sleep Efficiency	Reflect SQRT	Nil
Mean Activity Score	Log10	Nil
Movement and Fragmentation Index	SQRT	Nil

In the present study, poorer sleep quality, as measured by a higher movement and fragmentation index, was significantly more likely among those who reported caring for dependants, compared to those who did not (p <0.05).

The change in the mean values for MActSc and the median FragIn between weekdays and weekends is shown in Figure 4.6 and Figure 4.7 respectively. For both chronotypes, there is a pattern for increasing mean activity scores on weekends compared to weekdays. However the pattern is different between morning- and evening-types, when the movement and fragmentation index is considered. Among M-types, median FragIn values are greater on Friday and Saturday nights, however the opposite is seen for E-types, who have lower median values on the weekend. Post-hoc *t*-tests confirmed a significant difference between weekday and weekend sleep quality among morning-types, however all other comparison of interest did not reach significance (see Appendix 22).

There were no significant main or interaction effects detected in the models for ActSlpP or Sleep Efficiency.

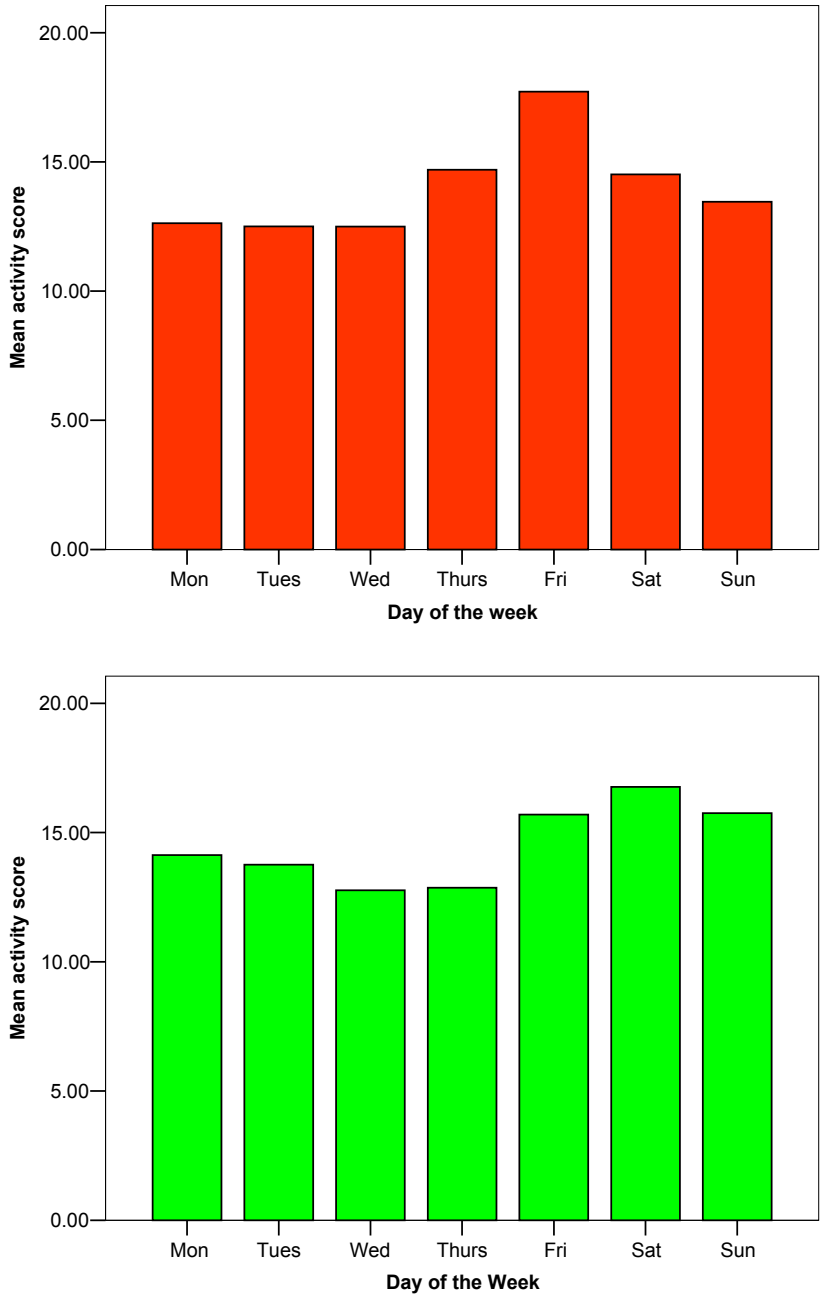


Figure 4.6 Changes in the average mean activity score across the week for morning- (red) and evening-types (green).

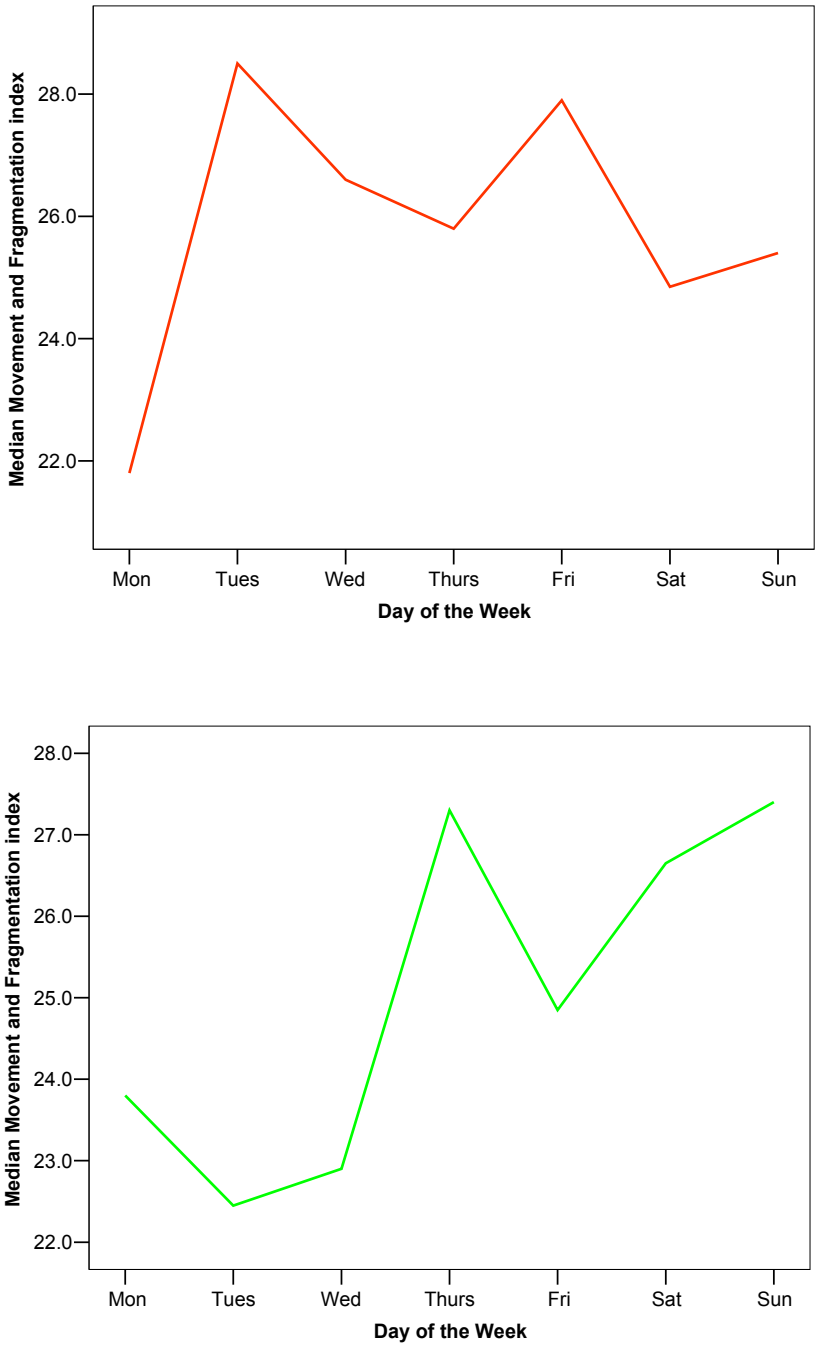


Figure 4.7 Changes in the median movement and fragmentation index across the week for morning- (red) and evening-types (green)

Table 4.25 Details and results of mixed model ANCOVAs for the sleep quality parameters of the main night sleep episode

Dependent variable	Fixed and Interaction Effects in the Mixed Model[a]	Significant Main Effects		Significant Interaction Effects	
Actual Sleep Time Percentage	ME, Age group, Dependents, ME*Weekday				
Sleep Efficiency	As above				
Mean Activity Score	As above			ME*Weekday	$F_{(2, 379)} = 4.66$, p=0.0100
Movement and Fragmentation Index	As above	Dependants	$F_{(1, 27)} = 4.29$, p=0.0479	ME*Weekday	$F_{(2, 379)} = 3.35$, p=0.0361

Note. [a] ME = M- vs. E-types. Age group = 30-39yrs. vs. 40-49yrs. Dependants = any dependants vs. none. Weekday = weekdays (Sun-Thurs nights) vs. weekends (Fri and Sat nights)

4.3.5 Differences in Total Sleep Duration Between Morning- and Evening-Types

Total sleep durations per 24-hours were calculated by combining all sleep episodes between midday on one day and midday on the following day. Of those variables that were created using this method of summing sleep, the parameters of interest presented in this section were total sleep duration parameters of total time in bed (TTiB), total assumed sleep time (TAssSlp) and total actual sleep time (TActSlp). A total of 419 sleep episodes were included in the analysis of total time in bed. There were four missing cases for the analyses on TAssSlp and TActSlp, as there were no actigraphic recordings on these days. Therefore these analyses included a total of 415 sleep episodes.

Table 4.26 and Table 4.27 present the mean, standard deviation, median and range of values for total time in bed, total assumed sleep time and total actual sleep time by chronotype and weekday/weekends respectively. In general, evening-type participants had longer sleep durations compared to morning-types. However, morning-types showed greater variability in total sleep duration, for all sleep parameters. There was also a general pattern for longer sleep durations on the weekends, for both chronotypes.

Table 4.26 Descriptive statistics for the total sleep duration parameters for morning- and evening-types

Sleep parameter	**Chronotype**	**Descriptive Statistics**				
		Mean (hrs)	*SD*	*Median (hrs)*	*Range*	*n*
Total Time in Bed	M	7.90	1.24	7.83	4.67-13.62	212
	E	8.31	1.38	8.00	5.08-13.53	207
Total Assumed Sleep Time	M	7.58	1.26	7.55	4.48-13.02	208
	E	7.93	1.34	7.68	4.42-11.73	207
Total Actual Sleep Time	M	6.69	1.12	6.70	3.60-10.73	208
	E	6.94	1.21	6.95	4.18-10.43	207

Table 4.27 Descriptive statistics for the total sleep duration parameters on weekdays and weekends for morning- and evening-types

Sleep parameter	Chronotype	Weekdays					Weekends				
		Mean (hrs)	*SD*	*Median (hrs)*	*Range*	*n*	*Mean (hrs)*	*SD*	*Median (hrs)*	*Range*	*n*
Total Time in Bed	M-type	7.72	1.06	7.76	4.67-9.82	152	8.36	1.51	8.08	5.60-13.62	60
	E-type	7.02	1.19	7.88	5.08-13.53	149	9.08	1.56	9.21	5.52-11.97	58
Total Assumed Sleep Time	M-type	7.42	1.12	7.45	4.48-9.78	149	8.00	1.49	7.77	5.20-13.02	59
	E-type	7.62	1.09	7.52	4.97-11.73	149	8.73	1.56	8.65	4.42-11.70	58
Total Actual Sleep Time	M-type	6.57	1.04	6.67	3.60-9.73	149	7.00	1.26	6.72	4.55-10.73	59
	E-type	6.70	1.00	6.73	4.75-9.93	149	7.56	1.45	7.41	4.18-10.43	58

As suggested in the tables below, chronotype was significantly associated with TTiB (Table 4.28), TAssSlp (Table 4.29), and TActSlp (Table 4.30). Age-group (30-39yrs vs. 40-49yrs) and weekdays vs. weekends were significantly associated with TAssSlp and TActSlp, whereas caring for dependants was only associated with TActSlp at the univariate level.

Table 4.28 Total Time in Bed: univariate associations with chronotype, age group, caring for dependents and weekdays/weekends

	Total Time in Bed		**Kruskal-Wallis Test**		
	Median (hrs)	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	7.50	1.34			
E	8.00	1.86	7.491	1	0.0062
Age group (yrs)					
30-39	8.21	1.84			
40-49	7.47	1.39	18.089	1	<0.0001
Caring for dependents					
Any	7.56	1.33			
None	7.58	1.44	0.062	1	NS
Weekdays/Weekends					
Weekdays	7.49	1.31			
Weekends	8.33	2.24	25.305	1	<0.0001

Table 4.29 Total Assumed Sleep Time: univariate associations with chronotype, age group, caring for dependents and weekdays/weekends

	Total Assumed Sleep Time		**Kruskal-Wallis Test**		
	Median (hrs)	*IQR*	χ^2	*df*	*p*-value
Chronotype					
M	7.55	1.64			
E	7.68	1.70	4.819	1	0.0281
Age group (yrs)					
30-39	7.98	1.60			
40-49	7.40	1.58	16.416	1	<0.0001
Caring for dependents					
Any	7.66	1.53			
None	7.65	1.80	0.516	1	NS
Weekdays/Weekends					
Weekdays	7.48	1.53			
Weekends	8.25	2.32	27.170	1	<0.0001

Table 4.30 Total Actual Sleep Time: univariate associations with chronotype, age group, caring for dependents and weekdays/weekends

	Total Actual Sleep Time		Kruskal-Wallis Test		
	Median (hrs)	*IQR*	$\chi 2$	*df*	*p*-value
Chronotype					
M	6.70	1.41			
E	6.95	1.75	3.146	1	0.0761
Age group (yrs)					
30-39	7.07	1.43			
40-49	6.63	1.57	8.943	1	0.0028
Caring for dependents					
Any	6.92	1.37			
None	6.72	1.73	4.173	1	0.0411
Weekdays/Weekends					
Weekdays	6.71	1.47			
Weekends	7.18	1.90	18.468	1	<0.0001

A mixed model ANCOVA was used to determine if the total amount of time in bed and actual sleep across a 24-hour period was influenced by chronotype, age group, dependants or weekdays versus weekends. As mentioned previously, the actigraphic measure of assumed sleep time correlates poorly with polysomnographically determined sleep duration and so only TTiB and TActSlp were used in these analyses, with separate models constructed for each parameter (see Table 4.31).

Table 4.31 Data transformations: Total sleep duration variables

Dependent Variable	Data Transformations	Number of Outliers Removed
Total Time in Bed	Log10	Nil
Total Actual Sleep Time	Nil	Nil

In the model for total time in bed, there was a significant main effect of age group, with participants aged 39-39yrs spending 34 minutes longer in bed than those aged 40-49yrs (p <0.05). The mixed model also identified a significant interaction effect of chronotype and weekday/weekends. As illustrated in Figure 4.8, the total amount of time spent in bed, and therefore made available for sleep, was greater on weekends compared to during the week, with morning-types spending 37 minutes longer in bed at weekends and evening-types spending 1 hour longer in bed at weekends. However, when M- and E-types were compared, there was no significant difference in weekday or weekend TTiB.

The interaction of chronotype and day of the week found in the mixed model for total actual sleep time is illustrated in Figure 4.8. As with TTiB, for both chronotypes the total amount of actual sleep was significantly greater on weekends compared to weekdays, however were no significant differences in total sleep duration between chronotypes when weekday and weekend sleep was compared.

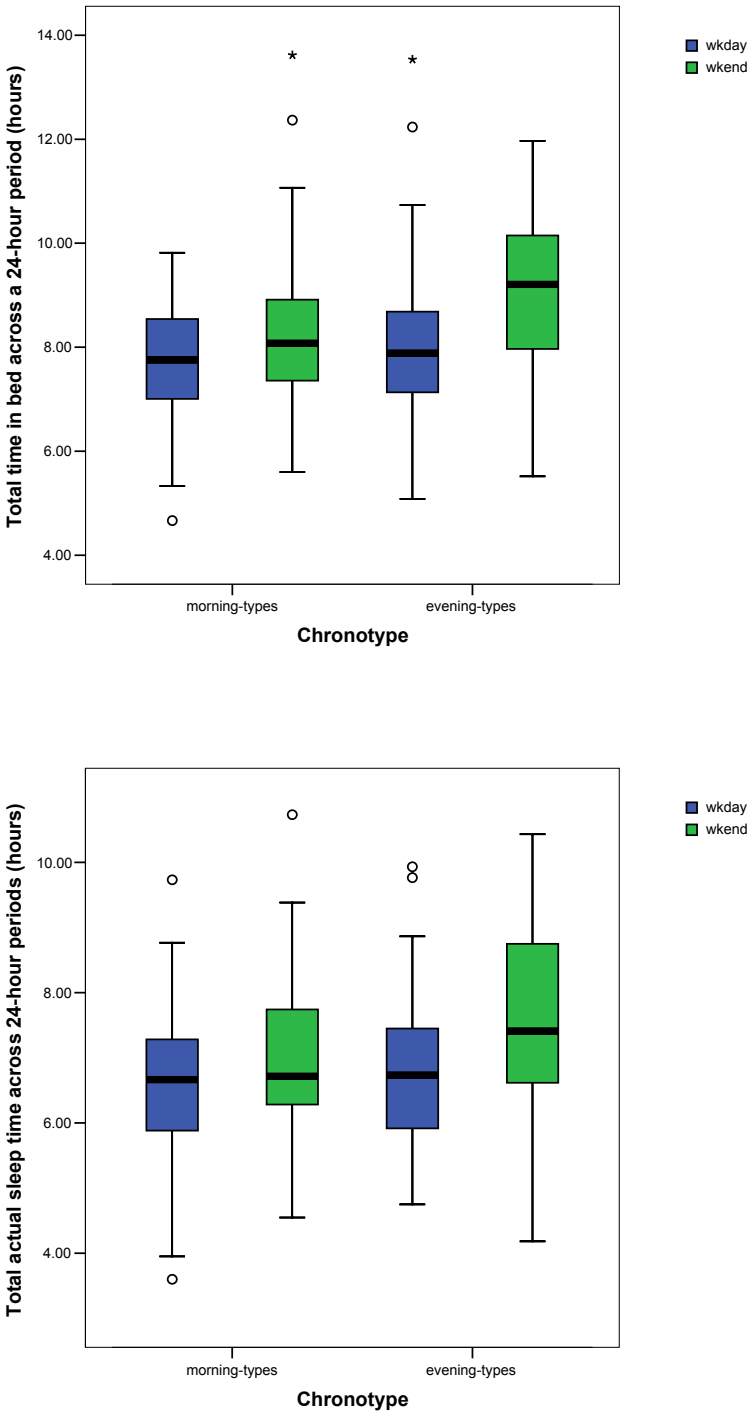


Figure 4.8 Median sleep durations across 24-hour periods for morning- and evening-types

The median, inter-quartile range and range for total time in bed (top panel) and total actual sleep times (bottom panel) on weekdays (blue) and weekends (green) are presented for morning- and evening-types.

Table 4.32 Details and results of the mixed model ANCOVAs for the sleep duration parameters across 24-hour periods

Dependent variable	Fixed and Interaction Effects in the Mixed Model[a]	Significant Main Effects		Significant Interaction Effects	
Total Time in Bed	ME, Age group, Dependents, ME*Weekday	Age group	$F_{(1, 26.8)} = 5.32$, $p = 0.0291$	ME*Weekday	$F_{(2, 386)} = 24.06$, $p < 0.0001$
Total Actual Sleep Time	As above			ME*Weekday	$F_{(2, 382)} = 22.11$, $p < 0.0001$

Note: [a] ME = M- vs. E-types; Age group = 30-39yrs. vs. 40-49yrs; Dependants = any dependants vs. none; Weekday = weekday main sleep periods vs. weekend main sleep periods

4.3.6 Differences in the Quality of Sleep Across 24-hour Periods Between Morning- and Evening-Types

The sleep parameters of interest in these analyses were total mean sleep efficiency (MSlpEff), the total mean activity score (TMActSc) and the Total Movement and Fragmentation Index (TMFragIn). There were four missing cases in these analyses because only sleep diary data was available. A total of 415 sleep periods were analysed.

Descriptive statistics for each sleep quality parameter grouped by chronotype are presented in Table 4.33, while Table 4.34 presents descriptive information for each chronotype comparing weekdays and weekends.

Kruskal-Wallis non-parametric tests found that sleep efficiency, mean activity scores and values of the movement and fragmentation index across a 24-hour period were significantly associated with age group and caring for dependants. There were no univariate relationships between the quality of the total sleep achieved and either chronotype or weekday/weekends (see Tables Table 4.35, Table 4.36, and Table 4.37).

Table 4.33 Descriptive statistics for the sleep quality parameters across 24-hour periods

Sleep parameter	**Chronotype**	**Descriptive Statistics**				
		Mean	*SD*	*Median*	*Range*	*n*
Total Mean Sleep Efficiency	M-type	85.11	6.26	86.45	61.0-100.0	208
	E-type	84.29	7.57	84.60	57.0-97.0	207
Total Mean Activity Score	M-type	13.46	6.99	12.05	0.56-50.08	208
	E-type	14.02	9.66	11.29	2.19-70.61	207
Total Movement and Fragmentation Index	M-type	27.68	11.77	25.90	5.0-71.0	208
	E-type	26.49	12.50	25.16	4.7-71.5	207

Table 4.34 Descriptive statistics for the sleep quality parameters on weekdays and weekends for morning- and evening-types

Sleep parameter	Chronotype	Weekdays					Weekends				
		Mean	*SD*	*Median*	*Range*	*n*	*Mean*	*SD*	*Median*	*Range*	*n*
Total Mean Sleep Efficiency	M-type	85.45	6.30	56.6	61.0-100.0	149	84.26	6.12	85.7	65.0-93.0	59
	E-type	84.24	7.31	84.2	62.0-96.0	149	84.42	8.26	85.55	57.0-97.0	58
Total Mean Activity Score	M-type	12.97	6.75	11.75	0.56-39.62	149	14.71	8.28	12.55	4.52-50.08	59
	E-type	13.59	8.22	11.29	2.19-44.43	149	15.13	12.66	11.24	2.51-70.61	58
Total Movement and Fragmentation Index	M-type	26.96	10.94	25.6	5.0-57.8	149	29.50	13.57	26.80	6.9-71.0	59
	E-type	26.32	12.35	25.5	4.7-71.5	149	26.93	12.98	23.70	5.2-66.9	58

Table 4.35 Total Mean Sleep Efficiency: univariate associations with chronotype, age group, caring for dependents and weekdays/weekends

	Total Sleep Efficiency		Kruskal-Wallis Test		
	median	*IQR*	*χ2*	*df*	*p*-value
Chronotype					
M	86.35	6.55			
E	84.60	11.60	1.012	1	NS
Age group (yrs)					
30-39	84.30	9.40			
40-49	85.60	8.90	6.760	1	0.0093
Caring for dependants					
Any	87.35	6.40			
None	83.70	11.80	19.577	1	<0.0001
Weekdays/Weekends					
Weekdays	85.70	9.15			
Weekends	85.80	8.90	0.240	1	NS

Table 4.36 Total Mean Activity Score: univariate associations with chronotype, age group, caring for dependents and weekdays/weekends

	Total Mean Activity Score		Kruskal-Wallis Test		
	median	*IQR*	*χ2*	*df*	*p*-value
Chronotype					
M	11.89	7.495			
E	11.29	12.09	0.419	1	NS
Age group (yrs)					
30-39	12.79	10.97			
40-49	11.21	8.71	5.887	1	0.0153
Caring for dependants					
Any	10.79	6.73			
None	14.11	11.92	11.192	1	0.0008
Weekdays/Weekends					
Weekdays	11.57	9.22			
Weekends	12.17	11.04	1.031	1	NS

Table 4.37 Total Movement and Fragmentation index: univariate associations with chronotype, age group, caring for dependents and weekdays/weekends

	Total Movement and Fragmentation Index		Kruskal-Wallis Test		
	median	*IQR*	$\chi 2$	*df*	*p*-value
Chronotype					
M	25.90	14.74			
E	25.16	16.30	0.928	1	NS
Age group (yrs)					
30-39	27.60	15.70			
40-49	24.20	16.40	11.561	1	0.0007
Caring for dependants					
Any	23.60	11.90			
None	28.50	17.30	29.529	1	<0.0001
Weekdays/Weekends					
Weekdays	25.55	15.50			
Weekends	25.40	15.88	0.443	1	NS

As for other analyses presented in this chapter, mixed model ANCOVAs were used to investigate whether the quality of all sleep episodes across a 24-hour sleep period was influenced by chronotype, age group, caring for dependants or day of the week (see Table 4.38 for model construction). However, no significant main or interaction effects were identified in any of the models.

Table 4.38 Data transformations: Sleep quality variables across 24-hour periods

Dependent Variable	Data Transformations	Number of Outliers Removed
Total Sleep Efficiency	Reflect SQRT	Nil
Total Mean Activity Score	Log10	Nil
Total Movement and Fragmentation Index	SQRT	Nil

4.4 General Summary

Q1: Does the timing of sleep differ between self-identified morning and evening-type individuals?

There was strong and consistent evidence that the timing of the main night sleep episode differs significantly between self-identified morning- and evening-type individuals who were categorised using the MEQ score cut-offs of Taillard and colleagues (2004). In support of the original hypothesis, after controlling for age and care-taking responsibilities, mixed model analyses confirmed that morning-type individuals had earlier sleep onsets and offsets than evening-types.

In addition, the present study also found that sleep timing of both chronotypes is later on the weekend (Friday and Saturday nights) compared to the rest of the week. When the weekday/weekend differences were considered, evening-types consistently demonstrated later sleep timing compared to morning-types.

Q2: Does the duration of sleep differ between self-identified morning- and evening-type individuals?

Contrary to the second hypothesis, there was no significant main effect of morningness/eveningness preference on the length of time in bed or the duration of actual sleep. However, in the analyses related to the main night sleep episodes, there was a significant interaction effect of chronotype and weekdays/weekends with *post-hoc* tests demonstrating that both morning- and evening-types spent longer in bed and spent longer sleeping on the weekends compared to weekdays. Moreover, when weekday and weekend main night sleep episodes were compared between chronotypes, E-types slept longer on weekends, but there was no significant difference in weekday sleep durations between the two groups. This might suggest that E-types used the weekend to catch-up on their sleep.

After controlling for chronotype, and care taking responsibilities there was a small but significant main effect of age group on the mean time in bed across the main night sleep episode, such that individuals aged 30-39yrs spent approximately 30 minutes longer in bed than those aged 40-49yrs.

In the present study, differences in sleep duration were also investigated by combining all sleep taken across 24-hours. After controlling for the confounding effects of age and caring for dependants, morning- and evening-types spent longer in bed on the weekends compared to weekdays, and it can be assumed that they had, or made, more time available for sleep. However, there was no difference in the mean actual sleep duration between M- and E-types.

Q3: Is there a difference in the quality of sleep obtained by self-identified morning- and evening-type individuals?

After controlling for age and chronotype, mixed model analyses found that caring for one or more dependants was significantly associated with poorer sleep as measured by greater mean activity scores and higher values on the movement and fragmentation index.

Inspection of the raw data for the main night sleep episode indicated that among morning-types there was a trend for poorer sleep (i.e. increase mean activity scores and higher values on the movement and fragmentation index) on the weekend, and conversely evening-types had poorer sleep during the week. However, after controlling for age and dependants, the only significant relationship that remained was the interaction between chronotype and day of the week, where morning-types had poorer weekend sleep, compared to their sleep across weekdays.

CHAPTER 5
CIRCADIAN PHASE DIFFERENCES BETWEEN MORNING- AND EVENING-TYPES

5.1 Tracking the Endogenous Circadian Clock

This chapter focuses on circadian phase which is used in chronobiology to describe where the circadian clock (or a marker rhythm) is up to in its cycle at a given point in time. An observable phase can be used as the hand of the clock to track its periodicity by measuring the elapsed time between occurrences of this phase marker and averaging these over successive cycles (Dawson et al., 1992). In order to evaluate changes in the position of the circadian clock, a number of techniques have been developed to accurately measure the characteristics of the overt physiological and behavioural rhythms that are driven by the circadian clock (Herman, 2005).

5.1.1 Core Body Temperature

Traditionally, the nadir of core body temperature was considered the 'gold standard' measure of circadian phase in humans. Although fluctuations in CBT are linked to normal thermoregulatory processes (Moore-Ede et al., 1982) and activity levels, the daily rhythm of CBT is under circadian control. Experimental studies (reviewed in (Heller, 2005)) have shown the persistence of normal rhythmic changes in CBT independent of muscle activity. Similarly, the circadian rhythm of CBT has been demonstrated in sleep deprivation studies.

The circadian rhythm of CBT exhibits a highly regular sinusoidal shape, reaching a maximum in the evening prior to the onset of darkness and a minimum during sleep at night (Cagnacci et al., 1992). Core body temperature was preferred over other rhythms because it can be measured at very frequent intervals (i.e. 1 minute) without disturbance (Duffy & Dijk, 2002). The rhythm of CBT is, however, modulated by a number of exogenous factors including increased activity (i.e. raised CBT) and sleep (i.e. lowered CBT). Thus, in order to tease out the circadian component in CBT rhythms, it is necessary to decrease the influence of these masking effects during experimental procedures.

One way of doing this is through the constant routine protocol (Czeisler et al., 1985) which assumes that the true amplitude and phase of the circadian clock can be determined by eliminating or controlling the influence of periodic changes in the environment and behaviour that may produce evoked effects (Dawson et al., 1992; Duffy & Dijk, 2002). During the constant routine protocol, individuals are maintained in temporal isolation and undergo enforced wakefulness across the day and night while light, posture, activity and the timing of meals are restricted to a constant minimal level (Herman, 2005). The duration of the constant routine

protocol is dependent on the variable that is being tracked, but typically the experimental procedure lasts longer than 24 hours to ensure that an entire circadian cycle is captured (Duffy & Dijk, 2002). Czeisler and colleagues (1986) illustrated the profound modulating effect of sleep and other external factors on human physiology in a study comparing the T_{min} in a healthy 66-year old woman and a group of healthy young men (n=29) under normal conditions (baseline) with a scheduled sleep episode from midnight to 0600hrs, and again during a 40-hour constant routine protocol. Examination of the CBT rhythm across the baseline night found that the woman had a rhythm not significantly different to the young men, with a T_{min} approximately halfway between bed time and wake time. However, during the constant routine protocol the T_{min} of this woman was phase advanced by 6.70 hours relative to her normal wake time (Czeisler et al., 1986), a finding that was masked by both activity and sleep during the baseline night (Czeisler & Wright, 1999).

Additional studies have confirmed that the amplitude of the CBT rhythm is also influenced by masking effects, with a larger apparent amplitude under entrained conditions compared to that under constant routine (Czeisler et al., 2005). Because the sleep episode itself (including the associated change in posture, light and activity level) masks the diurnal change in CBT, the phase marker T_{min} does not accurately reflect the circadian clock unless it is investigated under controlled conditions (Waterhouse et al., 2005).

5.1.2 Melatonin

The neurohormone melatonin (*N*-acetyl-5-methoxytryptamine) is primarily synthesised and secreted from the pineal gland which is located at the posterior end of the third ventricle (Claustrat, Brun, & Chazot, 2005; Weaver, 1999). Serotonin is derived from circulating tryptophan, and then converted to melatonin via a two-step process involving *N*-acetyltransferase (NAT) and hydoxyindole-O-methyltransferase (HIOMT)(Claustrat et al., 2005; Weaver, 1999). The mRNAs encoding the enzymes NAT and HIOMT are expressed with a day/night rhythm (Claustrat et al., 2005). In mammals melatonin secretion is driven by the SCN which imposes circadian rhythmicity onto the pineal gland via a circuitous pathway involving the sympathetic nervous system (Duffy et al., 2002; Scheer et al., 2005). This neural input signals the onset and offset of NAT activity which is the rate-limiting step in melatonin synthesis (Weaver, 1999).

The most important characteristic feature of melatonin is that it is produced and secreted in darkness with a highly regular circadian rhythm. During the subjective day, there is very little melatonin in the circulation, however with the onset of darkness, melatonin levels rise abruptly and secretion is maintained throughout the night, before levels begin to decrease prior to dawn. The changing temporal profile of melatonin secretion provides information about day length, which is the major time cue for the organisation of seasonal physiology in photoperiodic species

(Arendt, 2003, , 2005). Although the complex roles of melatonin in human physiology and disease is yet to be resolved (Claustrat et al., 2005), the circadian rhythm of melatonin plays a part in the organisation of adult circadian physiology (Arendt, 2005), perhaps acting as an endogenous synchroniser, stabilising and reinforcing other circadian rhythms and ensuring they maintain their phase relationships with each other (Claustrat et al., 2005).

Under constant routine conditions, the temporal profile of melatonin is relatively unchanged, suggesting that the circadian rhythm of melatonin is independent of the sleep/wake system (Czeisler et al., 2005; Czeisler & Klerman, 1999). However, melatonin secretion is extremely light sensitive, with as little as 2 lux reducing NAT activity by 50% in rats (Trinder et al., 1996). Light suppression of melatonin secretion is dose-dependent (Czeisler & Klerman, 1999). Although bright white light (>2500 lux) is needed to suppress the normal pattern of secretion (Arendt, 2005) even domestic intensity lighting (approx. 100 lux) can have a robust and significant suppressing effect (Zeitzer et al., 2000), a finding that may have important implications for shift workers who are exposed to artificial lighting across the night shift.

Interestingly, photic suppression of the melatonin rhythm can also occur in some blind individuals. Czeisler and colleagues (1995) measured plasma melatonin levels in sighted (n=6) and blind individuals who had no conscious light perception (n=11). Both groups exhibited the typical rhythmic patterns of decreasing CBT and increasing melatonin levels across the subjective night. On the second night of the constant routine protocol, each participant was exposed to bright light (10,000 lux) for 90-100 minutes, the timing of which coincided with the peak of the melatonin rhythm. As expected, all six sighted individuals showed decreased melatonin levels in response to the bright light stimulus. However, three of the blind individuals with no history of sleep complaints showed a similar response, with a sharp decrease in melatonin levels on exposure and a subsequent increase in levels 30-90 minutes after the end of the stimulus. This suggests that those blind individuals showing melatonin suppression are thought to still retain the RHT allowing light to affect the SCN but neurological problems further up the thalamo-cortical tracts may be the cause of blindness.

Under constant conditions, the timing of the melatonin rhythm is highly reproducible (Arendt, 2003; Benloucif et al., 2005), however the amount of melatonin secreted (amplitude) may vary considerably between individuals and by age (Waldhauser, Kovacs, & Reiter, 1998). There is a significant decline in melatonin levels across the human life span, with a steep fall occurring in the transition between childhood and adolescence, and a second moderate decline in old age (Waldhauser et al., 1998). Despite receiving considerable attention, the relationship between melatonin and ageing is still not fully understood. Several studies have reported a decrease in amplitude of the nocturnal melatonin profile with age, possibly beginning at 40 years (e.g.(Baehr et al., 2003; Carrier et al., 2002; Zhou et al., 2003)) while others have found no

significant difference in the characteristic features of the melatonin rhythm between young and old adults (Zeitzer et al., 1999).

5.1.3 Melatonin as a Circadian Phase Marker

The melatonin rhythm is argued to be the best marker of the endogenous circadian pacemaker (Arendt, 2003, , 2005; Benloucif et al., 2005; Klerman et al., 2002). In a study comparing the temporal parameters of the melatonin rhythm (onset, acrophase and offset) to T_{min} in morning- and evening-types (n=51, age range 16-32yrs), Griefahn (2002) argued that the temporal parameters of the melatonin rhythm were superior to T_{min} because:

(1) The correlation coefficients for the relationship between morningness/eveningness and melatonin parameters are considerably greater than for morningness/eveningness and T_{min}

(2) The relationship between morningness/eveningness and melatonin synthesis has greater resolving power; the temporal differences between M- and E-types are twice as large as for T_{min}.

(3) Only two known factors alter the melatonin rhythm: bright light and changes in posture.

Recently, Benloucif and colleagues (2005) reported that melatonin phase markers were more stable than estimates of T_{min} measured on two separate laboratory admissions (mean absolute difference between admissions: melatonin = 31 to 55 min; T_{min} >1.5hrs; ANOVA $p < 0.0001$). Klerman and colleagues (2002) also found that phase estimates derived from the melatonin rhythm were mathematically less variable than CBT markers. The authors explained that this variability may be a result of the different regulatory mechanisms of the endogenous rhythms; although the SCN directly controls the pineal secretion of melatonin, it may not be the principal oscillator driving the rhythm of core body temperature (Klerman et al., 2002).

Although ocular light exposure inhibits melatonin production and secretion in a dose-dependent manner (Arendt, 2005; Czeisler & Klerman, 1999; Lewy & Sack, 1989; Zeitzer et al., 2000), under dim light conditions the melatonin rhythm can be reliably measured. The nocturnal melatonin profile exhibits a square wave shape therefore onset, peak and offset are suitable candidates as makers of the circadian clock (Lewy & Sack, 1989). However, the onset of melatonin secretion (otherwise known as the dim light melatonin onset, or DLMO) is preferred for a number of reasons. Melatonin onset is theoretically least affected by any biochemical changes to the pineal gland across the night, which may alter the pattern of secretion (i.e. β-adrenergic subsensitivity in the pineal gland and the depletion of melatonin precursors) (Lewy, Cutler, & Sack, 1999). In addition, melatonin onset generally precedes sleep onset, and therefore the use of DLMO does not involve waking research participants from their sleep, nor does it require participants to stay in the laboratory for the entire night. This increases the utility of DLMO as a phase marker in field studies or for clinical and research laboratories that may not have the facilities or resources to maintain the requirements of a constant routine protocol

(Claustrat et al., 2005). Lewy et al. (1999) also suggested that any additional data points collected after DLMO may represent noise, and that the offset of melatonin secretion (DLMOff) was confounded by individual differences in amplitude, as those individuals with higher peak levels of melatonin would take longer to fall to baseline. However, Benloucif and colleagues (2005) recently reported that melatonin offset is more stable than estimates of melatonin onset. The correlations for melatonin offset markers assessed on two admissions to the research laboratory ranged from r =0.79 to r =0.82, where as correlations for onset phase markers ranged from r =0.70 to r =0.76. Furthermore, melatonin offset was more strongly associated with sleep onset and sleep offset (DLMOff50% vs. sleep offset r = 0.53; DLMOff20% vs. sleep offset r = 0.44; DLMOff20% vs. sleep onset r = 0.32; DLMOff50% vs. sleep onset r = 0.32; all p <0.01) (Benloucif et al., 2005).

The use of DLMO as the sole marker of the circadian clock also has some disadvantages. In particular, restricting the collection of melatonin samples to the first half of the night does not provide information about the amplitude or duration of melatonin secretion, potentially limiting the study outcomes. For instance, it was recently reported that the circadian clock programmes a longer biological night, evidenced by longer duration of high melatonin levels, among those who sleep more than 9 hours a night, compared to those who only sleep 6 hours per night (Aeschbach et al., 2003). Such a finding could not be replicated unless melatonin was measured across the entire night.

It has been reported that approximately 1-5% of the population have very low levels of melatonin (Waldhauser et al., 1998), and Zeitzer and colleagues (1999) presented data that indicated a greater than 10-fold variability in melatonin levels. Given the large inter-individual variability in melatonin levels, the exclusive use of DLMO as the sole marker of the circadian clock may limit the ability to determine circadian phase in some individuals.

The phase relationship between DLMO and the sleep/wake cycle has been comprehensively investigated by Martin and Eastman (2002) who used sleep diaries (verified by activity monitors) to track the sleep of 26 healthy young adults (age range 18-38yrs, unrestricted sleep schedules in the home environment) for 14 days prior to an overnight constant routine protocol to determine circadian phase. The authors reported that the timing of DLMO was approximately 2.8hrs before sleep onset and 13.7hrs after sleep offset. In addition, the parameter that best predicted DLMO was the midpoint of sleep averaged across the five days prior to the phase assessment (Monday to Friday, r =0.89, p <0.0001).

Similar results were found in a subsequent study of young adults following a fixed sleep schedule across a 7 day period, where DLMO was on average 1.98 hrs prior to average self-reported bedtime and 13.83 hrs after the average wake time. DLMO was significantly correlated with the average wake time (r =0.77, p =0.001) and the midpoint of sleep (r =0.68, p =0.001)

but not with bed time ($r = 0.36$, $p > 0.05$) (Burgess & Eastman, 2005). The authors found that the correlation between DLMO and sleep timing was more tightly associated with sleep parameters from individuals who were free to determine their sleep schedules compared with those who maintained a strict schedule based on their habitual sleep timing. More recently, Burgess and Eastman (2006) demonstrated that the timing of the melatonin rhythm may be more strongly influenced by alterations in wake time, compared to changes in bed time. In that study DLMO and DLMOff were significantly later following a two-week period of long nights (usual wake time delayed by 3 hours) compared with a two-week period of short nights (usual wake time advanced by 3 hours).

5.1.4 Definitions for the Dim Light Melatonin Onset (DLMO)

The best operational definition for DLMO remains at "the lower the level, the better the marker represents the endogenous circadian clock and the less it is influenced by differences in amplitude" (Lewy et al., 1999). The dim light melatonin onset was originally defined as the lowest level permitted by the limits of the available assay that would discriminate between daytime and night time levels (Lewy et al., 1999). At this time the proponents of DLMO proposed that a value of 10pg/ml would permit greater comparability between investigations (Lewy et al., 1999). However, other definitions for DLMO have been suggested and validated. For example, Voultsios and colleagues (1997) compared three methods of determining DLMO: (1) using 40pM as a threshold which approximated the Lewy threshold of 10pg/ml; (2) twice the average daytime concentration; and (3) two standard deviations above the baseline average. The authors found that method (1) provided good identification of DLMO using the plasma melatonin profile, however it was unable to determine DLMO from saliva samples in four out of six participants. Method (3) on the other hand identified DLMO in all but one of the participants. Voultsios and colleagues (1997) concluded that this definition was statistically superior to method (1) as it relied on melatonin levels being significantly different from baseline, and it allowed for individual differences in baseline values (Voultsios et al., 1997).

5.1.5 The Parameters of the Dim Light Melatonin Onset

Although it is less masked than many other circadian rhythms, measuring DLMO accurately requires particular experimental procedures. The current suggestion is that the intensity of background illumination during the study protocol should be < 30 lux and that absolute darkness should be avoided because it is more likely to cause an immediate phase shift in the circadian clock (Lewy et al., 1999). Similarly, individuals should be introduced to the dim light no sooner than 1 to 2 hours prior to the earliest expected melatonin onset (approx. 1700hrs) (Lewy et al., 1999) with sampling beginning no later than 1800hr (Lewy & Sack, 1989). In order to reliably capture the time of the DLMO, it is recommended that sampling occurs every 60-30 minutes (Lewy & Sack, 1989) as sampling less frequently than 30 minutes may lead to an

apparent episodic pattern of secretion (Arendt, 2005). Melatonin is readily detectable in plasma and the metabolite 6-sulfatoxymelatonin (aMT6s) is present in urine (Arendt, 2003; Bojkowski et al., 1987), however the frequent recommended sampling regime is problematic for measuring melatonin levels in these media.

Detecting melatonin in human plasma requires regular blood draws which can cause unnecessary discomfort. Blood sampling usually occurs at hourly intervals which have been sufficient to capture DLMO. Often an indwelling cannula is used which allows individuals to sleep throughout collection, however their use may require additional and often specialised staffing and research facilities. In contrast, the collection of urine samples to measure aMT6s is less invasive and the collection can be carried out by the individual in their own homes. However the sampling interval maybe < 3-4hrs across the day and longer overnight (Arendt, 2005). In addition, the collection of blood and urine samples may bring additional ethical questions and requirements for some individuals and communities.

Melatonin is also readily measurable in human saliva, however the levels of melatonin detected are much lower than in plasma, as salivary levels reflect the free plasma fraction which represents 23% of the total plasma concentration (Kennaway & Voultsios, 1998). Because of these relatively low levels, the utility of salivary melatonin was initially limited. However, recent developments in assay techniques have provided a valid and reliable method for assessing the circadian melatonin rhythm in humans (e.g. (Voultsios et al., 1997)). Saliva samples are easily collected using cotton swabs, which has increased the effectiveness of this method in field research. The sampling interval is usually 30-minutes, however unlike plasma samples, the collection requires waking the participants.

5.1.6 Research Objectives and Hypotheses

The specific objectives of the present study were:

1. *To estimate the time of the melatonin onset, peak, and offset under controlled conditions in 14 morning- and 14 evening-types.*

2. *To examine the relationship between the timing of the melatonin rhythm and self-identified morningness or eveningness.*

3. *To examine the contribution of circadian phase (as measured by the melatonin rhythm) to the variability in sleep variables, comparing morning- and evening-types.*

The relevant research hypotheses were:

1. *That there is a linear relationship between the timing of the melatonin rhythm and MEQ score.*

2. *That morning-type individuals will have significantly earlier melatonin phase markers than evening-types.*

3. *That preferred sleep timing is significantly related to the timing of the melatonin rhythm.*

4. *That weekday/weekend differences in sleep timing and duration are significantly related to the timing of the melatonin rhythm.*

5.2 Methods

The following section will provide an overview of the specific measures and the analytical methods which were used in this study. Full details of the methodological procedures including the details of the study protocol can be found in Chapter 3. Ethics approval for this study was granted by the Wellington Campus Massey University Human Ethics Committee (Protocol numbers 04/31).

Participants

A total of 32 participants were invited to take part in the present study however three participants did not attend because of illness. Of the 29 participants who did take part in the overnight laboratory protocol, the data from one participant was excluded from all analyses due to a failed urine toxicology test. The findings presented in this chapter are based on the analysis of data from 28 individuals (19 women and 9 men).

The participants had no obvious sleep, medical or psychological disorders as assessed by several questionnaires and a medical examination, and there were no reports of time-zone crossings in the month preceding the study. Four females reported taking oral contraceptives and one female reported using an intrauterine contraceptive device.

Setting

This study was conducted at the Sleep/Wake Research Centre Human Time Isolation Facility (HTIF) located at Massey University, Wellington, New Zealand. The HTIF is a 3-bed unit where the light intensity and temperature is controlled and sound is highly attenuated. The entire protocol was conducted under dim light conditions (<20 lux in all areas, range 2.75-15.51 lux) and the temperature maintained at 18-20˚C.

Design

The present study was carried out between April and October 2005. During this period the average monthly sunrise varied between 06:22 and 07:45 and the average monthly sunset between 16:59 and 19:44 (The National Observatory of New Zealand, 2005). Each participant attended the overnight laboratory protocol on a Saturday night, immediately following Phase

one of data collection (i.e. two weeks of actigraphic monitoring of habitual sleeping patterns). The protocol formally began at 1700hrs and concluded at 1000hrs on the Sunday morning. Saliva samples were collected every 30 minutes and performance testing (PVT) and sleepiness ratings (KSS) were conducted at one-hourly intervals. Participants were asked to maintain a semi-recumbent position throughout the protocol except when using the bathroom. They were instructed to maintain wakefulness for the entire protocol and were permitted to carry-out quiet activities in between study tasks. Meals and refreshments were provided at regular intervals, all of which were free of caffeine, dairy products, bananas and red food colourings (Martin & Eastman, 2002) (Dr. C. Eastman, personal communication, August 03 2003 and Dr. H.J. Burgess, personal communication, August 05 2003)

Radioimmunoassay

Salivary melatonin levels were measured using a direct radioimmunoassay (RIA) method (see Appendix 15 for details). All assays were conducted by Associate Professor David Kennaway and his staff at the Circadian Physiology Laboratory, Department of Obstetrics and Gynaecology at the University of Adelaide in South Australia. The intra- and inter-assay coefficients of variation were < 10% and < 16% across the range of the standard curve.

5.2.1 Measures

The collection of saliva samples permitted the investigation of the endogenous melatonin rhythm and the determination of a series of circadian phase markers. The thresholds for melatonin onset and offset were determined from the relevant literature and advice from academic colleagues (personal communication, D. Kennaway, November 25, 2005 and S. Benloucif, March 15, 2006). For each participant, their raw melatonin data was smoothed prior to the identification of the melatonin phase markers using a robust locally weighted regression scatterplot smoothing procedure (LOWESS, see Appendix 23 for details) (GraphPad Prism, GraphPad Software, Inc., San Diego, CA). The timing of each phase marker was then determined using 1-minute interpolation of the smoothed data. The following section outlines the specific procedures and definitions that were used to identify circadian phase.

Melatonin Onset:

Three methods of estimating the threshold for determining melatonin onset were employed in this study (See Figure 5.1 for an illustration).

DLMO: The threshold for the dim light melatonin onset was defined as the first sample to rise above the limit of detection for the radioimmunoassay (i.e. >4 pM) for one hour, followed by a continuous rise in melatonin levels with no subsequent values falling below the limit of detection. This method is a modified version of that reported by Voultsios and colleagues (1997).

DLMO25: Raw data (pM) for each individual were adjusted to a percentage of maximum which was defined as the average of the three highest values for that person. DLMO25 represented the first time at which melatonin levels rose to 25% of maximum followed by a continuous rise in melatonin levels (after (Benloucif et al., 2005)).

DLMO50: DLMO50 was recorded as the first time that melatonin levels rose to 50% of maximum levels (as defined above) followed by a continuous rise in melatonin levels.

Melatonin Offset

Three methods of estimating the threshold for the offset of the endogenous melatonin rhythm were also employed in the present study.

DLMOff: This estimate of melatonin offset was defined as the second to last sample before melatonin levels fell below the limit of detection for the RIA (after (Voultsios et al., 1997)). This threshold is equivalent to the time of the last hour of melatonin production.

DLMOff25: This phase marker represented the last time that the smoothed data declined to 25% of maximum levels followed by a continual decrease in melatonin levels.

DLMOff50: The time at which the smoothed data declined to 50% of maximum followed by a continual decrease in melatonin was called DLMOff50.

Circadian phase was also investigated using other characteristic features of the nocturnal melatonin profile.

Midpoint: The midpoint of the melatonin rhythm for each individual was determined as the average of DLMO50 and DLMOff50 from the fitted data.

Peak: It was hypothesised that the underlying circadian component is represented by the fundamental whereas higher order harmonics represent masking. Therefore the raw data (pM) was modelled using a second-order (or quadratic) polynomial regression equation and the peak of the melatonin rhythm was identified by visual inspection of the fitted curve.

MelStart**:** This phase marker was determined as the first sample above the limit of detection for this assay (i.e. > 4pM).

MelEnd**:** This phase marker represents the last sample above the limit of detection for this assay

In addition to identifying suitable markers of circadian phase, the raw melatonin data were evaluated to investigate whether there were observable differences in the shape of the waveforms between morning- and evening-types. The following characteristics were measured:

Area under the curve: Raw melatonin levels were converted to z-scores and the total amount of melatonin that was secreted across the night was investigated by calculating the area under the time*concentration curve (AUC).

The rate of melatonin production: This was represented by the steepness of the rising section of the melatonin curve which was defined as the difference between DLMO25 and DLMO50

The rate of melatonin decline: This represented the steepness of the falling section of the melatonin curve which was defined as the difference between DLMOff50 and DLMOff25

Duration of melatonin production: The time interval between DLMO and DLMOff was estimated as the duration of melatonin production

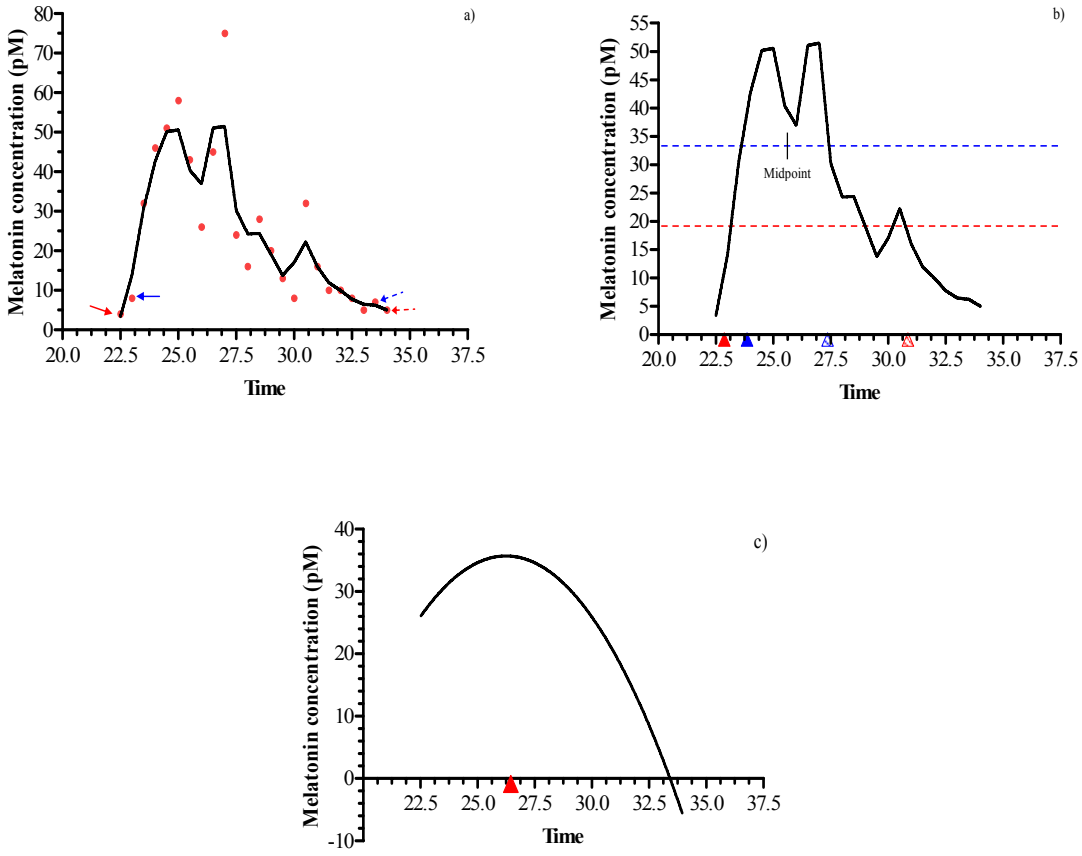


Figure 5.1 Circadian phase markers derived from the nocturnal melatonin profile.

Panel a) illustrates the raw (red circles) and LOWESS smoothed data (black line) for one participant (ID 20697). The red solid and dashed arrows indicate MelStart and MelEnd respectively, while the blue solid and dashed arrows indicate DLMO and DLMOff. Panel b) also illustrates the smoothed data for this participant. The red horizontal line represents 25% of maximum levels while the blue horizontal line represents 50% of maximum levels. The red solid and dashed triangles indicate the timing of DLMO25 and DLMOff25 respectively while the blue solid and dashed triangles indicate the timing of DLMO50 and DLMOff50 respectively. The midpoint was the average of DLMO50 and DLMOff50. Panel c) illustrates the 2nd polynomial regression fitted to the raw data for this participant. The red triangle represents the timing of the Peak melatonin level.

Sleep parameters

The sleep parameters of interest in the present study were sleep start time (SlpSt) and sleep end time (SlpEnd) which were derived from the *Actiwatch*™ and sleep diary data as described in Chapter 4. In addition, the midpoint of the main night sleep episode was also calculated as the average of sleep start time and sleep end time for that sleep episode. In order to investigate the relationship between the circadian melatonin rhythm and actual sleep timing, the parameters SlpSt, SlpEnd and midpoint for each participant were averaged across a number of different time periods. Recently, Martin and Eastman (2002) found that including more than five days of sleep data (derived from sleep diaries and verified by actigraphy) in the averaged estimates of habitual sleep did not necessarily improve the relationship with DLMO in young adults (18-32yrs).

Given the significant differences in weekday and weekend sleep timing and duration between M- and E-types (see Chapter 4), it was important to investigate whether these differences were related to the timing of the circadian clock. However Martin and Eastman (2002) also argued that the 'proximity' of the sleep data to the assessment of DLMO may be more important than possible weekday and weekend differences in sleep. In order to investigate these issues, the sleep data for each individual was averaged as follows:

(1) All 14 days of actigraphy and sleep diary data collection

(2) The last week (i.e. Friday – Friday nights inclusive) of data collection

(3) Weekdays only (i.e. Sunday night – Thursday night inclusive)

(4) Weekends only (i.e. Friday and Saturday nights only)

(5) The last five days (i.e. Monday – Friday nights inclusive)

(6) The final night (i.e. Friday night before attending the laboratory protocol)

Thus, there were 18 mean sleep parameters for each participant (3 sleep timing parameters x 6 averaged periods).

5.2.2 Statistical Analyses

Data management

As batches of saliva samples were assayed, the results of the RIA were e-mailed in an Excel spreadsheet from the University of Adelaide to the research leader. At the end of the data collection period, a final combined data file was produced and imported into specialised curve-fitting software (GraphPad Prism version 4.00 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com). For ease of recognition, any samples below the limit of

sensitivity for this assay (4pM) were assigned a value of 3 while any missing samples were assigned a value of 1.

Descriptive statistics

Descriptive statistics are presented in order to understand the overall pattern of data for the variables of interest. Raw melatonin concentrations in picomolar units (pM) were plotted against time (24-hour clock) to produce individual nocturnal profiles for each participant (see Appendix 24). Melatonin profiles were produced for grouped data (i.e. morning- and evening-types) by plotting the mean value at each time point.

The actigraphic sleep parameters sleep start time (SlpSt), sleep midpoint (SlpMid) and sleep end time (SlpEnd) were averaged over six different periods. The mean and standard deviation for each of these parameters under each of these conditions are presented in Appendix 25.

Univariate statistics

Pearson correlation coefficients and linear regression were used to determine significant relationships between the timing of the melatonin rhythm, actigraphically determined sleep parameters, and scores on the Morningness/Eveningness Questionnaire (MEQ) (Horne & Östberg, 1976). If the data followed a non-normal distribution, then Spearman rank correlations were used. Independent sample *t*-tests were used to assess significant univariate relationships between the circadian phase markers versus chronotype, and circadian phase markers versus mean sleep timing. Wilcoxon-Mann Whitney *U* tests were used where the distribution of data was non-normal.

Prior to running the multivariate analyses, Kruskal-Wallis chi-square tests were used to investigate the univariate association between sleep timing and the independent variables of age group (30-39yrs vs. 40-49yrs) and weekday vs. weekend. Spearman rank correlations were used to investigate the relationship between sleep timing and the circadian phase markers.

Multivariate statistics

Mixed model ANCOVAs for repeated measures were used to investigate the influence of circadian phase, age group and weekday/weekend on actual sleep timing. In these analyses, the actigraphic sleep parameters of sleep start time and sleep end time were treated as repeated measures recorded across a two-week period.

Table 5.1 and Table 5.2 present the details of the mixed models including the data transformations which were necessary to meet the assumptions of the mixed model. In all mixed model ANCOVAs used in this chapter, the covariance was modelled most appropriately by the compound symmetric structure.

Table 5.1 Dependent and independent variables for the mixed model ANCOVAs related to sleep start time

Model number	Dependent variable	Fixed Factors in the mixed models [a]	Data transformations (dependent variable)	Number of outliers removed
1	Sleep Start Time	DLMO, age group, weekday	Inverse	Nil
2	As above	DLMO25, age group, weekday	Inverse	Nil
3	As above	DLMOff, age group, weekday	Log10	Nil
4	As above	MelStart, age group, weekday	Log10	Nil
5	As above	MelEnd, age group, weekday	Log10	Nil

Note. [a] Melatonin phase markers were included as continuous variables age group = 30-39 vs. 40-49yrs. Weekday = weekdays vs. weekends.

Table 5.2 Dependent and independent variables for the mixed model ANCOVAs related to sleep end time

Model number	Dependent variable	Fixed Factors in the mixed models [a]	Data transformations (dependent variable)	Number of outliers removed
1	Sleep End Time	DLMO, age group, weekday		36
2	As above	DLMO25, age group, weekday		Nil
3	As above	DLMO50, age group, weekday		2
4	As above	DLMOff age group, weekday	SQRT	1
5	As above	DLMOff25 age group, weekday		1
6	As above	Midpoint, age group, weekday		2
7	As above	Peak, age group, weekday		2
8	As above	MelStart, age group, weekday		26
9	As above	MelEnd, age group, weekday	SQRT	8

Note. [a] Melatonin phase markers were included as continuous variables age group = 30-39 vs. 40-49yrs. Weekday = weekdays vs. weekends.

5.3 Results

5.3.1 Characteristics of the Study Participants

Table 5.3 presents the characteristics of the study participants (n=28). The mean age of the participants in the present study was 41 years (*SD* = 4.73yrs), and morning-type participants (n=14) were older than evening-types (n=14) (Table 5.4).

Table 5.3 Demographic information for the study participants

	All participants	**Morning-type**	**Evening-type**
	n (% of sample)	*n* (% of sample)	*n* (% of sample)
Men	9 (32.10)	6 (42.90)	3 (21.40)
Women	19 (67.90)	8 (57.10)	11 (78.60)
30-39yrs	11 (39.30)	5 (35.70)	6 (42.90)
40-49yrs	17 (60.70)	9 (64.30)	8 (57.10)
BMI1[a]	9 (32.10)	4 (28.60)	5 (35.70)
BMI2[b]	11 (39.30)	7 (50.00)	4 (28.60)
BMI3[c]	8 (28.60)	3 (21.40)	5 (35.70)
No Dependants	14 (50.00)	6 (42.90)	8 (57.10)
Any Dependants	14 (50.00)	8 (57.10)	6 (42.90)
Employed	25 (89.30)	13 (92.90)	12 (85.70)
Unemployed	3 (10.70)	1 (7.10)	2 (14.30)
DE-type	12 (42.90)		
ME-type	2 (7.10)		
MM-type	6 (21.40)		
DM-type	8 (28.60)		

Note. [a] BMI1 = normal range (Māori <26 kg/m^2); non-Māori <25 kg/m^2). [b] BMI2 = overweight range (Māori 26-32 kg/m^2); non-Māori 25-30 kg/m^2). [c] BMI3 = obese range (Māori >32 kg/m^2; non-Māori >30 kg/m^2)

Table 5.4 Average age and MEQ scores of the study participants

	Whole group	**Morning-types (n=14)**		**Evening-types (n=14)**	
	Age (yrs)	Age (yrs)	MEQ	Age (yrs)	MEQ
Mean	41.11	42.56	69.93	39.65	39.11
SD	4.73	4.22	3.05	4.92	6.84
Range	31-47	35-47	65-77	31-47	30-49

5.3.2 Characteristics of the Melatonin Profile Among Morning- and Evening-Types

The individual nocturnal melatonin profiles showed the characteristic shape of increasing melatonin levels throughout the evening, and decreasing levels towards morning. Some individuals showed a steep rising portion, while others showed steep falling portions. In addition, many of the individual profiles have a 'spiky' appearance, most probably due to some masking effect despite the constant conditions. There was considerable inter-individual variability in the nocturnal melatonin profiles. There was also some variation in the number of samples per participant that had melatonin levels >4pM (range 15-26 samples out of 34, mode=22/34 samples). Moreover, 9 participants had a maximum melatonin level < 40pM, which is approximately equivalent to the original definition for DLMO set at 10pg/ml.

The nocturnal melatonin profile was also evaluated within each chronotype, by averaging the melatonin levels at the half-hourly sampling points (17:30-10:00hrs). It is clear from Figure 5.2 that M-types have an earlier melatonin rhythm compared to E-types. The average onset of melatonin secretion, as measured by the mean of DLMO, DLMO25, DLMO50 and Start, was 1.03hrs earlier among morning types compared with evening-types (range of differences between phase markers 1.13 to 1.50hrs). However, as melatonin levels declined, the average difference between the two chronotypes reduced to an average of 42 minutes (range of differences from 0.38 to 1.06hrs, see Table 5.7 for details).

The morning-type profile appears to have a steeper rising portion, with a longer tail to the right as levels decrease towards morning. In contrast, the evening-type profile does not appear to show a rise in melatonin levels until 20:30hrs. Also it would seem that the morning-type profile has a slightly longer duration of high melatonin levels before the early morning decline whereas melatonin levels seem to decrease not long after the peak in the evening-type profile. Based on these observations it would appear that the M-type profile better illustrates the classic square-wave shape of melatonin secretion than the E-type profile.

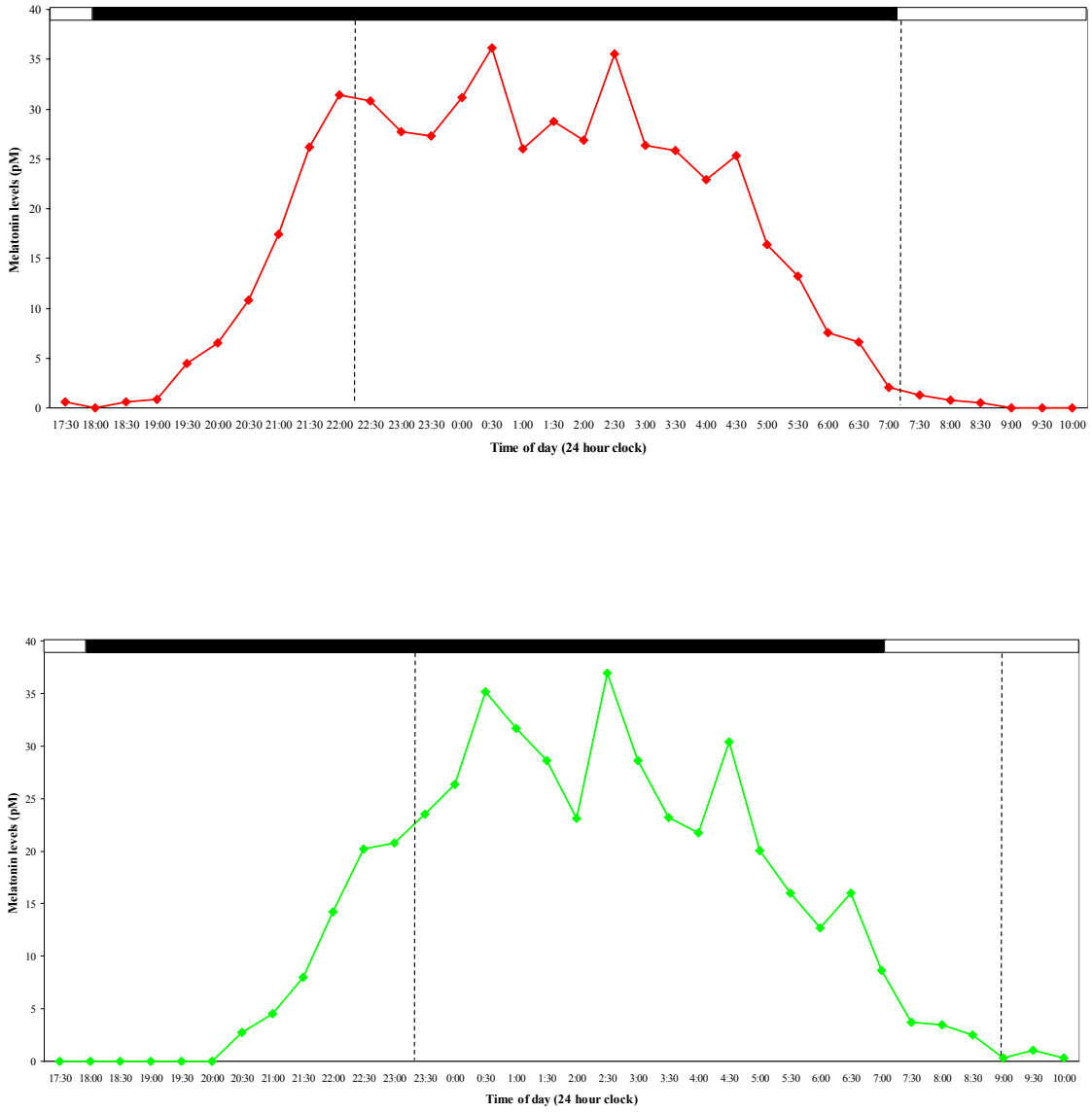


Figure 5.2 The nocturnal salivary melatonin profiles of morning- and evening-types

The mean melatonin level at each sample collection was calculated for morning (top panel) and evening-types (bottom panel) and plotted against time (24-hour clock). The two dashed vertical lines represent the mean sleep start time and sleep end time recorded on the night preceding the phase assessment (Friday night). The day/night is indicated by the black and white horizontal bar at the top of each panel.

The average nocturnal melatonin profile was also quantitatively evaluated by estimating the amount of melatonin that was produced (AUC), the duration of secretion, the rate of secretion across the evening and the rate of decline towards morning. As indicated in Table 5.5, morning-types secreted more melatonin across a longer duration compared to evening-types, which confirms the observations made during the visual inspection detailed above. Similarly, the duration of secretion (the time interval between DLMO and DLMOff) was approximately 38 minutes longer among M-types, however this difference was not significant.

The rising portion of the average nocturnal profile (DLMO to Peak) was similar for both chronotypes (M-types 4.39hrs ± 1.21hrs; E-types 3.92hrs ± 1.52hrs) as was the falling portion (Peak to DLMOff: M-types 4.95hrs ± 1.52hrs; E-types 4.94hrs ± 1.38hrs). As a measure of the relative steepness of these profiles, the rate of secretion was calculated as the time interval between the phase markers DLMO25 and DLMO50, while the rate of decline was the interval between DLMOff25 and DLMOff50. Again, none of these differences reached significance.

Table 5.5 Characteristics of the nocturnal melatonin profile by chronotype and age group

	Total Sample		M-type		E-type		30-39yrs		40-49yrs	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Area under the curve [a]	421.20	112.78	451.16	122.52	391.24	97.31	441.61	105.79	407.99	118.30
Duration of melatonin secretion [b]	8.89	1.25	9.14	1.26	8.50	1.75	9.14	1.38	8.74	1.17
Rate of melatonin secretion [c, e]	0.93	1.51	0.97	1.77	0.93	0.94	0.85	0.62	0.97	2.35
Rate of melatonin decline [d, e]	1.02	1.50	1.02	1.64	0.99	1.20	0.91	1.44	0.75	1.44

Note. [a] Values converted to z-scores prior to calculating the AUC from the raw data [b] The time interval between DLMO and DLMOff on the fitted waveforms [c] The time interval between DLMO25 and DLMO50 on the fitted waveform [d] The time between DLMOff50 and DLMOff25 on the fitted waveform. [e] Median and IQR presented for non-normal data

5.3.3 The Relationship between Melatonin Phase Markers and MEQ Scores

Scores on the MEQ were significantly associated with the timing of the melatonin rhythm, as measured by DLMO, DLMO25, and MelStart and MelEnd (Table 5.6). Significant correlation coefficients ranged from r = -0.39 (p =0.04) to r = -0.62 (p <0.001) with the strongest association between MEQ and DLMO25. All of the regression lines exhibit a negative slope indicating an earlier melatonin rhythm with higher scores on the MEQ (i.e. morningness). Figure 5.3 presents scatterplots and regression equations to illustrate the significant relationships.

Table 5.6 Regression parameters ($y=ax + b$) and correlation coefficients for the relationship between melatonin phase markers and MEQ scores

	Regression		**Correlation**	
	a	*b*	*r*	*p-value*
DLMO	-0.037	23.444	-0.607	0.0006
DLMO25	-0.040	23.582	-0.616	0.0005
DLMO50	-0.033	24.510	-0.355	0.0634
DLMOff [a]			-0.393	0.0575
DLMOff25	-0.019	30.691	-0.249	0.2020
DLMOff50	-0.018	29.321	-0.197	0.3153
Midpoint	-0.026	26.915	-0.324	0.0927
Peak	-0.026	26.797	-0.296	0.1260
MelStart	-0.044	23.202	-0.604	0.0007
MelEnd	-0.031	32.644	-0.391	0.0398

Note: [a] Spearman rank correlation used for non-normal data

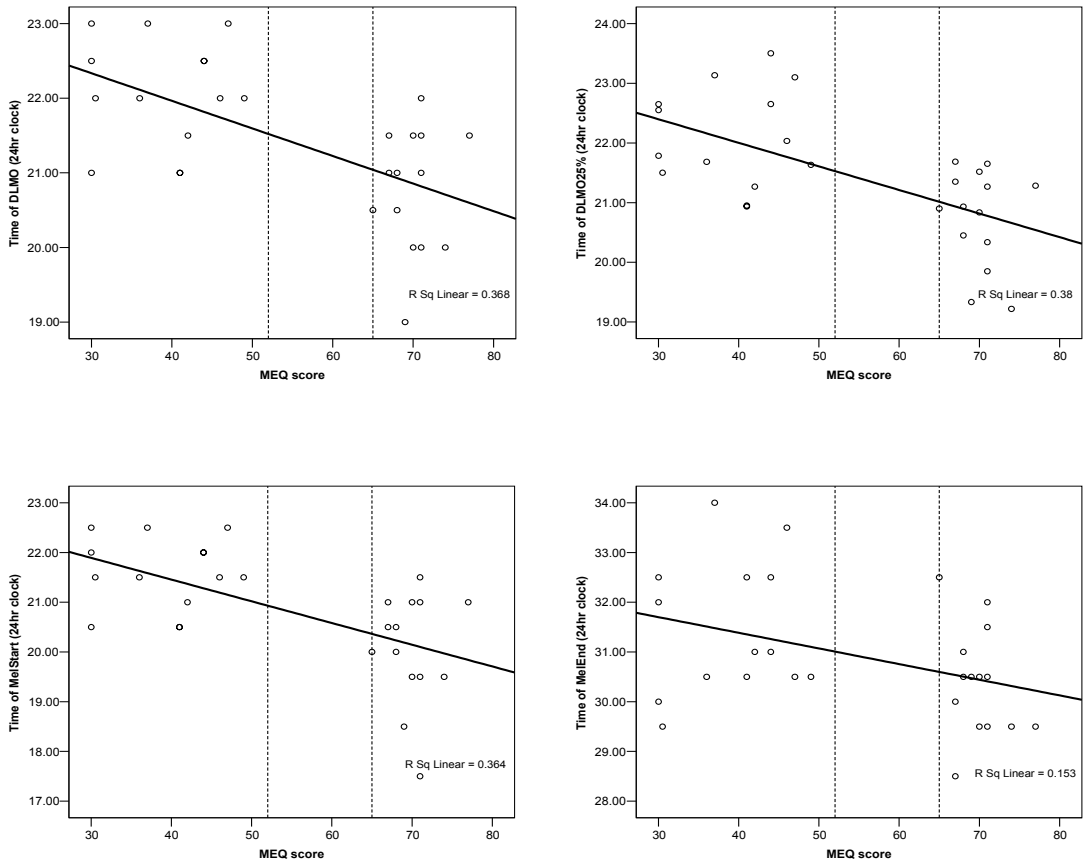


Figure 5.3 Significant linear relationships between melatonin phase markers and MEQ scores.

The dashed vertical lines indicate the score cut-offs for morning- and evening-types according to the criteria proposed by Taillard and colleagues (2004).

5.3.4 The Relationship between Melatonin Phase Markers and Chronotype

Table 5.7 presents descriptive information together with the findings of a series of univariate analyses investigating the relationships between circadian phase markers and chronotype. There was a significant difference in the timing of DLMO (p <0.001), DLMO25 (p <0.001), the first detectable sample (p <0.001) and the last detectable sample (p <0.05) between morning- and evening-types (Figure 5.4). Although the average DLMO50, midpoint, peak and all melatonin offset variables were earlier among M-types, they were not significantly different from E-types.

Table 5.7 Descriptive statistics and univariate relationships between melatonin phase markers and chronotype

	Total Sample		**Morning-types**		**Evening-types**		**M vs. E-types**		
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*t*	*df*	*p*-value
MEQ score			69.93	3.05	39.11	6.84			
DLMO	21:26	1.00	20:47	0.83	22:04	0.73	-4.366	26	0.0002
DLMO25	21:26	1.07	20:46	0.82	22:06	0.83	-4.292	26	0.0002
DLMO50	22:43	1.53	22:11	1.67	23:16	1.20	-1.975	26	0.0589
DLMOff [a]	6:00	2.25	6:00	1.63	6:30	2.13			0.0930
DLMOff25	5:40	1.25	5:23	0.88	5:57	1.52	-1.198	26	0.2417
DLMOff50	4:20	1.53	4:08	1.32	4:31	1.75	-0.656	26	0.5179
Midpoint	1:31	1.30	1:09	1.32	1:53	1.23	-1.525	26	0.1393
Peak	1:23	1.45	0:57	1.39	1:47	1.47	-1.485	26	0.1496
MelStart	20:49	1.18	20:04	1.10	21:34	0.73	-4.233	26	0.0003
MelEnd	6:56	1.33	6:24	1.10	7:28	1.37	-2.291	26	0.0303

Note. [a] DLMOff had a non-normal distribution, therefore the median and IQR are presented. Differences by chronotype were investigated using the Mann-Whitney *U* test. MelStart= the first detectable melatonin level in the nocturnal profile. MelEnd= the last detectable melatonin level in the nocturnal profile

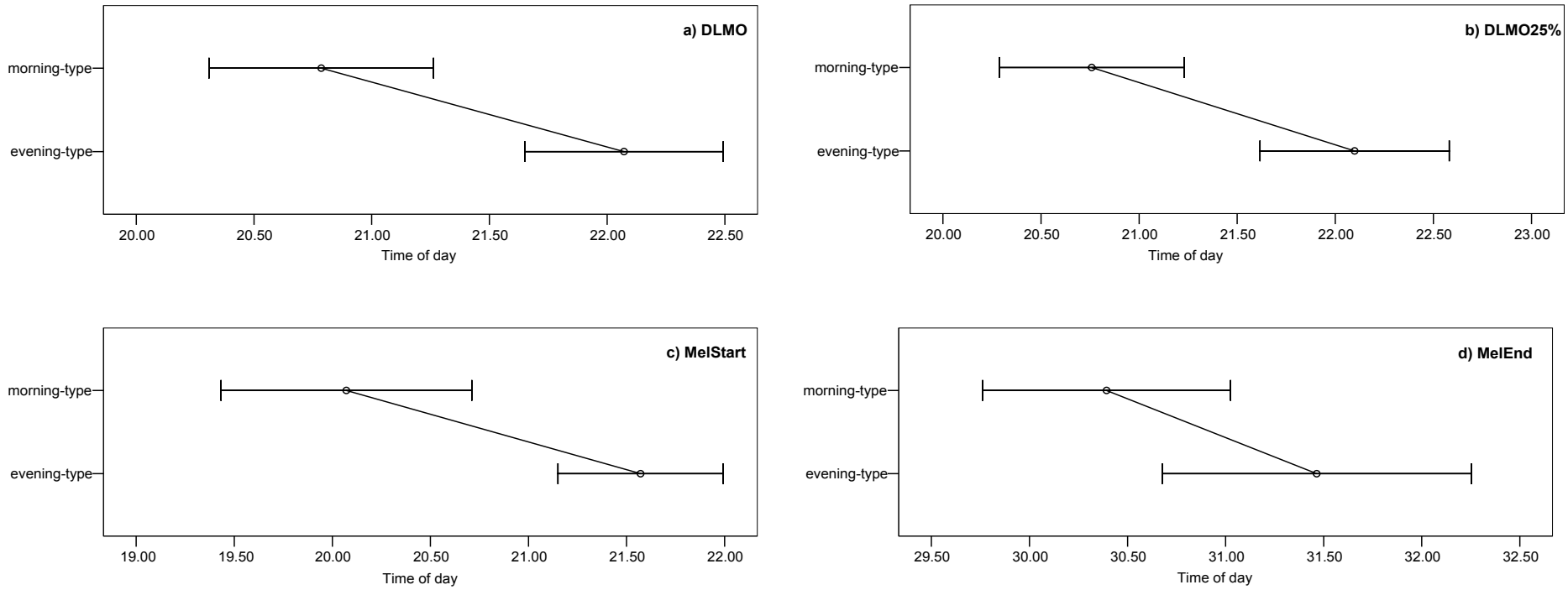


Figure 5.4 Differences in the timing of the melatonin phase markers between morning- and evening-types.

The error bars represent the mean ± 95%CI

5.3.5 Melatonin Phase Markers and Actual Sleep Timing

As expected, sleep start time, midpoint, and sleep end time were significantly earlier among morning-types compared to evening-types across all the averaging periods (all p <0.01, full tables can be found in Appendix 25).

The relationship between melatonin phase markers and actual sleep timing was investigated using Pearson correlation coefficients (or Spearman rank correlations if not normally distributed). The full details of these analyses are presented in Tables 1, 2, and 3 in Appendix 26.

The DLMO was consistently associated with sleep start time, midpoint and sleep end time across all averaging periods, with Pearson correlation coefficients ranging from r = 0.410 (p < 0.05) to r = 0.660 (p < 0.001). Regression parameters for these relationships are presented in Table 4 in Appendix 26. The tightest relationship was between DLMO and the midpoint of sleep averaged across the last five days of data collection. Figure 5.5 illustrates the linear relationship between these two variables, which indicates that an early main night sleep episode is significantly associated with an early DLMO (ANOVA F=20.07, df=27 p =0.0001).

The relationships between average sleep timing and the endogenous melatonin rhythm were also investigated separately for each chronotype, however few of these within group correlations reached statistical significance (see Appendix 26 for full tables). Among morning-types, there was a significant correlation between DLMOff and the midpoint of sleep on the final night (r =0.639, p =0.0188) whilst among evening-types, the following correlations were statistically significant: DLMO vs. average sleep end time across the last week (r = 0.571, p =0.033), DLMO vs. average midpoint of sleep across the last five days (r =0.541, p =0.046), the first detectable melatonin level vs. average sleep end time across the last week (r =0.571, p =0.033), and the first detectable melatonin level vs. the average midpoint of sleep across the last five days (r = 0.541, p =0.04).

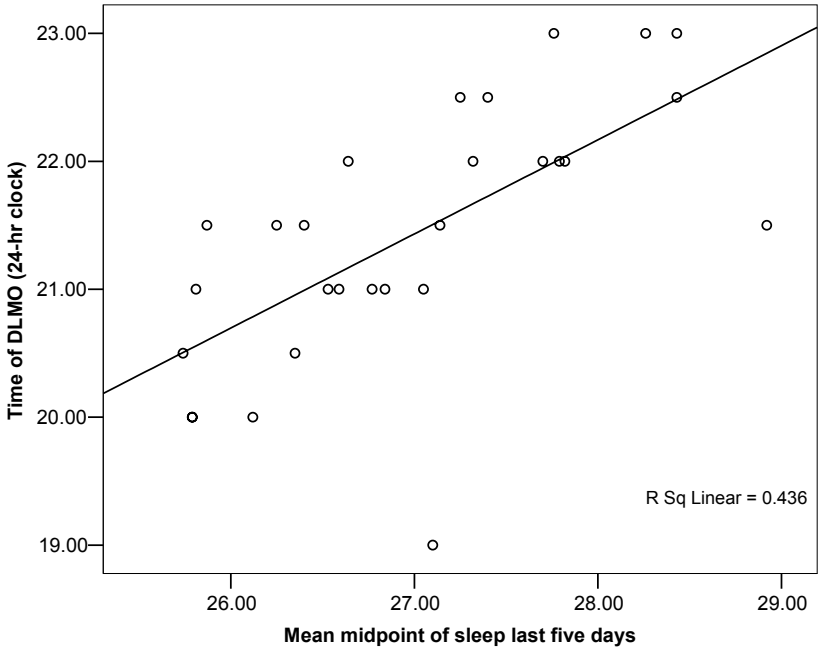


Figure 5.5 The relationship between the DLMO and the midpoint of sleep from the last 5d preceding the phase assessment

The equation for the regression line is: DLMO= 0.736 (midpoint of sleep) + 1.565

5.3.6 Phase Angles

Based on the consistent relationship between DLMO and actigraphic sleep timing, a series of analyses were used to investigate the phase angle between DLMO and sleep start time, midpoint and sleep end time across all averaging periods (i.e. 18 phase angles). Figure 5.6 presents a schematic representation of the phase relationship between DLMO and the main night sleep episode among morning- and evening-types.

Table 5.8 presents the descriptive statistics and univariate test results for the phase angles between DLMO and sleep start time, sleep midpoint, and sleep end time across each averaging period. Compared to weekdays, both morning- and evening-types had longer phase angles on the weekends as they shifted their main sleep episodes to a later clock hour.

A second set of phase angles were calculated based on the finding that sleep timing on the final night was significantly associated with DLMO, DLMO25, DLMOff, DLMOff25, MelStart and MelEnd (Table 5.9). In general, evening-type individuals tended to have a longer phase angle between the onset of the melatonin rhythm and the sleep timing parameters, indicating that E-types went to sleep at a later circadian time compared to M-types, however none of these differences were significant.

When the phase angle calculations considered melatonin offset, E-types tended to have a shorter phase angle to sleep start, and midpoint and a longer phase angle to sleep end compared to M-types. Univariate tests found that E-types had a significantly shorter phase angle from DLMOff to the midpoint of sleep and DLMOff25 to the midpoint of sleep (both $p < 0.05$, see Figure 5.7).

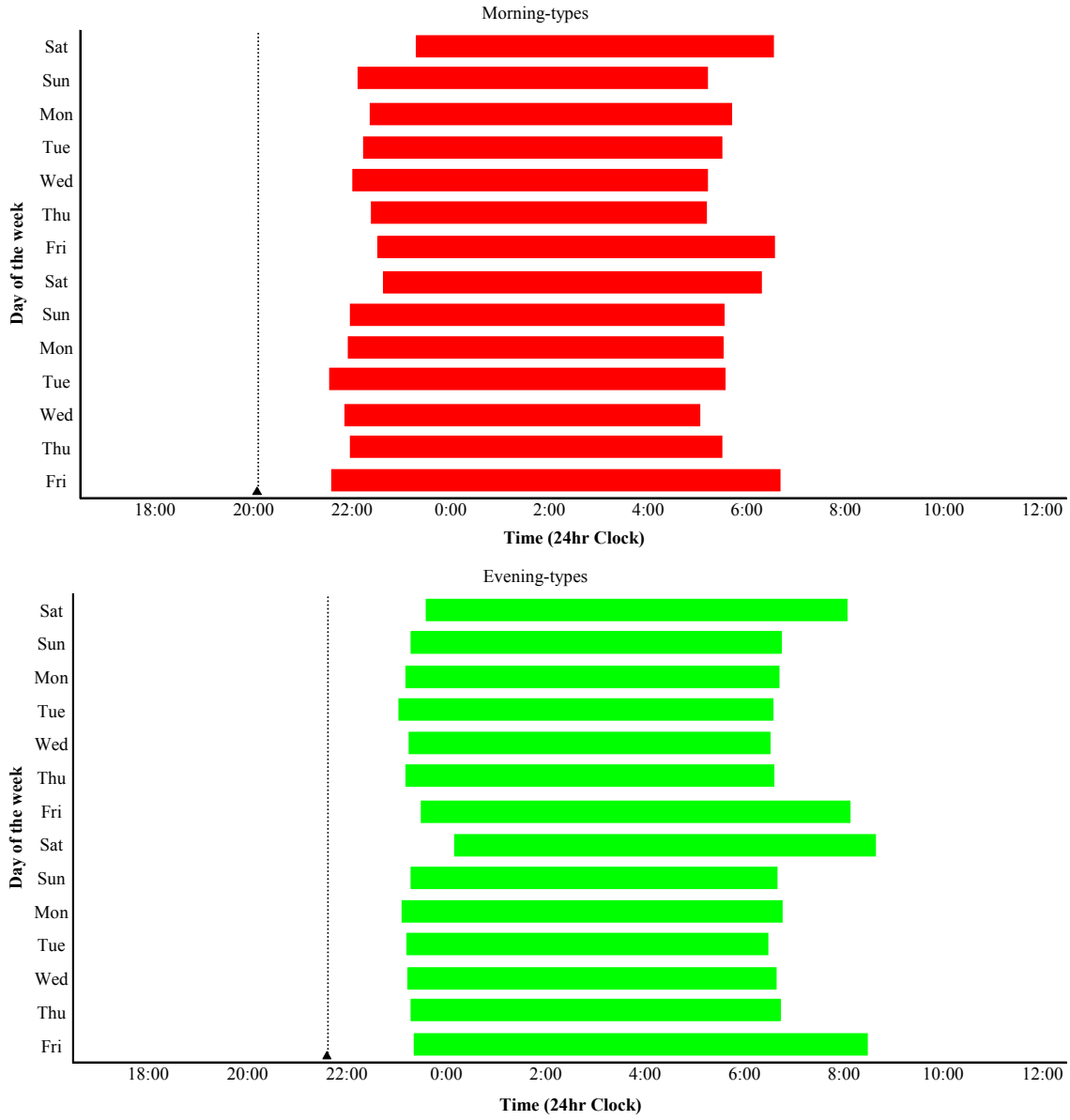


Figure 5.6 A schematic illustration of the relationship between the DLMO and habitual sleep timing among morning- and evening-types

The average main night sleep episode across a 14-day period is presented for morning-(top panel) and evening-types (bottom panel). The dashed vertical line represents the mean DLMO for each group.

Table 5.8 Average phase angle between DLMO and sleep parameters, and differences between morning- and evening-types

	Total Sample		Morning-types		Evening-types		M- vs. E-types		
All 14d	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*t*	*df*	*p*-value
SlpSt	1.91	0.90	1.98	0.95	1.84	0.87	0.383	26	0.705
SlpMid [a]	5.84	1.14	5.81	1.27	5.91	0.75			0.748
SlpEnd	9.55	0.93	9.48	1.12	9.62	0.71	-0.377	26	0.709
Weekdays									
SlpSt [a]	1.89	0.75	1.79	0.71	1.91	1.23			0.927
SlpMid [a]	5.54	1.11	5.49	0.92	5.44	0.76			0.854
SlpEnd	9.16	0.90	9.16	1.06	9.16	0.74	-0.001	26	0.999
Weekends									
SlpSt	2.25	1.12	2.33	1.14	2.17	1.31	0.380	26	0.707
SlpMid	6.41	1.14	6.31	1.25	6.52	1.05	-0.482	26	0.633
SlpEnd	10.58	1.30	10.29	1.45	10.87	1.12	-1.197	26	0.242
Last week									
SlpSt	1.87	0.97	1.85	1.09	1.90	0.87	-0.133	26	0.895
SlpMid [a]	5.89	1.16	5.64	1.15	5.95	0.93			0.358
SlpEnd	9.71	0.86	9.60	1.00	9.83	0.70	-0.705	26	0.487
Last 5d									
SlpSt [a]	1.63	0.76	1.60	0.93	1.80	0.84			0.448
SlpMid [a]	5.62	0.94	5.59	1.05	5.65	0.68			0.679
SlpEnd	9.47	0.84	9.44	0.96	9.51	0.74	-0.214	26	0.832
Final night									
SlpSt	1.67	1.27	1.49	1.26	1.84	1.30	-0.695	24	0.494
SlpMid [a]	5.95	1.22	5.84	0.56	6.67	1.48			0.166
SlpEnd	10.74	1.36	10.55	1.60	10.93	1.10	-0.704	24	0.488

Note. [a] The median and IQR are presented where the variable has a non-normal distribution. Differences between morning- and evening-types were compared using the non-parametric Mann-Whitney *U* test

Table 5.9 The average phase angle between circadian phase and sleep timing parameters measured on the night preceding the phase assessment (final night).

	Whole group (n=26)		Morning-types (n=13)		Evening-types (n=13)		M- vs. E-types		
DLMO	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*t*	*df*	*p*-value
SlpSt	1.67	1.27	1.49	1.26	1.84	1.30	-0.685	24	0.494
SlpMid [a]	5.95	1.22	5.84	0.56	6.67	1.48			0.166
SlpEnd	10.74	1.36	10.55	1.60	10.93	1.10	-0.704	24	0.488
DLMO25									
SlpSt	1.66	1.34	1.51	1.27	1.82	1.44	-0.571	24	0.573
SlpMid	6.20	1.21	6.04	1.27	6.36	1.18	-0.666	24	0.512
SlpEnd	10.73	1.45	10.57	1.60	10.90	1.34	-0.579	24	0.568
DLMOff									
SlpSt	7.31	1.41	7.81	0.94	6.81	1.65	1.900	24	0.070
SlpMid	2.78	1.31	3.29	1.12	2.27	1.34	2.108	24	0.046
SlpEnd	1.76	1.56	1.24	1.59	2.27	1.40	-1.760	24	0.091
DLMOff25									
SlpSt	6.60	1.63	7.20	1.07	5.99	1.90	1.997	24	0.057
SlpMid [a]	2.43	2.20	3.16	1.65	1.60	2.53			0.022
SlpEnd	2.47	1.70	1.85	1.65	3.09	1.58	-1.953	24	0.063
MelStart									
SlpSt	2.28	1.42	1.53	1.63	2.34	1.30	-0.208	24	0.837
SlpMid [a]	6.45	1.28	6.34	0.56	7.17	3.50			0.330
SlpEnd	11.35	1.46	11.28	1.79	11.43	1.10	-0.255	24	0.801
MelEnd									
SlpSt	7.85	1.37	8.31	0.94	7.39	1.59	1.804	24	0.084
SlpMid	3.32	1.29	3.79	1.12	2.85	1.32	1.964	24	0.061
SlpEnd	1.22	1.56	0.74	1.59	1.70	1.43	-1.610	24	0.120

Note. [a] Median and IQR presented for non-normal data. Differences between morning- and evening-types were compared using the non-parametric Mann-Whitney U test

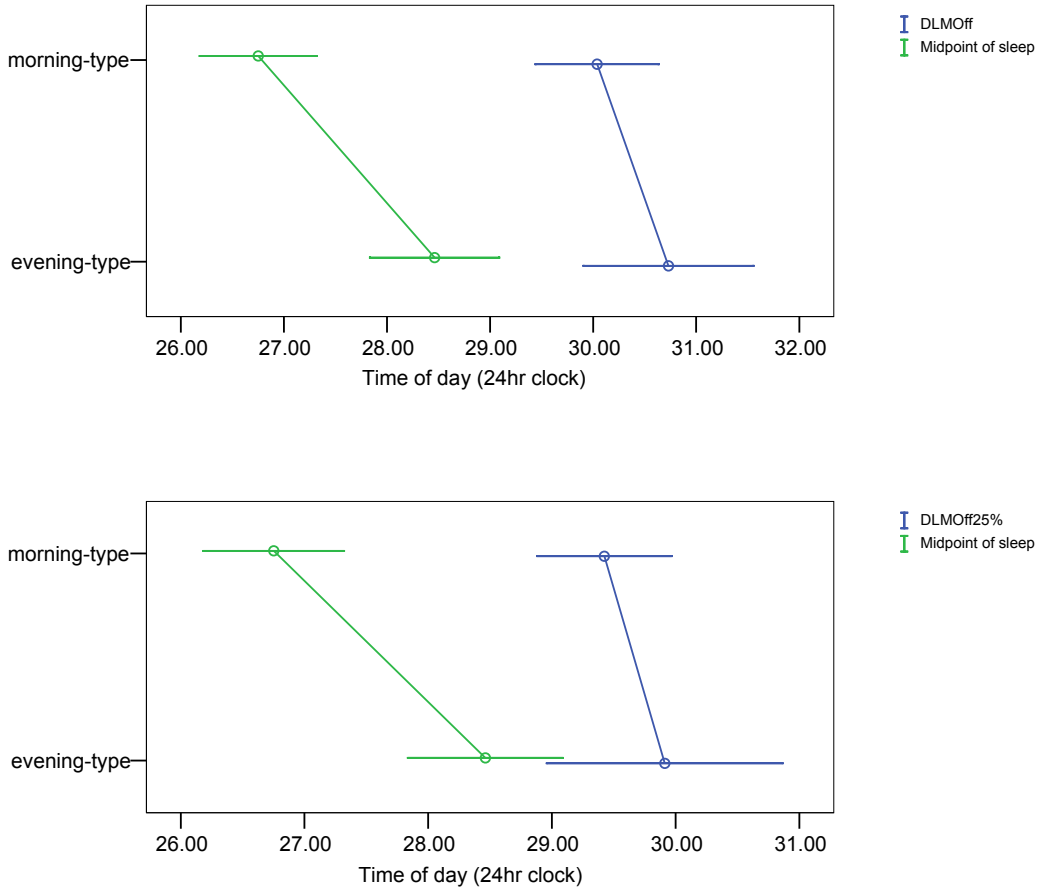


Figure 5.7 The phase relationship between melatonin phase and the average midpoint of sleep in morning- and evening-types.

The top panel illustrates the relationship between DLMOff and the average midpoint of sleep for the final night, while the bottom panel illustrates the relationship between DLMOff25 and the midpoint of sleep on the final night. The horizontal bars represent 95% CI.

5.3.7 The Contribution of Endogenous and Exogenous Factors to the Timing of Sleep

Table 5.10 presents the findings of the mixed model ANCOVAs used to investigate the influences of circadian phase, age, and weekday versus weekend sleep, on sleep start times for the main night sleep episode across a two-week period.

Overall, the estimates from each mixed model indicated that later sleep start times were associated with later circadian phase. Moreover, after controlling for age and circadian phase, there was a significant main effect of weekdays versus weekends. Table 5.11 presents the outcome of this modelling and provides an estimate of the change in mean sleep start times in relation to the timing of the endogenous melatonin rhythm.

For example, after controlling for age and differences in sleep on weekdays and weekends, the regression parameters describing the relationship between the estimated mean sleep start time and DLMO indicated that for every 30 minute delay in DLMO up to 23:00hrs, the estimated mean sleep start time was approximately 12.97 minutes later (range = 12.13-13.84). Substituting the average DLMO for morning- and evening-types separately into the regression equations, the estimated mean sleep start time was 22:51hrs and 23:25hrs respectively.

Similarly, for the relationship between mean sleep start time and DLMO25, MelStart and MelEnd. for every 30 minute shift in circadian phase the estimated start of the main night sleep episode became later by 10.19 minutes (range =9.60-10.80), 9.64 minutes (range =9.34-9.95) and 7.49 minutes (range=7.28-7.69 respectively).

Table 5.10 Details and results of the mixed model ANCOVAs for Sleep Start Time

Model number	Dependent variable	Fixed factors in the mixed model [a]	Significant main effects	
1	Sleep Start Time	DLMO, age group, weekday	**DLMO**	$F_{(1, 24.8)} = 10.83$, p=0.0030
			Weekday	$F_{(1, 347)} = 22.45$, p<0.0001
2	Sleep Start Time	DLMO25, age group, weekday	**DLMO25**	$F_{(1, 24.6)} = 6.52$, p=0.0172
			Weekday	$F_{(1, 347)} = 22.44$, p<0.0001
3	Sleep Start Time	DLMOff, age group, weekday	**Weekday**	$F_{(1, 347)} = 23.97$, p<0.0001
4	Sleep Start Time	MelStart, age group, weekday	**MelStart**	$F_{(1, 24.7)} = 7.67$, p=0.0105
			Weekday	$F_{(1, 347)} = 23.91$, p<0.0001
5	Sleep Start Time	MelEnd, age group, weekday	**MelEnd**	$F_{(1, 24.9)} = 4.55$, p=0.0431
			Weekday	$F_{(1, 347)} = 24.00$, p<0.0001

Note. [a] Melatonin phase markers were included as continuous variables age group = 30-39 vs. 40-49yrs. Weekday = weekdays vs. weekends. MelStart = the first detectable nocturnal melatonin level. MelEnd = the last detectable nocturnal melatonin level

Table 5.11 Estimated change in sleep start time for a 30-minute delay in melatonin phase markers

Regression equation	Time of melatonin phase marker	Estimated mean sleep start time
1/SlpSt = 0.06081 + (-0.00082*DLMO)	19:00	22:07
	19:30	22:19
	20:00	22:31
	20:30	22:44
	21:00	22:56
	21:30	22:10
	22:00	23:23
	22:30	23:36
	23:00	23:50
1/SlpSt = 0.05704 + (-0.00064*DLMO25)	19:20	22:23
	19:50	22:33
	20:20	22:43
	20:50	22:53
	21:20	23:03
	21:50	23:13
	22:20	23:24
	22:50	23:34
Log10SlpSt = 1.2354 + (0.006123*MelStart)	18:30	22:20
	19:00	22:29
	19:30	22:38
	20:00	22:48
	20:30	22:57
	21:00	23:07
	21:30	23:17
	22:00	23:27
	22:30	23:37
Log10SlpSt = 1.2202 + (0.004665*MelEnd)	6:30	23:02
	7:00	23:10
	7:30	23:17
	8:00	23:25
	8:30	23:32
	9:00	23:40
	9:30	23:48
	10:00	23:55

The significant main effects for weekday/weekend are described in Table 5.12. As in other sections of this thesis the *p*-values that are presented have not been adjusted for multiple comparisons. After controlling for age and circadian phase, sleep start times were significantly later on weekends (Friday and Saturday nights) compared to weekdays. The estimated difference between weekday and weekend sleep start times was approximately 28 minutes.

Table 5.12 Results of the post-hoc tests for differences between the estimated mean sleep start times on weekdays vs. weekends

Model	Fixed Factor	Estimated Mean Sleep Start Time (hrs:mins)	Significant Post Hoc Tests	Estimated difference between sleep start times (hours)
1	Weekday Weekend	23:11 23:39	$t_{(347)} = -4.74$, $p<0.0001$	0.46
2	Weekday Weekend	23:11 23:39	$t_{(347)} = -4.74$, $p<0.0001$	0.46
3	Weekday Weekend	23:12 23:41	$t_{(347)} = 4.90$, $p<0.0001$	0.48
4	Weekend Weekend	23:13 23:41	$t_{(347)} = 4.89$, $p<0.0001$	0.47
5	Weekend Weekend	23:12 23:40	$t_{(347)} = 4.90$, $p<0.0001$	0.47

Mixed model ANCOVAs were also used to investigate the influence of age, circadian phase and weekday versus weekend differences on sleep end times (Table 5.13). The model that included DLMO as the circadian phase marker did not meet the requirement of normally distributed residuals and so is not presented here.

Although each of the melatonin phase markers had a significant univariate association with sleep end time, after controlling for age group and weekday/weekend differences only DLMO25, Start and End reached significance in the multivariate analyses. Parameter estimates for the significant relationships indicate that a later circadian phase predicted a significantly later sleep end time (Table 5.14). For model 2, for every 30 minute delay in DLMO25 the estimated mean sleep end time was approximately 14 minutes later. Similarly, for model 8, a 30 minute delay in MelStart resulted in a sleep end time that was approximately 12 minutes later. Finally, for model 9, for every 30 minute shift in MelEnd, the estimated mean sleep end time becomes approximately 9 minutes later. This model applied a square root transformation to

sleep end time, so the range of differences in the estimated mean from the model is 8.45-9.48 minutes.

There was a significant main effect of age on sleep end times identified in models 2, 3, 6, 7 and 8, and post-hoc tests indicated for each model those aged 30-39yrs had a later sleep end time compared to those participants aged 40-49yrs (Table 5.15).

Post-hoc tests also indicated that sleep end times were significantly later on weekends, compared to weekdays (all p <0.0001). The estimated difference ranged from 1.30 to 1.38 hours.

Table 5.13 Details and results of the mixed model ANCOVAs for Sleep End Time

Model number	Dependent variable	Fixed factors in the mixed model [a]	Significant main effects	
2	Sleep End Time	DLMO25, age group, weekday	**DLMO25**	$F_{(1, 21.5)} = 18.22$, p=0.0003
			Age group	$F_{(1, 21.9)} = 10.42$, p=0.0039
			Weekday	$F_{(1, 314)} = 300.30$, p<0.0001
3	Sleep End Time	DLMO50, age group, weekday	**Age group**	$F_{(1, 24.8)} = 5.08$, p=0.0333
			Weekday	$F_{(1, 345)} = 239.15$, p<0.0001
4	Sleep End Time	DLMOff, age group, weekday	**Weekday**	$F_{(1, 346)} = 214.57$, p<0.0001
5	Sleep End Time	DLMOff25, age group, weekday	**Weekday**	$F_{(1, 346)} = 226.06$, p<0.0001
6	Sleep End Time	Midpoint, age group, weekday	**Age group**	$F_{(1, 24.8)} = 4.30$, p=0.0487
			Weekday	$F_{(1, 345)} = 239.24$, p<0.0001
7	Sleep End Time	Peak, age group, weekday	**Age group**	$F_{(1, 24.8)} = 4.30$, p=0.0487
			Weekday	$F_{(1, 345)} = 239.24$, p<0.0001
8	Sleep End Time	MelStart, age group, weekday	**MelStart**	$F_{(1, 23.1)} = 15.07$, p=0.0008
			Age group	$F_{(1, 23.2)} = 6.88$, p=0.0151
			Weekday	$F_{(1, 321)} = 292.35$, p<0.0001
9	Sleep End Time	MelEnd, age group, weekday	**MelEnd**	$F_{(1, 24.9)} = 6.25$, p=0.0194
			Weekday	$F_{(1, 339)} = 2934.76$, p<0.0001

Note. [a] Melatonin phase markers were included as continuous variables age group = 30-39 vs. 40-49yrs. Weekday = weekdays vs. weekends

Table 5.14 Estimated change in sleep end time for a 30-minute delay in melatonin phase markers

Regression equation	Time of melatonin phase marker	Estimated mean sleep end time
SlpEnd = -3.7047 + (0.4630*DLMO25)	19:20	5:15
	19:50	5:29
	20:20	5:42
	20:50	5:56
	21:20	6:10
	21:50	6:24
	22:20	6:38
	22:50	6:52
SlpEnd = -2.1058 + (0.4034*MelStart)	18:30	5:21
	19:00	5:34
	19:30	5:46
	20:00	5:58
	20:30	6:10
	21:00	6:22
	21:30	6:34
	22:00	6:46
	22:30	6:58
sqrtSlpEnd = 0.7147 + (0.05865*MelEnd)	6:30	6:16
	7:00	6:25
	7:30	6:34
	8:00	6:43
	8:30	6:52
	9:00	7:01
	9:30	7:11
	10:00	7:20

Table 5.15 Results of the post-hoc tests for differences between the estimated mean sleep end times by age group and weekday/weekend

Model	Fixed factor	Estimated mean sleep end time (hrs:mins)	Significant post hoc tests	Estimated difference between sleep end times (hours)
2	30-39yrs	7:40	$t_{(21.9)} = 3.23$, $p = 0.0039$	0.75
	40-49yrs	6:56		
	Weekday	6:40	$t_{(314)} = 17.33$, $p < 0.0001$	1.36
	Weekend	7:59		
3	30-39yrs	7:46	$t_{(24.8)} = 2.25$, $p = 0.0333$	0.81
	40-49yrs	6:57		
	Weekday	6:40	$t_{(345)} = 15.60$, $p < 0.0001$	1.38
	Weekend	8:03		
4	Weekday	6:37	$t_{(346)} = 14.65$, $p < 0.0001$	1.35
	Weekend	7:58		
5	Weekday	6:40	$t_{(346)} = 15.04$, $p < 0.0001$	1.37
	Weekend	8:02		
6	30-39yrs	7:43	$t_{(24.8)} = 2.07$, $p = 0.0487$	0.75
	40-49yrs	6:59		
	Weekday	6:39	$t_{(345)} = 15.47$, $p < 0.0001$	1.38
	Weekend	8:02		
7	30-39yrs	7:43	$t_{(24.8)} = 2.09$, $p = 0.0475$	0.75
	40-49yrs	6:59		
	Weekday	6:39	$t_{(345)} = 15.47$, $p < 0.0001$	1.38
	Weekend	8:02		
8	30-39yrs	7:38	$t_{(23.2)} = 2.62$, $p = 0.0151$	0.66
	40-49yrs	6:58		
	Weekday	6:38	$t_{(321)} = 17.10$, $p < 0.0001$	1.35
	Weekend	7:58		
9	Weekday	6:37	$t_{(339)} = 15.32$, $p < 0.0001$	1.30
	Weekend	7:55		

5.4 General Summary

Q1: Is there a difference in the nocturnal melatonin profile between morning-and evening-types?

Investigation of the averaged nocturnal melatonin profile found that there were no significant differences in the total amount of melatonin produced, the duration of secretion, the rate of increase or decline between morning- and evening-types.

There were large inter-individual variations in the levels of melatonin detected, with maximum values ranging from 14pM to 99pM. Despite such large differences, all of the methods used to determine circadian phase markers allowed identification of circadian phase for all participants.

Using the method proposed by Voultsios and colleagues (1997) DLMO was successfully identified in all 28 participants. It is interesting to compare this with the original definition for the determination of DLMO which Lewy and colleagues set at 10pg/ml (Lewy et al., 1999). In the present study only 9/28 participants had melatonin levels <40pM, which closely approximates the original threshold of 10pg/ml (Lewy et al., 1999; Voultsios et al., 1997). Thus the Lewy definition for the DLMO would not have allowed the identification of melatonin onset in these participants.

Q2: Is there a linear relationship between scores on the Morningness/Eveningness Questionnaire and circadian phase?

This study confirms previous reports of an inverse linear relationship between MEQ scores and circadian phase such that higher scores on the MEQ (i.e. increasing morningness) are significantly related to an earlier circadian phase of melatonin secretion.

Q3: What is the relationship between chronotype and circadian phase?

The greatest timing differences between morning- and evening-types were for markers of melatonin onset, which is consistent with the relationship between MEQ and melatonin phase described above. Furthermore, timing differences in markers of melatonin offset were smaller than that of melatonin onset, and only MelEnd reached statistical significance.

Q4: What is the relationship between circadian phase and actual sleep timing?

Actual sleep timing was estimated using the actigraphy and sleep diary data collected for each participant as part of the study presented in Chapter 4. The sleep parameters (sleep start, midpoint and end times) were averaged over different periods of time in order to investigate whether the inclusion of weekend main night sleep episodes (Fri and Sat nights), or the proximity of days to the overnight laboratory protocol, influenced the relationship between

sleep timing and circadian phase. As expected, mean sleep start, midpoint, and end times were significantly earlier among M-types compared to E-types, across each of the averaging periods.

(1) The univariate relationship between circadian phase and sleep timing.

The relationship between each of the circadian phase markers and sleep start time, sleep midpoint, and sleep end time, across each averaging period, was investigated to determine which sleep parameter was the best predictor of circadian phase. Correlation analyses found significant associations between each averaged sleep parameter and DLMO, DLMO25, DLMOff, DLMOff25, MelStart and MelEnd, such that an earlier melatonin phase position was associated with earlier sleep timing. The largest correlation coefficient was found for the association between DLMO and the midpoint of the main sleep episode averaged across the last five days preceding the phase assessment, which also remained significant among E-types.

When the relationship between circadian phase and actigraphic sleep timing were investigated within each chronotype, evening-types had an earlier DLMO which was associated with earlier sleep timing. This relationship was not found among M-types although the small number of participants in each group would have limited the statistical power to detect significant relationships.

(2) The internal relationship between circadian phase and sleep timing

Contrary to previous reports (Duffy et al., 1999; Hall et al., 1997; Liu et al., 2000) there were no significant differences in the phase angle between DLMO and sleep start, midpoint, or end time, between chronotypes in this study. This is possibly because the participants in the present study were able to follow their 'normal' sleep schedule which is likely to be influenced by other social constraints such as work patterns, and personal/family commitments (Mongrain et al., 2004). Typically, other studies have instructed participants to maintain a regular sleep/wake schedule or have investigated young adults who may have fewer constraints on their sleep. It is also likely that it is a consequence of the melatonin phase differences between chronotypes in this study, and that reported elsewhere

Both chronotypes demonstrated a longer phase angle between DLMO and the sleep parameters on the weekend, as they shifted their main night sleep episode to a later clock time.

In the analyses related to the phase angles calculated using the sleep parameters from the final night sleep episode, morning-types had a significantly longer phase angle from the midpoint of sleep to melatonin offset (DLMOff p =0.46 and DLMOff25 p =0.022). Although not significant at the 95% level, there was a tendency for M-types to have a longer phase angle between sleep onset and melatonin offset, and a shorter phase angle between sleep offset and melatonin offset. These observations suggest that evening-types wake at a later circadian time, when the levels of

melatonin begin to decline suggesting that societal norms truncate the sleep of E-types more than M-types.

On the other hand, the phase angles calculated on the final night suggest that E-types do not wake for 2 to 3 hours after melatonin offset (DLMOff and DLMOff25) and the average phase angle between the last detectable melatonin level and sleep end was 1.7hrs.

(3) The influence of circadian phase, age group and weekday/weekends on sleep timing

After controlling for age, mixed model ANCOVAs found that circadian phase (as measured by DLMO, DLMO25, MelStart and MelEnd) and weekday/weekends had a significant influence on sleep start times across a two week period. The modelling indicated that an earlier circadian phase predicted an earlier mean sleep start time, such that for every half hour delay in melatonin onset time, the estimated mean sleep start time was 10-12 minutes later. Weekday/weekend differences were found to have a stronger influence on sleep start times than circadian phase, with sleep start times approximately 28 minutes later on Friday and Saturday nights compared to weekdays.

The mixed model ANCOVAs indicated that circadian phase, age and weekday/weekend differences each have a significant influence on sleep end times. As for the sleep start models, the only phase markers which had a significant main effect on sleep end times were DLMO25, MelStart and MelEnd. With every 30 minute delay in circadian phase the estimated mean sleep offset was 7-10 minutes later.

When circadian phase was represented by DLMOff25, DLMO50, midpoint, peak, and MelStart, there was a significant main effect of age on sleep end times. Post-hoc analyses indicated that sleep end times were approximately 40-49 minutes later among younger participants aged 30-39yrs. There was also a consistent and significant main effect of weekday/weekend differences on sleep end times, such that the estimated mean sleep end time was approximately 1.30-1.38 hours later on weekends.

Q4. Are differences in weekday/weekend sleep timing related to differences in circadian phase between morning- and evening-types?

As expected, there was a significant difference in the timing of sleep between Ms and Es on both weekdays and weekends. Melatonin phase markers were more strongly correlated with weekday sleep timing for the whole group (i.e. *r* is larger for weekday comparisons) and were similar for each chronotype. Although not significant, there was a pattern for both M and E-types to shift their weekend sleep to a later time relative to DLMO, by approximately the same amount (i.e. no significant difference in DLMO phase angles on weekends or weekdays). Mixed models found that weekday/weekend differences had a stronger influence on sleep timing than endogenous circadian phase.

CHAPTER 6
THE DEVELOPMENT OF A KAUPAPA MĀORI ETHIC FOR GENETIC RESEARCH

6.1 A Personal Introduction

Ko Mataatua te waka
Ko Maungapohatu te maunga
Ko Waikaremoana te roto
Ko Tauarau te marae
Ko Ngāti Rongo te hapū
Ko Tūhoe te iwi
Ko Te Hereripine Sarah-Jane Paine taku ingoa
No Wairoa ahau.

This whakapapa (genealogy) defines my identity as Māori, but more specifically it determines my identity as distinctly Tūhoe. It describes the relationships with other iwi (tribes) who came to this place on the Mataatua waka (canoe) and landed in Whakatane, in the Bay of Plenty. It describes our strong spiritual relationships with the physical landscape of Te Urewera (the lands belonging to Tūhoe), the mountains, rivers and lakes which boundary and protect the rohe (tribal area) of Tūhoe and from which we derive our identity (Higgins, 2004). This whakapapa denotes my relationship with members of the Ngāti Rongo hapū (sub-tribe), descendents of the tipuna (ancestor) Rongokarae, and who find solace at Tauarau marae (a ritual site) in the Ruatoki valley. The name Te Hereripine, told to my mother before I was born, comes from a woman of Te Mahurehure and Te Whakatane hapū (Milroy, 2006), and so this whakapapa also describes the many interlocking relationships between the different hapū of Tūhoe. This whakapapa irrefutably determines my relationship to the Tūhoe iwi, the people of Te Urewera, who have maintained a unique cultural identity, despite social and political oppression including the raupatu, or illegal confiscation, of Tūhoe land by the Crown. It also affirms my relationship with other iwi. Growing up in Wairoa, Hawkes Bay, I lived amongst the Ngāti Kahungunu iwi who hold the mana (prestige) of this area. Conversely, my whakapapa also reflects the history of tribal war with Ngāti Kahungunu and other bordering tribes to consolidate and affirm the mana of Tūhoe.

It can be said that knowledge is a taonga, a most treasured possession. However, modern society presents significant challenges to the validity and integrity of traditional knowledge systems. In the preface to the second edition of *Tūhoe: The Children of the Mist* (Best, 1972) Elsdon Craig (the grand-nephew of the author) wrote

> …The ancestors saw the threat of changing ways to the sacred culture, when they commanded my tupuna: "Son! The day is far spent and night approaches swiftly. Therefore go you forth and collect the fragments of *Mataatua*, where for twenty generations of men, that sea-worn craft has swung to her stone anchor by the rocks of Hinga-rae." They were true scholars, those kaumatua, their academic roots firmly set in the old traditions, their fertile minds ready to grasp the learning of the Western world (p. vii).

The forethought of our old people, to allow Pākehā into Tūhoe lands to hear and record their stories, ensured that in this changing world, the sacred knowledge contained within our whakapapa would forever be in the possession of our people.

The interaction between old and new ways of knowing is a constant feature of my own journey towards te ao marama, the world of light. My understanding of our traditional mythology, tikanga Māori (traditional practices) and Tūhoe kawa (protocol) is juxtaposed to my formal education and training in Western schools of knowledge and science. No more so was this evident than in 2000 when I was a Masters student at the University of Otago. In my final year of this program I was awarded the Te Rangihau scholarship, named after an esteemed kaumatua and scholar from Tūhoe. In the same year, the Government established the Royal Commission on Genetic Modification (RCoGM) to look into and report on the issues of genetic modification (GM) in New Zealand. Prior to one of the regional hui (meetings) held by the RCoGM, I was contacted by the Tūhoe/Waikaremoana Trust Board (the governors of the Te Rangihau scholarship) and asked to assist them in their preparations for this hui by defining the issues of GM for Tūhoe. Here I was, a 'scientist' in the eyes of my tribe, yet I had no understanding of the process of genetic modification and had never considered the ways in which Western science challenged the cultural and economic sovereignty of my iwi. Despite my naivety, I set about the task asked of me because of the relationships and obligations that are inherent within my whakapapa. Luckily, my parents were much more knowledgeable on the issues than their university educated daughter and were willing to help me understand.

And so my personal history defines my role in this study. First and foremost I position myself as Māori. My own sense of identity was instilled in me by my mother, who showed me the pride that can be derived from knowing my whakapapa, tempered with the humility of knowing where we come from. While the whakapapa that opens this chapter defines my position in the present study, it also speaks to the heart of the issues raised in this chapter which are ultimately about relationships.

My identity as Māori facilitated the development of strong relationships with the other researchers involved in this study and each of the participants, all of whom also identified themselves as Māori. Being Māori defined the ways in which I carried out the research, which was also affirmed by the Kaupapa Māori theory underpinning this study. It also dictated that I

write this chapter in a manner that prioritises Māori experiences and aspirations. As the primary researcher in this study, I was concerned with maintaining the integrity and rigour of the research presented here. However in writing this chapter I have not separated myself from the discussions which were held, because they speak to the reality of Māori living in New Zealand society. Nonetheless, I also recognise and affirm my position as a scientist trained in Western scientific methods. While much of this chapter critiques Western scientific knowledge and methodologies, I acknowledge that these histories and experiences are as much about my own research practice as they are about any other researchers or scientists in Aotearoa/New Zealand. Now is the time for the scientific community to reflect on the ways in which we seek knowledge and it is hoped that the narratives presented in this chapter will be read as lessons for how we all can take a more responsible approach to science.

6.2 Background

This chapter presents the findings of a qualitative study that investigated Māori hopes and concerns for genetic research in Aotearoa/New Zealand. It begins by providing a background to Māori understandings of genetic research, which are derived from a traditional body of knowledge known as mātauranga Māori and our position as tangata whenua (indigenous people). An overview of Māori conversations about genetics is presented along with a description of Kaupapa Māori theory, both of which come together to provide the framework for the analysis used here. The rationale for the methodology is then summarised, along with a detailed description of the processes that were used to carry-out this study. The study findings are then presented within the context of the relevant literature, and finally the development of an ethical framework within genetic research is discussed in terms of Māori needs and indigenous rights.

Although this study does not have a particular focus on the ethical implications of sleep and circadian rhythms research in New Zealand, the issues that are raised are indeed relevant for this discipline given the possibility that sleep disorders, for example, might be treatable through interventions targeting genes of molecular systems that are involved in maintaining and regulating sleep timing.

6.2.1 Research as a Tool of Colonisation

Research on Māori (not *with* Māori) is deeply connected to our experience of being colonised within our own country. Linda Smith (1992) describes this as 'a stripping away of mana…to be colonized [sic] is to be defined by someone else and to believe it even though you are confronted daily by evidence to the contrary'. When research compares Māori realities against the 'norms' of Western society it disregards the unique history and culture of Māori people. Generally, Western forms of research have taken a deficit-based approach to their research of Māori communities. As Koro Dewes (Ngāti Porou) once said

> I'm sick and tired of hearing my people blamed for their educational and social shortcomings, their limitations highlighted, and their obvious strengths of being privileged New Zealanders in being bilingual and bicultural ignored (cited in (International Research Institute for Māori and Indigenous Education, 2002)).

One Māori experience of research has seen the perpetuation of colonial values and a belief that it is Māori who must make changes in order to fit the model of the mainstream Pākehā majority(Cram, 2001b). This 'researching down' experience is shared with other indigenous peoples who have been forced to exist within a victim-blaming culture which highlights the misfortunes of individuals whilst ignoring the insufficiencies of Western society (Cram, 2001b).

Research has also been used by local and central government 'as a control strategy on Māori' (Teariki, Spoonley, & Tomoana, 1992). From these experiences Māori understand that research is often about the control of information and resources (Te Awekotuku, 1991) and the maintenance of power and social hierarchy.

Research has been a key tool in the marginalisation of indigenous realities and many indigenous peoples argue that genetic research presents a new site for the further colonisation of our knowledges. Within the genetic research discourse, Māori concerns stem from scientific colonialism which describes an epistemological approach whereby a dominant view and knowledge system (e.g. positivism) is enforced onto minority groups. This is evident as (a) the removal of wealth from the population, through commercialisation of the information gained (b) the right of and unlimited access to the subject population, and finally, (c) the creation of an external power base. Cram (2002) explains that this reflects the power structures of society where scientists and their knowledges are regarded as 'truth' while other systems and ways of knowing are viewed as illegitimate and sometimes even completely ignored. Dell Small (cited in (Cram, 2002)) argued that the paradigm of scientific colonialism was limited, as the oppressors (with the assistance of their scientific tools) determined the research from the outside therefore the research was not the 'problem of the oppressed (p. 7).' As a framework for research in Aotearoa/New Zealand, scientific colonialism undervalues mātauranga Māori (traditional Māori knowledge), and legitimises Western knowledge.

Māori concerns about genetic research also speak to our indigenous rights and tino rangatiratanga (sovereignty, self-determination). The 1840 Treaty of Waitangi (Appendix 27) is recognised as the founding document of Aotearoa/New Zealand which regulates the relationship between Māori, as tangata whenua (the indigenous people), and the Crown. Māori participation in research is implicit within each article of the Treaty of Waitangi however the Treaty must also be recognised as a document and agreement that promises protection, participation and partnership within research. Importantly, Article II guarantees tino rangatiratanga (sovereignty, self-determination) over the research that we participate in and Māori rights and responsibilities to make decisions based on our cultural values and customary preferences (Putahi Associates, 1999). Within the context of genetic research Du Plessis and colleagues (2004) understood that the Treaty ensures the protection and promotion of Māori interests whilst also providing a pathway for debate and legislation.

Māori rights within genetic research are also enforced through the Mataatua Declaration on Cultural and Intellectual Property Rights of Indigenous Peoples (Appendix 28) which makes recommendations for indigenous peoples, states, national and international agencies and the United Nations, in regards to biodiversity (Mead, 1997). The Mataatua Declaration recognises that indigenous peoples are the guardians of their customary knowledge and that we have the

right to protect and control dissemination of that knowledge. It also recognises that indigenous peoples have the right to create new knowledge based on cultural traditions and that indigenous peoples must be the first beneficiaries of their cultural and intellectual property (Mead, 1997).

6.2.2 The Basis of Māori Knowledge on Genetic Research

Although the Treaty of Waitangi and the Mataatua Declaration provide legal frameworks for talking about Māori rights within genetic research, the depth and breadth of Māori understandings of genetic research and Western science more generally are based within a traditional knowledge system known as mātauranga Māori. In order to appreciate the ways in which Māori talk about genetic research, it is important to recognise the foundations on which these understandings are constructed.

Mātauranga Māori

Professor Hirini Mead (2003) described mātauranga Māori or traditional Māori knowledge as '…a tool for thinking, organizing [sic] information, considering the ethics of knowledge, the appropriateness of it all and informing us about our world and our place in it (p. 306)'. Māori cosmological narratives (Du Plessis et al., 2004) are set back in the ancient homelands of Hawaiiki, and tell the story of the origins of the world and the place of all living and non-living things within it. In her analysis of one of these narratives, Linda Smith (1992) learnt some important lessons about mātauranga Māori; firstly that knowledge was sought on behalf of everyone and secondly that traditional forms of knowledge are specialised. Similarly the sanctity of mātauranga Māori is clearly expressed in these stories, for instance traditional knowledge is highly valued and although knowledge belonged to the collective, it was not always available to all members of Māori society. Knowledge is also tapu (sacred) and guarded by sanctions or traditional practices (tikanga Māori) in order to protect the knowledge and ensure safe transmission from person to person. Knowledge is also hierarchical and that being entrusted with knowledge enhanced the mana (prestige, esteem) of those who received it (Smith, 1992b). Mead (2003) explains that research for Māori is about expanding knowledge outwards (te whanuitanga), in depth (te hohonutanga) and towards light (te maramatanga).

Tikanga Māori

Because traditional Māori knowledge was tapu, it was firmly connected to the system of beliefs and values of Māori society, known as tikanga Māori (Mead, 2003). Tikanga Māori focuses on the principles of tika (right or correct) and pono (meaning true or genuine) and is based on three interdependent elements: *background knowledge* – based on history, knowledge of the environments, religious views, beliefs and worldviews; *concept* – derived from the background knowledge which represent the ideas that are of key importance; and *practice* – what is actually performed or carried out (Mead, 2003).

Tikanga Māori provides a framework (Mead, 2003) for the actions of Māori as individuals and as whānau (family), hapū (sub-tribe) and iwi (tribe) and represents the values (or principles) of Māori society which include, but are not limited to:

Whānaungatanga: A fundamental principle which embraces whakapapa (genealogy) and focuses on relationships. It is also related to the principle of he kanohi kitea (the face seen), which expresses the importance of seeing family members in order to keep the bonds of Whānaungatanga strong.

Manaakitanga: Underpins tikanga Māori and refers to an expected standard of behaviour which is to be aspired to. Often described as hospitality, it places importance on taking care of people and nurturing relationships. Mead (2003) describes aroha (love) as an essential driving force of manaakitanga.

Mana: This value has many meanings including authority, control, influence, prestige and power. Mana is drawn from our ancestors and is socially confined and mediates human relationships. Mana is to be respected and maintained at all costs.

Tapu: Is the most important element of all tikanga. Tapu is everywhere and is present in all things living, and not living. Mead (2003) understands tapu as inseparable from mana, and from Māori identity and cultural practices.

Utu: is defined as compensation, revenge or reciprocity. Utu is invoked when tikanga has been transgressed, and is a necessary component in restoring balance.

Noa: refers to the restoration of balance and is usually paired with tapu, however Mead (2003) cautions against the common perception that it represents the opposite of tapu.

Ea: is related to noa, and among other things, indicates the successful restoration of relationships.

6.2.3 Māori Talk about Genetic Research

> It is within the main principles of mauri, mana and whakapapa that Māori raise their absolute disagreement regarding genetic engineering and modification. If these principles are damaged or tampered with in any way, thus upsetting the holistic world balance, so too will be the mauri, mana and whakapapa of Māori and following generations. (Ngā Wahine Tiaki o te Ao [IP64]. Interested Person Submission. Executive Summary (Eichelbaum et al., 2002)).

There is a growing body of literature that articulates the main issues and concerns for Māori with regards to genetic research. Representatives such as Aroha Mead, Moana Jackson, Cherryl

Smith and Maui Solomon[7] continue to challenge those who wish to justify and legitimate the misappropriation of our traditional knowledges and tino rangatiratanga via genetic research. Additionally, Māori views on genetic research and the related technologies have been expressed in a number of forums. The following section will provide an overview of the ways in which Māori have been talking and writing about genetic research in Aotearoa/New Zealand.

Wai262

The depth of Māori concerns regarding the control and ownership of genetic information is appropriately illustrated by the Wai262 claim to the Waitangi Tribunal, commonly referred to as the 'flora and fauna claim'. The scope and scale of this claim was wide-ranging seeking recognition and protection of indigenous flora, fauna and the genetic resources contained therein as well as cultural knowledge and property as taonga protected by Article II of the Treaty of Waitangi.

> The Wai262 effort to protect and enhance mātauranga Māori and to insist on te tino rangatiratanga o te iwi Māori in Aotearoa is not an isolated phenomenon. Throughout the world indigenous peoples are networking in order to preserve their culture, traditions and ways of life from the ever-threatening and often totally overwhelming impact of governmental policies of modernisation and development (p. 27 in (Williams, 2001)).

As the first example of Māori resistance to biotechnology, this claim brought to the fore critical issues that highlighted 'the importance of the respect of all traditional Māori knowledge, the need for active protection of the knowledge and … Māori rights to absolute chieftainship over Māori knowledge and ways of doing things'(Smith & Reynolds, 2000).

Whose genes are they anyway?

In 1995, the Health Research Council of New Zealand (HRC) sponsored a Consensus Development Conference on Human Genetic Information, which sought to facilitate discussion and debate about genetic information and identify issues for health research. The key questions were:

(1) Who should have the right to know genetic information?

(2) What criteria should be used for genetic testing?

(3) What ethical and legal controls do we need for testing? (Baird et al., 1995)

At this conference, Māori acknowledged and affirmed beneficial treatments derived from genetic research that would enhance the quality of life for Māori as Māori define it. However

[7] This is by no means an exhaustive list of Māori who are speaking, writing and representing Māori concerns around genetic research.

the was some concern that talking genetics undermined the importance of social, economic and political determinants of health.

The relevance of genetic research was questioned given that we are already able to 'map' our being through whakapapa and mātauranga Māori. The Māori caucus described iratangata, the term used for gene, as the life principle of mortals which connects the spiritual to the physical world and is held within Māori as the repositories of whakapapa. It was pointed out that ownership and kaitiakitanga (guardianship) of genetic information is therefore embedded within the particular whānau, hapū and iwi, and as such it may be out of reach for many Pākehā researchers. Concerns were raised around issues of ownership of any genetic material that is taken for research, and the need to ensure that Māori are able to make informed decisions regarding genetic research.

Although the use of stringent ethical procedures in research was confirmed, many Māori participants had little confidence in the research practices of scientists and were concerned that Western scientific knowledge and methodologies marginalised Māori world views. The Māori caucus was adamant that the preservation of dignity and respect is paramount; therefore genetic research must uphold the mana of the participant(s) involved and acknowledge different aspects of tikanga. Finally it was recommended that an ethical framework for genetic research in health must recognise the Treaty of Waitangi and Māori rights to tino rangatiratanga.

The Royal Commission on Genetic Modification

The Royal Commission on Genetic Modification (RCoGM) was established in 2000 to report on the issues surrounding genetic modification in Aotearoa/New Zealand. Māori voices throughout the consultation process were comprehensive, considering health and medicine, food and crop production, the environment, research, intellectual property rights and the Treaty of Waitangi. The concerns and issues that were highlighted by these voices were not only specific to the Māori community but often also shared by non-Māori (Durie, 2004).

Despite the unreasonable timeframe allocated to the consultation process, Māori were united in their concerns for genetic modification and at the National Hui this effort culminated in the development of 16 recommendations on genetic modification which were based within the Treaty partnership between Māori and the Crown and which sought to develop processes for constitutional change and the legitimisation of Māori concerns (see Appendix 29). In his submission to the RCoGM, Moana Jackson a lawyer and active campaigner for Māori sovereignty noted that Māori considerations are often '…marginalised as cultural, rather than scientific or intellectual…' Drawing on the notion of scientific colonisation, Jackson continued

> '…Māori are asked to offer a 'mere' perspective which easily leads to rejection on the grounds of unreasoned, if interesting, spirituality or minimalisation as something that may be noted but

> ignored if more compelling scientific or economic reasons can be discovered' (Appendix 3 Section 4.1 of (Eichelbaum et al., 2002)).

The RCoGM began with promises to listen to Māori however by the time the report was issued, the input of Māori had been both simplified and toned down. Sivak (2005) argued that the bureaucratic framework of biculturalism used by the RCoGM failed the Māori community, as notions of partnership did not translate to Māori involvement in the setting of the parameters of the Inquiry. In his analysis of the final report Simon Upton (cited in (Jackson, 2001)) observed that 'Māori have been listened to with exquisite politeness and cosmic tact and then basically passed by'. We should perhaps therefore consider the RCoGM to be a starting point for Māori conversations about genetics.

Māori and genetic engineering

The diversity and richness of Māori understandings were also expressed in a comprehensive report entitled Māori and Genetic Engineering (Cram, Pihama, & Philip Barbara, 2000). As the authors pointed out, the purpose was not to provide *the* Māori perspective, but to document the complexity of Māori talk and depth of engagement with the issues.

The use of scientific terminology was considered problematic and there was a need to clarify the definition of science and whose science we are talking about. It was agreed that genetic engineering was of major relevance to Māori because of the Treaty of Waitangi, our obligations to future generations and the need for Māori to control our own destinys. Tikanga Māori was a key feature in many of the conversations which highlighted the importance of wairua, whakapapa and mauri.

There was concern that GE food and food production was a mixing of whakapapa because of the insertion of genes from one species into another. The risk of pollution was both physically and spiritually unacceptable and there was a call to focus on increased production and availability of organic kai (food). The argument for 'feeding the world' was unjust and there was a strong concern that GE would have a 'potentially disastrous impact' on rongoa Māori (traditional medicines and healing practices (Jones, 2000)).

When talking about human health there was a need to weigh up personal beliefs against collective well being. It was proposed that arguments for GE medicine were driven by a 'colonised mindset' and that Māori should be weary about making decisions based on survival.

There was an urgent call for Māori to be included in the development of research protocols and the need for a 'by Māori for Māori' approach to research. Māori communities must be involved in the decision-making and dissemination processes and that as individuals or communities Māori have the right to say no to any forms of genetic engineering.

Māori talk around GE also included concerns regarding globalisation, multi-national corporations, cultural and intellectual property rights, commodification and the maintenance of iwi development within this context.

Constructive conversations

The Constructive Conversations/Korero Whakaaetanga programme takes a multi-disciplinary approach to '…explore the social, cultural, ethical and spiritual implications of new health biotechnologies … and to enhance public participation in discussion and decision-making…' Te Kopere (a caucus of Māori researchers) act as kaitiaki (guardians) of information generated through the involvement of Māori in this programme and have identified and explored five interconnected themes which represented Māori views on genetic testing and the storage of genetic materials (Du Plessis et al., 2004).

Mana describes the maintenance of the integrity of a 'specifically Māori world view and identity'. Mana was also understood in terms of ethicality (Durie 1998, cited in (Du Plessis et al., 2004) because it informs everyday actions and interactions. *Whakapapa* illustrates differences in Western- and Māori-views of relationships. In terms of genetics, the Western-view is that a gene is a separate entity within the genome whereas a Māori-view is that we are located in relation to all living and non-living things, including all parts of the cell. *Mauri* was the '…sense of the elemental forces or energy that bring into being all life forms – both animate and inanimate – and an understanding of that which makes them unique.' Mauri was central to the deep understanding of whakapapa, and a 'higher order mauri' was connected to the responsibility of Māori to the protection of the social structures of whānau, hapū, and iwi. Mauri was inferred through expressions such as tampering with life forces and the 'mystery' of life. *Kaitiakitanga* denotes 'the exercise of guardianship by the tangata whenua of an area in accordance with tikanga Māori and in relation to natural and physical resources.' It was noted that hapū and iwi require mana and tino rangatiratanga to exercise their kaitiaki role. The notion of guardianship was expressed in terms of the protection and maintenance of Māori interests. Kaitiakitanga also facilitates Māori scrutiny of issues such as genetic technologies. *Tino rangatiratanga* represented a way for Māori to unite within a common discourse of decolonisation and resistance and was a statement of authority (see (Smith, 1999)). Tino rangatiratanga expressed the 'regaining/retaining' of rights around whānau health and wellbeing and articulated the right to be Māori and to be involved in decision-making.

Te Kopere observed that Māori understandings of genetic testing were framed by our experiences of colonisation, however they recognised that their participants talked from 'the centre' so as to maintain tangata whenua rights, sovereignty, mana Māori and the integrity of a Māori world view.

Community initiatives

It is important to note that Māori are not 'anti-science', in fact many of the conversations affirm Māori rights to engage with Western-science, and genetic research, for the development and advancement of Māori society. Within our own communities Māori have been talking about and strategising their hopes for genetic research for some time. In 1994 a whānau from Tauranga-Moana initiated a research partnership with scientists from the University of Otago with the hope of identifying genes responsible for the unusually high incidence of gastric cancer among their whānau. As Rankine and McCreanor (2004) discovered

> This project was remarkable because the whānau team compiled their own genealogy and collected the tissue samples, being an active research partner rather than accepting the subject position more usual for affected families. The two teams negotiated an agreement involving culturally appropriate management and ownership of tissue samples, a shared patent for the genetic test and regular reporting by the genetics team at whānau hui (Rankine & McCreanor, 2004).

Whānau involvement throughout the process was critical for the success of the project, because without them, the researchers from the University would not have gained access to the whakapapa information which enabled the development of a pedigree vital for establishing inheritance patterns. For the whānau, working with the geneticists and clinicians put into motion their aspirations to understand the 'illness' and develop a screening and early intervention programme. Importantly, it also provided assurances that their taonga would be protected.

6.2.4 Māori Sovereignty within Research and Ethics in Aotearoa/New Zealand

The convergence of a number of factors and experiences made way for the development of new ways of thinking about Māori research. The Māori education movement, developments in iwi research capability and the general renaissance of Māori culture over the last 30 years have all been identified as significant features within Māori resistance and decolonisation of deficit-based models of research (Cram, 2001b).

The desire to regain control in health research is expressed in The Hongoeka Declaration for Māori Health Researchers, which states 'we believe Māori health research should be determined and coordinated by Māori, working with Māori, for Māori.' It endorses the Mataatua Declaration and includes guidelines for Māori undertaking health research that upholds the notions of tino rangatiratanga, control, empowerment, accountability and development (Harris, 2003).

Tino rangatiratanga in research is about controlling the research that is done with Māori and directing the future of research in Aotearoa/New Zealand. The Treaty of Waitangi affirms our right to conduct research that is by Māori, for Māori, using the tools that we see as valid thereby

ensuring that research does not marginalise and colonise us further (Jackson, M (1987/1988) cited in (Cram, 2001b)). Te Awekotuku (1991) suggested that in order to avoid the imperialist mistakes of the past, research needs should be expressed from within the community, not from the outside.

As part of the process of regaining control, questions have been asked about the role of Pākehā researchers in Māori research projects (for a review see (Powick, 2003)). One attempt to bring Pākehā into line with Māori aspirations for research have included the development of documents and guidelines outlining processes to be followed when researching in Māori communities (e.g. (Health Research Council of New Zealand, 1998)). Within the field of education, models have been proposed which outline how culturally appropriate research can be conducted by Pākehā researchers (Smith, 1992a) (Table 6.1).

Table 6.1 Models for Pākehā researchers working with Māori communities.

Model	Explanation
The Tiaki Model	The Mentor Model, where authoritative Māori guide and mediate the research enterprise
The Whāngai Model	The Adoption Model, where researchers are 'adopted' by the community or whānau to the extent that they are considered as part of the whānau, and therefore can be trusted to do it right
The Power-Sharing Model	Where researchers seek the assistance of the community to meaningfully support the development of a research enterprise
The Empowering Outcomes Model	Where the research enterprise has positive and beneficial outcomes for Māori first and foremost. This relates to the original research questions being designed to answer questions and provide information that Māori themselves want to know

Source: Smith, G.H. (1992) & Powick, K. (2003)

Linda Smith (1999) also suggests that the following questions must be asked within cross-cultural research to ensure that the research is respectful.

- Who defined the research problem?
- For whom is this study worthy and relevant? Who says so?
- What knowledge will the community gain from this study?
- What knowledge will the researcher gain from this study?
- What are some possible negative outcomes?
- How can the negative outcomes be eliminated?
- To whom is the researcher accountable?
- What processes are in place to support the research, the researched and the researcher?

However, culturally appropriate research for Māori is:

- not for everyone
- about developing ways to devolve power and control in the research exercise
- about adapting ourselves as researchers to fit Māori cultural preferences and aspirations and to recognise the local context in which we are placed
- and that research of benefit to Māori needn't necessarily focus on Māori; there is ample work and research to be developed by looking at the impediments within Pākehā structures (Smith, 1992a).

Māori researchers found that they also faced a number of hurdles in the struggle to conduct respectful research, which included convincing Māori of the value of research; convincing the various fragmented but powerful research communities of the need for greater Māori involvement in research; and developing approaches and ways of carrying out research that would take into account, without being limited by, the legacies of previous research and the parameters of both previous and current approaches (Smith, 1999). Reflecting on our own processes and methods of analysing our communities lead to the development of an indigenous methodology known as Kaupapa Māori research, or Māori-centered research.

Kaupapa Māori is not new (Cram, 2001b) but instead speaks to the active positioning of Māori as tangata whenua and our struggle for the recognition and legitmation of te reo Māori and tikanga (Pihama, L. (1993) cited in (Cram et al., 2000)). Although the main theoretical work was carried out within education, Kaupapa Māori has been applied across a range of projects using a number of different methods (Harris, 2003). Graham Smith (1992) suggests that Kaupapa Māori is a local theoretical positioning related to being Māori such that:

- The validity and legitimacy of Māori is taken for granted
- The survival and revival of Māori language and culture is imperative
- The struggle for autonomy over our own cultural well-being, and over our own lives is vital to Māori survival

Much of the discussion around Kaupapa Māori is related to notions of critique, resistance, struggle and emancipation (Smith, 1999). Leonie Pihama (1993) (cited in (Cram, 2001a)) explains that Kaupapa Māori theory inherently involves the analysis of power structures and social inequalities and the critique of the hegemonic practices which justify the continued oppression of Māori. In this way Kaupapa Māori allows for the analysis of the dominant Western worldview and provides space for Māori realities by naming this Western 'common sense' as just another alternative cultural perspective. Kaupapa Māori is about retrieving space for Māori voices and our right to be Māori within wider society. In this way, Kaupapa Māori is about social change.

Table 6.2 summarises five principles which are integral to Kaupapa Māori research and derived from Māori philosophy values and practices (Mead (1996) cited in (Powick, 2003)). As Cram (2001) acknowledges, not all Māori researchers choose to use these names or conduct their research within this frame. However, Linda Smith (1999) explained that this intentional naming was about bringing indigenous values, attitudes and practices to the centre. Some commentators have attempted to distinguish between Kaupapa Māori and Māori-centred research. For example, Cunningham (2000) developed a framework which categorises research according to its ability to contribute to the Māori knowledge base and Māori development. Using this taxonomy, research is defined as:

(1) Research not involving Māori

(2) Research involving Māori

(3) Māori-centred research

(4) Kaupapa Māori research

The boundaries of the categories are based on the level of Māori control, Māori involvement as participants, researchers and users, the methods and tools used to collect the 'data' and the type of analysis that is applied (Cunningham, 2000). However, others have argued that distinguishing between categories of research limits the potential of Kaupapa Māori research in terms of its growth and development. Similarly there are concerns that using narrow definitions provides an opportunity for Māori to be denied the right to define their research as Kaupapa Māori which challenges the principles of tino rangatiratanga and participation. There is also the potential that

these definitions may provide non-Māori with the power to define Kaupapa Māori research (Harris, 2003).

Table 6.2 The principles of Kaupapa Māori research

KMR principle	Explanation
Whakapapa	The most fundamental aspect of the way Māori think about and come to know the world. Whakapapa contributes to Kaupapa Māori research as it is embedded in Māori knowledge and thinking patterns
Te Reo	Māori worldviews are embedded within te reo me ona tikanga (the Māori language and traditional practices) and it is through te reo that a path to the histories, values and beliefs of Māori is drawn. Within the context of Kaupapa Māori research it is expected that some participants will choose to convey their knowledge in te reo Māori, and so for the benefit of the project the researcher must also possess a knowledge of the language
Tikanga Māori	Tikanga is important within Kaupapa Māori research as it ensures that the researcher conducts the project in the correct manner. The mentorship of a kaumatua may be an important part of Kaupapa Māori research as sometimes the importance of tikanga can be taken for granted by the researcher. Interwoven within this concept is the appreciation and awareness of tapu to ensure that the appropriate tikanga are followed
Rangatiratanga	This principle is directly related to the process of decision making and collectivism between the researcher, whānau, hapū or iwi involved. Rangatiratanga affirms the importance of addressing the kaupapa of the research to Māori who remain central to the project, rather than in consultation on the side.
Whānau	The principle of whānau provides support for the Kaupapa Māori research to develop and consequently Kaupapa Māori research requires a number of obligations and responsibilities on behalf of the whānau. The whānau principle is also divided into different dimensions (gender and age) due to the different roles that whānau members play in the research.

Source: Powick, K. (2003)

In Aotearoa/New Zealand ethical reflection within mainstream research is governed by eight 'cultural' principles (respect for persons, informed consent, privacy and confidentiality, validity of the proposal, minimisation of harm, justice, cultural and social responsibility and compensation for research participants (Ministry of Health, 2006)), which take into account the universal principles of autonomy, non-maleficence, beneficence, and justice. These notions of ethics are derived from the teachings of the Christian church, where God is an external force, and humans live and exist within His creation. However, when Māori are asked to reflect on ethics the talk often takes a broader view, drawing not only from Western philosophy and Christianity but also from the traditional intellect of mātauranga Māori, which considers humans as an integral feature of the world, existing within relationships and not merely as an observer of it.

The Operational Standard for Ethics Committees (Ministry of Health, 2006) lists a number of elements that are specifically relevant to Māori within the process of ethical review of health research which focus on the importance of collectivism and traditional values and practices (Table 6.3). Furthermore, 'ethical' research for Māori also considers mana tangata (dignity, safety and mutuality); mana whakahaere (collaboration, control) and mana motuhake (effective outcomes and evidence of benefit) (Durie, E 1998 cited in (Powick, 2003).

Table 6.3 Principles of ethical review of health research in Aotearoa/New Zealand

Main principles	Additional issues for Māori
Respect for persons	Respect for Māori collectives - whānau, hapū and iwi
Informed consent	Gaining consent of collectives
Privacy and confidentiality	Collective ownership of information
Validity of research proposal	Kaupapa Māori and Māori-focused methodologies
Minimisation of harm	Minimising harm to te taha whānau (family and community), te taha hinengaro (emotional wellbeing and state of mind), te taha wairua (spirit), te taha tinana (the body or physical self)
Justice	
Cultural and social responsibility	Cultural diversity, koha (donation, present or gift)
Compensation for research participants	

Note: from *The Operational Standard for Ethical Review in New Zealand* (p. 6), by the Ministry of Health, 2006, Wellington: Ministry of Health. Reprinted with permission

Kaupapa Māori theory dictates that tikanga is followed throughout the entirety of the research process 'from inception to the dissemination of results to the ongoing relationship formed between the researcher(s) and the participant(s) (Cram, 2001b)'. Mead (2003) explained that the notion of tika should be a guiding principle for those who conduct research '…so that in the end everyone who is connected with the research is enriched, empowered, enlightened and glad to have been part of it.' For many indigenous peoples, ethical principles reflect the same ideas which regulate our relationships with each other and the environment and that integral to these relationships is the maintenance of respect such that '…everything in the universe is kept in balance and harmony'(Smith, 1999). To respect these values Linda Smith (1999) listed seven 'sayings' which govern the ways in which we behave. Cram (2001) explored these value statements further and explained their relevance to addressing researcher ethics and behaviour in cultural terms, which have been summarised in Table 6.4.

Table 6.4 Māori cultural values as guidelines for research ethics

Cultural values (Smith, 1999)	Researcher Guidelines (Cram, 2001)
Aroha ki te tangata	A respect for people. About allowing people to define their own space and to meet on their own terms
He kanohi kitea	The seen face. About the importance of meeting with people, face-to-face
Titiro, whakarongo…korero	Look, listen…speak. About the importance of looking and listening so that you develop understandings and find a place from which to speak
Manaaki ki te tangata	Share and host people, be generous. About collaborative approach to research, research training and reciprocity
Kia tupato	Be cautious. About being politically astute, culturally safe and reflective about our insider/outsider status
Kaua e takahia te mana o te tangata	Do not trample over the mana of people. About sounding out ideas with people, about disseminating research findings, about community feedback that keeps people informed about the research process and the findings
Kaua e mahaki	Don't flaunt your knowledge. Also about sharing knowledge and using our qualifications to benefit our community

6.2.5 The Place of Public Consultation in Ethics

To ensure the effective monitoring of genetic research within Aotearoa/New Zealand the development of ethical guidelines should reflect the spectrum of views that is held within our communities. The way in which this is achieved is through public consultation. Burgess (2005) describes consultation in research and clinical ethics as 'an attempt to describe the various perspectives of the interested parties…in sufficient depth to enable a shared understanding and clear ethical analysis.' In this way, consultation requires what is meaningful and provides a clear pathway towards a shared understanding within the constraints of the situation (Burgess, 2005).

The rapid development of genetic technologies means that Māori consultation has consistently occurred long after the science has been put in to place. Māori dissatisfaction with the consultation process is not isolated to the debates around genetic science but part of a wider problem that is entrenched within our history as subjects of research. Hohua Tutengaehe (cited in (Jackson, 2004)) described the reactive nature of Māori consultation and the limitations of unreasonable and unrealistic timeframes

> …having to be reactive all the time is one of the hardest things for our people. It often limits how well we can address an issue because we are always rushing to meet someone else's time frame or someone else's ideas about what is important. Every time Māori are asked to give a perspective we are…..responding to something that's been decided or….the main ideas are already set in concrete….as a result our people have often been asked questions impossible to answer in time frames impossible to keep.

From these experiences concerns have been raised about the lack of information and resources that are made available for consideration by Māori communities. Recently, Cherryl Smith and Paul Reynolds produced two publications (Smith & Reynolds, 2000, , 2003) specifically for whānau, hapū and iwi to use when thinking about genetic research. Smith and Reynolds (2000) suggest that our history of colonisation, land confiscation and unsafe research provides the lens through which we must examine and understand the potential dangers of genetics for Māori (see Table 6.5).

Table 6.5 A summary of issues for Māori to consider when thinking about biotechnology

Biomedical research	GE food, plants and animals
Research may be misinterpreted or used against Māori	Interference of whakapapa: crossing human genetic material with animals and vegetables
Research may be used to perpetuate negative stereotypes	Increasing interest in conducting closed trial and open field research in Aotearoa
Targeting Māori because of the apparent homogenous gene pool.	GE food purported to be able to improve health and nutrition; to feed more people; increase yield for growers and farmers
Whānau may become prime candidates for research because of rare genes or because they may suffer from 'important' diseases or medical conditions	Concerns regarding genetic research ongoing in Aotearoa (e.g.: GE cows, GE sheep, GE corn, diabetes research)
Scientists looking to "discover" the medicinal properties of native plants and traditional healing practices.	Token efforts to consult with Māori and the general public.
Be weary of the potential for patenting traditional knowledges and rongoa Māori.	Regulatory and monitoring bodies disregard Māori opposition to GE research and technologies
Human Genome Diversity Project	**Intellectual Property Rights**
The 'vampire project' seeks to collect and sequence DNA from indigenous populations.	Free-trade agreements (such as GATT/WTO) have provided a mechanism whereby Māori knowledge and resources may be sold and globally exploited.
Scientists can claim 'ownership' to particular genes that are viewed as valuable and having commercial potential.	Commodification of indigenous culture (including knowledge, resources, art and language) with little regard for cultural sensitivity
Patenting of humans and human cell lines (e.g.: Hagahai people)	
Whānau need to ensure that they have mechanisms in place to protect their DNA if and when they are approached by researchers who wish to study a hereditary trait or disease	

Note: from Māori, Genes and Genetics, by Cherryl Smith and Paul Reynolds (2000)

Although many of the concerns considered in this section have focussed on the impact of genetic research on mātauranga Māori and tikanga, the conversations also highlight the ethical challenges that are raised by genetic research and biotechnologies. Science is a human activity that occurs within a social context (Battye et al., 1999) therefore talking about genetics must include an ethical analysis which is determined by the communities in which the scientists exist.

The place of public consultation within the ethics of genetic research has recently been evaluated by The Democracy, Ethics and Genomics project (see http://gels.ethics.ubc.ca/). This programme has taken an inter-disciplinary approach to the evaluation of methods of ethical analysis for the development of public policy. Burgess and colleagues recognised that governments depend on experts (researchers, industry representatives, lawyers, policy analysts, economists and ethicists) to describe and assess the benefits, risks and merits of research and development, whereas the interests of the public are '…a phenomena to be described, evaluated and, ultimately, moved, but not engaged'(Burgess, 2003a).

The importance of 'meaningful dialogue' between researchers, policy-makers and the public is vital for achieving and maintaining public trust and approval. Without this trust, public and government investment in genetic research is vulnerable (Burgess & Atkinson-Grosjean, 2004). On the recommendation of the RCoGM, Toi te Taiao/The Bioethics Council was established to "meet public concern that decision-making was not adequately addressing the ethical, cultural and spiritual dimensions of genetic modification and biotechnology". Toi te Taiao/The Bioethics Council have initiated dialogue and reported on a number of issues believed to be of significance to the New Zealand public such as human assisted reproduction, nanotechnology, the insertion of human genes into other organisms and xenotransplantation. Toi te Taiao/ The Bioethics Council described the diversity of Māori viewpoints as representative of the strength of spiritual beliefs and the presence of a Māori world view in 'all corners of everyday life'(Toi te Taiao/ The Bioethics Council, 2005b).

It has been argued that a central ethical question with regards to the governance of genetic research is how to ensure adequate representation and evaluation of diverse perspectives, particularly for those who are marginalised, or are unable to access those who have the power to set policy (Burgess, 2003b). As citizens of Aotearoa/New Zealand, Māori are concerned with the political, social, cultural and environmental impact of genetic research. As tangata whenua and Treaty partners our concerns need to be heard early and not merely in an advisory role. Some of the work conducted by Toi te Taiao/The Bioethics Council has been criticised for marginalising Māori views and creating a sentiment of 'tokenism' within the debate (see (Collins, 2004)). In addition, Toi te Taiao/The Bioethics Council recognise that their programme of public dialogue may not be reaching Māori who have a deep understanding and knowledge of 'core' Māori beliefs (Toi te Taiao/ The Bioethics Council, 2005b).

6.2.6 Rationale and Study Aims

There is increasing demand for research at the genetic level, and growing development of genetic-based technologies, however there are currently no agreed protocols for the handling and disposal of genetic material from Māori participants. Any procedures thus far have been *ad hoc* and developed on a project by project basis to control and direct research that aims to modify genes (Baird et al., 1995; Cram et al., 2000; Eichelbaum et al., 2002). Given recent events involving the handling of human tissue and advances in genetic research and technology, there is an urgent need within New Zealand for the development of a practical yet ethical framework around research involving Māori tissue or fluid samples that builds on previous work but establishes guidelines that will sit within a Kaupapa Māori theoretical paradigm. Efforts have been made to develop protocols for the use and handling of blood samples, but as of yet the formation of guidelines that take into account the needs and views of Māori have not been completed. Guided by Kaupapa Māori research methodologies, this study acknowledges He Korowai Oranga (The Ministry of Health's Māori Health Strategy (Ministry of Health, 2001)) and therefore critiques non-Māori views of genetic information and kaitiakitanga of this information. There was also an opportunity to interview Māori from the Wellington community who had been approached to take part in a series of sleep studies (described in Chapters 2, 4 and 5 of this thesis), one of which would involve providing a biological sample, (i.e. a saliva sample) for research. It was envisaged that running these studies in parallel would enable the research team to talk to these participants about their decision-making processes and the values they consider when thinking about, and taking part, in research. This study also presented an opportunity to bring together Māori researchers from different institutions, research backgrounds and interests and provided a collaborative way of investigating the effects of genetic research on Māori. The project aimed to bring te ao Māori (the Māori world) to a scientific doctrine, reflecting on issues of bioethics, biotechnology, indigenous cultural and intellectual property rights. Underpinning this study is Kaupapa Māori research methodology, providing a framework where Māori are centralised and tikanga Māori is recognised as having an ability to add special emphasis to the ethical and cultural obligations of many people to gene research and technology (Cram et al., 2000; Eichelbaum et al., 2002).

The specific objectives of this study were:

1. *To examine with Māori the issue of genetic research and to determine the possible risks and benefits of genetic research*

2. *To employ Kaupapa Māori research methodologies to investigate and prioritise Māori experiences of research*

3. *To develop a practical yet ethical framework for health research that involves Māori genetic material*

6.3 Methodology

6.3.1 Kaupapa Māori Research

In order to adequately address the concerns of Māori pertaining to genetic research, this study has employed Kaupapa Māori research methodologies to ensure that this research is not only acceptable and beneficial for Māori, but also consistent with the development of Māori. Smith (1999) explains that Kaupapa Māori research is concerned with methodology, more so than method, which Cram and colleagues (2000) differentiate as:

Methodology: a process of enquiry that determines the method(s) used

Method: the tools used to produce and analyse data

Kaupapa Māori research methodologies also allow for a more human relationship to develop between the researchers and the participants and are also compatible with Māori methods of passing on knowledge. Finally, Kaupapa Māori research theory provides an interface with genetic research which currently occurs within a non-Māori framework; Kaupapa Māori research facilitates a change in the power relationship.

From a researcher perspective, the use of a Kaupapa Māori theoretical framework was also about identity. Kaupapa Māori analysis requires critical thinking about Pākehā constructs and definitions of Māori, however it also demands that we reflect on the ways in which we research and analyse ourselves. Kaupapa Māori allows Māori researchers to acknowledge that the research we conduct will be based in different philosophical understandings than Western research (Cram, 2001b). However, being Māori does not mean that we won't approach the research in a systematic, ethical or indeed 'scientific' way (Smith, 1999).

6.3.2 Qualitative Methods

Although the main theoretical work has occurred within the fields of education and the social sciences, Kaupapa Māori research does not exclude the use of a wide range of methods, but

rather signals the interrogation of methods in relation to cultural sensitivity, cross-cultural reliability, and useful outcomes for Māori (Smith, 1999). While the majority of this thesis has taken a quantitative approach to answering the research questions, the study presented here utilised qualitative methods as a way of allowing the participants to be actively involved in the development of the ethical guidelines for genetic research. The use of qualitative methods also addresses a major concern among Māori with regards to a lack of information on the subject and the need for Māori to be more heavily involved in decision-making. Finally a qualitative approach allowed the research team to look for pattern and meaning in participants' experiences, while at the same time acknowledging the contradictions and complexity within and between those experiences.

Qualitative methods also mesh readily with Kaupapa Māori theory as emphasis is given to the freedom of expression and the principles of partnership and participation within the research experience. In their research on genetic engineering, Cram and colleagues (2000) listed the following strengths of qualitative methods, in that they

- allow participants to express their experiences fully and in their own terms;

- search for meaning and patterns within these experiences;

- allow for complexity and contradictions between and within participants;

- allow access to power structures and relationships that exist within society; and

- allow for social change.

6.3.3 Research Ethics

In accordance with the principles of Kaupapa Māori, this study was guided by Māori understandings of research ethics and as such was informed and directed by tikanga Māori. The study was also approved by the Wellington Campus Massey University Human Ethics Committee (protocol number 03/149, see Appendix 1).

6.3.4 Focus Groups

The first stage of the present study involved a series of focus group interviews. Focus groups facilitate interaction and encourage participants to talk and ask questions together, allowing participants to explore their own experiences and examine the ways in which they think about issues and clarify their positions (Rice & Ezzy, 1999). In this way focus groups can be empowering, as they promote the 'active' participant and encourage participants to learn from each other through sharing experiences.

Focus groups are also advantageous because they allow the researcher to examine the ways in which participants choose to talk about ideas and experiences, through anecdote, story-telling,

sharing jokes, and silence. Focus groups can illuminate ideas (Kitzenger, 1995) through the validation of everyday language, and in the present study the use of te reo Māori, which may be concealed when a quantitative approach is taken to the research. Kitzenger (1995) explained that focus groups can also provide mutual support when participants express feelings that may be common to the group, but considered deviant from the dominant, or mainstream, culture.

Sampling strategy

Potential participants were identified through a simultaneous programme of research conducted by the Sleep/Wake Research Centre (referred to as the Early Birds study, see Chapters 3, 4 and 5 for details).

The initial aim of the present study was to talk to five participants who consented to taking part in the sleep study (option 1 on the consent form) and five participants who declined the invitation but were happy to talk about their reasons why (option 2 on the consent form). This method of recruiting was selected because it was believed that the participants would be able to draw on their recent experience of research and also allow the research team to engage with them and talk about their decision making processes.

Potential participants were identified using the consent forms which were cross-checked against the original database used from the Early Birds Study. Because the objective was to listen to Māori voices and experiences of research, self-reported Māori ethnicity was ascertained using their questionnaire information which used the Census 2001 ethnicity question. Participants were eligible to take part in the focus groups if they identified as Māori, either alone or as one of multiple ethnicities. Potential participants were contacted by a member of the research team using the telephone number(s) provided. During this conversation the purpose and proposed methods for the present study were briefly explained and any questions addressed. All participants who agreed to take part in the study were given a range of focus group sessions to attend. Moreover, one-on-one discussions were also available to those who felt uncomfortable with the prospect of a group discussion or for those who could not attend one of the proposed dates and/or times. Transport was available for any participants who wished to take part in the study. Confirmation letters were sent to all participants who agreed to join a focus group discussion. Information sheets and consent forms were also given to each participant (Appendix 30).

Three focus group discussions and a single one-on-one session were conducted between June and August 2004. All focus group participants (4 male, 7 female) identified their ethnicity as Māori and were residents of the Wellington region. The focus group sessions were held in a meeting room in Te Pūmanawa Hauora, the Māori Health Research Centre based at the Wellington Campus of Massey University. As requested, the one-on-one interview was held in a private meeting room at the participant's workplace at a time that was most convenient.

A total of 16 participants agreed to take part in the present study, however only 10 participants were able to attend. It was hoped that the focus groups would provide a comfortable and safe environment and to encourage inclusiveness participants, and researchers, were invited to bring whānau or friends with them. This was exemplified during one focus group where a teenage-son in attendance was invited to take part in discussions by the adult members of this group. Although he may not have been part of the original 'sample' from which the participants were selected, the importance of his place and contribution was recognised by the group and as such his comments and stories have been included within the study findings.

Interview procedure

Each focus-group was two-hours long and followed an open-ended format with the interviewer encouraging people to talk rather than pursuing a question and answer session. Written consent was given prior to the focus group beginning. Each discussion was based around two questions:

- What are your hopes and dreams for genetic research?
- What are your fears and concerns for genetic research?

The focus group conversations were not limited to any particular technique or interest area (i.e. human health, environment etc.) thereby allowing participants to offer their own definitions and analysis of genetic research. This type of 'scoping research' was used during the consultation phase of the Democracy, Ethics and Genomic project and models a representative approach to ethics by 'enhancing ethical analysis through engaging broad or neglected perspectives, and doing so in a manner that supports participants' own identification and representation of their interests'(Burgess, 2003b). The ethical analysis required by this process is based on a more robust notion of the range of public interests held by diverse people and that the 'deficit-model' within the consultation process (which presumes that the public must be educated before they can provide relevant commentary) is minimised by respecting the participants' expertise as members of the public who are interested in the kind of society they wish to live in and the role of genetics within it (Burgess, 2005).

The focus group sessions were structured according to the facilitator guide developed by the research team (Appendix 31). Each focus group began with a mihi whakatau, welcoming those in attendance on behalf of the research team followed by participant introductions and ice-breaker exercises. The expectations of the focus group were outlined by the facilitator who also emphasised the importance of maintaining confidentiality and respect for the experiences of all involved.

The first half of the session focused on our hopes and dreams for genetic research. Our hopes were discussed first, in case talking about our concerns discouraged any of the focus group participants from raising their hopes at another time. Participants were asked first to write down

their hopes (either individually or in pairs) before presentation to the group, at which time the facilitator would write them on a whiteboard. This method ensured that all participants had an opportunity to contribute their hopes in a non-threatening manner and ensured that any dominant participants did not take control of the discussion. In addition, once the hopes were on the whiteboard they became the hopes and dreams of the group and as such participants were not restricted by the ideas which they had articulated individually but instead they could speak to any of the hopes that were identified.

Kai (food) and refreshments were shared in the break before the second half of the focus group sessions during which the participants explored their fears and concerns for genetic research using the same processes described for the session on hopes and dreams.

To finish, a form of conceptual mapping (p. 135 in (Greenbaum, 1998)) was used to help summarise and locate the participants' hopes and concerns for genetic research. The facilitator thanked the participants for their attendance and presented each participant with a koha[8] on behalf of the research team in recognition of their time and contribution to the study.

Each interview was audio-taped (with permission) and additional notes were taken by a research assistant. The interviews were transcribed *verbatim* and checked for accuracy against the tape recording by the research facilitator. Copies of the transcripts were sent to each participant for editing and commentary prior to analysis (Appendix 32). In addition, each participant was sent a copy of the initial findings from the thematic analysis (Appendix 33).

6.3.5 Key Informants

The second stage of the present study involved in-depth interviews of key informants who had knowledge or experience in aspects of genetic research and/or research ethics. Rice and Ezzy (1999) liken the in-depth interview to a good conversation, where one person talks and the other listens, responds and encourages. The in-depth interview also allows the researcher to come to a deeper understanding of experiences by exploring the complexity of meanings within the talk (Rice & Ezzy, 1999).

Sampling strategy

Key-informants were identified by members of the research team and accessed through personal or collegial networks. The key-informants were sent a letter briefly outlining the purpose of the research and inviting them to meet and discuss the focus group findings with the research facilitator. A copy of the invitation letter, information sheet and consent form can be found in Appendix 34. Of the seven key-informants who were contacted, six indicated that they were interested in taking part in the study, although only five key-informant interviews were

[8] The koha consisted of either a calendar or book celebrating matariki (the indigenous Māori New Year)

conducted. Four of the interviews were conducted on a one-to-one basis. The fifth interview involved a small group of colleagues who were invited by the key-informant to listen, observe and contribute to the conversation; an initiative which greatly enhanced the study findings. All of the key-informants interviewed for this study self-identified as Māori, and were currently involved in health research within academic institutions throughout New Zealand.

Interview procedure

The interview process began with a brief overview of the initial thematic findings from the focus group transcripts. Key exemplars from the focus group talk were used to illustrate the development of these themes and to assist the key-informants understandings of the discussions.

In the second part of the interview the key-informants were asked to reflect on their own experiences as Māori researchers and use these understandings to examine and interpret the focus group talk.

These conversations were not structured interviews, but were instead directed by the ways in which the key-informants explored the issues. Rice and Ezzy (1999) argue that the structured interview format limits the potential research findings as it focuses on the repeatability of the process of asking and phrasing questions to minimise interviewer bias.

The key-informants were also asked to evaluate the research questions, methods and analytical framework that were used in the present study. This process was critical for assessing the rigour of the study in terms of transparency, generalisability and also validity of the methods and subsequent findings.

Each key-informant interview lasted between 90-180 minutes and was audio-taped with permission. Again, the interviews were transcribed *verbatim* and checked against the tape recording for accuracy before being returned to the informants for editing and commentary.

6.3.6 Analysis

The analysis of the focus group and key informants interviews were carried out separately using the database of transcripts, researcher notes and audio-tapes.

Thematic analysis

The initial method of analysis used a general inductive approach to identify the key themes in the participants talk. This allows the research findings to emerge from the dominant themes which are inherent in the talk but which may be obscured or hidden by other methodologies that involve preconceived notions of what the talk means (Thomas, 2003).

Following the initial reading of the transcripts specific segments of the participants talk were highlighted and sorted into categories, some of which were deductive, or predetermined by the research objectives and prior reading of the relevant literature, whilst other categories were

inductive and therefore developed through the reading and re-reading of the transcripts. This process resulted in nine categories which included a label; a description of the category including the characteristic features of this category; exemplar quotes which illustrated the meaning(s) of the category; and the links with other categories. This process of reading and re-reading the categories continued with each level seeking to draw out the differences and commonalities in the participants' experiences. Six preliminary themes emerged from this process, which were presented to the key-informants for commentary and evaluation.

The analysis of the key-informant data used a similar process, however the categories that were identified were entirely inductive with the transcripts coded using themes identified from the focus group analysis. In this way the key-informants understanding of the focus group talk supplemented the final stage of analysis which borrowed some lessons from discourse analysis (Potter & Wetherall, 1994) (Wetherell, 2003; Wetherell, Taylor, & Yates, 2001a, , 2001b) to tease out the consistencies and contradictions in the focus group talk.

6.4 Findings

The following section presents a reconstruction of the themes that were identified during the initial thematic analysis of the focus group discussions (see Appendix 35). Supplemented by the key-informants experiences, a further deeper reading of the focus group participants talk, gave rise to a better understanding of the connections between the themes. It was envisaged that weaving the hopes and fears back together would better portray the meanings, relationships and departures in our thinking and illuminate the processes that we use to connect our lived realities back to the place of genetic research.

6.4.1 Humanity, Morality and Mātauranga Māori

Talking about genetic research involves thinking about some fundamental issues around our humanity, our culture and our relationships with each other and our environments. What knowledges and understandings do we draw on to make our arguments for and against genetic research?

To begin a conversation about genetic research the focus group participants found themselves talking about the rightness of this type of research; questioning the appropriateness of this technology and debating the validity of this 'new' knowledge against what we already know and understand about our humanity and te ao Māori.

Rightness and playing God

When considering the logic of genetic research, many of the participants were guided by their own understanding of morality to establish whether different applications of the technology were 'right' or 'wrong'. For example, developments in cloning technologies have been touted as one of the latest success stories for the Western scientific world. However, many of the participants shared their understanding of these events and used terms such as 'scary', 'terrifying', 'gaudy', 'awful', 'tormented' and 'frightening'. Although, supporters of cloning and stem-cell research continue to push the potential of these technologies, for many of the participants the element of risk involved in the procedures remained, while for other participants it was clear that these applications were not only unnecessary, but unwanted.

For the focus group participants (FGPs) in the present study, genetic research was either portrayed as

(1) Less than human – participating in research that is inconsiderate of the needs of humanity and driven by their own desires, doing things that the community deem unacceptable and unwanted. When considering the rightness of genetic research some participants talked about scientists as 'rogue' and 'faceless', people who could not be trusted to respect the moral

boundaries of society. Driven by a need 'to know', scientists often 'overstepped the mark' or 'didn't know when to stop'

> *You hear about some good stories in terms of medical breakthroughs and that type of thing, and yeah there's benefits there and then they go too far and grow ears on the back of mice and those types of things just, just a science experiment gone wrong really…*
>
> ***Focus group 3, Tane***

(2) Merely human – this talk draws on a commonsense that research is the pursuit of knowledge, extending and pushing the boundaries of knowledge that already exists (Smith, 1999). Research is perceived as a natural human activity and that as humans we are capable of making mistakes some of which may need to be forgiven

> *I think it's in human nature to continually make advances and discoveries and when they've made one discovery it opens the doors to a whole heap of other discoveries. People don't know when to not open the door any further, they're not content, that this is what they've discovered. So, I think partly it's our fault, just because we want to investigate, want more knowledge it's a matter of knowing where does that actually stop?*
>
> ***Focus group 3, Tane***

(3) More than human - acting above society and using the power of genetics to do work that was normally outside the realm of human beings

> *It does come back to, who is it that makes those decisions, y'know at the end of the day, who is it that plays, sort of, y'know God, for want of a better word, over and above all of these hugely, not really private things, but, personal sort of things…*
>
> ***Focus group 1, Wahine***

Recent public discussions on genetic technologies suggest that 'to play God' describes 'an interference with the natural order' (NFO New Zealand, 2003), that is manipulating the order of life which has already been determined by a higher, intangible power. Alternatively Jones (2004) suggested that 'playing God' symbolises the permissible human participation in the transformation of the world '…by sustaining, restoring and improving what has been temporarily entrusted to us'.

In the present study, to 'play God' described a fear that genetic research disturbs the balance of power and authority that is held within a community. The fear that scientists could wield such power is not new. As a member of the RCoGM, Jean Fleming reflected back on her experiences and found that the public concern that genetic modification was to play god, was driven by a fear of the power that is inherent within developments in science

> There is a perception that science, and scientists, are capable of changing the course of evolution and of playing God – and that they actually set out to do this…These concerns signify a fear of

loss of autonomy and lack of choice. For many people, gene technology is about the control of the new by a few elite (Fleming, 2002).

Human need and the sanctity of life

Human need and the sanctity of life (Toi te Taiao/ The Bioethics Council, 2005a) clearly challenged the thinking of many of these FGPs. In the following example, one focus group participant was sympathetic to the needs of others. However her understanding is that genetic engineering is 'playing around' with the creation of human beings which is a direct challenge to her beliefs on life and spirituality. She argued that any information gained from 'dormant cells' and 'DNA' would change everything she knew about how she lives her life. To protect her knowledge she detaches herself from the issues by not thinking or feeling anything for genetic research. It also provides a way for her to live with her view that genetic research was medically necessary

> *I actually, I don't have* [hopes]*, as far as genetic engineering goes, I only swing toward medical advances and to, as you say, for illnesses diseases things like that. I don't agree with but I can still understand the need for it, personally genetics and any sort of playing around with how we were all bought forward is not something that um, I'm comfortable with but I understand that medically there is a need for it, there really really is, but as far as hopes and dreams towards it, I'm probably quite detached…*
>
> ***Focus group 3, Wahine***

The use of *in vitro* fertilisation technology (IVF) exemplified the need to balance humanity and our 'duty' to protect and enhance the lives of others. Although society has largely accepted IVF techniques, as these participants have shown, the community still holds concerns for this technology. For some FGPs, IVF is only one step away from 'designer' babies.

> *In terms of looking at things like IVF, which, while that may be an OK thing, but the fear is really around genetically modifying those, I don't know the process or the technical terms, but I guess it's tampering with the DNA of some sort, to ensure a genius or a nice looking child or a something around that, so it's not taking away from infertile parents, not moving from that, but really not tampering with that process. At the moment they're human donors to our knowledge un-tampered sperm or egg… the fear is that they start tampering with that process in some regard…*
>
> ***Focus group 1, Wahine***

The talk around IVF also involved an analysis of rights, power, wealth and decision-making. While previously the FGPs have understood the necessity for genetic research within medicine, in the following example the participants show some concern about the extent to which genetic research will be used and where it will end

> ***Wahine 1****: The big thing is that kid that's either over in Australia or the States they did it through IVF and they changed the DNA makeup of the child in order so that it could have*

some bone marrow specific to save the older child and it's sort of like, you can see why they've done it and their argument's very strong, but at the end of the day where's it going to stop? And they only got it done because they could afford it and that testing has probably been done on some poor kid who's been on deaths door sort of thing and they've used them as the guinea pig to benefit the rich people who can actually afford half of these things. They still use their sperm or something, but they needed a certain gene inside this new baby in order to manufacture the correct type of bone marrow [someone asked if the baby was OK]…Oh yeah the baby's fine they've got to wait until it's a year old and then they've got to take off the bone marrow to fix the older kid.

Wahine 2: *Before the child's got any say in it.*

Wahine 1: *Yeah, the child was basically born to save the older child.*

Focus group 1

Individuality and spirituality are essential elements of our humanness

It was agreed that the notion of helping people is a critical component to our decision-making and general acceptance of genetic research. However, several of the participants struggled to accept many of the arguments for advancing genomics over the reality of what it means to be human. The sentiment of individuality was important in our uniqueness as human beings and this was apparent in some of the focus group talk. To use genetic technologies for the classification, categorisation or description of humans or the world that we interact with would not capture the essence of our spirituality or mauri.

Many applications of genetic research appear to be motivated by a desire to prolong or extend the natural course of a human life. In the following examples, two women discuss the value of individuality and spirituality, and argue that our humanity has nothing to gain from genetic research

I was thinking in terms of cures for illnesses that I wonder if the whole genetic engineering thing, I suppose it's a bit sweeping, but you know it's like man seeking immortality. What good is it really going to do for mankind? So say in terms of say human kind is it really the way we should be going or what about satisfaction with our existing life, not so much that, but I don't know, looking for fulfilment or greatness in what we have as humans.

Focus group 1, Wahine

This participant questioned the logic of using genetic technologies to prevent death over the reality of what it means to be human, and accepting our mortality. She sees a flaw in the argument that genetic research will provide cures for illness, and suggests that these arguments have diverted our thinking about the value of quality of life and how this can influence our personal and whānau wellbeing.

The second participant draws our attention to the fine line between arguments for genetic research based on human necessity, and those that are driven by human desire. The participant also questions the power in the decision making process and the potential for one sector of our communities (such as scientists) to determine societal positions on fundamental issues

> *It's probably the other side of the coin isn't it, about where do you stop I guess in terms of do you just look at cures for illnesses and I guess most of us can rationalise that as an OK thing to do, but then where do you draw the line if the next thing is to actually prolong life. So you start looking beyond the norm of the lifecycle of a human being to looking at genetically enhancing the length of someone's life to what end? Where do you start to draw a line I guess as to what is deemed necessary and what is deemed, or what is a necessity really and what is perhaps a desire or something like that and who makes those decisions ?*
>
> ***Focus group 1, Wahine***

From these discussions it appeared that decision-making with regards to genetic research involves taking a pragmatic approach to accepting some quite outrageous things just because they are a reality; even through they've often become a reality in advance of an ethical, cultural or spiritual debate or guideline. Is it then that pragmatic represents necessity, and that the question of 'where will it stop?' represents desire?

The importance of our uniqueness and spirituality as a critical component of our human-ness was discussed in length by many of the FGPs. For one participant, there is joy in being aware of our connections with the natural environment and the ways in which we can achieve wellbeing through these relationships, while for others there is a common fear that individuals may lose their autonomy through genetic research.

The potential for gene technologies to 'prevent death' and 'ease suffering' has been the catch-cry of many advocates of the genetic sciences. During the RCoGM advocates and supporters of GM in medicine freely described the technology as 'the only possibility' or 'the only hope' and 'a bright light on the horizon' (e.g. Chapter 9 in (Eichelbaum et al., 2002)). However, the position that humans should be able to determine our own mortality is in its simplest form, completely illogical with respect to a Māori view of life and death. Mead (2003) explores the important place of death in the continuation of life

> It is recognised in our beliefs that human beings are transient and are not permanent features of the social landscape…at death the mauri that a person is born with dies and disappears. It is extinguished when the spark of life ceases, breathing stops and the heartbeat throbs no more. But the wairua that is released either prior to or immediately after death leaves the body and journeys upwards towards Ranginui, the Sky Father… (p. 147)

Similarly, Jackson (2004) described the paradoxical use of gene technology to prevent death

> … the Māori intellectual tradition has never been fussed with the idea of eternal youth and the strange fascination with botoxed beauty, nor with the fear of death that has led to the particular Western pseudo-science of cryogenics. Growing old and dying are simply part of whakapapa, and there is always a beauty in the wisdom of age that matches the vivacity of the young. People would ask how someone died, but the why of death was and is a question where the moral and ethical issues about needing to know have yet to be resolved. In some ways they even seem almost unnecessary because in the wisdom that can be gleaned from the whakapapa stories the wonderful dying of Maui between the thighs of Hine-nui-te-Po is explanation and lesson enough that some things are indeed immutable (p.74).

Privileging science over other worldviews

A significant feature of each focus group discussion was the diversity of perspectives which the participants brought to their conversations. The FGPs felt comfortable talking around tikanga Māori, spirituality, medicine, science, religion and the environment. They respected the differences in these knowledge systems and spent time exploring each and giving value to their positions. However, as one FGP pointed out, genetic research does not pay the same respect or value other 'alternative' perspectives. It was felt by some FGPs that science shouldn't be privileged over human thought and that these beliefs, although often perceived as lacking 'objectivity', present a valid basis to our decision-making

> *I hope that science doesn't get in the way of human thought or spiritual beliefs…coming up for cures for illnesses is the logical thing, good logical thought, it makes sense, but then you don't want that sense to get in the way of Māori belief…and then suddenly that belief gets taken over by that other logic and you've got to go down that path but what you might create is the reason why, from a Māori view, based on Māori thinking, which then makes it OK to do this over here… but not just go straight, well, because science says this came from that and that came from this therefore you do this…What it does in terms of spiritual beliefs is it protects peoples own spiritual beliefs to say no I just don't believe in transplants because it's my own spiritual belief y'know, and you wouldn't want science, necessarily want science to be the stick that can jump in and destroy peoples own personal views.*
>
> ***Focus group 1, Tane***

For this FGP the difference between Māori and scientific communities comes from a difference in logic which is most evident in the ways in which reasoning and inference occurs. The divergence of knowledge between positivism and mātauranga Māori is obvious when one recognises that traditional Māori intellect is, 'a non-dualistic world that sees interrelationships rather than hierarchy, and positions the thinker as someone who is part of the work and not merely an elevated observer of it' (Jackson, 2004).

> *…the way a lot of research methods are devised…a lot of them were designed to maintain objectivity and remove people from the context of it, and that was a way of viewing it.*

And the Māori view of it was 'that doesn't make any sense' that they can be anymore removed from it…and I think that comes out of that difference in philosophy…

Key-informant, MH1

Understanding mātauranga Māori is to know that knowledge is not often universally available. However this concept alone is at odds with the Western assertion that there are no limits to what can be researched (Mead, 2003). The specialised nature of mātauranga Māori demands respect, and the improper handling and use of knowledge can lead to dire consequences

> When you are dealing with the knowledge of the past, you have to take it seriously. Otherwise you don't get inspiration or spiritual fertility from that knowledge. And if you ignore the tapu of sacred things, it can lead to sickness or even death (p.9) (Manihera, 2004).

However, as one key-informant explained, Western sciences do not recognise or respect the value of our traditional knowledges, nor does it uphold the sanctity of our diverse relationships

… genetic engineering research, shows a total lack of respect, a total lack of respect for life, for the dignity of any living thing, even down to the organism or gene level and respect for the gene, and there's no respect for the gene, I mean science is just sort of inherently arrogant and some aspects of science – not all science I should say but some areas or disciplines within science are hugely disrespectful to organisms or to life or just to all our relations you know a shot gun sort of – I don't know the terminology but the methods of ramming two genes together or placing a gene inside another organism to create another organism, the creation of life to support another life, the – using the blood from foetus's that have been aborted, a brain dead person – now this is more broader than genetic engineering but I mean science in general, using a brain dead person's organs or parts, body parts and that for another, I mean there's whole areas there of complexity of relationships and respectful relationships, some areas in science or some discipline areas within the science general area, don't monitor any relationship, you know science is paramount and progress in science takes precedence over everything else, everything and anything else so that respect then is not there, that disrespectfulness is inherent in science, in some of the sciences

Key-informant, PR

New Zealand society generally regards the 'commonsense' as the values and principles of Pākehā which largely occupy an ethnocentric space. Because of the diametrically opposed understandings on which Māori and the scientific communities are based, they are often found talking past each other. For some of the participants understanding the differences in philosophy allowed them to see that researchers can '… come up with a different answer' or 'get the wrong answer.' For many of the FGPs their experience of research was that scientific knowledge is prioritised and valued over our own beliefs and as a consequence the outcomes of research are often far from their own realities.

The privilege of Western scientific knowledge is evident within the structure of current governance bodies that are responsible for the regulation of genetic research and technologies in Aotearoa/New Zealand. For example, the Environmental Risk Management Authority (ERMA) was established by Government to take responsibility for assessing applications to introduce hazardous substances or new organisms (HSNO) into New Zealand, including the genetic modification of animals and plants. Amendments to the HSNO Act in 2003 reinforced consideration of the Treaty and provided ERMA with Ngā Kaihautu Tikanga Taiao (NKTT), a Māori Advisory Committee, however, the authority and decision making processes undertaken by ERMA have received considerable criticism from Māori (Smith & Reynolds, 2000). Māori raised serious and legitimate concerns on two separate occasions when applications were made to field-test transgenic sheep and cows which were being used to develop potential treatments for cystic fibrosis and multiple sclerosis respectively. The basis to these concerns was that transferring genes between species interfered with the whakapapa model which is a central component to both the practical and spiritual aspects of Māori life. However there were also concerns raised regarding the inadequacy of consultation and a failure to demonstrate the benefits of the research (Durie, 2004). After considering all of the evidence NKTT found recommended that the applications be denied, but in spite of this ERMA approved the research concluding that other factors (e.g. economic, environmental) outweighed these 'cultural' concerns.

This understanding came through some of the focus group discussions where the FGPs shared a common understanding that the control of genetic technologies is based within a specific (read scientific or medical) knowledge. Moreover, to be effective in this role one must have specialised skills and understanding of the science. There was also a high level of trust embedded within governance which one key-informant explained is related to the respect that the community hold for people in authoritative positions such as scientists and doctors.

> *…there is a real trust in people's positions, you know like scientists, scientists are sometimes held up there as trustworthy because you know, they just are. I mean, they're experts in the field so how can they go wrong, I mean that's the interpretation, there's a whole lot of trust in there. Similar thing for governance bodies or for regulatory bodies that are put in place by a government to monitor, to regulate this type of technology…any hazards within our communities…the perception sometimes is that they're trustworthy because why else would they be put in those positions?*
>
> ***Key-informant, PR***

Because of their education and training scientists and medical practitioners are seen as objective and are trusted to work effectively in regulatory roles. Objectivity is a central tenet of positivism, however, as Fleming (2002) remarked the true objectivity of positivism is arguable

given that 'no human activity can be completely objective or without "soul". All science is based on the perpetrator's world view or belief system'. Cram (1999) adds

> That even when 'scientists' claim that there are no biases in their research, it is the scientists who have constructed the research questions, who have decided how the data is to be collected who have decided what statistical tests to apply…

Because the discourse on genetic research privileges scientific knowledge systems, discussions about the regulation and control of genetic research often marginalise the considerations of the Māori community. The objectivity of Western-science has been perpetuated through a discourse that positions science as something that is separate from society. However this proposition neglects the Māori community's history and experience of science and research as a legacy of imperialism (Sivak, 2005).

6.4.2 Regulation, Control and Tikanga Māori

This section is about providing long-term assurances and protection of people, our environments and our knowledges. It is also about using frameworks of control which respect our right to tino rangatiratanga.

Trust and integrity

The aspirations for the regulation and control of genetic research were encapsulated by a theme originally described as governance. It was clear that the primary purpose of governance is the protection of our knowledges and our people.

> *I guess some of what we've talked about brings us back to having some reasonably well established guidelines as to what the parameters are of any sort of research now and in the future could possibly take some sort of shape or form because I guess if you're taking care of the protection of people either again, their property, for want of a better word, if you've got some sort of tikanga around how you're going to ensure that sort of safety…*
>
> ***Focus group 1, Wahine***

For the FGPs, good governance involved 'strict' and 'continual' monitoring, that 'challenges' the drivers of genetic research, whilst providing 'assurances' that genetic research would be 'contained and used in a productive way'. For one KI, effective governance was about protection: '…protecting ways of doing things, or protecting the environment, protecting communities.' As a member of a regional ethics committee this KI was disappointed that scientists do not always consider the potential negative outcomes of their research and thus do not ensure that there are effective strategies in place to manage those risks.

The FGPs were aware that the full impact of genetic research may not be realised for many years and so good governance was expressed as a means of providing long-term assurances to

communities and protecting our environments for future generations. From a researcher perspective this is also about bringing confidence and integrity to governance so that communities feel supported and safe

> *…my job is to provide confidence, bring some integrity at governance and at a control level and for whānau it's one thing less they have to worry about, you know that burden that you talked about, we take it away…*
>
> ***Key-informant, CR***

Good governance would also consider all of the fears and views held within the community as valid. As our representatives they would challenge the supporters and drivers of genetic research and make decisions that would reflect the best interests of all of the community. However, effective controls and regulations must also be flexible, allowing for changes to be made when new situations, challenges, or technologies arise.

Despite these hopes and aspirations for good governance, many of the FGPs questioned the trust that is currently bestowed upon regulatory bodies and committees, and the integrity of the scientists involved. When looking at trust, the FGPs remembered back to recent stories and experiences of research and science (e.g. the introduction of GE corn and seeds, and the discovery that the hearts of several deceased babies had been kept without consent) where the regulatory systems failed to protect the interests, health and safety of the community. Many of the conversations around governance were centered on the need for safety within the process of genetic research, however one FGP questioned the integrity of the people who conduct the research and the need to regulate and control the human component of research

> *… I think one of the things for me that I've seen that maybe lets the attractiveness of [research] fall down are the people that put it into place. The logic is there but what let it down was the people exercising the method didn't get consent. So the idea was good but the follow through and follow up was real bad and then 10 years down the track you find things suddenly discovered, it was a decision made by one health person who had control over the decision making and that was it and everyone followed. So I'm saying it's a mixture. It's how well it's put into place and practiced…*
>
> ***Focus group 1, Tane***

Tino rangatiratanga and governance

Many indigenous commentators (e.g. (Smith & Reynolds, 2000) and (Harry, 2001)) have stressed that genetic research is an extension of globalisation and as such it will diminish indigenous knowledges. True regulation and control of gene-based technologies is therefore particularly crucial for indigenous people, however there is a valid concern that Western systems of protection are unable to enforce the diversity of interests and resources that are held by Māori and other indigenous communities (Tipene-Matua, 2000). One key informant questioned the ability of current regulatory bodies to adequately protect our taonga because of

the political and economic pressures which act on them such, as international trade agreements. In the following example, one KI describes how the regulation and control of genetic research is informed by the perception that indigenous knowledges are a commodity for trade, and thus systems are created to protect the economic potential rather than the community from which this knowledge is sourced.

> *…it's all built basically on capitalism, capitalism is based on exploitation. That exploitation is generally exploiting marginalised people for whatever they have got to offer, which includes Māori, indigenous people and they have a lot to offer. There's a lot of money to be made in indigenous knowledge or Māori people's knowledge, there is so much there, so within these international and also national institutions and agreements and conveyance or mandates lie or sit these governance bodies, these regulatory monitoring bodies, and also sit the scientists. They each have their competing interests or interest groups, or responsibilities and obligations from other regulations, from other laws and so on. So that impacts hugely on how governance, how regulation and monitoring occurs and what actually is regulated and what actually is monitored as well as what is a scientists research agenda and how scientist needs to operate within a university, but also within a private industry setting…*
>
> ***Key-informant, PR***

Our hopes for good governance articulated a desire to control what research is done and the ability to choose the research that our communities will safely and happily engage with. However, one focus group participant criticised the influence of Government in the prioritisation and direction of health research in Aotearoa/New Zealand, which appear to be contrary to the hopes and needs of the community. One KI agreed with this analysis and suggested that certain areas of research are earmarked by central Government, which culminates in the loss of community control of the process.

Although the majority of participants had clear hopes for good governance there was an equally strong voice that feared that the Government could not be trusted to provide the protection that we need. In order to understand the ways in which the focus group participants constructed Government within the context of genetic research, it is useful to look at the relationship between Māori and the Government at the time these focus groups were held.

In 2003, a Court of Appeal ruling unanimously agreed that iwi from the top of the South Island could present a case before the Māori Land Court claiming the foreshore and seabed (the area between the high and low tide marks) in the area of the Marlborough Sounds is customary Māori land, and therefore could be converted to Māori freehold land (Hingston, 2006). This decision received considerable media coverage, which in the main incorrectly interpreted the ruling as a move by Māori to deprive "the New Zealand public" of the foreshore and seabed (Hingston, 2006) when instead it recognised the *possibility* that Te Ture Whenua Act 1993

would lead to private ownership of the foreshore and seabed. More importantly the Court of Appeal ruling affirmed the *right* of those iwi to redress. To quell the 'mass hysteria' that followed, the Government moved quickly to legislate Crown ownership of the foreshore and seabed and to extinguish Māori customary title. Hingston (2006) argued that the reaction by Pākehā was not a problem with ownership of the foreshore and seabed (which was assumed to be owned by the Crown), but instead reflected the state of race relations in New Zealand and a '…visceral anti-Māori feeling…exacerbated by negative reports in the media' (p.111). Jackson (2003) wrote

> The Crown's response seeks to retain that colonizing [sic] determination but rephrases it by emphasizing the need to consider the "public interest" and the rights of "all New Zealanders". However such reasoning actually confuses the "public (non-Māori) interest" with the right of the "Māori public" in terms of Te Tiriti o Waitangi and in fact constrains the ability of Māori to exercise the rights and authority contained therein. It subordinates both the nature and meaning of Māori-defined rights and rangatiratanga itself to the whim of the Crown (Jackson).

Māori anger at the actions of the Prime Minister and the Government was widely felt across Aotearoa/New Zealand, however our frustration was focused through multilevel action locally (regional/tribal hui), nationally (an urgent claim to the Waitangi Tribunal) and internationally (an appeal to the United Nations). In 2004, the Foreshore and Seabed Act was received, providing Crown ownership of the public foreshore and seabed 'on behalf of all New Zealanders'.

Within this context, the following section will examine the ways in which this relationship between Māori and the Crown framed some of the focus group talk on the regulation of genetic research.

Kōrero One (Example One):

> ***Wahine 1:*** *You can't trust the government you can't trust business, oh no, not business, they'll use it for whatever they want, that's the driving force in the world, we're at their mercy. I don't trust business, as far as genetic engineering goes, 'cos there's no value, its just, except money, making money…and we're just pawns, really. They'll experiment on all those millions of Africans y'know…*
>
> ***Wahine 2:*** *And, ah, you know government is really swayed by what economic forces and companies say*
>
> ***Wahine 1:*** *yip, what America might say?*
>
> ***Wahine 2:*** *They are pawns too, multinational American companies*
>
> ***Wahine 1:*** *Yeah absolutely*
>
> ***Wahine 2:*** *We're fodder, it's cynical but I can't see any other way actually.*
>
> ***Focus group 1***

In this first narrative, the participants have situated Government within a global framework. Their description of 'multinational American companies' also implies that there is a relationship between government and business, and that with regards to genetic engineering, business is driven by a desire for making economic profit. These global economic forces are powerful, and the participants are aware of the strong influence that business has on Government. The participants describe themselves as 'pawns' and 'fodder' which indicates a feeling of hopelessness against Government while also illustrating a lack of consideration for the effects that genetic research may have on the participants. The participants are clear that Government cannot be trusted.

Kōrero Two:

> *I feel like there's a loss of control. We are at the mercy of large companies and faceless scientists. 'Conspiracy, can we trust the government to act on our, with our best interests at heart? As people, but also as Māori I mean, how can we trust the government?*
>
> ***Focus group 1, Wahine***

In this next example, the participants have brought the genetic research discourse back within a local framework. The distrust of government remains, however there is also a strong anti-corporate sentiment in their voice. The concept of science as another body that cannot be trusted is introduced and their use of the phrase 'faceless scientists' implies that scientists are not accountable to the community and research participants have no control over who takes their information. The concerns raised here are informed by the power relationships that exist between government, science, and research participants. However, this example also suggests that Māori have specific concerns that parallel those of Pākehā.

Kōrero Three

> ***Wahine 1:*** *Well I think history would tell us no a definite and resounding no, and they're still not listening to pretty good evidence based research around the health arena now. They still preferring to hold onto a very Pākehā view, a colonists view to, of the state of our health. So I would say a resounding no. I can't imagine that we'd ever trust them. 'Cos I mean they're driven by so many other drivers, they're probably not interested, y'know in the individual, the particular whānau, hapū, iwi that may be involved, they're interested in outputs and all those good things*
>
> ***Wahine 2:*** *Lobby groups have their own agendas, like business and stuff.*
>
> ***Wahine 1:*** *That's right, most of the good lobby groups, y'know, affluent groups*
>
> ***Wahine 2:*** *like Federated farmers who are growing more corn per acre, and the other groups are just stirring activists,* [laughing] *don't want to listen to them*
>
> ***Wahine 1:*** *And they're the ones, the very ones they should be listening to….*
>
> ***Focus group 1***

As heard in the first narrative, the participants maintain that government is not interested in individuals, and therefore research participants. However in this final example the participants have positioned themselves as Māori and talk about a government that does not listen to Māori realities, and therefore continues to marginalise Māori in this country. Within the context of research, government focuses on 'outputs' over the welfare of whānau, hapū and iwi. The distrust of government within this talk draws specifically from our history of colonisation. Unlike the previous narratives, the participants talk about lobby groups and the influence they exert on government. As one of the participants implies, affluent groups such as federated farmers have successfully managed their influence over government. The participants recognise that these lobby groups themselves are influenced by business and are similarly driven by economics and outputs, and for these reasons, are not necessarily representative of the Māori community. The participants also recognise that when a Māori voice challenges government and indeed Pākehā beliefs, they are labelled as activists and radical and portrayed as hostile, separatist and divisive. However, another understanding of radical Māori is that we are looking for change in the ways tangata whenua are politicised.

Governance and ethics

Another prominent component in the construction of the regulation and control of genetic research was the focus group talk around ethics. Many of the FGPs strongly believed that ethics would ensure and maintain public safety in research. Western society developed ethics as a way of constructing moral boundaries for the protection of society by the provision of rules for living and behaving. As one key-informant explained, current ethical frameworks are informed by the values of Western society, which may or may not necessarily reflect Māori values, hopes and dreams for good governance and effective research practice.

The current system for the ethical review of health and disability research in Aotearoa consists of six regional ethical committees, that consider applications for research to be carried out in its entirety in one of the four ethics committee regions, and then one multi-region committee, who consider applications for research to be carried out in more than one of the four ethics committee regions. Other committees have been established with various responsibilities for human ethics including the Health Research Council Ethics Committee (HRCEC), the National Ethics Advisory Committee on Health and Disability and Support Services Ethics (NEAC), and the Ethics Committee on Assisted Reproductive Technology (ECART)(The Health Research Council of New Zealand, 2002 (revised in 2005)). In addition, Institutional and Private Sector Ethics Committees can be accredited by the HRCEC.

One key-informant described the role of the ethics committee as 'making sure that the research practices are good and that researchers have got ways to reduce the risks and protect the people'. However, this KI also explained that the purpose of ethical review of health research

was not to do the work of the researchers, instead researchers must explain to the committees their decisions and the logic behind it. For this key-informant the scrutiny of research practice is a fundamental component of ethical review and assessment. Moreover, ethical assessment must also consider the consequences of genetic research for community values

> Ethical review of genetics research and practice has to scrutinise both its methodology and its impact generally in relation to fundamental moral considerations. We need to look at not only the realisability of worthwhile objectives, but also the impact of genetics on the values that inform human relationships, like autonomy, kindness, not causing harm, dignity, truthfulness and justice (p.27) (Evans, 2000).

Taking this into account, it can be argued then that ethical assessment of genetic research must uphold and maintain the values of Māori society to the same level as Pākehā values.

Māori responsiveness in the ethical review of health research in Aotearoa/New Zealand is maintained through the inclusion of members on each committee who have a recognised awareness of te reo and an understanding of tikanga Māori, and the embedding of the principles of the Treaty of Waitangi in the proceedings and processes of the ethics committees (Ministry of Health, 2006). Moreover, the HRC also produced *Guidelines for researchers on health research involving Māori* to ensure that the outcomes of biomedical, clinical and public health research provide outcomes that contribute to improving Māori health and wellbeing and through the maintenance and enhancement of mana Māori (Health Research Council of New Zealand, 1998). The common issues to be considered by researchers when thinking about Māori responsiveness include utility, defining and identifying Māori, informed consent, confidentiality, the handling and disposal of tissue, genetic information, intellectual property, koha, and the involvement of regional Māori health services (Sporle & Koea, 2004).

Within health research, Māori consultation has become a key part of the development of research projects through the identification of potential issues and concerns, and for involving Māori as partners and participants in research (Ministry of Health, 2006). In the Operational Standard for Ethics Committees, consultation is contextualised within the Treaty of Waitangi principle of partnership and is described as

> … a two-way communication process for presenting and receiving information before final decisions are made, in order to influence those decisions. It is a dynamic and flexible process… (p. 79,(Ministry of Health, 2006))

However Māori consultation has attracted negative publicity, particularly from scientists who felt Māori were purposely ‘stalling’ scientific progress and ‘stifling’ academic freedom. The relevance of Māori consultation was questioned by those who believed that their research had little or no perceived impact on the Māori community. As many of the key-informants interviewed for this study explained, this misperception has created considerable frustration

among Māori researchers, particularly in the way that some scientists have approached the opportunity to develop relationships with Māori pessimistically and paid 'lip-service' to the process.

> *... there are a lot of people trying to go through the Māori health unit and I was saying its not up to them to review your projects... cos I kind of felt like they're getting paid as researchers to set up their research project and yet they're expecting the Māori health unit to read them all not being paid to do it and then provide some kind of advice or ensure that its being done in the right way and write a letter of support ...and when...I said to the* [research team] *why aren't you setting up your own group or roopu that you can go to that have got experts who can provide that advice and paying them to do it, and they just got really shitty, and going 'but we're not the ones to do this its Māori that want to be consulted'...and I just thought it was ridiculous and I think it isn't done right yet, not even addressed really, or they go 'its an issue for everybody' especially major health issues for Māori you think, actually, you need to put a bit more thought into how will this help Māori.*
>
> ***Key-informant, MH2***

Many of the key-informants interviewed for this study expressed their concerns regarding the process of Māori consultation in health research which included:

- the legitimacy of the consultation process, particularly when researchers have not necessarily approached the most appropriate individual(s) or groups with whom to consult.
- the ability of ethical review to assess whether research was responsive to Māori, particularly as many individuals/groups felt over-consulted.
- the additional strain and unfair burden of work and expectations enforced onto a relatively small Māori health workforce
- and the inability of current systems to validate and value Māori consultation.

In general, the key-informants believed that researchers and their institutions should take more responsibility for their research practice and engage more with communities in order to understand and appreciate the benefits of working with Māori.

The Treaty of Waitangi as a framework for regulation and control

The reality that Western-science is determined by those who are doing the research raises specific concerns for Māori, as the principle of tino rangatiratanga contained with The Treaty of Waitangi guarantees our fundamental right to control the research that we take part in or are subjected to. Another layer of complexity within the regulation and control of research is the influence of international trade agreements and policies which act to determine those areas of knowledge that are prioritised and funded. However, as some of the key-informants argued, research science must recognise that the relationship between the Crown and tangata whenua

demands the same level of respect. One key-informant explained that in the process of signing up to international trade agreements, the Government knowingly makes decisions without consultation with Māori, or consideration of our indigenous rights. The key-informant warned that international trade agreements extinguish Māori rights guaranteed through the Treaty of Waitangi and the Mataatua Declaration. He heartedly declared that Māori are not an interest group but a Treaty partner and we have a right to shared a voice in the decision making process.

The relevance of the Treaty of Waitangi within research was illustrated by the Memorandum of Understanding (MOU) between Te Runanga o Ngai Tahu (the Ngai Tahu iwi authority) and the University of Otago. One KI believed that this relationship provided a mechanism for facilitating iwi control of research within a legislative framework. In her experience, the Treaty has brought assurances for her iwi through the development of a process of consultation that sits alongside mainstream structures within her institution and the guarantee of iwi governance of genetic research within their rohe. Other KIs agreed that the MOU has provided a clearer pathway for research that is conducted through this institution and affirms the validity of policies and guidelines that specifically addresses Māori rights. The creation of structural support systems, policies and processes for consultation has also alleviated some of the pressures Māori researchers have experienced in the past.

6.4.3 The Consequences of Genetic Research

How can we ensure that the negative outcomes of genetic research are considered and managed? Can we guarantee that all members of our communities will be able to share in the benefits? This section illustrates our hope that genetic research, in any capacity, would be carried out for the good or well being of our communities, rather than for the benefit of the individual or institution driving the research. It is about enhancing our communities.

Increased community education

Early in the focus group conversations participants frequently claimed that they didn't know anything about genetics, and sometimes they felt confused about the difference between genetic engineering, genetic modification and other techniques. Other participants felt that they weren't 'qualified' or 'skilled' enough to engage with the issues. Similar disclaimer statements have been reported by others who have looked at public perceptions of genetics and new biotechnologies (e.g.(Cram et al., 2000; Roper, Zorn, & Waeaver, 2004)). Many of the participants in the present study found a way through this confusion by abandoning scientific jargon, choosing instead to share personal stories and anecdotes to communicate their understanding of genetics and the possible consequences of genetic research to the rest of the group. This created a comfortable and safe space for the participants to think and talk about genetic research.

One key-informant felt that this 'confusion' was common and largely attributable to mainstream media coverage of genetic issues. Another KI agreed that the talk is heavily-laden with scientific language. Although it could be argued that the use of specific terminology is a necessary component of the discourse, it frames the issues as 'scientific' which in turn restricts the questions, issues and concerns that are discussed and limits public participation in the conversations and ultimately shifts the power relationship away from the community. The KI argued that more often than not, the use of 'scientific language' is redundant, and in fact creates mysticism around Western science. The key-informant also challenges the belief that the public (or Māori) 'just don't understand' as unfounded, because when the discourse is changed such that it considers the human consequences, as well as the ethics and values of society, Māori communities have demonstrated that they hold informed and valid opinions about new technologies and their wider implications for New Zealand society.

For another key-informant using everyday language, and taking the time to explain what was involved in the genetic research, was vital to the success of her work.

> *My experience doing genetic work, you have to sit down with [the participants] and explain to them what you want to do, why you have chosen them and how its done and I had to sit down with people who had taken part in my project and explain to them the method I was doing in a layperson's terms and they really appreciate that. They would say, here, take my blood. They were quite keen to be involved …. But it took me months and I had to speak to every single person myself and do it, but they appreciate that and then going back, you have to go back and say to them what you found, what it means and what you hope to do with it …The feeling of being talked at rather than um being explained what is going on…. I had to explain to them what polymerase chain reaction was and it is quite a mind boggling concept but they understood in the end you know but I did have to sit down and it took maybe 15 or 20 minutes of explaining that, and then you talk about your family, where you are from and then it's a couple of hours later. That's just one person out of 300.*
>
> ***Key-informant, NP***

Appropriate language and communication are implicated in the researchers' duty to gaining informed consent from their participants and also addressing their fears and concerns in order to minimise risks and harm to participants.

Greater and improved education was also linked to trust. Some FGPs did not trust the information on genetic research that was presented to them by scientists and/or Government as it may be used as propaganda. The availability of good information, and sufficient time to form an opinion which considers both new and old knowledge, were identified as key aspects to ensuring equitable participation in the debate about gene technologies. However, some participants felt that a lot of the information was sensationalised through the media, and

therefore was not a useful resource for educating our communities. In general, there was a feeling that communities did not have the tools available to them to easily learn about and understand genetics.

Similarly, some key-informants were skeptical about the validity of some Māori voices who they believed may be purposely 'twisting our stories' in support of genetic technologies. Such people were perceived as 'mischievous' and 'dangerous' as they created confusion by purposely misleading the public and misrepresenting Māori concerns.

Increased community conversation

For many of the focus group participants, the present study provided the first opportunity to talk about genetic research and consider the wide-ranging implications for their families. It was agreed that genetic research is not a common topic of conversation. Finding the time to consider issues around human biotechnologies is a particular challenge for Māori communities (Roper et al., 2004), particularly when many whānau face daily challenges which are more relevant than the issues surrounding genetics. Some FGPs described a constant bombardment of media stories on new biotechnologies, which some FGPs perceived as another strategy for telling people how to live their lives. For many of the participants, keeping up to date with developments and issues was not a priority.

The focus groups explained that public acceptance of genetic research would require better communication and dialogue between researchers (who are conducting the research), government and policy-makers (who are seen to be a key driver of genetic research) and communities (who are participants and end-users of the research). Although scientists and the government are responsible for ensuring that good information is readily available, for some participants being responsible for their own education was about taking some control over the process of research. One key-informant suggested that the media could play a useful role in the information and education of Māori communities by providing opportunities for Māori to actively theorise about genetic research within contemporary situations

> *...I was talking to Papaarangi about it, she was saying there needs to be more debate, we are misinformed through the media a lot, we do rely on the media to get our information or education and of course they're going to be swayed to one way or the other just to make it newsworthy. And there does need to be a lot more debate down in the community level, y'know? We were talking about that show on Māori TV where they have the debates and they have different iwi, they also have radio versus TV, why not scientists versus anti-GM people or something like that so you do get to what are the actual issues. Or even at the school Manu Korero speeches, you know have an interesting topic around genetics so that kids have to be able to research it and find out more information and presenting it to that kind of group…*
>
> ***Key-informant, MH2***

Some of the FGPs hoped that increased public discussion and debate around genetic research would provide a space for Māori to talk about the ways in which genetic research challenges Māori traditional knowledge and practices. Tikanga Māori was particularly relevant for a discussion on genetic research for one FGP who felt that it reminded Māori of our values and those things that are central to a thriving Māori community. In this way tikanga protects and guides the decisions that we make. For this FGP, being Māori and respecting our 'heritage' should not hold our communities back, but in fact it gives Māori the tools to engage with Western research and technology. Effective communication around issues such as genetic research will allow Māori communities to find the balance between our maintaining our values and advancing ourselves in the Pākehā world.

Public dialogue, such as the RCoGM and those initiated by Toi te Taiao/The Bioethics Council, have indicated that there are issues of specific importance to Māori which centre around the effects of genetic research and biotechnologies on tikanga. Many of the current conversations on genetic research have framed Māori concerns as cultural or spiritual in comparison to scientific rationale which is perceived and understood as 'normal' (Sivak, 2005). This diminishes the integrity and authority of mātauranga Māori by privileging a Western discourse and excluding Māori voices from conversations about science.

> … At one level, as so often happens, Māori views and analyses have been regularly misrepresented as little more than a vaguely spiritual and quaint sub-text. Consultation on the issue has merely led to a feeling that the Māori 'perspective' being sought was only a cultural explanation of something in which normality and truth had already been determined… In the whole genetic modification discourse the parameters seem predetermined by non-Māori economic, scientific and political interests. In this context the serious concerns that Māori have been raising have sometimes been acknowledged but then consigned to an addendum of cultural side issues, or diverted in a dubious consent process that has taken a terrible toll in terms of resources, time and damage done to deeply held and reasoned perceptions (p.71) (Jackson, 2004).

The brochures and reports that have resulted from these discussions have probably increased public awareness of the connection between genetic research and concepts such as whakapapa, mauri and wairua. However the ability of these documents to express the validity of these concerns is questionable and in fact may have resulted in the labelling of Māori concerns as cultural rather than scientific and legitimate. In the production of information there has been a focus on translating and defining traditional concepts in order to gain greater Pākehā understanding of the issues and the need to find a 'universal' Māori opinion. Jessica Hutchings describes this as a 'trait of colonisation' which attempts to exclude certain voices from the conversation based on whether they can talk about science, or whether they represent an authentic Māori voice. Similarly, one key-informant feared that opening a discussion about

tikanga to the wider Pākehā community may provide a mechanism to take control of and define the conversations.

Genetic research and community wellbeing

> Altruism and trust lie at the heart of research on human subjects. Altruistic individuals volunteer for research because they trust that their participation will contribute to improved health for others and that researchers will minimise risks to participants (De Angelis et al., 2004)

The willingness of Māori to take part in research illustrates the common understanding that to gain knowledge is to uphold and enhance the mana of whānau, hapū and iwi such that it can be used to support and protect the wellbeing of our natural resources and environments. Historically, this willingness has been taken advantage of by some Pākehā researchers (Cram, 1999) who have viewed Māori communities as research projects. This continual denigration of Māori communities has fostered a long-lasting distrust of Western science and researchers in particular. For Māori communities the resistance and suspicion appears to be heightened when genetics is involved

> *I think Māori and indigenous communities have had a history of researchers coming in and taking stuff and leaving a mess or you know they've participated in the manaakitanga, hospitality of Māori who are, who have been very giving and all the with past experience, even present experience with some researchers, all it is, is take, take, take so these are definitely general issues related to research so I think even now within Māori communities, they hear the word research they go oh yeah what, what are you going to take or what are you going to try and rip off from our people because I think our hospitality has been taken advantage of so many times so there's a natural hostility, natural suspicion with any research but I think with genetic engineering research there is even more suspicion…*
>
> ***Key-informant, PR***

Some of the focus group participants believed that contemporary research often still involves these colonising practices. As one focus group participant pointed out, sometimes there is little to gain and very little reciprocity in the researcher-participant relationship

> *I think the only thing that I have is that sometimes personally I don't have a problem with people wanting to do that y'know just to be helpful, I think its good thing but sometimes you read about this stuff afterwards and people have sort of come out with these other conclusions that you might not necessarily agree with…*
>
> ***Focus group 2, Tane***

Despite these experiences, the focus group participants were encouraged by the hope that their involvement in research was going to 'help somebody' and ultimately enhance the wellbeing of others. Indeed, as these FGPs demonstrated, the altruistic nature of taking part in health research in particular, is often pivotal in our decision making process. The thematic analysis identified a

range of hopes for genetic research which included finding cures for illness and disease, feeding the poor, and providing greater community protection. For one key-informant, many of the hopes and dreams articulated by the FGPs reflected the promises that have been made by supporters of genetic research which are repeatedly highlighted within the media. Indeed, from the focus group conversations it became evident that many of the hopes and dreams were gathered from mainstream media sources such as radio, television, newspapers and magazines. Molina (2004) acknowledged that scientific journalism has been a major player in the progress and development of genetic research and that it is strongly influenced by 'scientists, academics, ethicists and other experts'. To fully meet the objectives of this study, it was necessary to examine the ways in which the promises that have been made and the expert opinion that is transmitted through the media may have influenced the participants talk about genetic research.

As mentioned earlier, story-telling and analogy were important linguistic tools used by many of the participants to communicate with the rest of the group. Stories about 'dolly the sheep', 'designer babies' and 'GM crops' were frequently heard, as were phrases and terms such as 'DNA maps', 'medical breakthroughs', DNA 'short cuts' and 'playing God'. Scientific journalism is often oversimplified and purposely loaded with metaphor and imagery to assist the publics' perception and understanding of genetics (Molina, 2004). As a consequence the metaphoric language is often taken literally and accepted by the community as truth.

Within the development of their hopes and dreams for genetic research, many of the focus group participants portrayed genetic research, and DNA technology in particular, as a 'tool' to be used by humans to enhance the wellbeing of our communities. The consistencies and contradictions within these arguments will now be explored.

Human health and medicine

The benefits for human health dominated the discussions around our hopes and dreams for genetic research. Developments in genomic medicine were seen to 'contribute' to finding a 'cure' and engendering a 'solution' or 'remedy' to 'rectify' 'genetic diseases' or 'disorders' that would otherwise have individuals or 'children' 'suffering'. For many of the focus group participants, genetic research would 'fix' our poor health.

The participants' descriptions of the possible health benefits were extensive. However they could be broadly illustrated in three ways: (1) Individual health benefits; including 'prolonging life' through the development of pharmacogenomics and individualised medical treatments (2) Whānau benefits; through the development of genetic screening services, preventative treatments and the provision of a DNA 'bank' and (3) Community benefits; by relieving the community from the heavy social and economic burden of disease by eliminating health problems prevalent within our communities and redirecting resources that are currently allocated to the health sector.

Although these focus groups promoted the potential for the advancement of genetic research in health care and medicine, the conversations also clearly expressed a desire to have some control over their personal health and the family wellbeing. For example, genetic research was viewed by some participants as a way of providing options in healthcare and medicine and they were eager to have a greater range of choices available. At the level of the individual, taking control of health and wellbeing was about being able to gather balanced information, and the ability to make an informed decision on behalf of their families. On the other hand, whānau control of health was about being able to take responsibility for the wellbeing of the family and taking back the caring roles from the medical profession and Western notions of family. For the wider community, taking some control of health was about ensuring that genetic research was being used to improve the health of all members of the community, and maintaining greater public involvement in decision making and consultation.

It was also evident that there were differing and often contrasting understandings of health and disease causation within each of the focus group discussions. For example, one participant spent some time exploring a reductionist view of disease

> *... the fact that people can get down to looking at DNA looking at individual genes and determining that a particular gene causes a problem or disorder genetically and that people can carry these genes without actually knowing it but when they are highlighted y'know they can generally follow it through the family tree I mean there are illnesses, isn't there that are carried down through the father and sleeps through the mother, what's that blood one? Haemophilia... So it's a sort of silent gene until two people marry, have kids and to be able to give those people a better life through, what would be,*

probably a simple genetic change, without impacting anything else I think has huge benefits ...

Focus group 3, Tane

In this example the FGP describes genes as wholly responsible for disease and the hereditary nature of illness. He uses emotive language to highlight the importance of genetic research and describes how the technology provides a 'simple' way to enhance life. The use of phrases such as a 'silent gene' and 'simple genetic change' are signposts that indicate the participant has derived his understanding through media reporting around genetic research which on the whole project scientists as heroic (Molina, 2004).

Several of the key-informants picked up on the scientific-framing of health within the participants talk and questioned the truth behind these understandings and discussed the responsibility of researchers to ensure that their research does not perpetuate victim-blaming policies. Another key-informant described the consequences of this frame to public understandings and truths about health

...it's how you frame the perceived problem and so if you frame it as all you Māori's and all you Pacific people you're dying of diabetes so I mean the problem is diabetes, where's that diabetes located or something, okay it's identifiable within a gene so you've got a diabetes gene ...so the framing and the definition of the problem is a genetic problem so there must be a genetic solution but if you reframe or you look at the perceived problem using a different lens, you see okay the lowest socio-economic ..., it's one of the contributing factors, diet is one of the contributing factors which may also impact, have an impact of how much money you make, exercise, which is related to could also be a lower socio economic thing but not necessarily but related to self esteem, it could be related to access, to within the city, where you're going to go, you're running to the streets or whatever, you don't even have shoes, whatever it is so there's a whole lot of other contributing issues to a particular problem so it's in the definition or how you frame a particular problem

Key-informant, PR

Rankine and McCreanor (2004) have suggested that the media play a critical role in how the public understand and interpret their own lived experiences. This key-informant extends this and suggests that researchers are also responsible for the representation of community realities. By talking about health and disease as genetic, there is the potential for certain diseases to be perceived as peculiar to the Māori population, and similarly encourage Māori communities to take a fatalist approach to their health and wellbeing. This KI recommends that scientists and researcher become more critically aware about how personal beliefs and values are translated through research, and can mould social understandings and public perceptions.

Some focus group participants challenged the reductionist view in their own analysis of the promise of health benefits through genetic research, and suggested that there are also social and political explanations of health and disease. One participant specifically questioned whether genetic research could sit within a Māori framework of health. Traditional Māori understandings provide a more holistic view of health and wellbeing where the importance of traditional elements such as tinana (the physical element), hinengaro (the mental state), wairua (the spirit), and whānau (immediate and wider family) are now contextualised within te whenua (land providing a sense of identity and belonging), te reo (the language of communication), te ao turoa (environment), and Whānaungatanga (extended family) (Cram, Smith, & Johnstone, 2003). Because of this broad definition of health and wellbeing, many conventional ways of looking at health fall short of Māori realities. For some focus group participants, a dominant question was the relevance of genetic research to the continued improvement of Māori health and the development of services. Reid and Robson (2005) explain that Māori health status reads as a disproportionate burden of risk, morbidity, disability and mortality for almost every major category of disease. The popular view of disease causation is perpetuated and highlighted in the debates surrounding genetic gene technologies, where 'malfunctions' and 'defects' are purported to be central to many health problems, such as cancer, heart disease, diabetes and asthma (Berridge, 2000). However, public health researchers are increasingly focusing on health inequities (a.k.a. inequalities, disparities or gaps) as determinants of poor health outcomes. Arguments for and against genetics as the basis of ethnic inequalities in health are described by Nancy Kriegar (cited in (Reid & Robson, 2006)) as located in two different theoretical positions:

(1) The racialised expression of biology – where the health of different ethnic groups is derived from their different biological or genetic mix

(2) The biological expression of racism – which understands that ethnic inequalities in health are determined by our social environments and social hierarchy

As Western-science becomes increasingly focused on 'uncovering' the knowledge that is held within the human genome and the potential for economic and commercial gain from research 'outcomes', Māori are developing methodologies that value traditional knowledges and relationships and advance our communities

> *…the Māori way of thinking is getting bigger and bigger and that Pākehā way is getting smaller and smaller that sort of scientific… that's where you kind of end up talking past each other, 'cos their narrowing the discussion and you're actually widening it 'cos you want to know "ok how does that work in the context of everything else" and they're trying to understand "oh how does that work".*
>
> ***Key-informant, MH1***

Crime.

The subject of DNA testing and criminal investigation was of considerable media and public interest, following an address by the leader of the Opposition, to the Sensible Sentencing Trust in July 2004. During his speech on Law and Order, Don Brash outlined his Party's Policy whereby every person who is arrested would be DNA tested and if convicted, their DNA would be added to a national database. In this address DNA testing was described as 'the modern equivalent of a fingerprint or photograph – it is an identification tool. It is an enormously powerful method of establishing either guilt or innocence, and can make a huge contribution to solving crime…'

There are a number of significant features which speak clearly to one of the focus group discussions on DNA sampling and criminal investigation

> *…So in terms of the DNA technology I think it's just a fantastic tool. I wouldn't quite go so far as to say everyone in New Zealand should be DNA sampled but, yeah, it should be, probably should be a, definitely if anyone's committed a crime, depending on the extent of the crime, I think they should be DNA* [sampled]. *I'm a firm believer that Brash has got it right there. I think as soon as somebody commits a crime against community, against their neighbours etc in New Zealand that they've lost the right, to not give DNA samples. I think that's fantastic and look what it's done over the last, to solve crimes over 10 years old in New Zealand alone. It's just fantastic. So I think in that respect, that technology is very useable and has great benefit.*
>
> ***Focus group 2, Tane***

For this FGP, DNA sampling is a 'fantastic tool', 'wonderful' and 'magnificent'. DNA is portrayed as 'safe' and 'passive' and it is described as a tool that can provide information about individuals and our world. In his address, Brash used analogy to convey his message on crime by likening DNA testing to fingerprinting or photography. This imagery is picked up on by the focus group participant who describes DNA technology as 'simple' and 'useable' and insinuates that it has been used successfully to solve crimes where perhaps more conventional policing and investigative techniques have been unable to do so. This reasoning is used by the participant to bring some proof to his argument that DNA testing is worthwhile.

In his address, Brash presented his policy as a way of protecting and keeping our communities safe. The focus group participant calls on this community concern, and reminiscent of the Brash address, argues that crimes are being committed against communities, and not just individuals which is significant because it leads to the participant's line of reasoning that DNA sampling is about community rights. One of the major ethical concerns around genetic testing and DNA sampling is the need to protect individual and collective rights, particularly from the potential for discrimination by insurance companies and employers. Govern et al. (2004) suggested that inherent in these rights are issues of power, informed consent, and the right of the individual(s)

not to know. Although the participant believes that criminals 'lose' their rights, he defends the rights of the community to decline DNA sampling. The participant goes on to raise support for his argument by calling on the economic concerns of the community and highlighting the costs of crime to society, together with the notion of community safety which he believes outweighs the cost of the application.

> *I'm certainly with Mr Brash about DNA samples for criminals. I believe people lose their rights as they commit crimes, even if it's a deterrent the costs, 56 million to sample everybody and it puts half the criminals off in New Zealand then you've probably saved a few 100 million dollars sending people to prison and maintaining them.*
>
> ***Focus group 3, Tane***

Identity

One focus group hoped that genetic research could be used to develop and maintain understandings of Māori identity

> ***Tane****…and y'know, I'd like to know a little bit more about my background as a Māori, because when my dad was bought up he was in that era where, in Christchurch, where being a Māori was not, they weren't allowed to speak Māori at school, they got strapped and disciplined for it and he never learnt it. He, y'know, he never, he was put in a home, he never knew his family, never knew where he originated from, he had dark skin that's all he knew and he got abused at school because of it, he got disciplined for speaking Māori. So when I was young I knew I was part Māori but I didn't know anything about my history so I think, um, DNA can have the benefits of finding out where you're from, which is good...*
>
> ***Wahine****: It makes it harder when you have to do it that way.*
>
> ***Tane****: yeah, it does, it certainly does.*
>
> ***Wahine:*** *And also being the generation that they were that was basically it. My mother never spoke Māori and yet I've learnt as an adult she speaks fluently, but all the time, we were actually brought up in Australia she actually had to leave New Zealand, so all the time I was trying to find out "why are you so much darker? Where are we from?" All that sort of stuff, yeah, she said she was just never allowed to speak Māori…*
>
> ***Focus group 3***

In these stories the participants locate their personal loss of Māori identity within their family's experiences of assimilation. Up until 1926, the majority of the Māori population lived in rural communities (Walker, 2004). However over the next three decades, many Māori moved away from their 'traditional' homelands (kainga) (Nikora et al., 2004) into the urban centres which were largely populated by Pākehā settlers. This urban 'drift' translocated Māori identity from a community based around a marae and the traditional practices this environment depended and thrived upon, into the 'economic milieu' (Walker, 2004) and capitalist practices of Pākehā

society. The esteemed Tūhoe kaumatua John Rangihau (known affectionately by our people as Te Rangihau), connected the urban drift to a loss of identity when he observed how Tūhoe managed to retain '…a little more of their Māoriness than others' by resisting the move to the city (Rangihau, 1975). Voluntary Māori associations such as cultural clubs, churches and sporting clubs became sites of struggle against assimilation (Walker, 2004). For Māori living in the new urban landscape, these were places where Māori could be together (Rangihau, 1975) and reconnect with their Māori identity, values and culture.

A second aspect of our colonial history which clearly influenced the participants talk is the government-run Native school system where Pākehā looked to assimilate Māori using a school curriculum that would 'reflect settler views about what non-European populations should be taught in order to bring them into line with accepted European societal norms' (Morris Matthews & Jenkins, 1999). In their overview of the Māori girl's schooling system, Morris Matthews and Jenkins (1999) connected this expression of assimilation to the colonial ideology of race, where differences between Māori and Pākehā became located within social differences and hierarchy giving rise to the concepts of 'Christianizing'[sic] and 'civilizing' [sic] the native Māori population. As part of this institution, the use of te reo Māori was generally prohibited in order to 'speed the progress' of the Māori children. As the focus group participants inferred, this prohibition was often enforced through corporal punishment, with long-lasting and detrimental effects to their identity as Prof. Ranginui Walker (2004) explained

> The damaging aspect of this practice lay not in corporal punishment *per se*, but in the psychological effect on an individual's sense of identity and personal worth. Schooling demanded cultural surrender, or at the very least suppression of one's language and identity (p. 147).

For these focus group participants, developments in DNA technology promised to ease the strangeness of being Māori. On the contrary, Te Rangihau believed that for young Māori moving into the cities, this strangeness is avoided when they do so knowing their histories and where they come from

> I also believe young folk can live with a greater amount of assurance if they know who they are. Then they can move into the Pākehā world full of self-confidence because they have no difficulty about the question of identity. They can recognise themselves fully because they know their history (Rangihau, 1975).

One participant pointed out that DNA would be a 'fantastic tool' for 'people [who] want to find out…where they originated from and their roots so to speak'. The participants described DNA as a 'short-cut for identification', that it is 'precise', 'accurate' and 'unique'. One participant suggested that DNA is 'much the same as a birth certificate' and a second participant agreed

that DNA would provide a useful alternative to the daunting current bureaucratic systems for those interested in researching a 'family tree'.

Using DNA to retrace the origins of indigenous people was thrust into the public mind with the creation of the Human Genome Diversity Project (HUGO) and its descendents. These 'vampire' projects (Smith & Reynolds, 2000) were fiercely opposed by indigenous researchers and communities worldwide, as scientists sought to map the diversity of isolated and threatened indigenous communities (Smith & Reynolds, 2000; Smith, 1999)and moved to claim ownership of genes which they perceived to be of economic value and commercial potential (Harry, Howard, & Shelton, 2000; Smith & Reynolds, 2000).

For these FGPs, the key to their identity as Māori was located within their genes. The basis of their understanding, and that of projects such as HUGO, relies on the theory of genetic determinism (Keller, 1993) which, alongside other racist ideologies, found a new audience with developments in genetic technologies (TallBear, 2000). From a local indigenous perspective, genetic determinism '…is the belief that Māori and other indigenous peoples are innately less intelligent, more predisposed to diabetes, more predisposed to alcoholism and so on' (Smith, 2006).

Once a technique confined to the laboratory, tracing indigenous ancestry is now a political act that 'involves judging the worth of genetic knowledge against other kinds of claims to authentic identity and group membership' (Brodwin, 2002). Indeed, these focus group participants believed that 'all they have to do is take a strand of your hair or something, … or maybe even a little touch pad that takes the DNA sample out of the oil from your finger and then suddenly you've got a match'. Brodwin (2002) warned that the question now is not whether genetic research is 'bad' science, but whether it serves to diminish personal esteem and self-worth, group cohesion, access to resources, and the redress of social injustices.

In Aotearoa/New Zealand, issues of race, genetics and identity intersect in the discourse around the collection of ethnicity data in government and health statistics (Pearce et al., 2004; Robson & Reid, 2001). Robson and Reid (2001) summarised early government definitions of who was (or was not) Māori as including 'persons greater than half Māori blood', 'half-caste', 'living as members of Māori tribes', and 'persons of half or more Māori blood'. All of these definitions were problematic as they were based around the flawed concept of race, which proposes that biological characteristics and differences between groups can be genetically determined (Pearce et al., 2004; TallBear, 2000). TallBear (2000) challenged the idea that genetics could be used to prescribe cultural affiliation, since identity was developed through immersion in cultural practices and not transferred across generations via DNA. More recently government and health statistics (i.e. census) have moved towards counting individuals based on their self-identified membership within an ethnic group. The New Zealand Health and Disability Sector defines

ethnicity as ‘a social construct of group affiliation and identity’ where members may share a sense of common origins; claim a common and distinctive history and destiny; possess one or more dimensions of collective cultural individuality; and who feel a sense of unique collective solidarity (Ministry of Health, 2004a). Based on this definition Robson and Reid (2001) discussed a ‘spectrum of identities’ where Māori express a range of individual and collective identities in various contexts that may depend on the situation and may develop or change over time.

Although the focus group participants took a Western approach, which values the importance of genetics within the construct of identity, at other times they also showed a closer understanding of a Māori worldview of belonging. Interpretations and understandings of identity are complex and changing, however a significant feature of these explanations is the importance of our relationships and whakapapa. Higgins (2004) understood the meaning of the term ‘Māori’ as connected to the ways in which the indigenous people viewed their spiritual relationships with the land (whenua) and their gods (aitua) and the respect that was held for this worldview.

The significance of the relationship between Māori and whenua is also evident within the term ‘tangata whenua’ which Jackson (2003, cited in (Robson & Reid, 2001)) defined as ‘not people in the land or over the land, but people of it’. The use of tangata whenua also locates Māori within a social and political relationship with the Crown. Many non-Māori have been resistant to the term tangata whenua as it is perceived that it recognises Māori ownership of the land (Higgins, 2004). In addition, our positioning as tangata whenua guarantees Māori international rights pertaining to indigenous people which recognise the right to self-determination, including the collective and individual right to identify ourselves as such (Robson & Reid, 2001).

The complexity of Māori identity is also encapsulated by the term Māoritanga, which incorporates cultural vales of the people in to their perception of reality (Higgins, 2004). For many people, their identity as Māori is intimately related to their hapū and iwi identity. Te Rangihau believed he was a product of his environment and his people and he understood identity as related to life experiences and the ways in which you lived with your culture. Te Rangihau’s understanding of the origins of the term Māoritanga speaks loudly to the indigenous opposition of DNA as a tool to map identity

> Because if you cannot divide and rule, then for tribal people all you can do is unite them and rule. Because then they lose everything by losing their own tribal histories and traditions that give them their identity (p. 190)(Rangihau, 1975).

Decision making and tikanga Māori

Making decisions about genetic research was a significant consideration for the participants involved in this study. For most of the FGPs, the decision-making process involved evaluating

the potential risks against the possible benefits, and judging the rightness or morality of the application of genetic research. Decision-making also involved the consideration of different knowledges and assessing the truths that are implicit within these knowledges. Finally, the decisions and positions changed depending on the challenge or the situation that was under discussion. For example, when discussing genetic modification of foods and crops, most participants agreed that the appropriate position is 'no'. However, when GE crops were framed as a solution to famine and starvation the decision was more involved

> ... [Genetic crops] *sort of have their place but, I don't think they have there place in New Zealand, in a place that is fertile and doesn't really need it but in places like Africa and Ethiopia and that where they do have problems growing crops because of the lack of water and that, the genetic crops can help.*
>
> ***Focus group 3, Tane***

Making decisions based on survival blurred the boundaries between what we consider is right and what is wrong, and required a more complex process of reasoning from the participants. This was most evident within the discussions around health and disease, where the wellbeing of whānau was central to their decision-making

> *I think it's interesting, I was saying before that for me when this was all first discussed I probably took a stance right down that continuum you talked about of saying no. What are we doing tampering with this, but when you actually apply it to a personal experience where say if it was your child or something that had some illness that you know some genetic research may end up contributing to finding a cure then I think you tend obviously, to look at things a bit differently. So I guess what I'm saying is that I've moved down that continuum as I've become aware of some of the benefits I guess of doing it where nothing else will suffice, so there's no other way of doing it that will engender some solution or remedy or some cure other than doing some sort of testing of some sort.*
>
> ***Focus group 1, Wahine***

Whānau acts as a basic support structure within Māori society, and therefore is it an integral part of Māori health and wellbeing (Cram et al., 2003). The important place of whānau within decision-making was also highlighted by the participants talk about parenting and caring, and the influence of genetic research and medicine on these roles. Some participants spoke of the necessity and pressure to put aside any personal or indeed cultural perspectives on genetic medicines and treatments in order to be a 'good parent'. Although the FGPs approached new situations and challenges from a position that respects and upholds their personal beliefs and values, they believed that their ability and right to reject a medical treatment is silenced when society is able to dictate what it means to be a good parent, or to provide the best for their families.

Although Western society has already accepted some forms of genetic research and technology (e.g. Guthrie Cards and IVF treatment), many of the FGPs believed that their fears and concerns have not been adequately addressed. As a consequence of this, some of the FGPs felt 'ignorant' or 'uneducated' when it comes to issues around genetic research and thus incapable of providing their children with the life lessons that they need to progress in modern society. Within the context of the RCoGM, Sivak (2005) found that cultural concerns (read Māori concerns) around genetic modification were 'managed' by focusing on methods to improve public education. In this way, the perception was that if the ignorant public was properly educated then the problem of social concern is solved. Aside from belittling the abilities of the community to engage with, and theorise about genetic research, it also removed Māori concerns from active public debate. In this way managing culture could also be perceived as an assimilatory goal (Sivak, 2005).

Balancing cultural obligations, values and principles against personal choice and whānau wellbeing were also difficult decisions for many of the focus group participants. It was clear that many of the conversations that addressed decision-making were situated within wider discussions about organ donation and transplants. For example, when talking about their decision to be an organ donor some participants felt that their right to make a personal choice was often challenged by whānau and friends

> ***Tane****: It's quite interesting because, um, this business about being a donor, like when you apply for your license you can say if you're a donor and I understand that the family can actually, even though you've said on there and agreed to be a donor, they can say no. It's quite interesting because you made that as a personal choice. I wouldn't like to think that my children or next of kin would say no you can't do that because, if you make a choice that should be, it's your choice.*
>
> ***Wahine****: I've made it very clear, and they know me well enough that I make these choices and even though I'm their mum I've always been an individual and they understand that relationship so hopefully, the only who might not, might be my husband…*
>
> ***Focus group 3***

Some participants believed these challenges were based within traditional understandings and preferences on how to do things

> *I guess I have some concerns and fears like when you're talking about DNA and um, taking of tissue, blood all those sorts of things, my biggest concern is, being from a culture, being the way that we are, we have concerns about how that's handled and, how sensitive people are to those sorts of procedures and how we view, um our bodies, our bits and pieces so to speak, how sensitive are they towards that? I mean Māori people are very sensitive about absolutely any part of their body if you're going to take it or take any of it anywhere, there's that aspect of who will be handling it? Who will be putting it*

in its little place or where it has to be or where it has to go? I mean, there still are some of my generation to who possibly wouldn't even consider this, there is no way you're taking anything out of y'know, and I've been, for lack of a better word slagged quite a bit through my life for the fact that I'm a donor and I've said "for goodness sake if I'm not using it and it can benefit or help someone else that is what it's about". I know quite a few people who wouldn't even sit in front of you basically and discuss those sorts of things….um, yeah…

Focus group 3, Wahine

However, other participants felt that these old ways of looking at organ donation were not as strong, particularly as younger generations developed new ways of understanding the issues in order to accommodate changes in society.

A popular argument within the organ donation discourse matches the low rate of donation from Māori against an urgent need for organ transplants because of the disproportionately high rate of diabetes and kidney failure within our communities (Toi te Taiao/ The Bioethics Council, 2005c). Concurrently the common perception is that the decision not to donate is dictated by cultural taboos. However one FGP disputed this, arguing that tikanga encourages her family to think about issues such as organ donation within a culturally-specific context. In her view, tikanga allows Māori to confront contemporary challenges from a position where our values are centred and in this way the decisions that we make will be safe and affirm our Māori identity. Another FGP proposed that Māori need to 'demystify' our cultural values and principles in order to develop informed decision-making processes. Moreover he suggested that demystifying tikanga Māori must occur using conversations that are free of Western constructions of Māori society

Tane: *On Marae[9] yesterday, it was about kidney transplants and donors and what I was thinking was that, and I don't know this for sure, but you read it or someone tells you that you know Māori theory, that you don't give your organs to others. I can handle that, OK, but, in my mind, I'm thinking, I wouldn't like Māori thinking to be blamed for things that it shouldn't be blamed for and maybe people just don't want to do it because they don't want to die themselves, they've got a fear of if they give it, their kidney, they're going to die. But then we put it under this mystique of, well there is this Māori tikanga and custom which says you don't do that…we can end up being lumbered for something that's not our fault, that's been put under this tikanga Māori thing*

Wahine 1: *people make the assumption that we're not going to consider transplants*

Tane: *…maybe if you look at Māori who have members of their family, immediate members like brothers or sisters whatever, who might need a transplant, on what do they base their decision not to do it? Is it because "I know from my tikanga"?*

[9] Marae is New Zealand's longest running Maori current affairs/magazine television programme

Wahine 2: *so they may say the same thing about DNA*

Tane: *and whether they're just fearful of it*

Focus group 1

The common (mis-)perception of tikanga portrays Māori society as obstinate and the resultant suspicion of tikanga Māori can also create uncertainty and unease about the relevance of tikanga among Māori communities. However, Māori have shown incredible flexibility within the field of gene technologies (Tipene-Matua, 2000). Māori communities are often asked to provide a universal perspective on contentious issues, however this request is driven by the perception that Māori society is a homogeneous group of people who are unable or unwilling to think about and talk about those things that are challenging New Zealand society. Reid (2005) disputes this and argues that making changes (or not making changes) to tikanga or kawa (protocol) is part of our sovereignty or tino rangatiratanga

> People ask what's the Māori way, or the Māori perspective, or whatever. It's plural, it's diverse, it's multiple, it's flexible, it's changeable. We must resist people trying to make us into museum exhibits of past behaviours. We are complex, changing, challenging and developing - as is our right (p. 47 in (Reid, 2005)).

As the FGPs demonstrated, Māori have been making decisions as individuals and as whānau about organ donation for a long time, therefore there is a space for better discussion and analysis which could investigate the ways and the means of making decisions. Within these spaces Māori can discuss the issues that we are faced with and the ways in which mātauranga Māori can create a uniquely indigenous and valid opinion. One key-informant proposed that a critical analysis of the impacts of gene technologies to tikanga would be best suited to whare wananga (traditional houses of learning, or universities) where people with a deep knowledge can meet and discuss the issues. However, other informants were wary that restricting the debate to the whare wananga would create a situation where only certain members of the community would be involved in the talk (i.e. only those fluent in te reo Māori and/or Māori men). As one key-informant pointed out, we should not limit our range voices in an effort to bring an 'authentic' Māori position to the conversation. In her experience Western researchers are sometimes unable to connect their science back to a fundamental philosophy, however they are readily perceived as 'experts'.

Recently, the NEAC proposed that good decision-making should consider the shared values of society to determine how issues should be governed and what decisions should be made (National Ethics Advisory Committee, 2006). By situating the process within a framework of values, NEAC expect that the there will be greater trust, goodwill and support for the decisions that are made. However, as the participants in the present study have shown, identifying shared values is complex, as it involves the consideration of the inherent truths within the talk about

genetic research which is based on different forms of knowledge, notions of power, and the maintenance of Pākehā hegemony within New Zealand society.

Generally speaking, most members of the community are not required to make a decision about genetic research unless they find themselves in a situation where a friend or whānau member is sick or dying. Once in this situation, individuals may find themselves making decisions from a place that is not safe; making compromises in order to alleviate the suffering that is often involved. For many of these participants, decision-making involved a careful balance of individual rights, personal responsibility, whānau needs and culturally-specific understandings. However it must be said that if reconciliation is the objective, then this will be out of our reach given that New Zealand society still favours Pākehā values and forms of research.

Mead (2003) stated that it is right for Māori to come to a position on how we might proceed with contemporary issues such as genetic research, but in coming to this position Māori must look to our own knowledge systems in order to navigate our way through the issues. To do this, Mead (2003) presented a tikanga framework of assessment which outlines five tests (the tapu aspect; the mauri aspect; the take-utu-ea test; the precedent aspect; and the principles aspect) that can be applied to new issues such as genetic research and its application through genetic modification. Derived from tikanga values and principles, these tests allow Māori communities to shift their thinking on genetic research away from Western ideas of what is 'right' and into a culturally specific framework which respects the traditional values of Māori society. By thinking about genetic research in culturally specific terms, individuals or communities should be able to form a specific Māori position from which they can address and move through the challenge in a way that is tika (right) and pono (true) to do so.

Arguments for the common good

Many of the arguments supporting different applications of genetic research such as stem cell research and genetic engineering, have framed the issues as being 'for the common good' or 'for the good of mankind'. By setting the discourse on the use of genetic research as a matter for humanity, it moves the ethical reflection away from the individual (autonomy) to the rest of society and becomes the paradigm on which subsequent decision making on genetic research is made. Vicini (1999) argued that pursuing the common good takes into account a larger range of concerns without diminishing the emphasis on the individual. In the development of their hopes and dreams for genetic research the focus group participants in the present study undertook their own analysis of the validity and truth within these claims.

Many of the focus group participants questioned the promises that are made by scientists to the communities that they work in. For example, when discussing the use and acceptability of genetically modified crops and seed, one focus group participant raised his scepticism of the messages that are given to communities about the safety of these crops, which contradicted his

own experience of genetic crops when living overseas. One key-informant also questioned the ways in which scientists portray the 'truth' about genetic research to communities, arguing that scientists and researchers must take some personal responsibility in the way they present 'scientific evidence' and information, although she also wonders whether scientists purposely hold back on the 'truth', choosing instead to present only the information that serves their purpose.

> *…another woman got up and talked about the cloning of that dolly sheep and she said oh you know we've cloned a sheep and everything's fine, and I said oh no hasn't she had alot of illness that they think has probably been due to the cloning process, arthritis and something else, and she went oh I didn't know that and I said well don't go around spouting that there are no problems because it's a lie actually and you're trying to, you're informing communities, or misinforming communities by saying that there are no problems without actually knowing it yourself…and either don't know about the problems, which is probably true cos I reckon scientists… they're not going to let people know the bad things so scientists themselves might not know it …how can you be so strong … assertive in saying that and…you can never be sure…*
>
> ***Key-informant, MH2***

One focus group talked at length about recent experiences where families had been betrayed by science and medicine

> *… But we've had recent examples in New Zealand where we've had body parts extracted during autopsies stored away in jars on a shelf for medical purposes and that's abhorrent as far as I'm concerned, and to have a parent see the body of a child with its organs missing, without their knowledge and their authorisation is just totally unacceptable, Thankfully they're doing something about it now but I believe they're still finding as they clear out some cupboard spaces, they're still finding bits and pieces and the hospitals that are doing something about returning them, but it must be devastating for those parents, to have buried a child 10 years ago, 15 years ago, then find some organs that they didn't give their consent for them to take in the first place, to receive them then to go through all the trauma again.*
>
> ***Focus group 3, Tane***

In their analysis of this situation, the FGPs uncovered the power that exists within researcher-participant relationships. As an illustration of research relationships there can be an abuse of power and also trust, the consequences of which not only effect those directly involved, but also the wider community's perception and beliefs about research.

> ***Tane:****…So as long as the processes are in place and authorisations, proper authorisations are agreed, taken, um, then I certainly don't have any issues with it, as such. But the process that we've seen in the past shows that 'can we rely on the process?'*

And people, will probably no doubt start saying "no", donors and that kind of thing, for fear of having body parts taken…

***Wahine**: Of not knowing where it's going it might end up on a shelf in a couple of years. They might not actually do with it what I personally intended when I went tick I know very rare, and few and far between, y'know it still happens*

***Tane**: So that's a fear. That's also probably some of the Doctors involved and pathologists involved thought they were above everybody else to some extent, I don't really know, but you sort of got that feeling that they took whatever they wanted to take because they had the power to do that…*

Focus group 3

In another focus group, one participant questioned the context in which individuals and communities make their decisions about genetic research. For this participant he warns that it may seem logical to make decisions based on the promises of good outcomes, however there are deeper issues that the community needs to consider such as ownership and intellectual property rights, as well as questioning the ability of the community to access the promised benefits. He wonders whether we are entering into dialogue excited about the prospects but ignorant of the realities.

***…** then you have issues of ownership and access, who gets access to the good benefits and if you're the only one in the street selling pineapple lumps and no one's had any for millions of years then you are obviously the best thing, but whose to say that research is actually any good it's just that it's the only one that's around so you might get caught grabbing at things that aren't good, just because they appear to be that, because someone's thought it up.*

Focus group 1, Tane

Participants in Focus Group One spent some time teasing out the relationship between genetic research and the common good. As an example, the participants evaluated the argument that genetic modification (GM) would help feed people. Although they agreed that this is a good and fair reason to engage with GM, the participants also looked at the underlying and often unspoken political and economic influences within this promise. The problem of GM in food production is presented as a global issue and there is a sense of responsibility to those 'Third World' countries. The participants feared that GM will continue the oppression of the poor

***Wahine 1:** Then there was the down end of genetic research, things like the food industry you can tamper with food as much as you like but again but nobody's going to know what the health effects are from genetically modified food substances are. Third World countries… obviously that's the cheapest form of getting them the right source of food in the short term and in a cheap way but only a couple of businesses are going to profit out of it, it's not going to be profitable to the country, whether it be ours or some small south African town. It's like a third world country or if we decided to go down that road we*

wouldn't benefit, it would be for the people who produced it in the first place, which at the moment are big companies in the States, or, its not going to be here that benefits…Well it's just like the smaller places now, a lot of the Third World countries are using genetically modified crops because it's the cheapest form of aid to get in there and of course they're buying it at a lower price but it's all getting bought from the States to come in because they're the ones who created it so they're the ones getting the money not the Third World countries they're growing it but it's also getting sold back off overseas or it's getting eaten there.

Wahine 2: *Or maybe they're palming it off to Third World countries so they don't have to eat the stuff themselves.*

Focus group 1

The participants looked at how these promises attempt to disguise issues of power and wealth

Tane*: It all comes down to money doesn't it? The large food providers and the growers they want better returns on their crops, they don't want to have to deal with this disease or that disease or they don't want to have to spray their crops…*

Wahine*: They want a big turn over*

Tane*: although if they can grow certain crops better in Ethiopia and they're hardier that will obviously benefit people as a whole.*

Wahine*: It will probably grow into a great big economical market that side of the world do they actually get to where they're supposed to be or where it's needed rather?*

Focus group 3

Smith (1999) argued that a contemporary feature of imperialism, and therefore colonisation, is letting indigenous peoples and communities believe that they are choosers in a 'culturally neutral marketplace' while hiding economic and political inequalities. This was illustrated by some focus group participants who believed that poorer members of the community are forced to accept genetic research and technology because having the right to choose is dependent on personal wealth and social position. Another member of this focus group recognised that the community is left to 'suffer' when researchers are driven by the prospect of personal benefit.

Another analysis of the common good focused on the use of genetic research within health and medicine. In the next example the use of the word 'pleb' describes a social hierarchy within our communities that is based on wealth. The promises of health benefits will be socially and economically unattainable for some

I was thinking in terms of cures for illnesses that I wonder if the whole genetic engineering thing, what good is it really going to do for mankind? Well firstly, whose going to be able to afford it, what countries actually going to import it? So it's going to be very rich people who are going to have access to those, and all the rest of the plebs will have nothing…

Focus group 3

Some of the focus group participants also examined the ways in which the common good discourse specifically marginalises the Māori community

> ***Wahine 1****: It's probably the other side of the coin isn't it, about where do you stop I guess in terms of... do you just look at cures for illnesses, particularly if we're talking about Māori , illnesses that perhaps weren't around 200 years ago, that have been imported or whatever way you may want to look at it…*
>
> ***Wahine 2:*** *it's like really being God but then a God that can do some people because they can afford it.*
>
> ***Wahine 1:*** *Absolutely. That's a big issue and I suspect Māori aren't going to rate up there very highly in terms of having access to the resources or the financial resources to attain some of it.*
>
> ***Tane:*** *It's access and who can afford the cures and it's also who identifies what is an illness because for Māori although we've got high use of the health system we don't know that the health system is geared towards our health issues. It's geared toward some other cohort. Not us.*
>
> ***Wahine 1:*** *The power remains with the decision makers really doesn't it? The decision makers hold all the power.*
>
> ***Focus group 1***

For these participants the promise of great and beneficial outcomes through genetic research raised issues of power, racism and marginalisation. They understood that Māori communities are not empowered by genetic research because they are not involved in the decision-making process, which is where power is held and maintained in research. Indigenous commentators such as Linda Smith have expressed their anger at the justification of genetic research based on the common good, because indigenous peoples' reality and experience is of a Western system that has continually failed their communities. If the discourse around genetic research values the potential for curing disease then the various forms of racism which frame a Māori experience of the healthcare system and the barriers which deny our communities access to treatment and services need to be addressed and spoken about with an equal voice.

Although the focus group participants in the present study shared striking hopes and dreams for genetic research in terms of supporting the wellbeing of our communities, in their own analysis they have shown that 'for the common good' and 'for the good of mankind' does not translate to 'for the good of Māori'. In this way, the participants have identified that genetic research and Western-science moves Māori to the territory of the uncommon, once again making us the 'Other' (Smith, 1999) in our own land.

6.4.4 Good and Bad Research Practices

This is about remembering our past and present experiences of research in Aotearoa/New Zealand and learning from these experiences to ensure that genetic research is a safe, respectful and empowering experience for Māori communities.

Throughout the present study it was clear that what the participants 'know' about research and the way it is practiced is based on our long history and experience as subjects of research. For many of the participants, these memories have moulded their fears and concerns for genetic research, while for others it had been the platform on which they derived their hopes and dreams. The following section will present the ways in which the FGPs perceived good and bad research practices and their development of a research ethic.

Our research memory

One participant asked his focus group, why is it that we trust research, given that our history and experience has shown that scientists have failed Māori communities. Some of the FGPs remember a loss of control during the research experience, which is sourced from an imbalance of power within the researcher-participant relationship, a manifestation of which was discussed in relation to ownership of research information and knowledge. For one FGP the tikanga principles of mana and tapu ensure that the traditional knowledge, including DNA, is on 'loan' to the research and thus forever remains in the possession of the participant and their whānau, hapū and/or iwi.

The participants' research memory allowed them to discuss the risks involved in taking part in scientific enquiry. Risks were inherent in genetic research because of the newness of the technology and the number of unknowns that are involved. One participant connected the use of genetically modified seeds and crops to the introduction of gorse and possums, as a warning against accepting genetic research before considering all of the unknown consequences.

Participation in research involved risks, particularly when there are doubts around the integrity of the researchers involved. Research was also risky because the participants knew that there are often different truths and interpretations of the study findings.

The distrust of science and researchers came through many of the focus group discussions however it was particularly clear within Focus Group Two, where the participants talked about how research has been used in a hurtful and disrespectful portrayal of Māori society. Another participant pointed out that the media is quick and willing to perpetuate these 'findings' in their reporting.

> *I think the only thing that I have is that sometimes, y'know like personally I don't have a problem with people wanting to do that y'know just to be helpful, I think its good thing but sometimes you read about this stuff afterwards and people have sort of come out with*

these other conclusions that you might not necessarily agree with so they take the genes and they say oh well all Māori are stuck with diabetes because they eat too much of something, so all Māoris eat too much. They come out with all these conclusions on the other side that I think 'I don't agree with what they've said' y'know all those general things that they might have made from a small sample or depends on their methodology.

Focus group 2, Tane

The FGP went on to explain that these research 'truths' are based on Western notions of the 'Other' and that Pākehā perceptions of Māori society are perpetuated through research, the media, and politics, and that these beliefs about Māori do not mesh with our own realities

But I wonder whether y'know sometimes Pākehā researchers sort of have this thing that they already have in their minds and then they come and do the research to support their thoughts already and that's the thing that might be it's picked up by the media because in the general public sort of already believe these thoughts and then this researchers come in and sort of got this information Some parts wouldn't have fitted in with their conclusion…so they sort of emphasise different parts of the research y'know. So I would sort of sit there and go oh well they've got it wrong but that's what they believe, and it's been reinforced by the media and that's what they believe. So sometimes, so we're sort of sitting on the outside once again or marginalised that's what Māori s do that's who, that's who they are and we have all the proof that sort of keeps them in this little box…with Pākehā people doing research amongst Māori then sometimes you get that feeling, aye … reinforcing their stuff, the governments doing their stuff to reinforce their policies, their just supporting their own stuff…

Focus group 2, Tane

Although this memory of research is connected to Māori understandings of Pākehā researchers, some of the key-informants also pointed out that there have also been Māori involved in these disrespectful experiences. Māori researchers are often trained in Western frameworks. However, by conducting research within our own communities, it keeps the connection strong and the researchers honest

…we do blame a lot of our bad research on Māori communities on non-Māori researchers but there has also been a lot of token Māori on those research things and there has also been some Māori research… become a bit more accountable because we have also had a lot of our communities being engaged with us for a long time and if this is still their reflection on how they feel about research… that it still talks about are we getting it right as Māori health researchers because most of us trained in mainstream frameworks and its getting the right fusion so that we are actually as accountable and I remember how Ngahuia Te Awekotuku talked about years ago, the importance of us actually researching our own communities because it keeps that link tight where a lot of research where I have seen Māori researchers names attached to stuff they are out everywhere. Doing stuff where they don't actually have um I cant see a connection to that

community so sometimes I think, I mean I could rant on about non-Māori researchers all day, but I think with this forum its quite good to say if we were to, as Māori researchers, if we were going to match the hopes of those participants, are we kind of looking at our own frameworks and skills that would help us meet their hopes. Because those hopes are quite fabulous and the fears are really just about are we developing good practices in our research

Key-informant, SP

…I think that it's important… getting those connections to our communities because a lot of the researchers I think who have been complicit in pushing through or promoting this type of technology, I don't think really have connections to their communities, you know they've distanced themselves from their communities or they already are distanced from their communities and so are operating almost by themselves you know under their own steam so that they therefore don't have any responsibility back or get any sort of rarururu around what their decision, around how they make their decision until they're pulled up in places like the Royal Commission by others or in other places where they're actually vulnerable because they're going public so they don't necessarily want to go public because then they leave themselves open to possible criticism or whatever

Key-informant, PR

What is good research practice?

From out of these uncomfortable and often unforgettable memories of research, the focus group participants were able to construct new understandings of good and safe research practice.

Many participants had very clear thoughts about how genetic research should be carried-out and how researchers should conduct themselves, particularly within our communities. The following narrative reminds us that participation in research is not about giving away our data, for researchers to use in a portrayal of Māori realities, or to 'discover' some new piece of information about what it means to be Māori.

…some of the hopes and dreams is that it would be really clear as to what is going to happen so that if people contributed any part of themselves to any research, all the cultural issues are taken care of, they knew what was going to happen down the road so it's not just a part of yourself that you're giving in terms of physical it's still a part of yourself anyway in some other form yeah so just real clarity around what would happen.

Focus group 1, Wahine

By viewing participation in research as an act of sharing time, information and sometimes highly specialised knowledge, the participants also hoped that their remarkable contribution to the research would be protected and kept safe. For one participant, a good research ethic would incorporate lessons from cultural safety as a method for bringing some trust and integrity back into the research experience

I wonder if maybe, one of the ways around addressing some of that [concern], is more around making something culturally safe and so like there is a transplant going to happen, y'know there's the opportunity for appropriate karakia or y'know that throughout some of those processes we're actually allowed to practice our tikanga in order to make it as safe as it could possibly be so y'know, and that could go as far as anything really in terms, um, y'know the whole sort of research process, the way in which you're allowed to move through it, the time out to go and make sure that you're safe and that what you're doing is tika and y'know all of those sorts of things, so even, and I guess, really, it does come swinging right back round to those ethics again cos it part of that y'know. Those ethics must incorporate the ability to practise your own tikanga and that's whether you'd be Māori, Indian, Aborigine whatever you are, but y'know, that the ethics must include a component that allows a participant to be culturally safe in whatever that may mean to them.

Focus group 1, Wahine

The concept of Cultural Safety was first introduced by Dr. Irihapeti Ramsden within the context of nursing theory and practice. As this focus group participant pointed out, cultural safety is relevant in the context of genetic research as it can provide a mechanism for the protection of individuals and their beliefs within their own research experience. Indeed, Moana Jackson (cited in (Ramsden, 2002)) saw cultural safety as a tool for considering issues of power

> The key to Cultural Safety for me is it's part of making our people strong again and protecting our people where ever they are….that our people could use the idea of being culturally safe as part of their reclaiming of our sovereignty, of our rights…because for me you can't claim rights unless you're safe in who you are and you can't express those rights unless you're safe and then have the power to do so (p. 126)

Within the construction of the hopes and dreams for good and safe research practice, many of the participants often located the discussions within ethics. For one participant, ethics provided the direction for the way in which genetic samples would be handled and cared for while another participant agreed that ethics would provide some assurances of good research practice now and in the future. Research ethics also mediated the power relationship between the researcher and the researched. An effective research ethic would empower the participants and allow them to set the rules of engagement

…It's like, well, who do you trust and who is it that determines, um, the type of methodology, or the ethics around methodology? I don't mean to be focussing so much on the ethics, but it's a big part of it really isn't it? When you think of it everything does come back to clear and concise guidelines and it's a bit frightening that there's been nothing put in place yet…. I suppose that's part of the key really is that participants y'know of research need to realise that they do perhaps have some power in what they decide they will give and what they won't, so maybe part of the trick is actually about

empowering the participants so that they are actively, y'know, putting their parameters around so they are prepared to walk away if it doesn't fit their thinking, or what would make them comfortable.

Focus group 1, Wahine

The focus group participants had many suggestions and ideas on how research could be a more empowering experience for those that take part, which are summarised below:

(1) Letting the participants have a voice

One participant felt that Māori need to have the power and confidence to raise our concerns at any stage of the research, and that a participant's voice is as valid and legitimate as the researchers or scientists. There is power in being an active research participant and part of this is putting into action their right to decide what should and shouldn't be given to research. We are reminded that participants have a responsibility to protect the knowledge that they hold, particularly if it is specialised knowledge, such as mātauranga Māori or if they are representing their whānau, hapū or iwi

(2) Involving whānau in research

One participant suggested that Māori communities could take a more active role in research particularly through the involvement and employment of whānau on the research team. This would be aligned with the aspirations for Māori development through upskilling and training and would also provide some safety and control for those participating in the research. One FGP described her own experience of conducting research within her whānau. This FGP believed that her role as a 'researcher' allowed her mother to talk about issues and share stories that may otherwise have been kept silent in daily conversation.

(3) Involving Māori communities in the development and planning of research projects

Another thread to the empowering processes talk was the need for greater consultation and facilitating Māori involvement in the design and conduct of a research project. For many of the participants, this involvement ensured that community aspirations were realised through research. It is important to involve those hapū and iwi who hold mana whenua within consultation and development of research. For one key-informant, the MOU between the University of Otago and Te Runanga o Ngai Tahu guaranteed iwi rights to be consulted and considered in the early stages of research planning and development

(4) Sharing the control

Having some control over the research experience was an important part of empowering research participants. Two key-informants explained that Māori communities are research savvy, and are actively looking at ways in which they can have more control over the process of research by initiating their own research committees and developing processes to deal with

researchers who come into their communities with a proposal. Looking back at these developments in iwi research capabilities, some key informants felt that this has been a direct result of Māori communities being 'over researched' such that they needed to come up with their own ways of 'critically appraising' research in order to protect their own interests and communities.

Reciprocity was also a key feature of gaining some control and correcting the power imbalance. Within the context of genetic research, reciprocity was exemplified in relation to the handling, storage and disposal of human biological samples, including blood, tissue and DNA. Each of the focus groups looked at the 'common' belief that Māori always want their samples back. However, this perception puzzled most FGPs and KIs as their understanding of reciprocity was about having access to the information gained from their participation and contribution, rather than the actual sample *per se*. For one participant, talking about access to samples gathered in research was related to issues around property rights and ownership, while for another FGP the discussion around access was about keeping research participants informed throughout the process and getting their consent every step of the way. One of the KIs reiterated that researchers and scientists need to be realistic about returning samples. In her experience, scientists have often made assumptions about the 'Māori view' which undermines the participants' right to make their own informed decisions and the right to have some control in the process. Other KIs found that some scientists tend to 'romanticise' tikanga Māori; focussing on ceremonial aspects of tikanga rather than understanding the practical benefits. One key-informant feared that too much time is being spent developing guidelines with a 'one size fits all' approach, instead of realising that Māori communities want some control over the process and developing strategies to ensure that their diverse personal and cultural needs are upheld and valued.

> *...take this for example they want to take say blood from a person and just find out OK can that be returned and how does it get stored and that. If you stub your toe and lose a bit of blood on the ground what do you do? So how are some of these things that we're framing around genetic research actually relevant? What they're trying to do is say we want to have control of this process we want to have some control over the process of how we're involved in the research and its been turned around into ok this is the process and oh yeah we can still do the process are you happy now? And it still hasn't given Māori control over anything... We've got this tikanga forensics project and its looking at all these issues and it's around how the crime scene, the forensic crime scene staff work at sites, like homicides sites and the body's there and then the whānau might be there. If the whānau want to do things, how do you weigh up the possibility of contamination against the needs of the whānau to do things? ... If the whānau come in and do karakia, what does the scientist do? Do they keep working or do they stop, and what about moving the parts and how do we give them back and all that sort of stuff and I've been going and*

looking and some of the samples have been taken, we take more off stubbing your toe so is it practical to say, we're gonna give it back. What are they gonna do with it when they get it back…and its so dependent on the context and with the family if it was the whole organ that was going then maybe they do want it back. But the important thing is that you've had the discussion to find out whether or not they want it back, not whether it goes back or not. It's not to say yeah it has to go back, maybe they don't want it. Its the control and so how do you structure this around control and that's where it gets too loose because then its dependent on the researchers ethics and those other things and how people conceptualise it so you end up turning it into a process and turning it into a code and you lose the kind of, the essence…..

Key-informant, MH1

From a management perspective, clarity and transparency in research is achieved through documentation that outlines not only the research methods, but also addresses key issues for Māori communities. Considering and addressing all of the issues which are of concern for Māori communities is a signal of a researcher's commitment to good ethicality in research.

Empowering research participants through Kaupapa Māori

Within the development of their hopes for an empowering and enriching research experience, many of the focus group participants believed that greater acceptance of research by the Māori community would be facilitated by research practices that acknowledge and respect a Māori world view.

For one focus group participant, the misrepresentation of Māori society through research is a reflection that most research is underpinned by Western ways of knowing and understanding the world

We talk about the abuse of research, where people have said things and y'know, then it's taken out of context and it's rewritten and y'know, interpreted in some other way, a lot of that's around research when you're using something other than a Kaupapa Māori framework and methodology. course you're going to come up with a different answer, if you do it's the same sort of thing around that, it's like, well, who do you trust and who is it that determines, um, the type of methodology, or the ethics around methodology?

Focus group 1, Wahine

One key informant argued that Western research methods are inherently disrespectful of Māori and other indigenous values and knowledges

…to use a word it's unethical, to go back to that word which is also problematic but to use their own words, it's unethical, it's unethical to – it's not a respectful relationship and in fact it never has been a respectful relationship so how do we get a respectful relationship I suppose is a big one, it's not going to fall in our lap, we have to fight for it all the time and by attending some of these consultations or calls for submissions or

> *presenting to different audiences is sometimes you know sometimes it really makes me want to vomit but that's what we have to do, we have to keep on pushing, we have to keep on going, keep on going and saying this … you have responsibilities to us, you have obligations to us, we ourselves have obligations and responsibilities to everything around us, all our relationships, all our whakapapa relationships with everything around us as Māori we have kaitiaki relationships but you have responsibilities as well and those responsibilities are not being they're just not being they're not respectful relationships being developed…*
>
> ***Key-informant, PR***

Many of the fears around genetic research would be alleviated by knowing that the research team had a high level of Māori involvement and a strong commitment to upholding the values and prestige of the communities who they are researching

> *I think one of the ways is for the research to be lead by Māori. Y'know, that certainly engenders a much higher level of trust for me, I would still query maybe the organisation driving the Māori that are doing the research, but I would certainly warm, I mean, for example, I probably wouldn't be participating if it was mainstream research now. So um, y'know, for me, personally, I would be more inclined to cooperate and participate if it's been lead by Māori for Māori essentially*
>
> ***Focus group 1, Wahine***

One key-informant understood greater Māori involvement within research as recognition of the validity of a Māori worldview which also addresses some of the issues of power and control

> *…essentially that kind of power issue or recognition of kind of, status and validation of a Māori worldview … which aren't just the perspectives on the science, this is what we about genetic research this is our position this is our this is the Māori science side and this is the other science side to make them equally as valid…and they talk about researchers come in and take the information, you talk about it happening in a process but its that same thing, kind of recognising that other person as having equal value…and a lot of, I think, the tikanga is about acknowledging the other person, the whole thing with a powhiri is acknowledging the other person, before you get into stuff…*
>
> ***Key-informant, MH1***

Linda Smith (1999) argues that Western-researchers often overlook the realm of commonsense when engaging in cross-cultural research

> When studying how to go about doing research, it is very easy to overlook the realm of common sense, the basic beliefs that not only help people identify research problems that are relevant and worthy, but also accompany them throughout the research process.

In the present study a focus group participant connected to this and proposed that understanding the logic of any research means asking 'what is the kaupapa?'

> *I think that, letting aside what you might look at, whether it's DNA or genetics or whatever, a foot or a toe or a heart or a kidney, before you consider what you might look at you have to have a reason that's good enough to look at anything, it's the kaupapa of why… If you can get something like that sorted and agreed to then you go to what to do*
>
> ***Focus group 1, Tane***

The FGP described kaupapa as the foundation of the research. From this base the kaupapa would guide the direction of the study and the questions that are asked and the tikanga that must be followed. As Marsden and Henare (1992) explain

> Kaupapa is derived from two words *kau* and *papa*. In this context kau means 'to appear for the first time, to come into view, to disclose' Papa means ground of foundations. Hence kaupapa means 'ground rules, first principles, general principles. Tikanga means method, plan, reason, custom, the right way of doing things. Kaupapa and Tikanga are juxtaposed in Māori thinking. When contemplating some important project, action or situation that needs to be addressed and resolved the tribe in council would debate the kaupapa or rules and principles by which they should be guided (p. 17).

Smith (1999) describes the concept of kaupapa as a way of framing how we think about our ideas and practices '…It is a way of abstracting that knowledge, reflecting on it, engaging with it, taking it for granted sometimes, making assumptions based upon it, and at times critically engaging in the way it has been and is being constructed.'

Like a scientific hypothesis, understanding the kaupapa involves taking into account the reasoning, logic and prior knowledge behind the proposition. However, the participant suggests that answering the question of the kaupapa has a broader purpose as it requires researchers to consider this logic from a spiritual and cultural perspective. This participant believes that these important questions are currently overlooked in research

> *You've got to get the kaupapa, you gotta get the foundation reasoning kind of sorted first. And then that might open doors to say, 'Ok, so, respect for that, alright, given that premise we want to look at this?' At the moment I think what happens is you look at this, you look at that, and then you look at this over there, but you don't know why you're doing, why you're doing all this, so you focus on a single issue at a time…example, you could say, like with organ transplants, you could say if that's about taking something out of this person and sticking it into that person over here that's the action, but then why would you do that? What's the reason? And how, once you get that sorted, how do you protect the mauri of that organ from that person into the mauri over here? You get those questions sorted first and then you can start to do some things. But at the moment the question's just, well, shall we take this out of here, and stick it in over here…in terms of research and acceptance of Māori, then I think you need to get some idea of what's the reason behind what…you're doing, what's the reason that'd driving all this? And how can you protect some of the Māori thinking along the way…*

Focus group 1, Tane

One key-informant talked about developing the kaupapa as a way of ensuring that the practice and outcomes of the research are respectful

> *... we had a talk, a presentation from a couple of scientists who would do a lot of genetic modification ... and um the scientists all thought it was great they were just laughing and thinking it was just wonderful this stuff they were doing and they were talking about taking the DNA from flounder and inserting it into tomatoes to stop them from rotting so quickly and we were all really shocked because we had never heard that this was happening, but also the fact that they thought it was a joke…. and then he goes oh and at the end of the study we found it didn't work, and I was just...so I said why did you do it, why? And he said oh well we figured it might work because flounder has this particular pathway that stops them from freezing or something like that and we thought it might help tomatoes….I don't know… what drove them to do it, and their whole state of mind while they were doing it. It wasn't respectful to, you know, the whakapapa of flounder which I mean in the end we kind of feel that we all can whakapapa to each, there is a common thread for all of us, whether it's flora fauna, Māori, and we do feel that we have to protect these other things, even if they're not just human and he had no, he didn't even consider that…and so I think that's why, why do it in the first place and what is driving you. It is important the process but also the outcome, the fact that they've done all of this just to help a tomato and it didn't work anyway ...*
>
> ***Key-informant, MH2***

By engaging with the kaupapa, researchers would take a more holistic and considered approach to research, questioning the methodology or epistemological stance that informs the research strategy. Researchers must go beyond simply *recognising* the implications of personal beliefs and assumptions but instead ask questions that evaluate the ways in which research is carried out and whether or not the research is respectful (Smith, 1999).

Penehira and colleagues (2003) found that having a clear kaupapa within governance determines how you: (1) decide what you're doing; (2) allocate power; (3) make sure things are secure; (4) monitor how well you're doing; (5) involve people in decisions; and (6) report on results achieved.

In the following example, understanding the kaupapa of the research is also an ethical reflection, evaluating whether the research is tika or right, and where caring for and helping others is paramount

> *I think…one question might be, and it goes back, not so much our hopes and dreams, but what's, why you're doing what you're doing, is there a good enough reason for why you do what you do? And that might come back to a Māori way of thinking, of why do that coz that's that tikanga stuff, you do it because, 'oh OK cos it's right to do'. If it's to help*

and assist people then maybe that's a good enough reason to give it all a go, if that's the underlining thing…

Focus group 1, Tane

For one of the key-informants, understanding and communicating the kaupapa was vital for achieving informed consent from the community being researched

KI 1: *I just reworded it. We just said… you know how everyone dies of heart attacks, he is like yeah, and I would go well we would really like to come and do some research about why that is happening to our family. He's like, oh that sounds like a good idea, and then he was going to a hui at the time so he said oh, Suzanne wants to come home and do this stuff … so it has been about rewording things so that the committee, we are not talking in high faluting academic, so people actually understand what we have said…so we have never used the word genetics, and we have got a year to talk them through it, so we are not rushing in and saying well come on you said I can have your blood. You know, it's going to be a year of going and when we take your blood this is what is going to happen. These are the processes, and how do you feel about those processes, what do you think we could do to make that more, where would you like them kept? Would you like all the samples kept in Kahungunu in a particular place and we can do the analysis from here?*

KI 2: *Realistically it takes a year to two years to develop these networks and a protocol to surround what you are going to do.*

KI 1: *Yeah, … But that is kind of about reducing those fears, that instead of us going in with a set agenda, they have got a year and we have got a year to actually negotiate what will be the best practice and then genetics will be a discussion we will have with them face to face when they understand actually what the kaupapa is.*

Key-informant group

In this example, focussing on the kaupapa gave the research team and the community a common language within a conversation on ethics. This key-informant recognised that focussing on the kaupapa involved taking the time to engage with the community she was working with, involving them in the decision making and planning processes. Importantly, focussing on the kaupapa of the research situates the power to control and define the research within the community.

6.4.5 Towards a Kaupapa Māori Ethical Framework for Genetic Research in Aotearoa/New Zealand

Māori have faced a number of issues when thinking and talking about genetic research, and one of the major tasks for Māori communities is making decisions and forming positions to manage these challenges. Many of the focus group participants talked about the need to consider tikanga Māori when thinking about the place of genetic research in their lives. For some of the FGPs, tikanga Māori restricts or prevents them from engaging with genetic research. However, many commentators disagree that Māori society cannot, or should not be involved in the active debate about genetics or indeed other contentious issues, arguing instead that tikanga and mātauranga Māori can provide a framework for making informed and valid decisions (see (Mead, 2003; Reid, 2005)).

A tikanga Māori framework for ethical review was paralleled to the paradigm of ethics by one key informant who believed that the utility and effectiveness of this system comes from the inherent and diverse nature of these frameworks within individual whānau, hapū and iwi. This KI agreed with Mead (2003) who questioned the efficacy and ability of current regulatory systems to address Māori concerns, given their philosophical and geographical distance from Māori communities.

> *…ethics is interpretation about what you think is moral, what you think is right, what you think is wrong and it's also culturally based and rohe, iwi, hapū, whānau, national, international, indigenous, non-indigenous based.* (International Research Institute for Māori and Indigenous Education) *have our own ways of assessing, we have our own ways of looking at the merit or not of particular research projects that are brought to our notice because not all research projects are brought to our notice or brought within our communities for permission, to ask for permission but we have our own ways of assessing these. What should happen and what ought to happen is that any research related to any rohe, iwi, hapū, whānau or Māori generally should go through an assessment of its merits, or not, using our own assessment.*
>
> ***Key-informant, PR***

A primary objective of the present study was to develop some ethical guidelines which would regulate the ways in which genetic research is conducted among Māori. Through the analysis of the focus group and key-informant talk it became clear that these 'ethics' must be located within a specifically Māori framework to ensure that the aspirations of the Māori community are upheld.

The following section will outline some key ethical principles[10] which could be used by researchers wanting to conduct genetic research, or perhaps any research, among Māori communities. The participants' hopes for an empowering research experience were expressed through their understanding of what is right or tika, which is intimately connected to ethicality within research. In accordance with the hopes for good research practice, these principles are derived from tikanga Māori and as such take their beginnings from a mātauranga Māori knowledge system.

Connecting these ethical principles within tikanga Māori has several advantages. Firstly, it acknowledges the work of other Māori researchers, commentators and communities who have been talking about ethics and research for a long time. Although some prefer to differentiate between tikanga Māori and Māori ethics (Hudson, 2004), in the present study talking about ethics was a way of centering those values which Māori hold close within a discussion about genetics and science. Situating these ethics within tikanga Māori also facilitates Māori control of research. The principles are located at the level of governance as a reflection of Māori hopes and dreams for rangatiratanga. It also provides opportunities for participants and researchers to consider and be informed by the principles, but with the freedom of choice and flexibility to decide how Māori communities want to manage research, in collaboration with the researchers.

Te Rangihau explained that Māori are shaped by their experiences and histories as individual iwi. Because of these different histories and the diverse and dynamic nature of Māori society, tikanga also vary between iwi and by geography (Mead, 2003). Stating these ethics in terms of tikanga Māori will allow communities to interpret the principles in ways that meet the needs of the whānau, hapū or iwi. It also speaks to the concern that researchers and scientists often take a 'one size fits all' approach to their engagement with Māori. Respecting this diversity within a tikanga framework for ethics restricts researchers from entering different rohe and telling Māori what these principles mean.

Based within tikanga Māori, these ethical principles are connected to each other and are informed by shared values and as such they can not be understood or applied in isolation. That is not the purpose of tikanga Māori, and it is not the purpose of these guidelines. Only when taken together can they enhance the research experience and bring benefits for all involved.

Whānaungatanga

This ethic is about spending time building and developing trusting relationships and seeking out common connections and aspirations

[10] In the description of the ethical principles, italics are used to differentiate between the traditional understanding of the tikanga and the application of the principle within research ethics.

The importance of Whānaungatanga was described by Te Rangihau as the 'warmth' and 'strength' that can come when people are bound together within a situation (Rangihau, 1975). For Rose Pere, Whānaungatanga means that the work she undertakes, even far from home, upholds the beliefs and aspirations of her people (Pere, 1979). For Timoti Karetu Whānaungatanga talks about a community spirit linking neighbouring villages closely together and a childhood where he was indulged, loved, cared for and nurtured (Karetu, 1979). Whānau is a basic support structure for Māori communities, and for these Tūhoe rangatira it is a significant feature of their identity. Therefore it is only right that the ethic of *Whānaungatanga* is discussed first.

Whānaungatanga reinforces the importance of relationships. It embraces whakapapa (Mead, 2003) and locates Māori firmly within the geography and chronology of this place. It connects Māori to the physical and spiritual elements of our world and reminds us that we are not alone. Whānaungatanga extends beyond whakapapa to non-kin people who are connected through shared experiences (Mead, 2003). For Māori, some of these experiences are connected to colonisation and imperialist research practices.

The ethical principle of *Whānaungatanga* situates research relationships within a culturally-specific framework, which is underpinned by values such as manaakitanga, tapu, and mana and legitimises the use of te reo and tikanga. Whānaungatanga reinforces the traditional understanding that to know ones whakapapa is to know ones identity. Formally, Whānaungatanga is established through mihimihi (introductory speeches) where connections are made through common ancestors, common landscapes, common marae, and common hapū or iwi. Furthermore, mihimihi is the first step in the development of a trustworthy relationship (Edwards, McManus, & McCreanor, 2005). Mead (2003) implicates he kanohi kitea (the face seen) as part of establishing Whānaungatanga. For researchers, this ethic means facing up to the community, showing them who you are and what you have to offer.

Whānaungatanga acknowledges that individuals will have different roles within the relationship, however these differences are to be respected, as they are each vital to the effective running and management of the community. Too often within research, these roles have been determined by the researchers, who have entered into a community and enforced hierarchy through their use of Western scientific methodology. As a research ethic, *Whānaungatanga* reduces the space (Cram, 2001b) between researchers and the researched, and addresses issues of power. The relative equivalence of researchers and participants could be visualised through the tuakana/teina system

Ma te tuakana ka totika te teina, ma te teina ka totika te tuakana

From the older sibling the younger one learns the right way to do things, and from the younger sibling the older one learns to be tolerant

Tuakana/teina addresses issues of seniority and mana (Mead, 2003) however as this whakatauki (proverb) illustrates, everyone can prosper from a respectful relationship, and support and mentorship can move in both directions.

Whānaungatanga also involves aroha, which is an expression of love and trust for those in the relationship. Because of these deep feelings, individuals often go out of their way or tackle things which may seem too hard. Building research relationships takes time and effort, however through aroha, maintaining the ethic of *Whānaungatanga* means prioritising the development of research relationships during the very primordial stages of the project (i.e. development and planning of research questions, methods). This might involve dedicating some of the research costs to the relationship-building stage and setting timelines and milestones that incorporate a 'honeymoon' period. When research is recognised as a relationship, it also invokes transparency within processes and behaviours, and as a research ethic it highlights the importance and validity of these steps.

Manaakitanga

About caring for and nurturing our research relationships and being generous with our skills and knowledges

Manaakitanga underpins all tikanga Māori and involves nurturing and looking after guests and being very careful about how they are treated (Mead, 2003). Manaakitanga focuses on human behaviour, and care is taken to ensure that the mana of the manuhiri (guests, visitors) is respected and upheld (Mead, 2003). Manaakitanga is highly valued, and Māori communities take great pride in their ability to care for manuhiri particularly as it can enhance the integrity of the hosts.

Māori have extended their manaakitanga to Western-research, devoting considerable time and pride to ensure that researchers are welcomed into their communities (with powhiri), nourished (with a bountiful supply of kai) and enriched (through the sharing of stories and experiences). Te Rangihau (1975) understood that Whānaungatanga mediated the expression of manaakitanga through hospitality

> The whole basis…is the business of showing concern for your neighbour, concern for him as a person, and therefore sharing his daily life and sharing the things of the community. And caring….In other words there is as much joy - or perhaps greater joy – in giving as in receiving. And so we give of one another to one another – we give the talents we have so everybody can share in these sorts of experiences.

The ethic of *manaakitanga*, and its connection to *Whānaungatanga*, provides an important lesson for researchers, because it is a reminder that our behaviours not only reflect on ourselves

as researchers, but also the research team, the communities involved, the institutions that we work within, and the way in which the study findings are perceived and received.

Manaakitanga is related to the notion of empowerment, as it nourishes relationships and people and allows those involved as researchers and participants to grow through the experience. *Manaakitanga* validates traditional ideas of hospitality within the research experience, which might include practices such as powhiri, mihimihi and sharing kai before any business is discussed. Mead (2003) explains that manaakitanga can be thought of as 'the common good' where one can evaluate the research in terms of whether it is helpful to humankind or to people who suffer. By situating the common good discourse within the ethical principle of manaakitanga, it centres te ao Māori as normal. For scientists and researchers, this research ethic means sharing the research voice, by developing strategies to ensure that Māori aspirations and realities are heard through the research findings.

Another concept which is relevant to the ethic of *manaakitanga* is the practice of koha, or gift giving. Koha involves the principles of reciprocity, equivalence, and manaakitanga mediated by whakapapa and the notion of tika or good grace (Mead, 2003). Koha is about giving something back to the hosts as a sign of respect, thanks and aroha. Although manuhiri often present money because of its convenience, koha can take many forms including kai and taonga, because it was about giving what was available and making a contribution which reflected what was needed. For those who receive koha they do so knowing that there is reciprocity involved and that one day they would be expected to repay this gift.

Koha in research is contextualised as part of the social and cultural responsibility of reseachers working with Māori communities. Although the Operational Standard reminds researchers that koha is not to be thought of as a payment (Ministry of Health, 2006), it is often situated within the ethical practice of compensation of research participants (see (Massey University., 2005)). When koha is perceived and understood as compensation, it permits Pākehā notions of gifts and donations and definitions of what is, or isn't, acceptable as koha. Similarly the tikanga practices that are involved in koha (Mead, 2003) is limited by Western understandings of coercion.

Māori involvement in research can be viewed as the 'gifting' of a space within our communities to be occupied by research, however it is important to clarify that this space remains connected to the mana and the rangatiratanga of the Māori communities as hosts; researchers are effectively guests within these territories and therefore cannot claim ownership or control.

The ethic of *manaakitanga* (and koha) might include the sharing of skills, knowledge, expertise, and training opportunities as a sign of gratitude and respect. Mead (2003) explains that making an effort to visit and be seen is an important aspect of koha which adds a meaningful social dimension to the exchange. For researchers, he kanohi kitea might mean being actively involved

with Māori communities not only during the collection of data but also to present results and generally keeping the Whānaungatanga connection strong.

Kaitiakitanga

This is about protecting our participants and their knowledge as taonga. It is also about respecting the guardianship roles that Māori have to protect our resources and knowledges.

The principle of kaitiakitanga is recognised as the obligation to guard, keep, preserve, conserve, foster, protect, shelter and keep watch over (Marsden & Henare, 1992) because of our whakapapa connections with all life forms. The ethic of *kaitiakitanga* reminds researchers that decision-making must focus on the protection of the research participants, their values and their knowledges. This principle reinforces the hope that research will be an empowering experience; therefore the research methodology should reflect the aspirations of the Māori community. When thinking about the protection of people within research, it is useful to remember a number of points. The role of kaitiaki is to protect the mauri of the life form and ensure that it is kept healthy and strong. This is taken very seriously, because if the mauri is depleted then the kaitiaki must do all that it can to replenish the mauri and restore their own mana (Mead, 2003). *Kaitiakitanga* reminds us that the governance of research is about protecting the mana of the Māori community and the mana of the research knowledge. As an ethical principle, *kaitiakitanga* also protects Māori views about research and knowledge and therefore it can be used as a framework for addressing the undue privilege of Western knowledges and forms of research.

The ethic of *kaitiakitanga* also protects the communities' rights to say no within the research experience. The role of kaitiaki is to protect our taonga to ensure that they would be available and healthy for future generations. In this way, *kaitiakitanga* means making decisions about research (as researchers and as communities) and developing guidelines which not only protect Māori communities in the present, but also bring assurances that our children and grandchildren will have a research 'memory' that is happier than ours.

Some researchers and/or research groups may prefer to maintain an alliance with one particular Māori body through whom they consult. However, kaitiaki roles are determined by mana whenua, with whānau, hapū and iwi acting as guardians of the natural and physical resources within their own territories. This understanding encourages researchers to engage with and forge respectful relationships with those communities who hold the mana whenua in the region where the research is taking place. The ethic of protection implies that researchers must respect and acknowledge the variations in iwi authority as kaitiaki, and their rights to control the research that is happening within their own landscapes.

The ethical principle of *kaitiakitanga* also speaks to Māori hopes for good governance and decision-making. Set within a Treaty of Waitangi discourse, kaitiakitanga relates to customary

and intellectual property rights and as such tino rangatiratanga mandates Māori rights to control their resources and knowledges as taonga. *Kaitiakitanga* is also about self-determination, which is essential to the development of indigenous models for good governance (Penehira, Cram, & Pipi, 2003). *Kaitiakitanga* facilitates Māori rights and rangatiratanga to determine the parameters of research, the tools that are used, and the questions that are asked.

6.5 General Summary

Q1: What are our hopes and dreams for genetic research in Aotearoa/New Zealand?

The present study has convincingly demonstrated that Māori have strong and clear hopes and dreams for genetic research in Aotearoa/New Zealand. The initial thematic analysis found that these desires encompassed broad hopes for social and particularly community enhancement, safe research practices and good governance. The focus group participants affirmed the right to engage with genetic research in order to maintain or elevate whānau health and wellbeing. The participants hoped that there would be more talking, between researchers, policy makers and communities to ensure that Māori aspirations are realised through genetic research. The participants also hoped that Māori would use genetic research as place to talk about tikanga and how it can be applied to manage the challenges of Western sciences and to help whānau make decisions which respect our cultural understandings. The participants also expressed a desire for better information about genetic research which fairly represents the diversity of beliefs and perspectives that are held close within our communities. In the end, the participants hoped and dreamed that genetic research was about helping people.

The participants hoped that any form of genetic research or application of new biotechnologies would be regulated and controlled so that Māori communities are protected now and in the future. Good governance involved transparency within processes and policies, and greater accountability to the communities. Good governance also provided representation of community values and protected Māori knowledges. Māori communities are well-equipped to assess the value and integrity of research. The participants' hopes and dreams for genetic research included their desire for research practices and protocols that encourage the ideal of an active participant. The FGPs articulated their understanding of ethicality in research and suggested ways in which the research experience could be improved.

Q2: What are our fears and concerns for genetic research in Aotearoa/New Zealand?

The thematic analysis confirmed that Māori concerns for genetic research are wide ranging and reinforce many of the ideas that have been raised within other discussions (e.g. (Cram et al., 2000; Eichelbaum et al., 2002; Smith & Reynolds, 2000)). Māori are concerned about the appropriateness of many applications and techniques used in genetic research, such as xenotransplantation and cloning. From a mātauranga Māori perspective, they disregard the importance of whakapapa and mauri, however they also bring into question the significance of individuality and spirituality as distinct features of our human-ness. The participants were suspicious of the many claims that genetic research will support and enhance the wellbeing of our communities. Anecdotes and memories acted as careful reminders that genetic research requires proper consideration of the full spectrum of possible consequences. Some of the

participants were unsure whether the current regulatory systems have the capacity to effectively monitor genetic research and uphold Māori values, particularly as such contentious issues often challenge mātauranga and tikanga Māori. There was a sense of dissatisfaction with the availability and quality of resources and information that is available for our communities. Many of the participants were concerned that public education and consultation has received minimal attention and shown a level of tokenism in efforts to include an informed and independent Māori voice. Finally, these FGPs reinforced Māori concern for their continued right to claim collective intellectual property rights over their knowledges and the misperception and misinterpretations of 'what Māori want' from their research experience.

CHAPTER 7
DISCUSSION

The main purpose of this study was to improve scientific understanding of the circadian clock and its role in controlling the timing of sleep in daily life. To do this it was necessary to investigate the distribution of self-reported morningness/eveningness in the general population, the timing, duration and quality of sleep of morning- and evening-types, and the influence of the circadian clock vs. psychosocial factors on sleep timing.

It had been proposed that this research could be extended to investigate polymorphisms in the clock genes of morning- and evening-types in the general population. Thus, the final objective of this programme was to develop an ethical framework for genetic research in New Zealand that would take into account a Māori world view. To do this the final study of this thesis explored Māori hopes and concerns for genetic research in New Zealand using a Kaupapa Māori framework. Taking a Kaupapa Māori position was important as it facilitated a change in the power relationship since genetic research currently occurs within a non-Māori view point.

This chapter provides a synthesis of the main study findings within the context of the relevant literature. The strengths and limitations of each study are considered, the problems encountered are discussed, and questions for future research are posed. In conclusion of this thesis, a number of challenges for the scientific and academic community are raised which highlight the growing need for a balanced and ethically responsible approach to conducting research in Aotearoa/New Zealand.

7.1 A Survey of Morningness/Eveningness in the General Population

7.1.1 Study Strengths and Limitations

Generalisability

The specific age-range of participants in the questionnaire survey, and indeed across all of the studies, was 30-49yrs. While this limited age range captures those in the population who are less likely to be experiencing age-related changes in sleep timing, it restricts the generalisability of these findings to other age groups. Similarly, because of the specific comparisons between Māori and non-Māori in the survey study, the generalisability of these findings to other ethnic groups is unknown. The structure of the electoral rolls does not permit systematic over-sampling of other ethnic groups, for example Pacific peoples.

Despite this, there are several unique features of the survey presented in Chapter 2 which mean that the findings add to the large body of literature on morningness/eveningness.

An important strength of this study is the Kaupapa Māori methodological approach that guided the research questions, study design and interpretation of data. The principles of equal explanatory and analytical power affirm a Kaupapa Māori research (KMR) position in epidemiology, through Māori participation at all stages of the study, a commitment to achieving similar numbers of responses from Māori and non-Māori, and analysis and interpretation of data to the same breadth and depth as for non-Māori. As a framework for conducting health research in Aotearoa/New Zealand, KMR ensures that Māori needs and aspirations are prioritised such that Māori are 'centred' and viewed as the norm.

There are also important considerations for sleep and circadian rhythms research more generally. Although this approach has been developed within a framework that is informed by the Treaty of Waitangi, the methodological techniques used have the potential to benefit human sleep and circadian rhythms research internationally. First, they broaden the range of factors considered in the aetiology of self-identified morningness/eveningness. The interaction between the endogenous control of sleep timing and the modifying effects of exogenous components, such as work schedules and societal demands, must be taken into account if we are to understand the distribution of self-reported circadian phenotypes within the general population. Second, as a framework for conducting sleep research, the approach employed in this study illustrates the value of research partnerships, both with other research groups and with the communities of interest. Through these partnerships it is possible to provide study outcomes that are of relevance to the entire population.

Another important aspect of this study was the simultaneous investigation of the associations between morningness/eveningness and demographic and socioeconomic factors. Although this study was limited to residents of the Wellington region, it has an advantage over other large surveys which have been limited to college-aged student (Adan & Natale, 2002; Chelminski et al., 1997) or specific working populations (Ishihara et al., 1988). The use of the electoral rolls provided a sampling frame which permitted the selection of a random sample of New Zealand adults. Similarly, the information provided in the electoral rolls permitted the stratification of this sample by age and Māori descent. This study is also unique because it addresses a significant gap in the literature regarding the relative influence of age, sex, ethnicity, socio-economic deprivation and work status on self-reported morningness/eveningness.

The findings of Chapter 2 are also significant because they present population prevalence estimates for five categories of chronotype according to the new criteria of Taillard and colleagues (2004), which were validated for use in a middle-aged working population, and a comparison of these to the more well-known cut-offs of Horne and Ostberg (1976). Given the importance of accurate classification of chronotypes, the information provided in Chapter 2 will

therefore be of relevance to those interested in the genetic basis of the regulation of human sleep.

Selection bias

Selection bias occurs when systematic differences are identified between those selected to be in the study and those who are not. In the present study selection bias is an important consideration for two reasons.

Firstly, the use of the electoral roll as a sampling frame permitted the random selection of study participants stratified by age and Māori descent. However, selection bias may be introduced if there is a systematic difference between those people who are enrolled and those not enrolled. The 2001 electoral roll captured approximately 93% of eligible voters (Electoral Enrolment Centre, 2003) suggesting that selection bias is not a significant confound in this study (Table 7.1).

Table 7.1 A comparison of the eligible voting population to enrolled electors by parliamentary electorate 2001

Age (years)	Population	General roll	Māori roll	Difference	% enrolled
30-39	585270	490181	41430	53659	90.83
40-49	541190	480378	31572	29240	94.60
Total	1126460	970559	73002	82899	92.64

Source: Electoral Enrolment Centre 2001

Secondly, selection bias, in the form of response bias, must be considered, by determining whether there are systematic differences between those who choose to be in the study (the respondents) and those who choose not to participate. As with our previous surveys of sleep disorders among New Zealand adults ((Harris, 2003; Mihaere, 2004; Paine et al., 2004)), there was a concern that those individuals who have problems with their sleep may be more likely to respond than those who do not. To minimise this type of response bias all participants were offered the opportunity to enter an incentive prize draw.

Response bias is also minimised when adequate response rates are achieved. Although there is no official standard for a minimum acceptable response rate, a benchmark is often set at 70%. The final response rate (RR4) in the present study was 55.7%. Reasons for the modest response are unknown. However possible deterrents to response may have included the length of the questionnaire; the number of items included in the study packages; and misinterpretation of the purpose of the study. Although Māori were less likely to respond than non-Māori, logistic regression showed that the differences in response rate which were observed were mainly due to differences in the socioeconomic deprivation profile of the Māori and non-Māori populations, rather than ethnicity *per se*.

Information bias

Information bias can occur when there are systematic errors in the way information is gathered from an individual (Rothman & Greenland, 2005). Therefore the possibility of information bias is an important limitation in the present study because all of the data are subjective reports. However, the MEQ has been validated against physiological circadian rhythms in healthy subjects (Van Dongen, 1998) and additional information (i.e. demographics, work status, sleep habits and general health) was gathered using previously used or validated questions.

In addition, information bias may be introduced by those who complete the questionnaire incorrectly (i.e. ticking two boxes or ticking between boxes) and those who enter the data (i.e. data entry error). To minimise this type of bias, a conservative set of data entry rules was developed to enable consistency of coding. In addition, all questionnaires were double-entered and any inconsistencies were evaluated and corrected on an individual basis by the research team.

Confounding

The potential for confounding is worthy of serious attention in any epidemiological study, because of the potential to mix or confuse the effects of the exposure of interest (e.g. night work) with other factors (e.g. socio-economic deprivation) which may also contribute to the health outcome under investigation (e.g. sleep timing) (Pearce & Greenland, 2005). In this way, confounders can lead to an over- or underestimate of the effect observed, due to the complexity of relationships between various exposures and outcomes (Hennekers & Buring, 1987).

For example, the potential for age to act as a confounding variable was considered during the planning and design of the study, given the continual changes to the pattern of human sleep with ageing (Bliwise, 2005), and the known differences in the age structure of the Māori and non-Māori populations. Confounding can, however, be controlled in a number of ways, some of which were employed in this study. The first measure undertaken to control for the confounding by age, was to restrict the age-range of the target sample to 30-49yrs. A second strategy was to stratify the sample by age, which allowed for confounding by age to be controlled for in multivariate analyses.

7.1.2 The Epidemiology of Morningness/Eveningness in the General Population

Using the original scoring criteria provided by Horne and Ostberg (MEQ1), 49.8% of the total population were morning-type, while only 5.6% had an evening-type preference. This is comparable to other large surveys (Taillard et al., 1999; Taillard et al., 2001). However, using new scoring criteria validated among middle-aged working adults (MEQ2, mean age 51.2yrs ± 3.2yrs (Taillard et al., 2004)), the prevalence estimates of chronotypes were more balanced, with approximately one-quarter of the population aged 30-49 years reporting either a morning-

type or evening-type preference. This finding was important, as previous studies had indicated that evening-types are relatively rare among middle-age and working populations. There were also no differences in MEQ scores or the prevalence of chronotypes by ethnicity or gender.

This study supports the reported trend for increasing morningness with age for which a number of possible mechanisms have been proposed (see (Bliwise, 2005) for a review). Longitudinal studies with blind individuals, and studies comparing the free-running periods of young and elderly participants in 28-hour forced desynchrony protocols, suggest that age-related shortening of the circadian period is unlikely to be a major contributing factor. Age-related changes in the visual system (e.g. cataracts, macular degeneration), and behavioural changes that alter light exposure patterns, could affect the phase angle of entrainment. There is also some evidence for a reduction in the strength of the homeostatic sleep drive with age, which might alter the timing of the sleep/wake cycle. However, the present study found significant differences across a very limited age-range (30-49yrs). It is unclear whether this finding represents an early indicator of aging in the visual system, or other unidentified age-related changes.

It has been suggested that age and work schedule are greatly influential with regards to morningness/eveningness preference (Adan & Amirall, 1991; Chelminski et al., 2000), and if taken into consideration, may eliminate any gender differences (Adan, 1992). The results in Chapter 2 confirm this, with multivariate analyses establishing that ethnicity, gender, and socioeconomic deprivation are not important determinants of morningness/eveningness preference. The relationship between sleep patterns and socioeconomic status was also examined in a study of 356 ‘larks’, 318 ‘owls’, and 555 ‘others’ aged 65ys and over (determined according to self-reported bed and rising times) who were identified from the 1973-4 Department of Health and Social Security survey. Of this group, owls were reported to have the highest self-reported mean income as well as being most likely to have access to a car and own an indoor lavatory, although none of these relationships reached statistical significance (Gale & Martyn, 1998).

This study supports the work of Taillard et al. (2004) and suggests that the Horne and Ostberg scoring criteria, developed in UK adolescents, may not be useful for studying morningness/eveningness in middle-aged working populations. It is acknowledged that the chronotype categories identified by the scoring criteria are defined by arbitrary boundaries on a normally distributed variable, and many investigators now prefer to consider chronotype as a continuous variable. However, the identification of categories is a useful tool when one is interested in identifying extreme chronotypes for investigation (e.g. in genetic screening studies) which was the original intention of this study.

7.1.3 Morningness/Eveningness as a Risk Factor for Health Problems

The temporal disorganisation experienced during night work can have serious effects on an individual's health and wellbeing. While shift work is associated with a range of work-related disorders, problems with sleep are the most common health complaint of shiftworkers (Gander, 2003).

The finding that E-types were more likely to be unemployed or involved in night work, compared to M-types, provides a good example of the influence of endogenous versus psychosocial factors on preferred sleep timing. If one was to interpret these findings according to the endogenous model, then the findings might suggest that E-types are in some way self-selecting themselves into jobs involving night work, or that E-types find it difficult to maintain a regular 'nine-to-five' job because of a biological preference to sleep late.

However, according to the psychosocial model, the findings might suggest that work patterns have a significant impact on an individual's self-reported chronotype, with night workers for instance reporting a sleep timing preference which matches their work schedule. Similarly, it could be speculated that unemployed individuals are not exposed to the numerous social cues which stem from having a regular work pattern, thus unemployed individuals may demonstrate a drift in their sleep timing to a later clock hour. Whatever the interpretation the possible negative consequences of having an evening-type preference on health (via chronic sleep restriction), is worthy of consideration here.

The only New Zealand evidence (Driscoll T et al., 2004) for a relationship between work status and ill-health, was provided in a recent national survey of insomnia symptoms and sleeping problems. After controlling for ethnicity and sex, being involved in night work (OR=1.61, p <0.01) or being unemployed (OR=1.49, p <0.001) significantly increased the risk of reporting a chronic sleeping problem compared to those who were employed, but not working nights (Paine et al., 2004). The increased likelihood of night work among evening-types found in the present study may therefore indicate a greater risk of chronic sleeping problems among this chronotype.

In the present study, night workers were more likely to report abnormal sleep duration and excessive levels of daytime sleepiness (ESS scores >10). In a study of 346 white-collar workers aged 19-64 years, Ishihara et al. (1988) concluded that the significantly shorter sleep length found among evening-types (compared to morning-type workers) was attributable to the constraints of a regular work schedule (all participants started work at 8:30am). Taillard et al. (1999) also reported that E-types tended to shorten their weekday sleep more than others, compared to their subjective sleep need. However, it was suggested that the sleep debt experienced by E-types is a result of a greater sleep need associated with this chronotype, rather than the imposition of a habitual work schedule that truncates their sleep.

There is increasing experimental evidence that sleep restriction can suppress immune function (Spiegel et al., 2002; Van Cauter & Spiegel, 1999), induce glucose intolerance and increase appetite (Van Cauter & Spiegel, 1999), and may cause elevation of blood pressure and the inflammatory cytokines, potentially increasing cardiovascular risk (Pollmacher et al., 2000). Moreover, there is a rapidly expanding body of literature implicating short habitual sleep duration as a risk factor for serious co-morbidities, notably obesity, type-2 diabetes, and cardiovascular disease (Knutson & Turek, 2006). In the present study, E-types were more likely than M-types to report poor/fair general health, after controlling for ethnicity (OR=2.46, p <0.0001) but the chronotypes did not differ in their self-reported sleep durations (categorised as short, normal or long sleepers). Instead, the independent risk factors for short sleep (< 6.5hrs in a 24-hour period) were increasing age, living in a less-deprived decile, and being involved in night work. In contrast, after controlling for sex, socioeconomic deprivation and chronotype, being a long sleeper (> 7.5hrs in a 24-hour period) was more likely among Māori, younger adults, the unemployed, and those working nights.

A longitudinal investigation of all-cause mortality found a lower risk of death among E-types and M-types (categorised according to bed and wake-up times) compared to others. However, this was attributed to differences in time spent in bed, rather than chronotype *per se* (Gale & Martyn, 1998). Taillard et al. (2001) reported significant relationships between different aspects of self-reported morbidity (i.e. sleep and mood disorders) and morningness/eveningness were independent of age, sex or sleep quality.

7.1.4 Differences in Sleeping Patterns between Māori and non-Māori

There is extensive evidence of ethnic disparities in health in New Zealand. As a population group, Māori have on average the poorest health status of any ethnic group in New Zealand, with disparities existing across a range of health mortality and morbidity indicators (Blakely et al., 2004; Ministry of Health, 1999a, , 2002; Te Puni Kokiri, 2000). Recent epidemiological evidence suggests that Māori also suffer disproportionately from self-reported sleeping problems including OSA and insomnia (Harris, 2003; Mihaere, 2004; Paine et al., 2005).

To the best of our knowledge, there have been no systematic investigations of ethnic differences in MEQ scores among adults, although there is limited evidence for possible ethnic differences among 13-16 year olds (Kim et al., 2002) and a tendency for greater eveningness among Spanish students, as compared with Italian students (Adan & Natale, 2002).

The findings presented in Chapter 2 provide strong evidence that self-reported morningness/eveningness is independent of ethnicity. In this study there were no significant differences between Māori and non-Māori in terms of the mean MEQ score, or the weighted proportions of chronotype using either MEQ1 or MEQ2 scoring criteria. Moreover, being Māori was not a significant independent predictor of morningness/eveningness.

In accordance with our national survey of insomnia, Māori in the present study were 1.5 more likely to report current night work compared with non-Māori, although there was no significant difference in self-reported unemployment by ethnicity. While there was no relationship between ethnicity and MEQ, differences in morningness/eveningness may be of importance to Māori because of our greater participation in night work.

While there was a significant univariate association between self-reported poor or fair general health and ethnicity (p <0.001), this relationship was no longer significant at the multivariate level (p =0.09). Similarly, there was also a significant univariate association between ethnicity and self-reported sleep duration categorised as either short-, normal- or long-sleepers. Multivariate analyses indicated that being Māori was not significantly related to short-sleep, however Māori were more likely to sleep more than 7.5hrs in a 24-hour period.

The distribution of daytime sleepiness among New Zealand adults (30-60yrs) was comprehensively investigated by Gander et al. (2005). In that study, Māori had a higher mean ESS score than non-Māori and were significantly more likely to report excessive levels of daytime sleepiness (Gander et al., 2005a). In the present study after controlling for chronotype, being Māori was a significant independent risk factor of excessive daytime sleepiness (ESS score > 10).

The finding that ethnicity was not a significant independent predictor of chronotype is important considering the interaction between circadian physiology and psychosocial factors on sleep timing. Firstly this finding may suggest that there are no fundamental biological differences between Māori and non-Māori in the timing of sleep. Thus, if a genetic screen for human clock genes in the general population was to proceed then it need not address genetic differences between Māori and non-Māori populations. However, this does not mean to say that developing our understanding of the regulation of sleep timing is not of relevance to Māori. As the previous section has shown, the impact of differences in sleep timing on the health and wellbeing of Māori may well be exacerbated by other risk factors, such as our high participation in night work.

Thus, the present study contributes to a considerable body of epidemiological evidence that there are significant disparities between Māori and non-Māori in sleep health, but indicates that these are not mediated by differences in the distribution of chronotypes. To reduce these disparities, additional work will be needed to identify the specific sleep disorders (in addition to OSAS) that affect Māori disproportionately, and to develop diagnosis and treatment services that are accessible and appropriate for Māori communities.

7.2 Sleeping Patterns and Circadian Phase among Morning- and Evening-Type Individuals

7.2.1 Screening Participants for Research

Despite the significant response to the call for participants during the survey phase of this programme, the number of individuals who met the study inclusion criteria was surprisingly small (approximately 29%). In addition to the significant effect on the size of the study sample, this has raised a number of issues regarding the use and validity of screening tools in research, which deserve discussion here.

The screening process described in this thesis was carefully developed by paying close attention to the procedures described in the literature and on the advice of professional colleagues. However, it appeared that for this population, some of the screening criteria may have been too rigid. For instance, a global score greater than five on the Pittsburgh Sleep Quality Index is indicative of a 'poor sleeper' (Buysse et al., 1989). However, it is possible that the considerable work and family commitments experienced at this stage of life may have a significant impact on an individuals' perception of sleep quality. Thus the scoring rules were modified such that an individual with a PSQI <8 (Carpenter et al., 2004) would still be considered to take part in the sleep studies

It was also observed that a number of potential participants with extreme eveningness scores on the MEQ had a history of using anti-depressants , which excluded them from participation. It is likely that for these participants their medication and/or condition may affect their sleep and thus have influenced their self-rated morningness/eveningness preference. Lower MEQ scores (i.e. greater eveningness) have been reported for depressed populations, compared to normal age- and gender matched controls (Drennan et al., 1991). It is also possible that these individuals were misdiagnosed sufferers of the circadian sleep disorder, Delayed Sleep Phase Syndrome.

Similarly, each person was required to complete the MEQ for a second time as part of the screening process, to ensure that their self-rated MEQ score was still within the appropriate range. However it was observed that the second MEQ score for many individuals differed to their original score, and in some instances individuals who were originally M- or E-type were rated as neither-type (N-type) during screening. There are at least two possible explanations for this observation. Firstly, the time interval between the survey and the screening process was approximately one year, so it is reasonable to assume that changes to personal, family, and/or work circumstances during this period may have affected an individual's morningness/eveningness preference. While others have reported that the MEQ has good

test/re-test reliability (see (Taillard et al., 2004; Van Dongen, 1998)), this was not specifically evaluated in the present study.

The observation of moving MEQ scores may also be explained by the statistical phenomenon of regression towards the mean (Bland & Altman, 1994). Respondents to the questionnaire survey were ranked according to their MEQ score and telephone recruitment purposely started from either end of the distribution with the aim of recruiting the most extreme chronotypes in order to enhance the size of the difference between the morning- and evening-type groups. Thus, because participants were recruited based on their original 'pre-test' MEQ score, regression towards the mean predicts that their 'post-test' MEQ score will be closer to population mean than the pre-test score. This would result in some definite E-types having a higher post-test score and some definite M-types having lower post-test score. Although the exact cause is unknown, the effect of this shift in MEQ chronotypes is that a small number of respondents (n=32) were excluded from participation because they were considered N-type at screening.

Ethical issues raised by screening

Screening in research appears to have two functions. On one hand, screening embodies the ethical principle of minimising harm to study participants. For example, by asking individuals to complete a health checklist it is possible to assess whether or not an experimental condition (e.g. extended periods of sleep deprivation) may aggravate an existing medical condition (e.g. epilepsy). The National Screening Unit also offer this explanation of screening

> 'Screening is a health service in which members of a defined population, who either do not necessarily perceive they are at risk of, or are already affected by a disease or its complications, are asked a question or offered a test, to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of a disease of its complications'

Thus, screening could be considered a researcher's ethical and moral responsibility to protect the study participants and to provide them with information that is useful. In this way screening requires consideration of the broader clinical, social, ethical and economic issues (National Health Committee, 2003). In screening for health issues (e.g. genetic disorders), there is an obligation to develop processes whereby the individual under investigation is provided with long-term follow up. Although we were not screening for disease in the present study, we were entering into a relationship with the potential participants, including those who failed screening. These people were sufficiently interested to give up a Saturday morning to undertake the screening process, but arguably received very little in return for their participation. A lack of funding and time restricted a more reciprocal engagement of the research team with these people.

On the other hand, screening tools and processes are commonly used to assess the suitability of an individual to meet the particular constraints of the study design. For example, in the present study the screening tools and processes described in Chapter 3 were deemed an appropriate method to determine whether an individual was considered 'normal' and/or 'healthy'. The more homogeneous the study participants, the smaller the sample size needed to detect differences between groups on the variable(s) of interest. However this approach, usually driven by resource limitations, also restricts the generalisability of the findings to the general population.

The screening process was problematic at a human level. The research team went to great lengths to provide a comfortable environment for the participants during screening (i.e. morning tea provided, family and friends welcomed, and koha given). However, the objectification of those individuals was a natural feature of this positivistic process. Many of the potential participants were happy to take part in the project, finding the subject area of great interest, and also finding some level of satisfaction knowing that their information would be useful and helpful. The large majority of these people were turned away from the project, because they had high scores on the DASS-21, or had poor sleep, or had a history of medication use etc. Thus, by our standards they were not considered normal, or healthy, however this did not meet their realities. In the process of maintaining objectivity in science, there is the potential to objectify the study participants. Thus there is a disjuncture between screening to protect the research participants and screening to protect the research. There is an ethical issue that needs to be addressed when individuals consider themselves healthy but after screening, are identified as potentially 'ill' (National Health Committee, 2003). In addition to the ethical dilemma, the practise of studying small homogeneous sub-groups, in order to achieve statistically significant results, may itself compromise the value of the science.

In the context of this thesis, the screening process was initially considered problematic because of the high rate of decline/attrition of potential study participants. The aim was to admit 60 participants through the study protocol, but after nine months of screening only 32 participants were invited to take part. On a practical level, this also had a significant impact on the financial and human resources available to this programme. In this context, screening processes are also determined by the funding and resources available to the research programme. Working with tight budgets and the constraints of the timeline means that fewer individuals can be put through the screening and also that stricter screening criteria are adopted in order to provide a 'tighter' study design.

7.2.2 Strengths and Limitations

Generalisability

Issues of generalisability are also important when considering the findings presented in Chapters 4 and 5, given that the all of the study participants were recruited from the survey

population. Thus, the findings related to differences in the timing of sleep and circadian phase by chronotype may not be applicable to other age-groups. In addition, the generalisability of these findings is affected by the small number of study participants (n=31 for Chapter 4 and n=28 for Chapter 5). On the other hand, the selection of participants from a general population sample is notable, compared to others that have used clinical case series.

Differences in the timing of sleep between morning- and evening-type individuals have been reported by several other authors. However the present study design and findings provide important new information for this area of research in many ways.

Firstly, despite the small sample size the findings presented in Chapters 4 and 5 confirm that the MEQ score cut-offs proposed by Taillard and colleagues (2004) accurately define morning- and evening-types who differ in terms of the timing of sleep and the circadian phase of the nocturnal melatonin profile.

The second significant feature of these studies is the use of validated objective measurement tools. In Chapter 4 the timing, duration, and quality of sleep were measured using a combination of actigraphy and sleep diary data. This contrasts with several similar studies which have estimated differences in sleeping patterns based solely on self-report (Carrier et al., 1997; Horne & Östberg, 1976; Ishihara et al., 1988; Ishihara et al., 1987; Roenneberg et al., 2003b; Taillard et al., 1999; Taillard et al., 2004). In Chapter 5, the circadian phase position was estimated using validated methods of determining the onset, midpoint, peak and offset of the endogenous melatonin rhythm described by Voultsios et al. (1997) and Benloucif et al. (2005).

Thirdly, sleep was monitored in the participants own home (i.e. a 'naturalistic' approach) and therefore the estimates of sleep timing take into account any psychosocial factors that influence the timing of sleep/wake scheduling in daily life, as compared to previous studies which have enforced strict sleep schedules and/or conducted studies within the laboratory environment. The duration of sleep monitoring (i.e. up to 14 days) is also an important feature of this study.

Missing data

The amount of missing actigraphy, sleep diary and melatonin data was minimal, and in all instances the data was missing at random. As mentioned in Chapter 4, there was some variability in the amount of actigraphy and sleep diary data that was collected by each individual, dependent on when a participant was able to take part in the overnight laboratory protocol. It would have been preferable to collect 14 days of sleep data from each individual, however it was considered more important to be able to co-ordinate with the participants personal/family/work needs and commitments, and include them at their convenience. The effect of this variability was minimised by the use of the mixed model ANCOVA procedure in the analysis of data, which is able to cope with unbalanced data.

Monitoring sleep in the participants own home is considered a significant strength of the study presented in Chapter 4. However the disadvantage of this study design is that it was impossible to control for and/or monitor the level of light exposure and the effect of prior sleep on circadian phase.

Given the length of the study period (up to 16 days including both actigraphy and circadian phase assessment) and the level of commitment that was required of the study participants, the small amount of data that was lost is remarkable.

Limitations of actigraphically determined sleep parameters

Actigraphy has been shown to have good correlation with polysomnographic measures of sleep and wakefulness, however it performs less well when sleep is short or of poorer quality (Ancoli-Israel, 2005). Because the actiwatch device relies on changes in activity to determine sleep from wake, it generally tends to overestimate sleep and underestimate wakefulness. Several steps were taken to account for these potential sources of error. Firstly, participants were instructed to complete a validated sleep diary in combination with pressing the event marker on the *Actiwatch*™. This was useful for the differentiation between sleep and periods of still wakefulness. Secondly, a series of rules were developed for determining Bed Time and Get Up Time parameters which were used by the *Actiwatch*™ software to set several other sleep parameters. Finally, a consistent approach was taken in the analyses presented in Chapter 4, which included that development of a protocol for meeting the requirements of normality necessary for the mixed model analytical procedure.

It is noted that there were very few significant findings in the univariate and multivariate analyses related to sleep quality. However this may reflect the fact that actigraphic estimates of sleep quality are poor in comparison with the gold standard PSG measurement of sleep quality (Signal et al., 2005).

Limitations of melatonin phase markers

Monitoring the nocturnal profile of the endogenous melatonin rhythm was undertaken using a modified constant routine protocol. Thus, the potential for masking of the circadian melatonin rhythm was minimised by the study design. However, visual inspection of the raw melatonin profiles found some evidence that masking may have occurred despite the highly controlled experimental conditions. The effect of this is diminished by the use of graphical smoothing methods prior to the identification of circadian phase, using established methods (e.g. (Benloucif et al., 2005; Voultsios et al., 1997)).

Another potential limitation of the study design is the use of saliva samples, rather than blood samples, for the detection of melatonin concentrations given the small amount of melatonin detectable in saliva. However, it is contended that the potential for error was diminished through

the use of standardised collection and preparatory procedures, and a well-known and validated radioimmunoassay technique (Voultsios et al., 1997). Moreover, the use of blood samples would have significantly increased the discomfort experienced by the study participants, and the work and responsibilities of the research team, not to mention that some participants may have been unwilling to take part if required to give blood samples.

7.2.3 The Sleep of Morning- and Evening-Types in Daily Life

The MEQ relies on the respondent's self-reported preferred timing for sleep/wake scheduling to determine chronotype. However, for most individuals, their ability to follow this ideal is limited by societal expectations, work demands and other family and personal commitments. Thus it is likely that a myriad of psychosocial or behavioural factors also contribute to the individual variability observed in sleep timing. In order to establish the relationship between *preferred* and *actual* sleep timing it was considered important to monitor the sleeping patterns of morning- and evening-types in their natural environment free from any restrictions on behaviour.

Individuals who reported current night work were excluded from participation, as the intention was to investigate preferred sleep times that were minimally impacted by work schedules. Moreover the age-range of the participants was restricted to 30-49 years to minimise the impact of age-related changes in sleep. Thirty-one individuals took part in this study (16 M-types and 15 E-types), with a mean age of 41yrs. There were more women participants than men, however similar numbers in both groups reported care-giving responsibilities.

Mixed model ANCOVAs confirmed that the timing of main night sleep episodes (i.e. bed time, sleep start time, sleep end time and get up time) was about an hour earlier for morning-types compared to evening-types. The estimated difference in sleep timing between chronotypes reported here (range of differences 1.08hrs – 1.60hrs) is similar to other sleep diary studies of morning- and evening-type workers (Ishihara et al., 1988) and students (Horne & Östberg, 1976; Ishihara et al., 1987). However these differences are much smaller than those reported in a more recent study of 12 M- and 12 E-types, who were assigned sleep schedules according to their preferred sleep times from a 1-week screening diary and their responses to the MEQ (Mongrain et al., 2004). In that study, morning- and evening-types differed by 2.55hrs in their bed times and 2.80hrs in their rising times (both $p < 0.0001$). This discrepancy may be explained by the strict screening criteria that were used by Mongrain et al. (2004) to select chronotypes, including the exclusion of those volunteers with more than 2-hour variability in sleep schedules across a week.

It has been reported that E-types demonstrate larger day-to-day variability in sleep timing and that E-types show larger shifts in sleep timing on free days (i.e. weekends or holidays) versus work days (i.e. during the week), regardless of whether individuals are workers or come from student populations (Ishihara et al., 1988; Ishihara et al., 1987; Lavie & Segal, 1989). It is

purported that this variability is due to the influence of social factors, and in particular work schedules, dictating when an individual must go to sleep and wake up during the working week (Taillard et al., 1999).

Taillard and colleagues (1999) investigated this relationship in age, gender and employment-matched groups of M-, N- and E-types (n=219 in each) who completed the reduced version of the MEQ (Adan & Amirall, 1991), as well as the Basic Nordic Sleep Questionnaire which includes more precise questions on sleep. During the weekend, all chronotypes went to bed later, woke later and subsequently slept more. While M-types delayed their bed time and rising times by 30min and 90min respectively, E-types delayed their bed time by 60min and their rising time by 2.3hrs.

In the validation of their new MEQ score cut-offs, the Taillard group (2004) found that E-types had larger weekday/weekend differences in self-reported bed times (0.46hrs vs. 0.35hrs respectively) and rising times, compared with M-types (1.73hrs vs. 1.18hrs respectively).

The findings presented in Chapter 4 support this hypothesis, with both chronotypes delaying their sleep at weekends, by comparison with weekdays, although the delay was greater for E-types than M-types. Although Taillard et al. (1999) and Taillard et al. (2004) report larger weekday/weekend differences, this may be explained by their use of subjective vs. objective measurement tools.

Unlike the Horne and Ostberg MEQ, the Munich ChronoType Questionnaire (MCTQ) specifically addresses differences in sleep timing on work days and free days (Roenneberg et al., 2003b). Following the analysis of the first 500 completed questionnaires, Roenneberg and colleagues (2003) reported that early chronotypes (~ morning-types) fall asleep almost two hours earlier than late chronotypes (~ evening-types) on weekdays, however rising times are similar between the two groups (approximately 30 minutes difference). Differences are more marked on free days, with late chronotypes indicating a larger range and later timing of sleep times (Roenneberg et al., 2003b).

Weekday/weekends differences in sleeping patterns were also investigated in a study of 73 young women who wore an activity monitor and completed sleep diaries across multiple nights (range 2-10) while sleeping in their own homes on unrestricted schedules (Tworoger et al., 2005). As in other studies, individuals had later bed times and rising times on weekends compared with weeknights.

As expected, participants aged 30-39yrs in the present study also had later sleep times than participants aged 40-49yrs, confirming several previous studies using self-report (Carrier et al., 1997; Roenneberg et al., 2003b; Touchette et al., 2001) and objective measurement tools (Yoon et al., 2003).

In contrast to the analyses related to sleep timing, mixed model ANCOVAs indicated no difference in the duration of the main night sleep episodes of morning- versus evening-types on weeknights. However, E-types spent longer trying to sleep (TIB) and slept longer (ActSlp) on weekend nights than did M-types. While such a finding has been reported in several other studies of sleeping patterns among morning- and evening-types (e.g. (Carrier et al., 1997, , 1998; Taillard et al., 1999; Taillard et al., 2004), this relationship does not appear to be consistent. For example, Ishihara et al. (1988) found that M-types slept 30 minutes longer than E-types (p <0.05), although they did not specifically investigate differences on weekdays and weekends. Similarly, Roenneberg and colleagues (2003) found that on average participants in their study slept 1 hour longer on free days. These authors concluded that on workdays sleep timing, particularly sleep end times are largely dictated by social timing, and for later chronotypes sleep duration is kept near its minimum. On the other hand sleep duration on free days tends to vary over a broader range. Thus, while sleep duration on work days is directly influenced by the alarm clock, it may still be influenced on free days by the work schedules as an after-effect, because working people, particularly later chronotypes, have to compensate for the sleep debt accumulated during the work week (Roenneberg et al., 2003b).

In the present study participants aged 30-39yrs spent more time in bed, but did not obtain more sleep, than those aged 40-49yrs. Roenneberg et al. (2003) grouped their participants by age as follows: <21yrs, 21-30yrs and >30yrs. While sleep durations were similar on weekdays (7.40hrs, 7.20hrs and 7.50hrs respectively), sleep durations on weekends (or free days) decreased with increasing age (9.30hrs, 8.20hrs, and 8.00hrs respectively).

If differences in sleep scheduling between chronotypes are based on a fundamental difference in the timing of the circadian clock, then it could be expected that E-types and M-types differ in terms of the timing of their evening wake-maintenance zone and sleep gates. Thus, E-types may have a later wake maintenance zone and be unable to initiate sleep until late evening. Their sleep is then truncated by early rising times, in order to begin work at a socially acceptable time, or to meet the needs of their family (e.g. getting children to school).

Using the MCTQ Roenneberg et al. (2003) found that during the workweek, early chronotypes fall asleep almost 2 h before the late chronotypes do. This difference shrinks down to 30 min at wake up, leading to a systematic shortening of sleep from early to late chronotypes (Roenneberg et al., 2003b).

This is consistent with the finding that E-types had larger weekday/weekend differences in TIB and ActSlp compared with M-types. Using TIBdiff (the difference between weekend and weekday TIB, (Monk et al., 2000)) indicated that E-types accumulate a significantly larger sleep debt across the working week, which must be dissipated on the weekend (mean TIBdiff E-types 1.31hrs ± 0.72hrs vs. M-types 0.69hrs ± 0.85hrs, t = 2.240, df =29, p =0.033). On the other

hand, while M-types may alter their sleeping patterns more on weekends to meet social expectations, it is probable that two nights of restricted sleep is not sufficient to accumulate a sleep debt to cause significant extension of weekday sleep episodes.

On measures of sleep quality, the only difference by chronotype for main night sleep episodes was that M-types had a higher fragmentation index (indicating more disturbed sleep) on weekend nights versus week nights, while E-types showed a non-significant trend in the opposite direction. Participants who reported caring for dependents had higher mean activity levels during sleep, and higher fragmentation index values, than those not caring for dependents. There were no significant differences in sleep quality measures comparing the age decades. These findings are not surprising given the limitations of actigraphy for estimating sleep quality (Signal et al., 2005).

Similar relationships were found when considering total sleep across 24-hour periods measured noon to noon. Mixed model ANCOVAs indicated that both chronotypes spent longer in bed and obtained more actual sleep on weekend nights. However, the weekday/weekend difference was larger for E-types than M-types. Participants aged 30-39 years spent more time in bed, but did not obtain more actual sleep, than participants aged 40-49yrs. There were no differences in the sleep quality variables between chronotypes.

The study presented in Chapter 4 confirms that the MEQ cut-offs proposed by Taillard and colleagues (2004) do identify people with objectively verified differences in sleep timing.

7.2.4 Melatonin Phase Markers and Self-Reported Morningness/Eveningness

Morning-types had an earlier melatonin onset (mean difference 1.03hrs), melatonin offset (mean difference 42 minutes), secreted more melatonin, and tended to have a longer duration of secretion compared to E-types. However, the rates of increase and decline were similar for both chronotypes. Although the temporal pattern of melatonin secretion was earlier among M-types than E-types, Griefahn (2002) also found there were no significant differences in the duration, maximum and AUC of the salivary melatonin profile, or any differences in the minimum, maximum, mesor or amplitude, between morning- and evening-type students aged 16-32yrs. This author explains that others have assumed an association between the amplitude of the circadian rhythm (as measured by CBT) and morningness/eveningness, although the previously reported differences are not consistent. The findings of the present study support the conclusion of Griefahn (2002) that the overall shape of the melatonin profile is independent of morningness/eveningness.

There were significant correlations between MEQ scores and markers of melatonin onset, but not melatonin offset. Although few studies have reported a correlation between MEQ scores and the endogenous melatonin rhythm (e.g. (Griefahn, 2002; Liu et al., 2000)), several studies have

reported an earlier T_{min} with increasing morningness (Baehr et al., 2000; Duffy et al., 1999; Hall et al., 1997). In the present study, MEQ scores were negatively correlated with the timing of DLMO, DLMO25, the first detectable melatonin level and the last detectable melatonin level. Moreover, linear regression indicated that, for every one-point increase in scores on the MEQ, (i.e. increasing morningness) circadian phase was approximately 2 minutes earlier.

This study presents the first physiological data for chronotypes classified according to the MEQ scoring criteria proposed by Taillard and colleagues (2004). In particular, the present study demonstrates that using these criteria, the endogenous melatonin rhythm of morning-types is significantly earlier than that of evening-types with differences in DLMO, DLMO25, DLMO50 and MelStart ranging from 1.09hrs - 1.50hrs. Phase differences between M-types and E-types were more apparent in the early subjective night. In M-types, melatonin secretion (DLMO) began 1.28hr earlier but this phase difference was not maintained throughout the dark period. By the late subjective night, the circadian clock among morning- and evening-types was at a similar phase position relative to the external world (difference in DLMOff = 0.5hrs). Carrier et al. (2002) reported a similar finding for the core body temperature rhythm, however there was a possibility that the phase advance observed in the rising limb of the CBT rhythm during the early subjective day was an evoked effect of the preceding sleep episode (Carrier et al., 2002).

Although the findings presented here confirm the previously reported phase difference between M- and E-types, the size of the difference in this study is smaller than others. While earlier studies have reported a 2-3 hour difference in the average melatonin onset between M- and E-types (Griefahn, 2002; Lack & Bailey, 1994; Mongrain et al., 2004), in the present study, the difference between morning- and evening-types in terms of their average DLMO was only 1.28hrs ($p < 0.001$).

One possible reason for this discrepancy is the difference in scoring criteria that have been used to identify chronotypes. Earlier studies have generally used the original criteria proposed by Horne and Ostberg (1976), where evening-types have a MEQ score between 16 and 41 while morning-types score between 69 and 86 (Horne & Östberg, 1976). In contrast, Taillard et al. (2004) proposed that evening-types could be accurately identified by a MEQ score between 16 and 52, while morning-types would score between 65 and 86. Thus, some of the participants classified as E- or M-types in the present study, would be considered neither-type according to the original criteria. It is therefore possible that these 'N-types' may have affected the size of the difference in circadian phase, by essentially shifting the average DLMO for both groups closer together. To investigate this, the average DLMO for both groups was calculated using the data from those participants who would meet the Horne and Ostberg scoring criteria for morning- and evening-types. Again, M-types (n=9) had a significantly earlier mean DLMO compared to E-types (n=8), however the difference between the two groups was still only 1.22hrs, which is

comparable to the difference between the mean DLMO presented here, suggesting that the different scoring criteria for categorising chronotypes does not account for the smaller difference in phase between M- and E-types.

The dim light melatonin onset has been the preferred marker of the circadian phase in studies which have investigated the phase relationship between morning- and evening-types however it was recently reported that the offset of melatonin secretion is a more stable marker than DLMO (Benloucif et al., 2005). The findings presented here indicate that, although the average offset of melatonin occurred at an earlier clock hour among M-types, the differences in DLMOff, DLMOff25 and DLMOff50 between the two chronotype were small (0.50hrs, 0.56hrs and 0.38hrs respectively) and did not reach statistical significance. Only one other study has compared morning- and evening-types using melatonin offset as a marker of circadian phase. In that study, self-identified morning- and evening-types demonstrated a 2.20hr difference in the timing of melatonin offset (p <0.0008) (Griefahn, 2002). If, as the findings suggest, on workdays E-types are required to wake earlier than they would prefer, then this would result in them receiving longer light exposure during the phase advancing portion of the circadian cycle. This would tend to reduce the phase differences between E-types and M-types.

The strongest relationship between sleep timing and the endogenous melatonin rhythm was between DLMO and the midpoint of sleep averaged across the five nights prior to the constant routine protocol. It is interesting to note that this is in agreement with the findings of Martin and Eastman (2002), who reported that DLMO (20% of maximum melatonin levels) was most strongly correlated with the mean midpoint of sleep calculated from the five days preceding circadian phase assessment (r =0.89, p <0.0001) in a sample of healthy young adults (n=26, 18-38 years of age).

For sleep timing parameters averaged across the 14-days of actigraphy recording, M-types and E-types slept at a later circadian phase on weekends than on week nights, but there were no significant phase angle differences between chronotypes. For the sleep parameters from the final night of actigraphy recording, there was a tendency for E-types to sleep later with respect to the DLMO than M-types, but the differences did not reach statistical significance. Similarly, E-types tended to sleep later with regard to measures of melatonin offset, than M-types. Significant differences between chronotypes were found for the phase angle from mid-sleep to DLMOff, and from midsleep to DLMOff25. While several authors have reported a longer phase angle among morning- compared with evening-types (Duffy et al., 1999; Hall et al., 1997; Liu et al., 2000; Taillard et al., 2003), the relationship is still not clear (see (Mongrain et al., 2004)).

Duffy and colleagues have comprehensively investigated the biological basis of morningness/eveningness using both the constant routine and forced desynchrony protocols. Duffy et al. (1999) found that while evening-types woke at a later clock hour, morning-types

woke at a later circadian phase (i.e. longer time interval between T_{min} and habitual wake time), although this relationship only reached statistical significance for the phase angle using T_{min} and not melatonin maximum. Thus, these authors have assumed that the observed difference in entrained circadian phase reflects a difference in one or more fundamental properties of the circadian system between chronotypes. Duffy et al. (2001) subsequently determined that this may be related to a correlation between the intrinsic circadian period, morningness/eveningness preference, and habitual wake time, with shorter τ associated with increasing morningness. Thus it was proposed that M-types wake at a time when the circadian sleep drive is decreasing, while E-types are waking shortly after the T_{min} when the circadian sleep drive is high (Duffy et al., 2001). This was supported by the findings of Liu et al. (2000). However, this is confused when age is considered. Although increasing age is associated with a greater preference for morningness, older adults wake at a circadian phase reminiscent of young evening-types (i.e. shorter phase angle to wake time (Duffy et al., 1999)).

Mongrain et al. (2004) proposed that this difference may be explained by the different social pressures to adjust their sleep timing that are experienced by morning- and evening-types, and young vs. old adults. To investigate this possibility, these authors compared the phase angles (DLMO to averaged wake time and T_{min} to wake time) of morning- and evening-types (12 M- and 12 E-types, age range 19-34yrs) who were free of work and school constraints. While the phase angles were similar for both groups, a later circadian phase was correlated with a shorter phase angle. Moreover, this relationship was different for both groups, such that the regression line for the relationship between phase angle and circadian phase was steeper for M-types because of an earlier sleep schedule (Mongrain et al., 2004). Thus the findings were paradoxical. In the first instance there was an association between a later circadian phase and a shorter phase angle (as described by (Duffy et al., 1999)), but on the other hand, M- and E-types had identical phase angles despite different circadian phase. The authors concluded that the MEQ correctly identifies an individual preference for morning or evening activity, but that this reflects two different circadian patterns: (1) a preference that is associated with a difference in the period and phase of entrainment and (2) a preference that is associated with some other aspect of sleep regulation such as a faster decline of homeostatic sleep pressure.

While the small sample size in the present study may have limited the power to detect significant differences between chronotypes, on the final night of actigraphy recording E-types slept later in the circadian cycle than M-types.

7.2.5 The Contribution of Circadian Phase versus Other Factors to Sleep Timing in Daily Life

A series of mixed model ANCOVAs examined the associations between different melatonin phase markers and sleep timing across the 14 nights prior to the circadian phase assessment,

after controlling for age group (in decades) and weekday vs. weekend nights. This model confirmed significant main effects for sleep start time and DLMO, DLMO25, MelStart and MelEnd. For sleep end times, there were significant main effects for DLMO25, MelStart and MelEnd. These relationships were all in the direction of later sleep with later melatonin phase markers.

All of the models related to sleep start and end times also showed significant main effects of weekdays versus weekend nights, with later sleep at weekends. In addition there were significant main effects for age group and sleep end times in five out of nine models, with participants aged 30-39yrs having later sleep end times than those aged 40-49yrs. This finding is consistent with the difference in MEQ scores between these groups identified in the preceding chapter.

The modelling indicated that for every 30 minute delay in melatonin onset time, the estimated mean sleep start time was 10-12 minutes later. Similarly the modelling indicated that for every 30 minute delay in circadian phase, the estimated mean sleep offset was 7-10 minutes later.

It is notable that the mixed model ANCOVAs indicated that the weekday/weekend night differences in sleep timing (at weekends, sleep start 28 minutes later, sleep end 1.3-1.4 hours later) were greater than the differences between chronotypes. This suggests that psychosocial factors may have a greater effect on sleep timing in daily life than does circadian physiology. While this is perhaps not surprising, it does indicate some need for caution assuming how much differences in circadian clock genes affect sleep timing for people between the extremes represented by advanced and delayed sleep phase syndrome.

7.3 Towards the Development of Guidelines for Research Involving Māori Genetic Material

7.3.1 Strengths and Limitations

Generalisability

This study presented in Chapter 6 began with a desire to hear Māori voices within discussions about genetic research in Aotearoa/New Zealand. To achieve this, a Kaupapa Māori methodological framework was adopted as a way of ensuring that the views and opinions of the participants were considered legitimate. As the theoretical framework underpinning this study, Kaupapa Māori situated Māori hopes and concerns at the interface of genetic research. This is considered a significant strength and indeed defining feature of this work, as it facilitated a change of the power relationship, since genetic research currently occurs within a non-Māori view-point.

It is acknowledged that many of the issues raised within this study will be shared by Pākehā and there will be much common ground. For instance the distrust of science, government and multi-national corporations may not be specific to the Māori community, and many other cultures emphasise the importance of family in the well-being of their communities. However, it must be reiterated that the Kaupapa Māori positioning of this study was about retrieving space for Māori voices within conversations about genetic research and affirming our right to be Māori within wider society.

In Aotearoa/New Zealand we have a unique opportunity to contribute to the larger global debate around genetics through the inclusion of a strong indigenous voice. For these reasons, the findings will have some relevance for many communities and indeed other indigenous populations worldwide. The diversity of interests of relevance to Māori has an important place in wider discussions about research, and should be considered in the development of public policy and research ethics.

The small number of participants and the limited geographical residency of those who took part in the focus group study is worthy of discussion here. The purpose of this study was not to seek out and present *the* Māori perspective of genetic research in Aotearoa/New Zealand. Instead it was hoped that the study would provide a space where Māori could feel safe to talk about genetic research and know that their opinions would be considered valid and meaningful. The methodological framework used in the present study provides a model for conducting further conversations with other members of the Māori community (e.g. kaumatua, rangatahi, rural Māori). It is interesting to note that the model presented here was recently used in a similar study commissioned by the Māori Indigenous Health Institute (MIHI) and the Cardioendocrine Research Group, both of the Christchurch School of Medicine and Health Sciences, in preparation for a study investigating the genetic factors influencing cardiovascular disease in two Māori communities (Tawhara, 2006).

Burgess (2005) has argued that representativeness within ethics is not measured by the size of the group who hold the view, but instead looks at whether the ethical analysis is adequately inclusive and considerate of perspectives that are present in the population, but which are often marginalised or misunderstood. While the number of focus group participants may be small, this study has clearly demonstrated that many Māori positions and interpretations of genetic research are shaped by our traditional mātauranga Māori intellect and our experience of colonisation, a feature which not given due consideration in other studies. Thus the Kaupapa Māori framework used here was crucial for the development of a research ethic for genetic research which valued the needs and expectations of the Māori community.

Validity and reliability

Qualitative research methods do not focus on generalising the information gathered to the whole population (Davidson & Tolich, 2003). Instead the value and rigour of the study is gained through transparency in analysis, the face validity of the results and the development of valid and accurate descriptions of the participants talk (Cram et al., 2000).

In the first instance this was facilitated by returning the transcripts and research findings back to the participants. This process provided individuals with an opportunity to make any editions or add supplementary comments to the transcriptions before any analysis was undertaken. Then, following the initial thematic analysis, a summary of the key themes that were identified were mailed to the participants and again they were invited to make any changes they felt were necessary. In addition, each focus group participant was invited to reconvene and take part in a feedback discussion which would provide an opportunity for the participants to develop the themes further or clarify their positions. While it is noted that all of the focus group participants declined this invitation, it is recognised that this does not necessarily indicate that the analysis was without fault, but perhaps that the participants had given as much time and commitment to the study as was available.

The validity and indeed credibility of the focus group study was also improved and assessed through the key-informant process. This also provided some triangulation in the research process, through the incorporation of multiple research methods. Each key-informant interview began with a summary of the themes identified in the focus group discussions and each key-informant was asked to consider these findings in the context of their own experience as Māori researchers. The key-informants were also invited to critique the study design and analytical method used, and many offered their own thoughts on what issues required further elaboration and also provided some suggestions on how to situate the themes within the current framework of health research in Aotearoa/New Zealand. During the interviews with the key-informants, it was confirmed that the present study uncovered a broad range of hopes and concerns which encompassed many of the social, political and economic implications of genetic research. Finally, each key-informant was offered the opportunity to review and make editions to their transcript prior to analysis and incorporation into the main research findings.

The reliability of the study design was also enhanced through the use of the following logistical measures:

(1) The use of inclusion criteria for participation in the focus group discussions

(2) A discussion guide was used for each focus group, and the same facilitator and note taker were used in each session.

(3) The focus groups were held across a three-month period, thus the social and political environment at the time was similar. This is important because it was obvious that the focus group participants drew on their personal experiences, analogy and media reports to help form positions on different issues.

(4) Each focus group was digitally voice-recorded and these recordings were used to check the accuracy of the transcripts.

(5) Finally, advice and commentary was regularly sought from other members of the research team throughout the analysis of the transcripts and the development of the themes.

7.3.2 The Ethical Implications of Conducting Genetic Research in Aotearoa/New Zealand

The study presented in Chapter 6 has shown that Māori are able to articulate and justify their understandings of genetic research when given the opportunity, tools and a culturally-safe environment to do so. From the surface, many of the issues discussed are reminiscent of the promises and concerns that have been voiced in other spaces. However, from the unique position of being tangata whenua, Treaty partners, marginalised and colonised, the participants have named and claimed these hopes and concerns and brought truth to Māori talk about genetic research and the type of society that we live in.

Many of the hopes presented in this study are not new, often meeting and intersecting with the many promises that have been made to Māori communities by those who advocate genetic research. However these findings are important because they confirm that Māori are not anti-science, and in fact Māori communities accept genetic research that would enhance the quality of life for Māori, as *we* define it (Baird et al., 1995). On first glance, Māori hopes for genetic research are shared by the wider New Zealand society in that we all aspire for good health, plentiful food supplies and safe communities. However, a deeper reading of these hopes uncovered the richness and complexity of the ideas that were raised which were ultimately about affirming our tangata whenua status, our tino rangatiratanga, and our right to be Māori.

Despite a concentrated effort to re-centre research and prioritise Māori aspirations through the development of by Māori for Māori approaches to research, the voices heard within the present study still talk about research practices which pass over and silence Māori communities. Within these conversations, the FGPs talked about unequal power relationships and the prioritisation of Western knowledge systems over Māori ways of knowing and doing things. They were also concerned that genetic research reinforces racist ideologies and negative stereotypes about Māori society and gives weight to Pākehā misperceptions of Māori. The focus group participants also feared that the outcomes of research marginalise Māori values and perspectives and in doing so, will diminish the mana of mātauranga Māori and validate the belief that traditional Māori knowledge is devoid of any truth or logic. Indigenous peoples, including

Māori, have long questioned the links been research and imposed ideals about the Other. Smith (1999) explains

> Researchers are in receipt of privileged information. They may interpret it within an overt theoretical framework, but also in terms of a covert ideological framework. They have the power to distort, to make invisible, to overlook, to exaggerate, and draw conclusions, based not on factual data, but on assumptions, hidden value judgements and often downright misunderstandings. They have the potential to extend knowledge or perpetuate ignorance (p.176).

As the participants in the present study have shown, Māori understandings and truths about genetic research are based within our experiences of colonisation within the research landscape. Recently, Bates and colleagues (2005) have argued that the public use complex and informed understandings of genetic research to generate warrants (or good reasons) for the acceptance or rejection of genetic technologies.

> When arguing about genetics, genetic researchers may collect the data of microbiology and use warrants based on the scientific method to justify their claims. The lay public may use social knowledge and experiential data interpreted through analogic and inductive warrants to support their claims.

The complexity of Māori understandings was demonstrated in the weighing up of the hopes and concerns that were raised within the focus group discussions. The participants brought together their shared and overlapping experiences as tax-payers, as humanitarians, as environmentalists, as the oppressed and as the sick, to construct their understandings of the implication of genetic research to Māori.

The findings presented here extend the conceptual framework provided by Bates and colleagues (2005), in that the focus group participants were able to dichotomise the issues as being of significance to all New Zealanders, or as being of specific significance to Māori. The participants demonstrated an informed understanding that was not reliant on a detailed appreciation of the specific techniques or methods used in gene-based research, but instead was evident in the way that they were able to draw on the experiences and histories of Māori communities to generate the warrants for their positions. The concern that 'Māori thinking' would be blamed for holding-back science draws on more modern experiences where our rights as tangata whenua as guaranteed by the Treaty of Waitangi, are disregarded and misrepresented as race-based preferential treatment. Our knowledge of racism supported participants concerns around the availability of beneficial treatments derived from genetic research, while our recent experience regarding the Foreshore and Seabed Legislation fuelled our distrust of governance and regulatory bodies.

This present study demonstrated that the Māori community draws on sources such as fiction, history, news events and personal accounts to discuss their hopes and concerns for genetic research (Bates et al., 2005). Moreover it has shown that Māori are equally able to draw on a traditional intellectual framework to generate warrants for their positions.

The security of tino rangatiratanga within genetic research was expressed as the need to develop Kaupapa Māori approaches to manage this form of Western-science. Linda Smith (cited in (Cram, 2001b)) listed the following questions to guide decision-making process in research and to facilitate reflection on our own processes by asking ourselves whether the research that we conduct is respectful.

- Who is the research for?
- What difference will it make?
- Who will carry out the research?
- How do we want the research to be done?
- How will we know that it is a worthwhile piece of research?
- Who will own the research?
- Who will benefit?

This list would sit comfortably alongside the question of the Kaupapa which was identified by one focus group participant as a necessary and obvious part of the process of genetic research. The term Kaupapa has been described as providing 'ground rules, customs, and the right way of doing things' (Pihama, Cram, & Walker, 2002). Thus, engaging with the Kaupapa, involves a comprehensive approach to the research process that would require researchers to question their own methodology or epistemological stance that informs the research strategy.

A significant outcome of the present study was the development of some key ethical principles for genetic research conducted in Aotearoa/New Zealand. *Whānaungatanga* values the importance of developing meaningful and trusting relationships with our research participants and being committed to this relationship as a vital part of the scientific process. *Manaakitanga* speaks to the human element within the research endeavour and encourages us to leave communities with the gifts of knowledge in recognition of their commitment to the work. While *kaitiakitanga* reflects our responsibility to protect our research participants, it also reminds us of the rights and needs of Māori communities to protect and enhance their own wellbeing which may necessitate sharing control of the research.

Located at the level of governance, these ethics take their meaning from tikanga Māori and validate the use of Kaupapa Māori methodology within genetic research. Importantly these principles provide a link between the Māori and Western scientific communities and as rules for

conduct, these guidelines affirm Māori values and provide a mechanism for control within the research process.

7.4 The Future of Sleep and Circadian Rhythms Research in Aotearoa/New Zealand

7.4.1 Summary of Key Findings and Suggestions for Future Research

The thesis presents the first estimates of the phenotypic variability of morningness/eveningness in a large random sample of adults in the general population. Using the new MEQ score cut-offs suggested by Taillard and colleagues (2004) approximately 25% of the population report either a morning- or an evening-type preference, and these groups differ in their habitual sleep timing and the timing of the endogenous melatonin rhythm. This research also shows that ethnicity, sex and socioeconomic deprivation are not important determinants of sleep timing preference, after taking into account age and work schedules. Together with the literature on circadian clock genetics, these findings suggest that the distribution of naturally occurring circadian phenotypes in the general population may involve a complex interaction of a number of core clock genes regulating sleep, as well as an interaction with societal factors such as work schedules.

While this thesis supports the hypothesis that an individual's MEQ chronotype has a significant effect on the timing of sleep, it has also shown that differences in sleep on weekdays and weekends accounted for more of the variability in sleep timing, duration and quality, than did MEQ chronotype (Chapter 4).

In a similar vein, an inverse relationship was confirmed between MEQ scores and circadian phase of the melatonin profile, with a significant difference in the timing of the dim light melatonin onset, but not offset, between MEQ chronotypes. However, differences in the timing of the melatonin rhythm between MEQ chronotypes were smaller than the overall differences in sleep timing (Chapter 5).

It has been argued that differences in circadian clock phase between extreme morning- and evening-types should be greater than differences in their sleep timing and that evening-types should sleep earlier in their circadian clock cycle because of societal pressures tending to impose a restricted range of bedtimes. This hypothesis would argue that evening-types are required to wake relatively earlier in their circadian clock cycle, and are therefore exposed to light for longer during the phase advance portion of the phase response curve.

However, this thesis found the opposite, for instance, evening-types slept later in their circadian clock cycle than morning-types. In addition, evening-types slept later in the day (external clock time) than morning-types. There are several possible factors that might contribute to this unexpected finding. The E-types studied may have chosen lifestyle options that enable them to

sleep later. There may also be differences between E-types and M-types in the homeostatic sleep drive, which also influences sleep timing.

Regardless of the causes, the later sleep timing of E-types in these studies would result in them receiving less exposure to morning light (the phase advancing portion of the phase response curve) and more exposure to evening light (the phase delaying portion of the phase response curve) which would be expected to contribute to the delayed circadian clock phase of E-types, compared to M-types.

While these explanations are speculative, overall, the findings point to the complexity of the factors that affect our preferred timing for sleep in daily life. This may not be surprising, however this thesis adds to the argument for not over investing in studies of the variability in clock gene polymorphisms, as a research focus limited to the genetics of the circadian clock will not be sufficient to explain differences in preferred sleep timing. Future research efforts would be better directed at increasing our understanding of the ways in which psychosocial factors influence sleep timing in daily life, and the possible consequences of this for our overall health and wellbeing. For instance, several related issues of relevance to shiftworkers have received minimal research attention. These include how much flexibility in sleep timing is possible without compromising sleep quantity and quality, and whether different chronotypes differ in the "rigidity" of circadian regulation of sleep timing.

7.4.2 Conclusions

As this thesis has convincingly shown, the question of sleep timing is not just an esoteric scientific problem. The timing of contemporary society favours the early bird, with early morning start times dictated by the structures of work and school.

Adapting to the demands of a 24-hour society depends on a complex interaction between the endogenous circadian pacemaker and exogenous factors such as work schedules. This thesis suggests that for evening-type individuals, this may have consequences for their health and be a contributing factor to sleep restriction.

Recent experimental evidence suggests that restricted sleep has a significant impact on health, safety and social participation. The results of this thesis suggest evening-type people in particular are likely to experience sleep restriction due to a preference for sleep and other activities that is at odds with societal norms. This thesis has also conclusively shown that evening-types may be at greater risk of chronic sleep restriction because of their high participation in night work

Although it is recognised that genotype does not necessarily predict phenotype, the scientific sleep community still does not know the extent to which genetics determines sleep timing, the extent to which morningness/eveningness is modifiable, and the relative contribution of

circadian physiology versus other psychosocial factors in determining sleep/wake scheduling. While differences in the circadian clock between morning- and evening-types are detectable against a background of daily life, this thesis has also addressed a significant gap in the literature by demonstrating that circadian physiology explains only a small percentage of the individual variability in sleep timing.

Greater understanding of the molecular mechanisms underpinning sleep regulation would provide valuable information on the development of the circadian sleep disorders and assist in the development of personalised treatments for ASPS and DSPS. Having the ability to determine whether an individual is physiologically suited to different work schedules or able to cope with night work is also of great interest to many. However we must also ask ourselves whether focusing on genetics is indeed worthwhile, given the constraints of the current research environment and the significant ethical, social and economic issues which are yet to be addressed. In what ways is information about shift work suitability meaningful and relevant for individuals or communities who have no choice but to be involved in night work because of geographical, social and political circumstances? Similarly, is it sensible to direct financial resources and research effort towards developing treatments for circadian sleep disorders, which probably only affect a small proportion of the population, given that there is still no standardised approach to the diagnosis and treatment of insomnia in New Zealand, and no formal training of health care professionals in this area.

Taking a balanced and systematic approach to studying the distribution of morningness/eveningness, this thesis has also shown that there is some merit in investigating the genetic variability of sleep timing for the general population versus that which is currently focussed on families. It has provided much needed evidence to show that a population screen for clock gene polymorphisms must consider not only the likely biological predisposition but also the numerous psychosocial influences which determine the phenotypic expression of chronotype.

The participants in the qualitative study also provided valuable insight into the risks and benefits of genetic research as they are perceived by the Māori community. Importantly this thesis has uncovered the urgent need for more respectful research relationships in order to advance scientific knowledge and understanding in this country.

While the findings from the focus group study signify Māori needs within the research experience, they are intimately relevant for wider New Zealand society as it is likely that the issues raised will be true for other communities and cultures in this country.

As a model for conducting research in New Zealand this thesis contains important lessons for the scientific community. To build respectful relationships we must be prepared to ask participants about their aspirations and goals for the research, to listen to and incorporate their

diverse needs, and to commit to the ideal of engaging in a long-standing relationship, rather than focusing on seeking informed consent. This has significant implications for science funding and institutional approaches to research. To conduct research according to the model proposed here will require a revision of the time and financial resources that are needed for this work. This is a significant challenge for the research establishment, but the work in this thesis persuasively indicates that it is a challenge we must address.

The issues raised here are also of fundamental importance to public health. We spend a third of our life sleeping, a significant proportion of the workforce have provisions for shift work in their employment contracts, our geographical location requires us to fly across multiple time zones, and there is an increasing move towards 24-hour operations. There are also broad normal variations in human sleep patterns that exist in the general population and change systematically with age.

For these reasons, the elucidation of the genetic components regulating sleep timing is relevant to the entire community, as compared to genetic screening for a disease, which although important, often affects only a small proportion of New Zealanders. The nature of sleep and circadian research in this country means that we are often working with communities and industries who are innately aware and indeed interested in the impact that sleep has on their daily lives. Thus it is vital that our approach to building research relationships, and conducting research with communities, continues to provide outcomes that are relevant.

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APPENDIX 1
ETHICS APPROVAL

Massey University
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Human Ethics Committee: Wellington

28 August 2003

Sarah-Jane Paine
HRC Maaori Health PhD Scholar
Sleep/Wake Research Centre
Massey University
WELLINGTON

Dear Sarah-Jane

Re: MUHEC: WGTN Protocol - 03/126
The Epidemiology of Advanced Sleep Phase Syndrome

Thank you for your letter of 20 August 2003 in response to the question and comments of the Massey University Wellington Human Ethics Committee.

The amendments you have made now meet the requirements of the Massey University Human Ethics Committee and the ethics of your protocol are approved. Approval is for three years. If this project has not been completed within three years from the date of this letter, a new application must be submitted at that time.

Any departure from the approved protocol will require the researcher to return this project to the Massey University Human Ethics Committee for further consideration and approval.

A reminder to include the following statement on all public documents: "This project has been reviewed and approved by the Massey University Human Ethics Committee, WGTN Protocol 03/126. If you have any concerns about the conduct of this research, please contact Mr Jeremy Hubbard, Acting Chair, Massey University Wellington Human Ethics Committee, telephone 04 801 2794 ext 6358, email J.J.Hubbard@massey.ac.nz.

Yours sincerely

Jeremy Hubbard (Acting Chair)
Massey University Wellington Human Ethics Committee

Cc: Professor Philippa Gander

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Human Ethics Committee: Wellington

26 January 2004

Sarah-Jane Paine
C/o Sleep/Wake Research Centre
Massey University
Adelaide Road
WELLINGTON

Dear Sarah-Jane

Re: MUHEC: WGTN Protocol - 03/149
Towards the development of guidelines for the handling, use and storage of Maori genetic material in research.

Thank you for your letter of 8 January 2004 together with the amended documents, as required by the Massey University Wellington Human Ethics Committee.

The amendments you have made now meet the requirements of the Massey University Human Ethics Committee and the ethics of your protocol are approved. Approval is for three years. If this project has not been completed within three years from the date of this letter, a new application must be submitted at that time.

Any departure from the approved protocol will require the researcher to return this project to the Massey University Human Ethics Committee for further consideration and approval.

A reminder to include the following statement on all public documents: "This project has been reviewed and approved by the Massey University Human Ethics Committee, WGTN Protocol 03/149. If you have any concerns about the conduct of this research, please contact Mr Jeremy Hubbard, Acting Chair, Massey University Wellington Human Ethics Committee, telephone 04 801 2794 ext 6358, email J.J.Hubbard@massey.ac.nz.

Yours sincerely

Jeremy Hubbard (Acting Chair)
Massey University Human Ethics Committee: Wellington

Cc: Dr Fiona Cram, Katoa Limited

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Human Ethics Committee: Wellington

31 August 2004

Sarah-Jane Paine
Sleep/Wake Research Centre
Massey University
102 Adelaide Road
WELLINGTON

Dear Sarah-Jane.

Re: MUHEC: WGTN Protocol - 04/31
Sleeping patterns across the circadian cycle

Thank you for the above protocol that was received and considered at the Massey University Human Ethics Committee: Wellington meeting on 18 August 2004.

The protocol was unconditionally approved.

Approval is for three years. If this project has not been completed within three years from the date of this letter, a new application must be submitted at that time.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

A reminder to include the following statement on all public documents: "This project has been reviewed and approved by the Massey University Human Ethics Committee, WGTN Protocol 04/29. If you have any concerns about the conduct of this research, please contact Mr Jeremy Hubbard, Acting Chair, Massey University Wellington Human Ethics Committee, telephone 04 801 2794 ext 6358, email J.J.Hubbard@massey.ac.nz

Yours sincerely

Jeremy Hubbard
Acting Chairperson
Massey University Human Ethics Committee: Wellington

Cc: Professor Philippa Gander, Director, Sleep/Wake Research Centre

APPENDIX 2
THE NEW ZEALAND MORNINGNESS/EVENINGNESS QUESTIONNAIRE

EARLY BIRDS AND NIGHT OWLS QUESTIONNAIRE

1. What sex are you? *Please tick* 1 ☐ Male 2 ☐ Female

2. What is your date of birth? ..... /..... /.....
(day) (month) (year)

3. Which ethnic group do you belong to? *Please tick the box or boxes which apply to you.*

a ☐ Māori b ☐ Samoan c ☐ Niuean d ☐ Indian
e ☐ NZ European f ☐ Cook Island Māori g ☐ Tongan h ☐ Chinese
k ☐ other (such as Dutch, Japanese, Tokelauan). Please state.....

4. Do you currently work for pay, profit or income?

0 ☐ No *Comments welcome →..... (please go to question 6)*

1 ☐ Yes, one paid job 2 ☐ Yes, more than one paid job

5. In the last 4 weeks did you work for pay, profit or income for at least 3 hours between midnight and 5am?

1 ☐ Yes 2 ☐ No

6. How many hours sleep do you usually get in 24 hours?..... hours .....minutes

7. How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times.

	PLEASE TICK ONE BOX ON EACH LINE would never doze	slight chance	moderate chance	high chance
Sitting and reading	0 ☐	1 ☐	2 ☐	3 ☐
Watching TV	0 ☐	1 ☐	2 ☐	3 ☐
Sitting inactive in a public place (e.g. theatre, meeting)	0 ☐	1 ☐	2 ☐	3 ☐
As a passenger in a car for an hour without a break	0 ☐	1 ☐	2 ☐	3 ☐
Lying down in the afternoon when circumstances permit	0 ☐	1 ☐	2 ☐	3 ☐
Sitting and talking to someone	0 ☐	1 ☐	2 ☐	3 ☐
Sitting quietly after a lunch without alcohol	0 ☐	1 ☐	2 ☐	3 ☐
In a car, while stopped for a few minutes in traffic	0 ☐	1 ☐	2 ☐	3 ☐

8. In general, would you say your health is

0 ☐ Excellent 1 ☐ Very good 2 ☐ Good 3 ☐ Fair 4 ☐ Poor

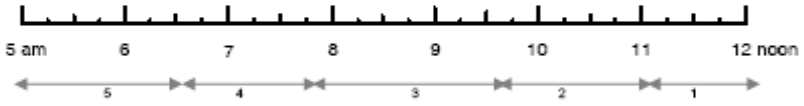
Please answer the following questions in order.
Do not go back and check or change your answers.

What time of day do you like to sleep?

Imagine that you are completely free to plan your day. Think only about what feels best for you.

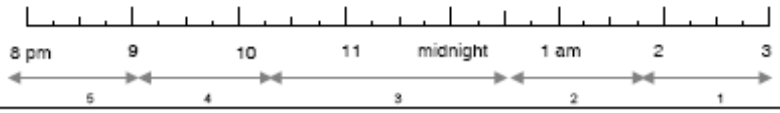
9. **What time of day would you get up?**

Please put a cross at the time closest to your best time.



10. **What time of day would you go to bed?**

Please put a cross at the time closest to your best time.



Waking Up In The Morning

11. **You have to get up at a particular time in the morning. How much do you need to depend on the alarm clock to wake you up?** *Please tick the box that applies to you.*

4 ☐ Not at all dependent 3 ☐ Slightly dependent 2 ☐ Fairly dependent 1 ☐ Very dependent

12. **If nothing is disturbing you (noise, light etc), how easy do you find it to get up in the morning?**

1 ☐ Not at all easy 2 ☐ Not very easy 3 ☐ Fairly easy 4 ☐ Very easy

13. **How alert do you feel in the first half hour after waking up in the morning?**

1 ☐ Not at all alert 2 ☐ Slightly alert 3 ☐ Fairly alert 4 ☐ Very alert

14. **How is your appetite in the first half hour after waking up in the morning?**

1 ☐ Very poor 2 ☐ Fairly poor 3 ☐ Fairly good 4 ☐ Very good

15. **How tired do you feel in the first half hour after waking up in the morning?**
Please tick the box that applies to you.

1 ☐ Very tired 2 ☐ Fairly tired 3 ☐ Fairly refreshed 4 ☐ Very refreshed

16. **When there is nothing that you have to do tomorrow, what time do you go to bed, compared to your usual bedtime?** *Please tick the box that applies to you*

4 ☐ Seldom or never later 3 ☐ Less than 1 hour later 2 ☐ 1-2 hours later 1 ☐ More than 2 hours later

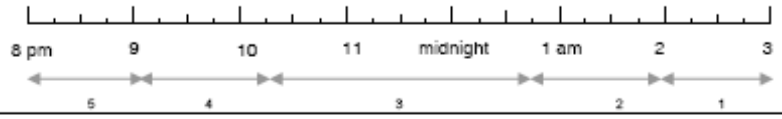
17. **You and a friend have decided to do some physical exercise.**
- **Your friend wants to train twice a week from 7-8 am**
- **How well do you think your would perform at this time?**

Please tick the box that applies to you

4 ☐ Would be on good form
3 ☐ Would be on reasonable form
2 ☐ Would find it difficult
1 ☐ Would find it very difficult

18. **What time in the evening do you start to feel tired and in need of sleep?**

Please put a cross at the time that suits you best.



19. **You want to do your best on an exhausting mental test that lasts 2 hours. Which one of these 4 test times would suit you best?** *Please tick the box that is closest to your best time.*

6 ☐ 8-10am
4 ☐ 11am–1pm
2 ☐ 3-5pm
0 ☐ 7-9pm

20. **If you went to bed at 11 pm, how tired would you normally be at that time?**

Please tick the box that applies to you

0 ☐ Not at all tired
2 ☐ A little tired
3 ☐ Fairly tired
5 ☐ Very tired

21. **If you go to bed a few hours later than usual, but don't have to get up at any special time in the morning, what is most likely to happen?** *Please tick the box that applies to you*

4 ☐ I wake up at the usual time and do not fall back to sleep
3 ☐ I wake up at the usual time, then doze
2 ☐ I wake up at the usual time, then fall back to sleep
1 ☐ I do not wake up until later than usual

22. **Imagine that you have to be at work, and stay alert, between 4-6 am. You don't have anything in particular to do the next day. Which of these strategies would suit you best?** *Please tick the box that applies to you*

1 ☐ I would not go to bed until work was over
2 ☐ I would take a nap before work, then sleep after
3 ☐ I would take a good sleep before work, then nap after
4 ☐ I would take all my sleep before work

23. **You have to do 2 hours of hard physical work. You are completely free to plan your day. When would you choose to do this work?** *Please tick the box that is closest to your best time.*

4 ☐ 8-10 am
3 ☐ 11 am – 1 pm
2 ☐ 3-5 pm
1 ☐ 7-9 pm

24. **You and a friend have decided to do some physical exercise.**
- **Your friend wants to train between 10-11 pm**
- **How well do you think you would perform at this time?**

Please tick the box that applies to you

1 ☐ Would be on good form
2 ☐ Would be on reasonable form
3 ☐ Would find it difficult
4 ☐ Would find it very difficult

25. Imagine you can choose your own work hours. You have to work for 5 hours a day (including breaks). Your job is interesting, and you get paid for the amount of work you do. Which 5 hours <u>in a row</u> would you choose to work? *Please tick 5 boxes for the time that suits you best.*

26. At what time of day do you feel your best? *Please tick 1 box to indicate your best time.*

27. You hear about "morning types" and "evening types". Which of the following types do you think you are? *Please tick the box that applies to you*

6 ☐ Definitely a morning type
4 ☐ More a morning type than an evening type
2 ☐ More an evening type than a morning type
0 ☐ Definitely an evening type

28. Please read and complete the information sheet and consent form in Booklet 2

29. Please tick this box if you would like to enter the draw for a rimu wall mirror sponsored by dm ☐

Thank-you for your help. Please send us the questionnaire in the reply-paid envelope provided or you can phone your response to 0800 SLEEP WAKE (0800 753 379).

APPENDIX 3
QUESTIONNAIRE SURVEY STUDY PACK

Massey University
WELLINGTON

Private Box 756
Wellington
New Zealand
T 64 4 801 5799
F 64 4 801 2692
www.massey.ac.nz

<Date>

<FIRST>gap<SURNAME>
<ADDR1>
<ADDR2>
<ADDR3>
<ADDR4> *(if applicable)*

E te rangatira, tēnā koe

E ngā waka, e ngā mana, e ngā reo,
e ngā karangatanga maha o ngā hau e whā
ko tenei te mihi atu ki a koutou.
Tēnā koutou hoki i roto i ngā āhuatanga o tēnei wā.
Nō reira, tēnā koutou, tēnā koutou, tēnā koutou katoa.

We are trying to find when people prefer to sleep – are you an "early bird" or a "night owl". We are interested in understanding how much of this preference is due to biology (the body clock).

We are doing a survey of people aged 30 to 50 years, and your name was randomly selected from the electoral roll as part of a sample of 5,000 people in the Wellington region.

We are trying to obtain as wide a sample of people in Wellington as possible. We would greatly appreciate your help in answering the questionnaire and sending it back to us. Your information is just as important to us whether you have a sleep problem or not.

The questionnaire will only take about 10 minutes. Please fill in your questionnaire and send it back to us in the post-paid envelope provided, or you can give us your answers by calling our toll-free number 0800 SLEEP WAKE (0800 753 379).

It is important for you to know that **your information will be kept confidential.** You will not be identified in any feedback or reports about the study. Please answer as much of the questionnaire as possible.

We will be recruiting some participants for a further study "*Sleep and your Body Clock*". We have included a booklet that will provide you with information about this study and also a consent form, where you can show if you want to be in the next study, or not. Please be aware that answering the questionnaire does not mean that you have to take part in the second study.

This project has been reviewed and approved by the Massey University Human ethics Committee, WGTN Protocol 03/126. If you have any concerns about the conduct of this research, please contact the following person:

Mr Jeremy Hubbard, Acting Chair
Massey Human Ethics Committee
Massey University Wellington
Private Box 756
Wellington

Telephone: 04 801 2794 x 6358
E-Mail: J.J.Hubbard@massey.ac.nz

You can also contact us directly with any concerns or queries about the survey at the address and phone number given.

To thank you for helping us with the survey, we are offering you the opportunity to go into a draw to win a stunning rimu wall mirror valued at up to $480.

This prize has been kindly sponsored by Design Mobel Ltd. and will be drawn on 15th December 2003. Please tick the appropriate box on the questionnaire if you would like to enter. All participants will be sent a pamphlet summarising the key results once the study has been completed.

Thank-you for your help.

Nō reira, noho ora mai ra
nā

Sarah-Jane Paine (Tuhoe, Ngati Rongo)
PhD Student
Sleep/Wake Research Centre
Massey University
Private Box 756
WELLINGTON

Professor Philippa Gander
Director
Sleep/Wake Research Centre
Massey University
Private Box 756
WELLINGTON

Encl.4 (1 questionnaire, 1 information booklet, 1 consent form, 1 post-paid reply envelope)

Massey University
WELLINGTON

Private Box 756
Wellington
New Zealand
T 64 4 801 5799
F 64 4 801 2692
www.massey.ac.nz

<Date>

<FIRST>gap<SURNAME>
<ADDR1>
<ADDR2>
<ADDR3>
<ADDR4> *(if applicable)*

Dear Sir/Madam

Sleep is very important for our health. We are from the Sleep/Wake Research Centre at the Wellington Campus of Massey University.

We are trying to find out when people prefer to sleep – are you an "early bird" or a "night owl"? We are interested in understanding how much of this preference is due to biology (the body clock).

We are doing a survey of people aged 30 to 50 years, and your name was randomly selected from the electoral roll as part of a sample of 5,000 people in the Wellington region.

We are trying to obtain as wide a sample of people in Wellington as possible. We would greatly appreciate your help in answering the questionnaire and sending it back to us. Your information is just as important to us whether you have a sleep problem or not.

The questionnaire will only take about 10 minutes. Please fill in your questionnaire and send it back to us in the post-paid envelope provided, or you can give us your answers by calling our toll-free number 0800 SLEEP WAKE (0800 753 379).

It is important for you to know that **your information will be kept confidential.** You will not be identified in any feedback or reports about the study. Please answer as much of the questionnaire as possible.

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This prize has been kindly sponsored by Design Mobel Ltd. and will be drawn on 15th December 2003. Please tick the appropriate box on the questionnaire if you would like to enter. All participants will be sent a pamphlet summarising the key results once the study has been completed.

Thank-you for your time.

Yours sincerely,

Sarah-Jane Paine
PhD Student
Sleep/Wake Research Centre
Massey University
Private Box 756
WELLINGTON

Professor Philippa Gander
Director
Sleep/Wake Research Centre
Massey University
Private Box 756
WELLINGTON

Encl.4 (1 questionnaire, 1 information booklet, 1 consent form, 1 post-paid reply envelope)

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai

Massey University

INFORMATION SHEET

Sleep and Your Body Clock.

You are invited to take part in a study to assess how much the body clock affects your preferred sleeping time.

The aims of the study:

- To collect and compare data on the quantity and quality of sleep of two groups of people: those who report that they are - "morning types", and people who are neither morning-type nor evening-type ("neither-types").
- To determine whether morning-types go to sleep earlier and wake earlier in the morning, during their usual daily lives, compared to neither-types.
- To confirm that the body clock is earlier in morning-types compared to neither-types.

Who are we looking for?

- Your name was randomly selected from the electoral roll as part of a sample of 5,000 people from the Wellington Region, asked to fill out the "Early Birds and Night Owls" questionnaire.

- We are looking for people who match the following criteria:
  (1) Answered the "Early Birds and Night Owls" questionnaire.
  (2) The questionnaire answers show a morning- type person or a neither-type person.
  (3) Aged between 30-50 years
  (3) Not involved in shift work.

Melatonin.

- *Melatonin* is a hormone produced naturally in the brain. During the day very little melatonin is produced, however, in the evening there is a sudden increase in melatonin and it stays this way until just before dawn, when the levels of melatonin decrease again.
- Because we know melatonin is present only at night, we believe it also has something to do with sleep. We are able to measure how much melatonin is in your body by taking samples of saliva. By taking samples at regular intervals we are able to find out when your body begins to produce melatonin, and therefore when your body clock is telling you it is time for sleep.

What is involved if you decide to participate?
This study has 2 phases. If you decide to be in the study you will be asked to:

- Come to the Sleep/Wake Research Centre to meet with the project leader and discuss each phase in detail, and answer any questions you may have.
- In Phase One: wear a small watch-sized activity monitor and complete a sleep diary for 14 days.
- In Phase Two : visit the Sleep/Wake Research Centre for approximately 12 hours on a Saturday, during which time we will ask you to provide saliva samples.

The following information explains what will happen during each phase of the study.

PHASE ONE:

- A member of the research team will contact you in August 2004 and arrange to meet with you at the Sleep Wake Research Centre.
- During this first meeting Ms. Sarah-Jane Paine will explain the activity monitor (Actiwatch™) and sleep diary to you and give you one to take away with you.
- The Actiwatch™ is the same size as a watch and is worn on your non-dominant wrist. The sleep diary is filled out by you, to help us know when you tried to fall asleep, and when you have decided not to try to sleep any more. Together, the activity monitor and sleep diary give information on when you are sleeping, how long you are sleeping, and the quality of each sleep period.
- You will wear the activity monitor and complete the sleep diary for 14 days in a row. The first day that you wear the activity monitor will be a SATURDAY.
- The activity monitor recording and logbook data will not have your name on them. Instead they will have a code number and all data will be stored in a secure cabinet at Massey University. **No material which could personally identify you will be used in any reports on the study.**

PHASE TWO:

- At the end of the Phase One you will come to the Sleep/Wake Research Centre to take part in the next phase of the study. This will happen on a SATURDAY.
- At the Sleep/Wake Research Centre, Ms. Paine will collect the Actiwatch™ and sleep diary from you. She will then explain what will happen for the rest of the day. **While you are at the Sleep/Wake Research Centre you will be supervised by a member of the research team. They are available at all times to provide assistance and to answer any questions you may have.**
- The Sleep/Wake Research Centre has a lab facility with 3 hospital-style beds. This study requires you to remain in the lab for approximately 12 hours, between 10am and 10pm or between 12pm and 12am. YOU ARE NOT REQUIRED TO STAY OVERNIGHT.
- For some of this time you will be required to remain in a bed. You will not be able to get out of bed and move around during this time except to use the bathroom.
- You will be allowed to doze while you are in the bed.

- Certain foods and liquids are not allowed to be consumed on this day. Ms. Paine will let you know in advance what these are. While at the Sleep/Wake Research Centre your snacks and drinks will be provided.
- The research team will provide entertainment such as T.V/Video, books and magazines while you are at the Sleep/Wake Research Centre.
- Between 5-5:30pm the lights in the lab will be dimmed and will remain that way until the end of the session.
- Every 30 minutes from 6pm until the end of the session, Ms. Paine will collect a saliva sample from you. To do this you will be asked to chew on a cotton swab for a few minutes. **It is important for you to know that this is a totally painless procedure.**

What are the outcomes of the study?

- You will receive a summary of the findings of the study and have access to a copy of the final report.
- This is an opportunity for you to learn about your sleep and how varied sleep can be. You will be shown your own sleep data. A member of the research team will sit and explain to you what the data means.
- You will also learn about morningness/eveningness. You will have an opportunity to find out what your questionnaire answers mean and also what your melatonin profile looks like.

Risks and benefits

- There are no personal risks involved in wearing an activity monitor and it will not detect any medical disorders.
- Providing a saliva sample is totally painless and there is no risk to you by doing this.
- You may feel thirsty or have a dry mouth after providing a saliva sample. We are able to provide drinks and snacks to help with this except during the 10 minutes before giving a sample.

Important points

- This project has been reviewed and approved by the Massey University Human Ethics Committee, WGTN Protocol 03/126. If you have any concerns about the conduct of this research, please contact the following person:

Mr Jeremy Hubbard, Acting Chair
Massey Human Ethics Committee
Massey University Wellington
Private Box 756
Wellington

Telephone: 04 801 2794 x 6358
E-Mail: J.J.Hubbard@massey.ac.nz

- Your name and details will be kept confidential at all times. There is no way that you will be able to be identified in any reports on the study.

- Your saliva samples will be kept until they are analysed. Only members of the research team will be able to access your samples. The samples will be destroyed after analysis.
- For the Saturday lab visit, you will be provided with a taxi to travel to and from the Sleep/Wake Research Centre.

What do I do now?

- **Please read the consent form carefully.**
- You will notice that there are 3 options for you to choose from. **Please ensure that you tick the appropriate box and sign at the bottom**. Send this form back to us in the postage-paid envelope along with your questionnaire.

We believe that it is important to understand why people may or may not be interested in being part of this study. We hope to recruit some people to discuss with the researchers their reasons for or against being in this study. The results from this discussion will help form guidelines for scientific research in New Zealand.

Participation

- Your participation is entirely voluntary. If you do agree to take part you are free to withdraw from the study at any time without having to give a reason.
- You are free to contact the research team at any time during the study to ask questions. Our toll-free number is 0800 SLEEPWAKE (0800 753 379)
- Only the names of those who agree to participate or agree to talk with the research team will be retained.

Thank you for taking the time to consider being involved in the study. Any of the following members of the research team would be happy to answer questions you may have about this study.

Researchers:

Sarah-Jane Paine
PhD Student
Sleep/Wake Research Centre
Massey University
Ph: 801 5799 ext. 6039

Professor Philippa Gander
Director
Sleep/Wake Research Centre
Massey University
Ph: 801 5799 ext. 6033

Date: *(insert date here)*

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai

Massey University

CONSENT FORM

Sleep and your Body Clock.

- I have read and I understand the information sheet dated *(insert date from bottom of information sheet here)* for volunteers taking part in the study designed to intensively follow my sleep patterns over a two week period. I am aware that this also involves a day-visit to the Sleep/Wake Research Centre.
- I have had the opportunity to discuss this study. I am satisfied with the answers I have been given, and understand that I may ask further questions at any time.
- I understand that participation in this study is voluntary and that I may withdraw from the study at any time.
- I understand that participation in this study is confidential and that no material, which could identify me, will be used in any reports on this study.
- I have had sufficient time to consider whether to take part.
- I know whom to contact if I have any questions about the study.

☐ I agree to take part in this study. My phone number is _____ and I give consent for a research team member to contact me.

☐ I do not wish to take part in this study, but I am happy to discuss my reasons with the research team. My phone number is _____ and I give consent for a research team member to contact me.

☐ I do not wish to take part in this study, please do not make any further contact.

Please print your full name here _____

Signature _____ Date _____

Researchers:	Sarah-Jane Paine	Philippa Gander
Contact phone number:	801 5799 x 6039	801 5799 x 6033

APPENDIX 4
SURVEY RESPONSE CODES

Mailout 1	
10	Non-responder
10.2	Study pack sent to new address (i.e. was GNA)
11	Response by mail 1
11.1	Response by phone
11.2	Response from 10.2
14	Gone, no address (GNA)
14.1	GNA by phone
14.2	GNA from 10.2
15.1	Overseas by mail
15.2	Overseas by phone
16.1	Deceased by mail
16.2	Deceased by phone
17.1	Refuse by mail
17.2	Refuse by phone
18.1	Language difficulties
Mailout 2	
20	Non-responder
20.2	Study pack sent to new address (i.e. was GNA)
21	Response by mail 1
21.1	Response by phone
21.2	Response from 20.2
24	GNA
24.1	GNA by phone
24.2	GNA from 20.2
25.1	Overseas by mail
25.2	Overseas by phone
26.1	Deceased by mail
26.2	Deceased by phone
27.1	Refuse by mail
27.2	Refuse by phone
28.1	Language difficulties

Mailout 3

30	Non-responder
31	Response by mail 1
31.1	Response by phone
34	GNA
34.1	GNA by phone
35.1	Overseas by mail
35.2	Overseas by phone
36.1	Deceased by mail
36.2	Deceased by phone
37.1	Refuse by mail
37.2	Refuse by phone
38.1	Language difficulties

Phone follow-up (Telematch numbers)

40	Non-responder
40.2	Send another questionnaire
41	Response by mail 1
41.1	Response by phone (ie. called the SWRC)
41.2	Response by phone follow-up
44	GNA
44.1	GNA by phone
44.2	GNA phone follow-up
44.3	Wrong number/no such number
45.1	Overseas by mail
45.2	Overseas by phone
45.3	Overseas phone follow-up
46.1	Deceased by mail
46.2	Deceased by phone
46.3	Deceased phone follow-up
47.1	Refuse by mail
47.2	Refuse by phone
47.3	Refuse phone follow-up
48.1	Language difficulties
48.2	Does not qualify i.e. hospitalised, disability etc
49	Moved out of Wellington

Phone follow-up (White pages)

50	Non-responder
50.2	Send another questionnaire
51	Response by mail 1
51.1	Response by phone (ie. called the SWRC)
51.2	Response by phone follow-up
54	GNA
54.1	GNA by phone
54.2	GNA phone follow-up
54.3	Wrong number/no such number
55.1	Overseas by mail
55.2	Overseas by phone
55.3	Overseas phone follow-up
56.1	Deceased by mail
56.2	Deceased by phone
56.3	Deceased phone follow-up
57.1	Refuse by mail
57.2	Refuse by phone
57.3	Refuse phone follow-up
58.1	Language difficulties
58.2	Does not qualify i.e. hospitalised, disability etc
59	Moved out of Wellington

Mail out 4 (Māori non-responders only)

60	Non-responder
60.2	Send another questionnaire
61	Response by mail 1
61.1	Response by phone (ie. called the SWRC)
61.2	Response by phone follow-up
64	GNA
64.1	GNA by phone
64.2	GNA phone follow-up
64.3	Wrong number/no such number
65.1	Overseas by mail
65.2	Overseas by phone
65.3	Overseas phone follow-up
66.1	Deceased by mail

66.2	Deceased by phone
66.3	Deceased phone follow-up
67.1	Refuse by mail
67.2	Refuse by phone
67.3	Refuse phone follow-up
68.1	Language difficulties
68.2	Does not qualify i.e. hospitalised, disability etc
69	Moved out of Wellington

APPENDIX 5
DATA ENTRY RULES

Field Description	Field Length	Comments		Programme Defaults
ID number	5n	10001-12326 20001-22674	Pre-printed bottom left-hand corner Hand-written may vary	MUST BE PRESENT
Question 1	1n	1-2	Transsexual: key as indicated otherwise default	9
Question 2	8n	DDMMYYY		15/06/YOB if missing i.e. mid year, where YOB is from the electoral roll If age in years is given, key in 15/06/YOB, where YOB is based on age
Question 3	8 x 1a	A-H		Space fill
Question 3 'K'	1a	K	K can be ticked and have no "please state"	Space fill
Question 3 'Please state'	20a		Key as supplied	
Question 4	1n	0-2	If ticked 1 & 2 key 1	9
Question 'comments'	1a	Y	Key 'Y' if ticked	Space fill
Question 5	1n	1-2		9
Question 6 – Hours	2n	HH	Key as supplied in 'hours' Key middle of hours i.e. 10-12 key 11	Space fill
Question 6 – Minutes	2n	MM	Key as supplied in 'minutes' Key middle of minutes i.e. 30-40 key 35 "don't know" or "sometimes" etc, leave blank Where average of range results in _.25 or _.75, round to _.5	Space fill
Question 7	8x 1n	0-3	Double tick or tick between boxes (0,1) key 1 (1,2) key 1 (2,3) key 2	Space fill
Question 8	1n	0-4	Double tick or tick between boxes (0,1) key 1 (1,2) key 2 (2,3) key 3 (3,4) key 3	9

Field Description	Field Length	Comments		Programme Defaults
Question 9	1n	1-5	(5:00am-6:30am) key 5 (6:31am-7:45am) key 4 (7:46am-9:45am) key 3 (9:46am-11:00am) key 2 (11:01am-12:00pm) key 1 If range indicated then key midpoint. If multiple times indicated then key the extreme left time. If tick falls to left of timeline key 5 If tick falls to right of timeline key 1 If tick on score line key as indicated If tick on score falls on intersection between 2 scores, key conservative i.e. (1,2) key 2 (2,3) key 3 (3,4) key 3 (4,5) key 4	If missing key 7
Question 10	1n	1-5	(8:00pm-9:00pm) key 5 (9:01pm-10:15pm) key 4 (10:16pm-12:30am) key 3 (12:31am-1:45am) key 2 (1:46am-3:00am) key 1 If range indicated then key midpoint. If multiple times indicated then key the extreme left time. If tick falls to left of timeline key 5 If tick falls to right of timeline key 1 If tick on score line key as indicated If tick on score falls on intersection between 2 scores, key conservative i.e (1,2) key 2 (2,3) key 3 (3,4) key 3 (4,5) key 4	If missing key 7
Question 11	1n	1-4	Double-tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 12	1n	1-4	Double-tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 13	1n	1-4	Double-tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 14	1n	1-4	Double-tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7

Field Description	Field Length	Comments		Programme Defaults
Question 15	1n	1-4	Double-tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 16	1n	1-4	Double-tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 17	1n	1-4	Double-tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 18	1n	1-5	(8:00pm-9:00pm) key 5 (9:01pm-10:15pm) key 4 (10:16pm-12:45am) key 3 (12:46am-2:00am) key 2 (2:01am-3:00am) key 1 If range indicated then key midpoint. If multiple times indicated then key the extreme left time. If tick falls to left of timeline key 5 If tick falls to right of timeline key 1 If tick on score line key as indicated If tick on score falls on intersection between 2 scores, key conservative i.e (1,2) key 2 (2,3) key 3 (3,4) key 3 (4,5) key 4	If missing key 7
Question 19	1n	0,2,4,6	Double-tick key as follows (0,2) key 1 (2,4) key 3 (4,6) key 5	If missing key 7
Question 20	1n	0,2,3,5	Double tick key as follows (0,2) key 1 (2,3) key2.5 (3,5) key 4	If missing key 7

Field Description	Field Length	Comments		Programme Defaults
Question 23	1n	1-4	Double tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 24	1n	1-4	Double tick key as follows (1,2) key 1.5 (2,3) key 2.5 (3,4) key 3.5	If missing key 7
Question 25	1n	1-5	(12:00am-3:59am) key 1 (4:00am-7:59am) key 5 (8:00am-8:59am) key 4 (9:00am-1:59pm) key 3 (2:00pm-4:59pm) key 2 (5:00pm-12:00am) key 1 If range indicated then key midpoint. If tick falls to left of timeline key 5 If tick falls to right of timeline key 1 If tick on score line key as indicated THIS APPLIES IF 6 BOXES ARE TICKED INSTEAD OF 5.	If missing key 7
Question 26	1n	1-5	(12:00am-4:59am) key 1 (5:00am-7:59am) key 5 (8:00am-9:59am) key 4 (10:00am-4:59am) key 3 (5:00pm-9:59pm) key 2 (10:00pm-12:00am) key 1 If consecutive boxes are ticked key predominant band If 2 boxes are ticked key 7	If missing key 7
Question 27	1n	0,2,4,6	Double tick key as follows (0,2) key 1 (2,4) key 3 (4,6) key 5	If missing key 7
Incentive prize	1a	Y	Key 'Y' of ticked	N
Response type	2a	M, P, PU	If questionnaire is blue then key M (mail) If questionnaire is white with no initials then key as P (phone) If questionnaire is white with initials then key as PU (phone follow-up)	Space fill
Flag	1a	Y	Key if ANY question is keyed 7	Space fill

APPENDIX 6
THE RELATIONSHIP BETWEEN MORNINGNESS/EVENINGNESS AND SELF-REPORTED GENERAL HEALTH

Table 1. Self-reported general health, by ethnicity, sex, socioeconomic deprivation, work status and chronotype

	Poor/Fair General Health		Excellent/Very Good/Good General Health				
	%	*95% CI*	*%*	*95% CI*	*χ2*	*df*	*p*-value
Māori	8.99	7.32-10.91	91.01	89.09-92.68	14.94	1	0.0001
non-Māori	5.08	4.01-6.32	94.92	93.68-95.99			
Men	6.64	5.21-8.32	93.36	91.68-94.79	0.007	1	0.933
Women	6.73	5.49-8.14	93.27	91.86-94.51			
Quin1	2.52	1.56-3.83	97.48	96.17-98.43	64.96	4	<0.0001
Quin2	4.44	2.80-6.64	95.56	93.36-97.20			
Quin3	10.19	7.50-13.43	89.81	86.57-92.50			
Quin4	8.52	5.82-11.94	91.48	88.06-94.18			
Quin5	13.55	10.23-17.47	86.45	82.53-89.77			
Unemployed	13.65	10.36-17.51	86.35	82.49-89.64	42.96	2	<0.0001
Employed, no nights	4.83	3.90-5.91	95.17	94.09-96.10			
Nights	9.30	6.05-13.52	90.70	86.48-93.95			
E-type	10.80	8.52-13.45	89.2	86.55-91.48	24.59	2	<0.0001
N-type	5.66	4.44-7.10	94.34	92.90-95.56			
M-type	4.47	2.99-6.40	95.53	93.60-97.08			

APPENDIX 7
THE RELATIONSHIP BETWEEN MORNINGNESS/EVENINGNESS AND USUAL SLEEP DURATION

Table 1. Usual sleep duration, by ethnicity, sex, age group, socio-economic deprivation, work status and chronotype

	<6.5hrs		**6.5-7.5hrs**		**>7.5hrs**				
	%	*95%CI*	*%*	*95%CI*	*%*	*95%CI*	*χ2*	*df*	*p*-value
Māori	19.20	16.80-21.78	45.00	41.89-48.14	35.80	32.82-38.86	66.44	2	<0.0001
non-Māori	9.4	7.31-11.84	64.46	60.74-68.06	26.14	22.87-29.61			
Men	17.67	14.91-20.71	54.74	50.96-58.48	27.59	24.29-31.07	12.32	2	0.0021
Women	13.5	11.43-15.80	51.57	48.40-54.74	34.92	31.94-37.99			
30-34yrs	23.45	19.33-27.99	39.95	35.04-45.01	36.60	31.79-41.61	23.27	6	0.0007
35-39yrs	26.52	22.23-31.15	38.64	33.82-43.63	34.85	30.16-39.77			
40-44yrs	28.99	25.10-33.12	38.72	34.48-43.08	32.30	28.27-36.53			
45-49yrs	35.51	30.71-40.53	40.99	36.02-46.10	23.50	19.34-28.07			
Quin1	10.17	7.62-13.22	59.54	55.01-63.96	30.29	26.22-34.61	33.59	8	<0.0001
Quin2	15.29	11.49-19.75	54.14	48.45-59.75	30.57	25.52-35.99			
Quin3	13.07	9.51-17.37	54.25	48.49-59.93	32.68	27.45-38.25			
Quin4	17.10	12.80-22.14	49.07	42.95-55.21	33.83	28.20-39.82			
Quin5	23.45	18.69-28.75	43.45	37.66-49.37	33.10	27.71-38.84			
Unemployed	16.80	12.38-22.02	42.40	36.20-48.79	40.80	34.65-47.17	61.61	4	<0.0001
Employed, no nights	12.42	10.63-14.38	57.18	54.37-59.95	30.40	27.85-33.05			
Night work	31.15	24.52-38.40	38.25	31.18-45.71	30.6	24.02-37.83			
E-type	16.80	12.38-22.03	42.40	36.20-48.79	40.80	34.65-47.17	5.54	4	0.2362
N-type	12.42	10.63-14.38	57.18	54.37-59.95	30.40	27.85-33.05			
M-type	31.15	24.52-38.40	38.25	31.18-45.71	30.60	24.02-37.83			

APPENDIX 8
THE RELATIONSHIP BETWEEN MORNINGNESS/EVENINGNESS AND DAYTIME SLEEPINESS

Table 1. Daytime sleepiness, by ethnicity, sex, age group, socio-economic deprivation, work status, and chronotype

	ESS ≤ 10		ESS > 10				
	%	*95%CI*	*%*	*95%CI*	*χ2*	*df*	*p*-value
Māori	83.17	80.70-85.44	16.83	14.56-19.30	19.47	1	<0.0001
non-Māori	89.30	87.60-90.84	10.70	9.16-12.40			
Men	86.82	84.60-88.83	13.18	11.17-15.40	0.0003	1	0.98
Women	86.80	84.93-88.51	13.20	11.49-15.07			
30-34yrs	88.13	85.15-90.70	11.87	9.30-14.85	5.23	3	0.16
35-39yrs	88.23	85.34-90.72	11.77	9.28-14.66			
40-44yrs	86.71	85.34-90.72	13.29	10.91-15.97			
45-49yrs	84.25	81.03-87.11	15.75	12.89-18.97			
Quin1	87.59	85.14-89.77	12.41	10.23-14.86	8.26	4	0.08
Quin2	89.34	86.26-91.94	10.66	8.06-13.74			
Quin3	87.09	83.53-90.12	12.91	9.88-16.47			
Quin4	83.87	79.53-87.61	16.13	12.39-20.47			
Quin5	83.95	79.67-87.65	16.05	12.35-20.33			
Unemployed	87.53	83.72-90.73	12.47	9.27-16.28	23.45	2	<0.0001
Employed, no nights	87.98	86.41-89.44	12.01	10.56-13.59			
Night work	76.92	71.16-82.03	23.08	17.97-28.84			
E-type	85.62	82.65-88.26	14.38	11.74-17.35	1.50	2	0.47
N-type	86.84	84.80-88.69	13.16	11.31-15.20			
M-type	87.97	85.13-90.43	12.03	9.57-14.87			

APPENDIX 9
RESPONSE CODES FOR SLEEP STUDY RECRUITMENT

10 NO CONTACT, PHONE NUMBER DISCONNECTED NO NEW CONTACT DETAILS.

11 INTERESTED IN STUDY, ATTENDED APPOINTMENT TO COMPLETE QUESTIONNAIRE AND MEDICAL CHECK

11.1 INTERESTED IN STUDY, MADE AN APPOINTMENT BUT DID NOT TURN UP

11.2 INTERESTED IN STUDY, QUESTIONNAIRE SENT TO PERSON IN THE MAIL

12 INTERESTED IN STUDY, BUT CANNOT TAKE PART DUE TO FAMILY, UNAVAILABLE BECAUSE OF WORK, SPORTS ETC...

12.1 INTERESTED IN STUDY, BUT CANNOT TAKE PART BECAUSE OF CAFFEINE, SMOKING OR ALCOHOL RESTRICTIONS.

13 INTERESTED IN STUDY, BUT CANNOT TAKE PART BECAUSE OF MEDICAL CONDITION, PHYSICAL DISABILITY

14 NOT ELIGIBLE FOR STUDY, OUTSIDE AGE RANGE FOR THIS STUDY (30-50 YEARS)

15 NOT ELIGIBLE FOR STUDY, CURRENT SHIFT WORKER

16 LANGUAGE DIFFICULTIES

APPENDIX 10
SCREENING QUESTIONNAIRE

SLEEP AND YOUR BODY CLOCK QUESTIONNAIRE.

Please read each question carefully and answer ALL of the questions in this booklet.

Please remember that all of the information you provide for this study is strictly confidential. Your name is not kept with this information and so you cannot be identified.

If you have any questions or concerns please ask a researcher.

Pre-lab questionnaire. ID..... 15/11/2006

HEALTH CHECKLIST

GENERAL

What sex are you? *(Please tick)* ☐ Male ☐ Female

What is your date of birth? ..... /..... /.....

(day) (month) (year)

How tall are you? .....metres

What is your weight? .....kg

YOUR WORK AND HOME LIFE

How many people in your household are in each of the following age groups?

0-5yrs	____	6-12yrs	____	13-18yrs	____
19-24yrs	____	25-60yrs	____	60+yrs	____

How many of these people need looking after by you?

0-5yrs	____	6-12yrs	____	13-18yrs	____
19-24yrs	____	25-60yrs	____	60+yrs	____

Have you travelled overseas in the last four weeks? 1☐ Yes 0☐No

If yes, where did you travel? ……..

Do you currently work for pay, profit or income?

☐ No *Comments welcome* →.....

☐ Yes, one paid job ☐ Yes, more than one paid job

In the last 4 weeks did you work for pay, profit or income for at least 3 hours between midnight and 5am? 1☐ Yes 0☐No

Does your work mean that you:

- **go to bed after midnight?** 1☐ Yes 0☐No
- **get up before 5am?** 1☐ Yes 0☐No
- **are unable to sleep at night?** 1☐ Yes 0☐No

Does this happen <u>more than 50 days</u> of the year? 1☐ Yes 0☐No

PREFFERED WORK TIME

Preferred work time was defined as 'time you would prefer to work in your main area of paid employment across the week, irrespective of current work patterns or any future work pattern you believe you may be expected to work'.

Please complete the table below by using a scale 1 to 10. The number represents the priority or preference allocated to WORK activities for a specific hour on a particular day of the week. Place a number in each square. The higher the number the more you would prefer to work at that time on that day.

	AM												PM											
	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11
Mon																								
Tues																								
Wed																								
Thu																								
Fri																								
Sat																								
Sun																								

PREFFERED SOCIAL TIME

Preferred social time was defined as 'time you would prefer to spend with family and friends involved in fun and entertainment, visiting friends and relations, (social clubs are included here) also eating and drinking and social life activities. This time may include children, work colleagues, partner, friends, relatives and strangers' (Argyle, 1996, p.4).

Please complete the table below by using a scale 1 to 10. The number represents the priority or preference allocated to SOCIAL ACTIVITIES for a specific hour on a particular day of the week. Place a number in each square. The higher the number the more you would prefer to socialise at that time on that day.

	AM												**PM**											
	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11
Mon																								
Tues																								
Wed																								
Thu																								
Fri																								
Sat																								
Sun																								

PREFERRED SLEEP TIME

Preferred sleep time is defined as 'the time you would prefer to spend asleep irrespective of your current work pattern'.

Please complete the table below by using a scale 1 to 10. The number represents the priority or preference allocated to SLEEP for a specific hour on a particular day of the week. Place a number in each square. The higher the number the more you would prefer to sleep at that time on that day.

	AM												PM											
	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11
Mon																								
Tues																								
Wed																								
Thu																								
Fri																								
Sat																								
Sun																								

Please list the average amount of **caffeine** you consume per day. (For example, how many cups of tea/coffee, cans of caffeinated soft drink and chocolate bars would you have in one day).

.....

.....

SMOKING

Do you describe yourself as a:

1☐ Regular smoker
(I smoke one or more cigarettes per day)

2☐ Occasional smoker
(I do not smoke every day)

3☐ Ex-smoker
(I used to smoke but not any more)

4☐ Non-smoker
(I have never smoked regularly)

ALCOHOL

How often do you drink alcohol?

0☐ Never 1☐ Less than once per week 2☐ Once or twice per week 3☐ Once every 2 days 4☐ Daily

On a typical drinking occasion, how many drinks do you have? (One drink equals a glass of beer, a glass of wine or a nip of spirits).

0☐ None 1☐ Less than 2 drinks 2☐ 2-4 drinks 3☐ 5-6 drinks 4☐ More than 6 drinks

STRESS

Are you currently experiencing a greater than your normal amount of stress? (e.g. a sick relative, relationship break-up, getting married, etc.) 1☐ Yes 0☐No

Do you have any academic or other test scheduled for one week before and during the study? 1☐ Yes 0☐No

In general, would you say your health is?

0☐Excellent 1☐Very good 2☐Good 3☐Fair 4☐Poor

How do you rate yourself on the following? PLEASE TICK ONE BOX ON EACH LINE

	Poor	Fair	Good	Excellent
Your ability to concentrate	0☐	1☐	2☐	3☐
Your ability to get things done	0☐	1☐	2☐	3☐
Your ability to cope with minor problems	0☐	1☐	2☐	3☐
Your relationship with family / friends	0☐	1☐	2☐	3☐
Your physical wellness	0☐	1☐	2☐	3☐
Your general quality of life	0☐	1☐	2☐	3☐

How often do you have trouble remembering things?

0☐ Never 1☐ Rarely 2☐ Often 3☐ Always

SLEEP

Do you <u>normally</u> take a nap during the day? 1☐ Yes 0☐No

If yes:

How often do you take naps? (e.g. once a day, two times per week) _____

Please tell us why you take naps (e.g. because I work late at night/ I get up early to get the children ready for school etc.)

_____

_____

Have you ever been diagnosed with a sleeping problem? 1☐ Yes 0☐No

If yes, please describe

.....

.....

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times.

PLEASE TICK ONE BOX PER LINE

	Would never doze	Slight chance	Moderate chance	High chance
Sitting and reading	0☐	1☐	2☐	3☐
Watching TV	0☐	1☐	2☐	3☐
Sitting inactive in a public place (e.g. theatre, meeting)	0☐	1☐	2☐	3☐
As a passenger in a car for an hour without a break	0☐	1☐	2☐	3☐
Lying down in the afternoon when circumstances permit	0☐	1☐	2☐	3☐
Sitting and talking to someone	0☐	1☐	2☐	3☐
Sitting quietly after a lunch <u>without</u> alcohol	0☐	1☐	2☐	3☐
In a car, while stopped for a few minutes in traffic	0☐	1☐	2☐	3☐

GENERAL HEALTH (please use the back of this sheet if you require more space.

Have you had any serious accidents, head injuries, or concussion? 1☐ Yes 0☐No

Are you currently on any medication?

(prescription or over the counter) 1☐ Yes 0☐No

If so, what medication? .....

Have you been on any medication in the past week? 1☐ Yes 0☐No
(prescription or over the counter)

If so, what medication? .....

Do you currently have any physical illness? 1☐ Yes 0☐No

If yes, what illness(es)? .....

Do you have any personal or family history of epilepsy, or other neurological disorders?
(e.g. migraines) 1☐ Yes 0☐No

If yes, what disorders? .....

Do you have any personal or family history of respiratory problems?

(e.g. asthma, allergies, bronchitis) 1☐ Yes 0☐No

If so, what illness(es)? .....

Do you have any personal or family history of a mental illness? 1☐ Yes 0☐No

If so, what illness(es)? .....

INSTRUCTIONS:

The following questions relate to your usual sleep habits during the past month *only*. Your answers should indicate the most accurate reply for the *majority* of days and nights in the past month. **Please answer all questions.**

1. During the past month, when have you usually gone to bed at night?

USUAL BED TIME _____

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?

NUMBER OF MINUTES _____

3. During the past month, when have you usually gotten up in the morning?

USUAL GETTING UP TIME _____

4. During the past month, how many hours of *actual sleep* did you get at night? (this may be different than the number of hours you spend in bed.)

HOURS OF SLEEP PER NIGHT _____

For the remaining questions, check the one best response. **Please answer *all* questions.**

5. During the past month, how often have you had trouble sleeping because you……

a) Cannot get to sleep within 30 minutes

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

b) Wake up in the middle of the night or early morning

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

c) Have to get up to use the bathroom

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

d) Cannot breathe comfortably

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

e) Cough or snore loudly

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

f) Feel too cold

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

g) Feel too hot

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

h) Had bad dreams

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

i) Have pain

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

j) Other reason(s), please describe _____

_____

_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

6. During the past month, how would you rate your sleep quality overall?

Very good 0☐	Fairly good 1☐	Fairly bad 2☐	Very bad 3☐

7. During the past month, how often have taken medicine (prescribed or "over the counter") to help you sleep?

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month 0☐	Less than once a week 1☐	Once or twice a week 2☐	Three or more times a week 3☐

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all 0☐	Only a very slight problem 1☐	Somewhat of a big problem 2☐	A very big problem 3☐

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you **over the past week**. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:
0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

		Please circle			
1)	**I found it hard to wind down**	0	1	2	3
2)	**I was aware of dryness of my mouth**	0	1	2	3
3)	**I couldn't seem to experience any positive feeling at all**	0	1	2	3
4)	**I experienced breathing difficulty** (e.g. excessively rapid breathing, breathless ness in the absence of physical exertion)	0	1	2	3
5)	**I found it difficult to work up the initiative to do things**	0	1	2	3
6)	**I tended to over-react to situations**	0	1	2	3
7)	**I experienced trembling (e.g. in the hands)**	0	1	2	3
8)	**I felt that I was using a lot of nervous energy**	0	1	2	3
9)	**I was worried about situations in which I might panic and make a fool of myself.**	0	1	2	3
10)	**I felt that I had nothing to look forward to**	0	1	2	3
11)	**I found myself getting agitated**	0	1	2	3
12)	**I found it difficult to relax**	0	1	2	3
13)	**I felt down-hearted and blue**	0	1	2	3
14)	**I was intolerant of anything that kept me from getting on with what I was doing**	0	1	2	3
15)	**I felt I was close to panic**	0	1	2	3
16)	**I was unable to become enthusiastic about anything**	0	1	2	3
17)	**I felt I wasn't worth much as a person**	0	1	2	3
18)	**I felt that I was rather touchy**	0	1	2	3
19)	**I was aware of the action of my heart in the absence of physical exertion** (e.g. sense of heart rate increase, heart missing a beat)	0	1	2	3
20)	**I felt scare without any good reason**	0	1	2	3
21)	**I felt that life was meaningless**	0	1	2	3

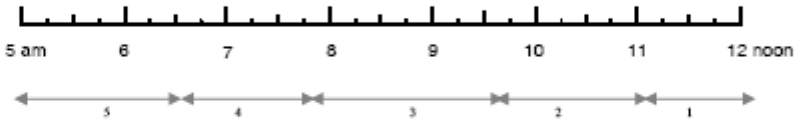
Please answer the following questions in order.
Do not go back and check or change your answers.

What time of day do you like to sleep?

Imagine that you are completely free to plan your day. Think only about what feels best for you.

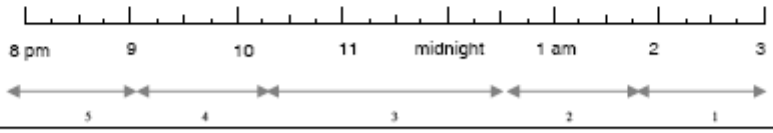
1. What time of day would you get up?

Please put a cross at the time closest to your best time.



2. What time of day would you go to bed?

Please put a cross at the time closest to your best time.



Waking Up In The Morning

3. You have to get up at a particular time in the morning. How much do you need to depend on the alarm clock to wake you up? *Please tick the box that applies to you.*

4 ☐ Not at all dependent 3 ☐ Slightly dependent 2 ☐ Fairly dependent 1 ☐ Very dependent

4. If nothing is disturbing you (noise, light etc), how easy do you find it to get up in the morning?

1 ☐ Not at all easy 2 ☐ Not very easy 3 ☐ Fairly easy 4 ☐ Very easy

5. How alert do you feel in the first half hour after waking up in the morning?

1 ☐ Not at all alert 2 ☐ Slightly alert 3 ☐ Fairly alert 4 ☐ Very alert

6. How is your appetite in the first half hour after waking up in the morning?

1 ☐ Very poor 2 ☐ Fairly poor 3 ☐ Fairly good 4 ☐ Very good

7. How tired do you feel in the first half hour after waking up in the morning?
Please tick the box that applies to you.

1 ☐ Very tired 2 ☐ Fairly tired 3 ☐ Fairly refreshed 4 ☐ Very refreshed

8. When there is nothing that you have to do tomorrow, what time do you go to bed, compared to your usual bedtime? *Please tick the box that applies to you*

4 ☐ Seldom or never later 3 ☐ Less than 1 hour later 2 ☐ 1-2 hours later 1 ☐ More than 2 hours later

9. You and a friend have decided to do some physical exercise.
- **Your friend wants to train twice a week from 7-8 am**
- **How well do you think you would perform at this time?**

Please tick the box that applies to you

4 ☐ Would be on good form 3 ☐ Would be on reasonable form 2 ☐ Would find it difficult 1 ☐ Would find it very difficult

10. What time in the evening do you start to feel tired and in need of sleep?

Please put a cross at the time that suits you best.

11. You want to do your best on an exhausting mental test that lasts 2 hours. Which one of these 4 test times would suit you best? *Please tick the box that is closest to your best time.*

6 ☐ 8-10am 4 ☐ 11am–1pm 2 ☐ 3-5pm 0 ☐ 7-9pm

12. If you went to bed at 11 pm, how tired would you normally be at that time?

Please tick the box that applies to you

0 ☐ Not at all tired 2 ☐ A little tired 3 ☐ Fairly tired 5 ☐ Very tired

13. If you go to bed a few hours later than usual, but don't have to get up at any special time in the morning, what is most likely to happen? *Please tick the box that applies to you*

4 ☐ I wake up at the usual time and do not fall back to sleep 3 ☐ I wake up at the usual time, then doze 2 ☐ I wake up at the usual time, then fall back to sleep 1 ☐ I do not wake up until later than usual

14. Imagine that you have to be at work, and stay alert, between 4-6 am. You don't have anything in particular to do the next day. Which of these strategies would suit you best? *Please tick the box that applies to you*

1 ☐ I would not go to bed until work was over	2 ☐ I would take a nap before work, then sleep after	3 ☐ I would take a good sleep before work, then nap after	4 ☐ I would take all my sleep before work

15. You have to do 2 hours of hard physical work. You are completely free to plan your day. When would you choose to do this work? *Please tick the box that is closest to your best time.*

4 ☐ 8-10 am	3 ☐ 11 am – 1 pm	2 ☐ 3-5 pm	1 ☐ 7-9 pm

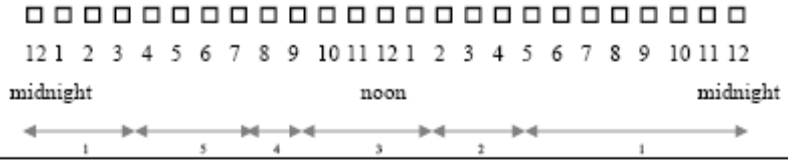
16. You and a friend have decided to do some physical exercise.

- **Your friend wants to train between <u>10-11 pm</u>**
- **How well do you think you would perform at this time?**

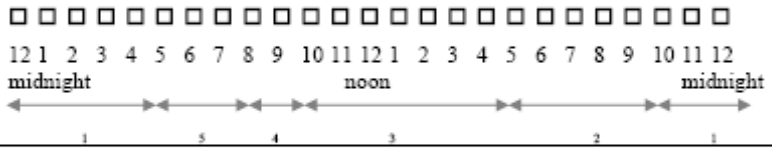
Please tick the box that applies to you

1 ☐ Would be on good form	2 ☐ Would be on reasonable form	3 ☐ Would find it difficult	4 ☐ Would find it very difficult

17. Imagine you can choose your own work hours. You have to work for 5 hours a day (including breaks). Your job is interesting, and you get paid for the amount of work you do. Which 5 hours <u>in a row</u> would you choose to work? *Please tick 6 boxes for the time that suits you best.*



18. At what time of day do you feel your best? *Please tick 1 box to indicate your best time.*



19. You hear about "morning types" and "evening types". Which of the following types do you think you are? *Please tick the box that applies to you*

6 ☐ Definitely a morning type	4 ☐ More a morning type than an evening type	2 ☐ More an evening type than a morning type	0 ☐ Definitely an evening type

If you are selected for this study you will be required to come to the Sleep/Wake Research Centre and stay overnight. This visit will be on a SATURDAY NIGHT.

- We will try and accommodate your other commitments as much as possible.
- Please indicate the weekends when you would be available to take part in the study.

Please note that the final date for taking part in this study will be

SATURDAY 26TH NOVEMBER

PLEASE INDICATE ALL WEEKENDS THAT YOU WOULD BE AVAILABLE.

Date	Yes, I'm available (please tick)
Saturday 15th – Sunday 16th October	
Saturday 29th – Sunday 30th October	
Saturday 5th – Sunday 6th November	
Saturday 12th – Sunday 13th November	
Saturday 19th – Sunday 20th November	
Saturday 26th – Sunday 27th November	

Sarah-Jane Paine will contact you to confirm your study date. Please leave your contact details below.

Name: _____

Address: _____

_____

Telephone number: _____ (home)

_____ (work)

_____ (mobile)

E-mail: _____

THANK-YOU FOR COMPLETING THIS QUESTIONNAIRE.

APPENDIX 11
TEMPLATE FOR THE MEDICAL EXAMINATION

MEDICAL EXAMINATION CHECKLIST

Doctor: _____

Date: _____

PATIENT DETAILS

ID number: …….. **Age:** …….. **Sex:** M or F

Weight (kg): …….. **Height** (cm): ……..

MEDICAL HISTORY

List medical conditions (e.g. Asthma, HTN, heart disease, thyroid, renal, DM, DVT, PE, CVA, cancer, previous surgery):

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

Specifically:

☐ Depression/psychiatric ☐ Epilepsy ☐ Sleep apnoea /Narcolepsy/Insomnia

☐ Migraine ☐ Fibromyalgia ☐ Recreational drug use

Did the participant say YES to any of the above? ☐ **yes** ☐ **no**

If YES, please advise participant that because of their condition they may not be able to take part in the study

Comments_____

_____

_____

_____

MEDICATIONS

List regular medications:

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

Specifically:

☐ Antidepressants ☐ Beta blockers ☐ sedating antihistamines

Did the participant say YES to any of the above? ☐ yes ☐ no

If YES, please advise participant that they may not be able to take part in the study due to their regular medications.

List pain relief (non-regular) and OTC preparations:

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

Specifically:

☐ Codeine (e.g. in OTC cold medications) ☐ Melatonin

☐ Pseudoephedrine (e.g. in OTC cold medications)

Did the participant say YES to any of the above? ☐ yes ☐ no

If YES, please advise participant that OTCs containing codeine, caffeine or psuedoephedrine cannot be taken during the study

Comments_____

_____

_____

_____

List any allergies or reactions to drugs:

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

FAMILY HISTORY

_____
_____
_____
_____

SOCIAL HISTORY (incl. Smoking, EtOH, occupation, living situation. dependants)

_____
_____
_____
_____

REVIEW OF SYSTEMS

General:

☐ appetite ☐ weight ☐ fevers/night sweats ☐ recent cold/ infection

Respiratory:

☐ cough ☐ sputum ☐ wheeze ☐ SOB

☐ exercise tolerance

CVS:

☐ chest pain ☐ palpitations ☐ dizziness ☐ orthopnoea

☐ claudication

Abdominal:

☐ nausea/vomiting ☐ indigestion ☐ abdo. pain

☐ nature and frequency of bowels

Urinary:

☐ frequency ☐ dysuria ☐ nocturia ☐ stress-urge

☐ UTI

Gynaecological:

☐ any menstrual cycle problems ☐ pregnant ☐ nursing

Neurological:

☐ vision ☐ hearing ☐ headache

☐ numbness and/or weakness in arms/legs

Comments_____

_____

_____

EXAMINATION (may require Chaperone)

Cardiovascular:

☐ Pulses ☐ BP ☐ Oedema

☐ JVP ☐ Heart sounds ☐ Heart rate/rhythm

Comments_____

_____

_____

Respiratory:

☐ Resp. Rate ☐ Percussion ☐ Breath Sounds

☐ Added sounds

Comments_____

_____

_____

Gastrointestinal:

☐ Softness ☐ Tenderness ☐ Masses

☐ Organomegaly ☐ Bowel Sounds ☐ Scars

Comments_____

_____

_____

Neurological:

☐ Cranial nerves ☐ Upper limb: tone / power / reflexes

☐ Lower limb: tone / power / reflexes ☐ Gait

Comments_____

_____

_____

Mental Status Examination:

☐ alert ☐ orientated ☐ attention ☐ memory

☐ mood ☐ affect ☐ insight

Comments_____

_____

_____

Consent to Release Information

I……

Date of Birth……

Give consent for the medical information gathered about me by

……..to be released to:

- Other health professionals (including my General Practitioner and specialists)

Name: _____

Address: _____

_____

_____

- Other

Name: _____

Address: _____

_____

_____

And to the release of my medical information from my family doctor and specialists

to……..

Signed……..

Date……..

APPENDIX 12
THE RESULTS FROM THE SCREENING PROCESS

Of the 523 morning- and evening-type individuals who indicated their willingness to take part in the studies of sleep timing and circadian phase, a total of 358 individuals (134 E-types and 224 M-types) met the initial study inclusion criteria (30-49yrs of age, and not currently involved in shift work) and were eligible for further screening. Of this group, 243 individuals were able to be contacted by the RA and were verbally invited to take part in the screening process (Table 1).

Table 1. The number of participants contacted to take part in the sleep studies

	Whole group		E-types		M-types	
	n	**%**	**n**	**%**	**n**	**%**
Contacted	243	67.88	95	26.54	148	41.34
Not contacted	115	32.12	39	10.89	76	21.23
Total	358	100.00	134	37.43	224	62.57

Table 2 summarises the acceptance rate for the entire contact group. Approximately 45% of the contact group did not take part in the screening process. Reasons for this varied but can be broadly categorised as follows:

- Not available/eligible (n=66). The main reasons why individuals were not available or eligible to attend the screening sessions were family, work and sporting commitments (n=32); outside the age range (30-49yrs) at the time of contact (n=20); current medical condition or physical disability preventing their ability to take part in the study (n=9); currently involved in night work (n=4); and a perceived inability to refrain from smoking, drinking alcohol or taking caffeine as required by the study protocol (n=1).
- Not interested (n=10; no reason given).
- No response (n=34; participants requested a screening questionnaire be sent to them by post, but did not complete and return it to the research team).

Of those who attended a Saturday morning screening session (the *screening* group, N=133), 10 individuals did not complete the screening process.

Table 2. Results of the screening process for the whole group and by chronotype

	Whole group		M-types		E-types	
	n	*%*	*n*	*%*	*n*	*%*
Consenting participants						
Not contacted	115	32.12	76	21.23	39	10.89
Contacted	243	67.88	164	45.81	95	26.54
Contact group						
Not available/eligible	66	27.16	41	16.87	25	10.29
Not interested	10	4.12	6	2.47	4	1.65
No response	34	13.99	34	13.99	16	6.58
Attended screening session	133	54.73	83	34.16	50	20.58
Screening group						
Did not complete screening	10	7.52	6	4.51	4	3.01
Accepted						
Passed screening but no response	3	2.26	2	1.50	1	0.75
Passed screening and completed full study	32	24.06	16	12.03	16	12.03
Passed screening but did not complete full study	3	2.26	3	2.26	0	0.00
Declined						
Passed questionnaire, failed medical	14	10.53	10	7.52	4	3.01
Failed questionnaire, passed medical	21	15.79	12	9.02	9	6.77
Failed questionnaire and medical	9	6.77	5	3.76	4	3.01
Failed questionnaire, no medical	41	30.83	29	21.80	12	9.02

Approximately 64% of the attending group (n=85) failed to meet the study inclusion criteria. The high rate of failure during the screening process was of particular concern to the research team, and therefore the possible reasons for this were further investigated.

Thirty-two individuals were not permitted into the study because their scores on the MEQ completed as part of the screening process fell within the neither-type range. Sixteen individuals were not recommended to take part in the full study protocol as a result of their medical examination. Of those remaining, 27 individuals scored as mild, moderate, severe or extremely severe on one or more of the scales used in the DASS-21. Finally, 13 individuals from the attending group were not invited into the full study on the basis of the combined information gathered during the screening process.

On the other hand, 38 individuals met the requirements of the study and were invited to take part in the full study protocol. However, of this group three individuals did not respond to the invitation and a further three individuals did not begin the protocol due to unforeseen illness. Thus, a total of 32 individuals took part in the study.

APPENDIX 13
INSTRUCTIONS ON HOW TO USE THE ACTIWATCH AND SLEEP DIARY

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai

Massey University

SLEEP AND YOUR BODY CLOCK

Actiwatch and sleep diary instructions

The small watch-sized object you are about to put on your wrist is an actiwatch. It is designed to sense movement through a small accelerometer. The recorded movements are downloaded onto a PC at a later date.

The data from the actiwatch is analysed in conjunction with the information from the sleep diary to determine sleep length and sleep quality.

Information about wearing the actiwatch:

- Wear the watch on your non-dominant wrist (the hand you don't write with)
- It is important that you do not change wrists as this may change the information that we get from the watch
- Place the watch on your wrist with the event marker closest to your thumb.
- Wear the watch with the face on the outside of your wrist. It should be attached reasonable firmly so that it does not move about on your wrist. If it does move about tighten the strap slightly.
- The watch is water-resistant, not waterproof, so please do not wear it in the bath/shower or swimming. This means you will need to take it off, but please try to remember to put it back on again.
- If you take the watch off for any reason (to shower, swim etc...) then please note in your diary the times that you took the watch off and put it back on again.
- It is not uncommon for people to take the actiwatch off and forget to put it back on again after having a shower. If this happens, please put the watch on again as soon as you remember and note in your diary when you put the watch back on.
- Please note that we can not tell what you are doing from the actiwatch data. We can only tell whether you are moving or not.
- On the face of the watch is a small indentation. This is called the EVENT MARKER. If you push this a small mark will appear on the data output. It

does not stop the watch. The watch will keep going the entire time you are wearing it.

- We would like you to push the event marker when you start trying to sleep and again when you stop trying to sleep. Please do this whenever you intend to sleep for **10 minutes or longer.**

Information about filling out the sleep diary.

- The sleep diary is set out so that each line represents 24 hours, from midnight to midnight in one day
- Please write the date for each day beside the start of the line
- We are interested in **any** sleep that is 10 minutes or longer. It does not matter whether this is during the day or during the night.
- The information that is essential to us is the times that you **begin trying to sleep and the times when you finished trying to sleep.**
- **BGN** is the time when you begin trying to sleep. Some people may get into bed and read etc, but we do not need to know this, we only need to know when you begin trying to sleep.
- **FSH** is the time when you wake up and are no-longer trying to sleep. At this time you may either get out of bed, or begin reading etc, but you are no longer trying to sleep.
- Please place a mark on the line at each of these times and then write the abbreviations underneath what the line relates to (i.e. **BGN** and **FSH**). These abbreviations can be found on the top of each page of your diary.
- Please remember to push the event marker when you being trying to sleep and again when you finish trying to sleep.

On the night before you come to the Sleep/Wake Research Centre (**Friday night**) we would like you to call us (ph. 801 5799 x 6039) and leave a message when you begin trying to sleep and again when you wake up **(Saturday morning).**
This is gives us an extra measure of what your sleep is like before you come to stay overnight in our isolation facility.

ID #:_____
6039

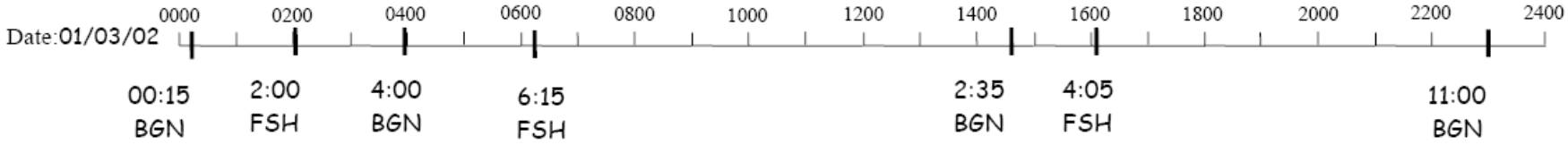
For enquiries contact Sarah-Jane Paine (04) 801-5799 extn.

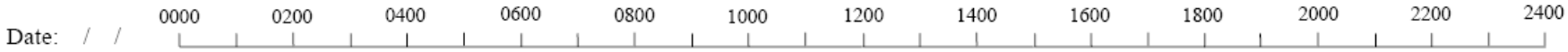
SLEEP LOG

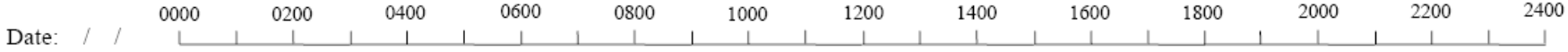
Each line represents 24 hours from midnight one day to midnight the following day
Please enter on each line:

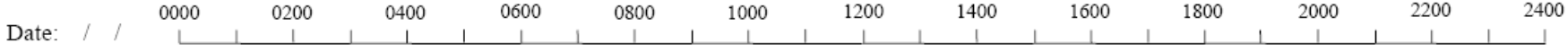
1. When you begin trying to sleep **(BGN)** and finished trying to sleep **(FSH)** for any sleep **10 minutes or longer** (including minutes)
2. Times you have taken the watch off (OFF).
3. Please **push the event marker** on the watch **only** when you begin trying to sleep and finish trying to sleep.

This line gives you an example on how to fill out the log. Carry sleep time over to the next line if necessary.









APPENDIX 15
RADIOIMMUNOASSAY FOR THE DETECTION OF MELATONIN IN HUMAN SALIVA

Salivary melatonin was assessed from saliva samples collected by gently chewing on polyester swab salivettes for 2 min (Sarstedt, Numbrecht, Germany). Samples were centrifuged and stored frozen until delivery to the Department of Obstetrics and Gynaecology, The University of Adelaide, Australia.

APPENDIX 16
STUDY PACK FOR SLEEP STUDIES

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai

Massey University

SLEEP AND YOUR BODY CLOCK.
Participant information sheet

You are invited to take part in a study to investigate how much your body clock affects your preferred sleep timing. This study is being conducted by researchers from the Sleep/Wake Research Centre, Massey University.

The aims of the study:

- To collect and compare data on the quantity and quality of sleep in two groups of people: those who report that they are - "morning types", and people who are "evening-types".
- To determine whether morning-types go to sleep earlier and wake earlier in the morning, during their usual daily lives, compared to evening-types.
- To see whether the circadian clock is advanced in morning-types compared to evening-types.

Who are we looking for?

- We are looking for 60 participants who match the following criteria:
  (1) The questionnaire answers show a morning- type person or an evening-type person.
  (2) Aged between 30-50 years
  (3) Not involved in shift work.

What is involved if you are interested in taking part?

If you decide that you would like to be in the study you will be asked to:

- Complete a brief questionnaire about your general health and lifestyle.
- You may need to undergo a medical examination with a physician. It is possible that staying awake all night may effect some pre-existing medical conditions.

If you are selected for the full study, you will be asked to :

- Come to the Sleep/Wake Research Centre (SWRC), 102 Adelaide Road, Newtown, to meet with a member of the research team to discuss the procedures involved in the study.
- Wear a small watch-sized activity monitor and complete a sleep diary for 14 days.
- Come to the SWRC on a SATURDAY and **stay overnight**.
- Provide a urine sample to screen for medications/drugs that may interfere or disguise your normal sleeping patterns.
- It is important to us that if you decide to take part, that you are able to participate in both parts of the study. We will make every effort to accommodate you and your other commitments.

Even if you are not selected for the full study, your questionnaire information is valuable to us and will be useful when describing the study. **Please remember that none of the data collected will have your name recorded on it**.

The following information explains what will happen during each part of the study.

PART I:

- A member of the research team will contact you and arrange to meet with you at the Sleep/Wake Research Centre. Transportation will be provided if necessary.
- During this first meeting Ms. Paine will explain each part of the study as well as the procedures that we will use to investigate your sleeping patterns. You will be asked to fill out a questionnaire about your general health and lifestyle. A medical physician will also conduct a physical examination during this meeting.
- Ms. Paine will explain the activity monitor (Actiwatch™) and sleep diary and give you one to take away with you. The Actiwatch is the same size as a watch and is worn on your non-dominant wrist. The sleep diary is filled out by you, to help us know when you have gone to sleep and woken up again. Together, the activity monitor and sleep diary give information on when you are sleeping, how long you are sleeping, and the quality of each sleep period.
- You will wear the Actiwatch and fill out the sleep diary for 14 days in a row. The first day that you wear the activity monitor will be a SATURDAY.
- On the last night that you wear the Actiwatch we will ask you to call the SWRC when you go to bed and call again when you wake up the next morning.

PART II:

- After wearing the Actiwatch for 14 days you will come to the SWRC to take part in the next part of the study. This will happen on a SATURDAY. Ms. Paine will meet with you and explain the procedures to you.
- You will be required to provide a urine sample when you arrive at the SWRC. It is important to us that we screen for drugs/medication that may interfere or disguise your sleep. All of the samples will be sent to the Institute for Environmental Sciences and Research (ESR), Porirua to be analysed. **Please be assured that the results of the screening test WILL remain CONFIDENTIAL. This information WILL NOT have your name on it and WILL NOT be shared with anyone else.**
- The SWRC has a room where we can control the light, temperature and noise. This room has 3 hospital-style beds, and each bed is separated by screens for your comfort and privacy. This study requires you to remain in a bed from 5pm on Saturday until approximately 10am on Sunday morning. You will not be able to get out of bed and move around during this time except to use the bathroom.
- Every 30 minutes Ms. Paine will collect a saliva sample from you. To do this you will be asked to chew on a cotton ball for 2 minutes and then put it into a container. Your samples will be stored in a freezer at the SWRC until they are analysed.
- You will not be allowed to sleep during this part of the study. You may experience some discomfort and extreme sleepiness at certain times during the night. Please be aware that you will not feel like this all night and you will probably find that you feel better early Saturday evening and again on Sunday morning.
- We are also interested in how your alertness changes across the night and so each hour you will need to perform a short reaction time exercise.
- Certain foods and liquids are not allowed to be consumed on this day. Ms. Paine will let you know in advance what these are. While at the SWRC your snacks and meals will be provided.
- While you are at the SWRC all of your entertainment will be provided including DVD movies, board/card games, Xbox games and music. You are welcome to bring some items with you to the SWRC, however please be aware that you need to check these items with the researcher on your arrival, as some items may not be permitted.
- At the end of the study you will be able to stay and sleep at the SWRC if you would like. We have shower facilities available and will provide you with clean towels to use.
- All participants will be provided with transport home again on Sunday.

- Analysis of your saliva samples will be carried out at the Circadian Physiology Laboratory, at the University of Adelaide, Australia. All of your samples will be transported to the laboratory where they will be analysed to detect how much melatonin is being produced in your body during the night. Melatonin is a hormone which is naturally produced in your brain. Melatonin is only produced at night time and therefore it is believed to have a relationship with your sleeping patterns.

Risks and benefits

- **None of the data collected will have your name recorded on it.** Instead it will have a code number. No material which could personally identify you will be used in any reports on the study.
- There are no personal risks involved in the activity monitor and it will not detect any medical disorders.
- You may find it difficult to provide a saliva sample every 30 minutes for an entire night. We will provide water and orange juice for your comfort; however there are some rules as to when you can drink these.
- You may find it difficult staying awake while at the Sleep/Wake Research Centre, however we will provide a DVD player, music and games for your entertainment.

What are the outcomes of the study?

- This is an opportunity for you to learn about sleep and how varied sleep can be. If you take part in the full study you will be shown your own sleep data.
- You will receive a summary of the findings of the study and have access to a copy of the final report.
- These findings will also be presented in the PhD thesis of Ms. Paine.
- Information from these studies will be described and submitted for publication in international sleep and biological rhythm journals.
- We envisage that there will be widespread interest in this study and so information from this study will be available to the media. **Please remember that none of the data collected will have your name recorded on it**.

What are my rights?

You have the right to:

- Decline to participate;
- Decline to answer any particular question;
- Withdraw from the study at any time;
- Ask any questions about the study at any time during participation;
- Provide information on the understanding that none of your data will have your name on it (an ID number is used instead), and you will not be identified in any reports on the study;
- Have any of your personal data handed back to you;
- Be given access to a summary of the study findings when it is concluded.

Project Contacts

- The researchers responsible for this study are Ms. Sarah-Jane Paine and Professor Philippa Gander.
- If you have any further questions about this study please do not hesitate to contact any of these individuals at the address or phone number below.

Important points

- This project has been reviewed and approved by the Massey University Human Ethics Committee, WGTN Protocol 04/31. If you have any concerns about the conduct of this research, please contact the following person:

  Professor Sylvia Rumball
  Chair
  Massey University Campus Human Ethics Committee
  Wellington,
  Telephone: (06) 350 5249
  E-mail: humanethicswn@massey.ac.nz

- Although we do not believe that you are at risk of injury or harm by being part of this study it is important that you are aware that if physical injury results from your participation in this study, you should visit a treatment provider to make a claim to ACC as soon as possible. In the unlikely event that your ACC claim is not accepted you should contact the researcher.
- Because you are required to stay awake all night while at the SWRC we advise that you do not drive home after the study. Instead, you will be provided with a taxi to travel to and from the Sleep/Wake Research Centre, or you may organise for a friend or relative to drop you off and pick you up again.

What do I do now?

- Please read and complete the consent form. If you have any questions or would like to discuss the study further please do not hesitate to contact one of the researchers listed below.
- Please complete the questionnaire and send it back along with your consent form in the envelope provided.

Thank you for taking the time to consider being involved in the study. Any of the following members of the research team would be happy to answer questions you may have about this study.

Researchers:

Ms. Sarah-Jane Paine
PhD Student
Ph: 801 5799 ext. 6039

Professor Philippa Gander
Director
Ph: 801 5799 ext 6033

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai

Massey University

SLEEP AND YOUR BODY CLOCK

CONSENT FORM

This consent form will be retained for a period of five (5) years.

- I have read and I understand the information sheet dated 22 March 2005 for volunteers taking part in the study designed to intensively follow my sleep patterns. I understand that I may undergo a medical examination with a physician, and that if I am selected I will be required to undergo a urine drug/medication test.
- I have had the opportunity to discuss this study. I am satisfied with the answers I have been given, and understand that I may ask further questions at any time.
- I understand that participation in this study is voluntary and that I may withdraw from the study at any time.
- I understand that participation in this study is confidential and that no material, which could identify me, will be used in any reports on this study.
- I understand that I can have any of my personal data handed back to me.
- I have had sufficient time to consider whether to take part.
- I know whom to contact if I have any questions about the study.

Signature: _____ **Date:** _____

Full Name - printed _____

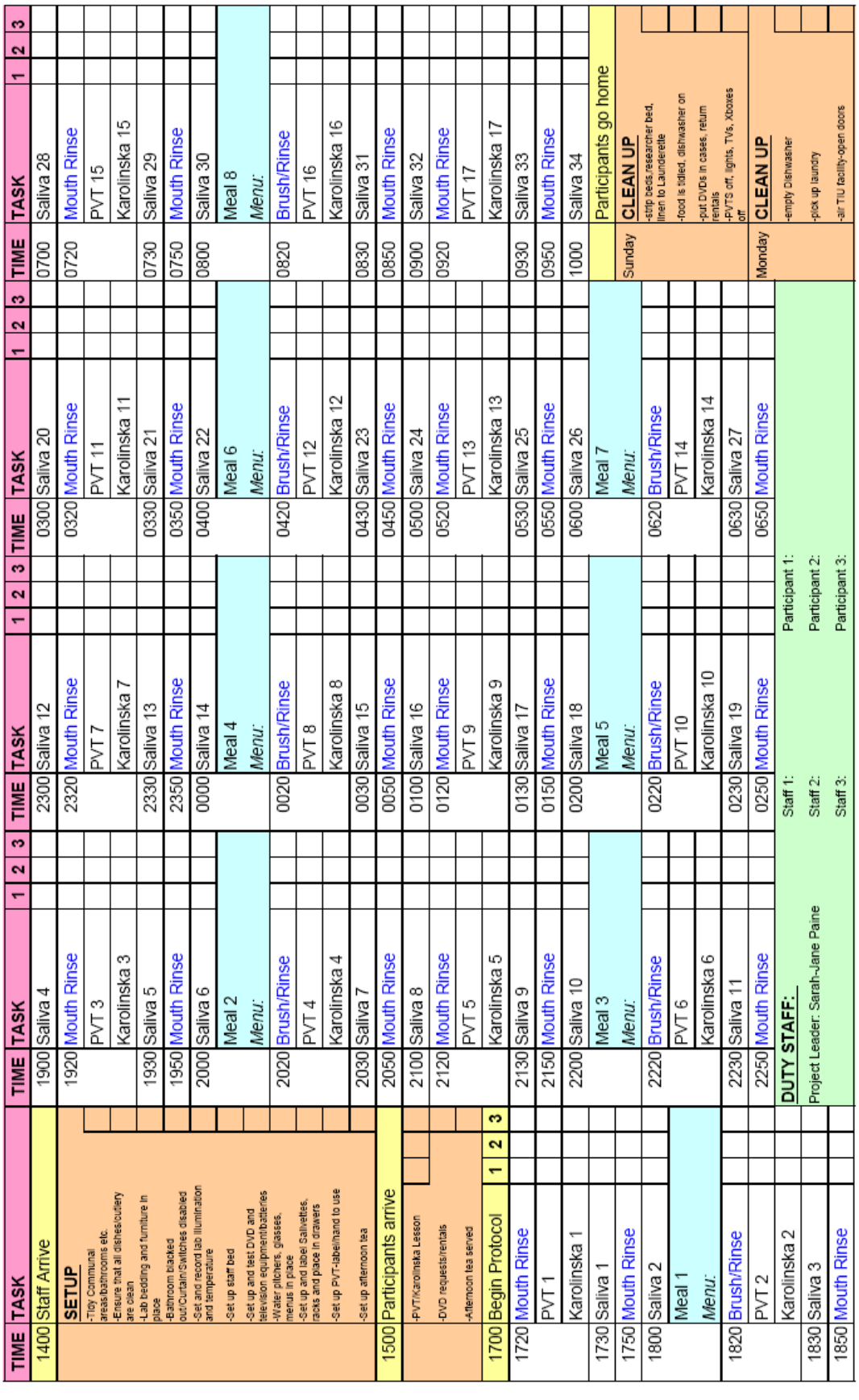
Researchers:	Sarah-Jane Paine	Philippa Gander
Contact phone number:	801 5799 x 6039	801 5799 x 6033

APPENDIX 17
THE KAROLINSKA SLEEPINESS SCALE

How do you feel at this moment?	
1	Extremely alert
2	
3	Alert
4	
5	Neither sleepy nor alert
6	
7	Sleepy, but no difficulty remaining awake
8	
9	Extremely sleepy, fighting sleep

Please circle <u>one number</u> that best describes how you feel right now.

APPENDIX 18
CONSTANT ROUTINE PROTOCOL



APPENDIX 19
PROTOCOL FOR DETERMINING BED TIME AND GET UP TIME IN ACTIGRAPHY

A set of rules were developed for determining bed time and get up time in the Actiware-Sleep software, which are summarised in the table below. For example, if the event marker (EM) was pressed, and the bed time was confirmed by actigraphy (AD), but the sleep diary (SD) was not completed, then the information from the event marker and the actiwatch was used to set bed time. Similarly, if the event marker was missing, but a sleep diary time was given that matched the actigraphy data, then bed time was set using AD and SD.

EVENT MARKER (EM)	ACTIGRAPHY DATA (AD)	SLEEP DIARY (SD)	BED TIME & GET-UP TIME CALCULATED USING…	REASON
√	√	X	EM and AD	• Sleep diary may have been completed retrospectively
X	√	√	AD and SD	• EM pressed in anticipation of Bed Time • EM not pressed at Bed Time but pressed on awakening • EM pressed at earlier awakening and then participant gone back to sleep • EM forgotten at awakening but pressed at later time
√	X	√	EM and SD	• Could be caused by restless sleep or still wakefulness
X	√	X	AD only	• AD alone used if the EM and SD are discrepant or missing
X	X	√	SD only	• SD alone used if the changes in AD not clear and EM not used
X	X	X	AD only	• If EM, AD and SD are discrepant then AD alone used
• *Note.* Adapted from Signal et al. (2004)				

APPENDIX 20
POST-HOC TESTS OF SLEEP TIMING

Table 1. Estimated mean Bed Time by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean bed time	Significant post-hoc tests for chronotype by weekdays/weekends	Estimated difference (hours) between bed times
M-type	Weekday	22:29	$t_{(382)} = 3.39$, p=0.0008	0.41
	Weekend	22:53		
E-type	Weekday	23:33	$t_{(383)} = 3.52$, p=0.0005	0.44
	Weekend	23:59		
M-type	Weekday	22:29	$t_{(30)} = 5.05$, p<0.0001	1.07
E-type		23:33		
M-type	Weekend	22:53	$t_{(50.3)} = 4.53$, p<0.0001	1.10
E-type		23:59		

Table 2. Estimated mean Sleep Start Time by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean sleep start time	Significant post-hoc tests for chronotype by weekdays/weekends	Estimated difference (hours) between sleep start times
M-type	Weekday	22:34	$t_{(377)} = 3.31$, p=0.0010	0.40
	Weekend	22:58		
E-type	Weekday	23:49	$t_{(377)} = 2.65$, p=0.0083	0.34
	Weekend	0:10		
M-type	Weekday	22:34	$t_{(29.5)} = 5.54$, p<0.0001	1.25
E-type		23:49		
M-type	Weekend	22:58	$t_{(47.4)} = 4.62$, p<0.0001	1.19
E-type		0:10		

Table 3. Estimated mean Get Up Time by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean Get up time	Significant post-hoc tests for chronotype by weekdays/weekends	Estimated difference (hours) between get up times
M-type	Weekday	6:11	$t_{(381)}$ =10.40, p<0.0001	1.09
	Weekend	7:17		
E-type	Weekday	7:25	$t_{(381)}$ = 12.46, p<0.0001	1.66
	Weekend	9:04		
M-type	Weekday	6:11	$t_{(29.2)}$ = 5.92, p<0.0001	1.22
E-type		7:25		
M-type	Weekend	7:17	$t_{(44.8)}$ = 6.48, p<0.0001	1.79
E-type		9:04		

Table 4. Estimated mean Sleep End Time by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean sleep end time	Significant post-hoc tests for chronotype by weekdays/weekends	Estimated difference (hours) between sleep end times
M-type	Weekday	6:00	$t_{(377)}$ =9.47, p<0.0001	1.10
	Weekend	7:06		
E-type	Weekday	7:20	$t_{(377)}$ = 12.66, p<0.0001	1.68
	Weekend	9:00		
M-type	Weekday	6:00	$t_{(29)}$ = 5.64, p<0.0001	1.32
E-type		7:20		
M-type	Weekend	7:06	$t_{(43.5)}$ = 6.69, p<0.0001	1.90
E-type		9:00		

APPENDIX 21
POST-HOC TESTS FOR SLEEP DURATION

Table 1. Estimated Time in Bed by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean time in bed	Significant post-hoc tests for chronotype by weekdays/weekends	Estimated difference (hours)
M-type	Weekday	7.74	$t_{(383)}$ =4.11, p<0.0001	0.62
	Weekend	8.36		
E-type	Weekday	7.88	$t_{(384)}$ = 7.91, p<0.0001	1.27
	Weekend	9.15		
M-type	Weekday	7.74	*NS*	0.14
E-type		7.88		
M-type	Weekend	8.36	$t_{(57.6)}$ = 2.74, p=0.0083	0.79
E-type		9.15		

Table 2. Estimate Actual Sleep Time by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean actual sleep time	Significant post-hoc tests for chronotype by weekdays/weekends	Estimated difference (hours)
M-type	Weekday	6.60	$t_{(379)}$ =3.33, p=0.0010	0.44
	Weekend	7.04		
E-type	Weekday	6.67	$t_{(380)}$ = 8.04, p<0.0001	1.10
	Weekend	7.77		
M-type	Weekday	6.60	*NS*	0.07
E-type		6.67		
M-type	Weekend	7.04	$t_{(44.1)}$ = 2.46, p=0..0177	0.73
E-type		7.77		

APPENDIX 22
POST-HOC TESTS FOR SLEEP QUALITY

Table 1. Estimated mean movement and fragmentation index by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean movement and fragmentation index	Significant post-hoc tests for chronotype by weekdays/weekends
M-type	Weekday	26.81	$t_{(379)}$ =2.43, p=0.0158
	Weekend	30.10	
E-type	Weekday	24.76	*NS*
	Weekend	25.94	
M-type	Weekday	26.81	*NS*
E-type		24.76	
M-type	Weekend	30.10	*NS*
E-type		25.94	

Table 2. Estimated mean activity score by chronotype and weekdays/weekends

Chronotype	Weekdays vs. weekends	Estimated mean activity score	Significant post-hoc tests for chronotype by weekdays/weekends
M-type	Weekday	13.17	$t_{(379)}$ =2.95, p=0.0034
	Weekend	15.56	
E-type	Weekday	12.5	*NS*
	Weekend	13.08	
M-type	Weekday	13.17	*NS*
E-type		12.5	
M-type	Weekend	15.56	*NS*
E-type		13.08	

APPENDIX 23
LOCALLY WEIGHTED REGRESSION SCATTERPLOT SMOOTH PROCEDURE (LOWESS)

The LOWESS procedure (Chambers, Cleveland, Kleiner, & Tukey, 1983; Cleveland & Devlin, 1988) uses weighted least squares to fit a polynomial regression line to a set of points on a scatter plot. To begin, a value point of interest (x_i) is selected from the scatterplot to which a *y*-value will be fit from the LOWESS curve. First the size of the 'window' must be defined which determines the number of data points neighbouring x_i which will be taken into consideration by the weighting procedure. The GraphPad Prism software utilised in this study allows the user to select either 5- (coarse), 10- (medium), or 20-points (fine) within the window. The effect of each setting can be seen in Figure 1 below, however the medium setting was applied in all curve fitting procedures used in this study.

Neighbourhood weights are defined for each point in the window, giving more weight to those points closest to x_i. The important features of the weight assignment are:

(1) x_i has the largest weight

(2) The weight function decreases smoothly as the neighbouring values (x) move away from x_i

(3) The weight function is symmetrical about x_i

(4) The weight function hits zero just as the furthest values on either side of x_i hit the boundary of the window (Chambers et al., 1983).

Next, a polynomial regression line is fit to the points within the window using weighted least squares. The neighbourhood weight determines the amount of influence any one point within the window has on the fitted line. That is, those points with the largest weight (i.e. those nearest x_i) have a much greater influence than those with a smaller weight. Finally a *y*-value that corresponds to x_i is estimated from the fitted line giving the coordinate x_i y_i on the LOWESS curve. This process continues until regression function values have been completed for each value in the data set and an entire LOWESS curve has been created.

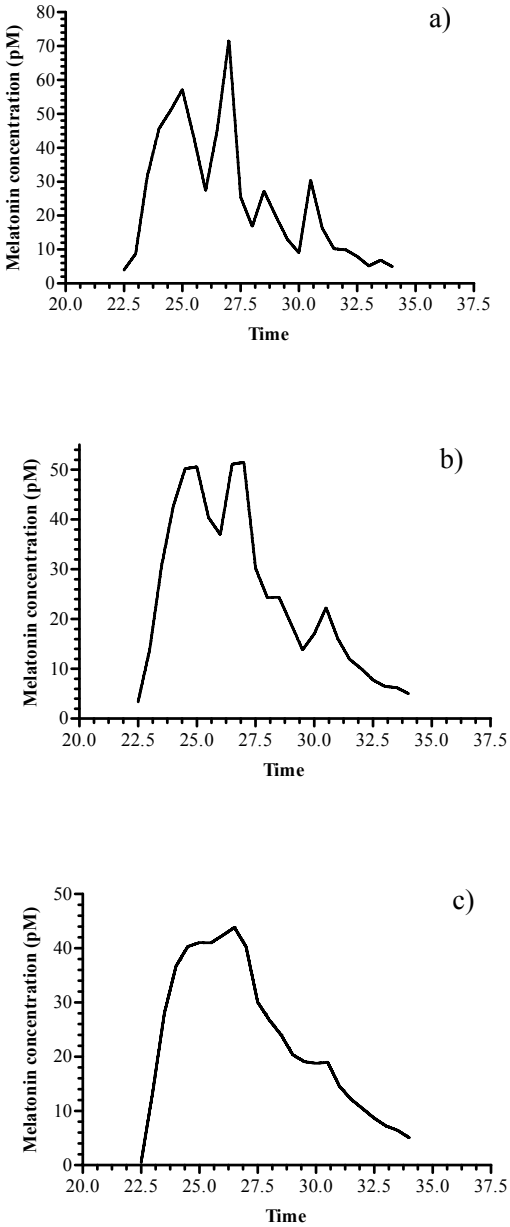
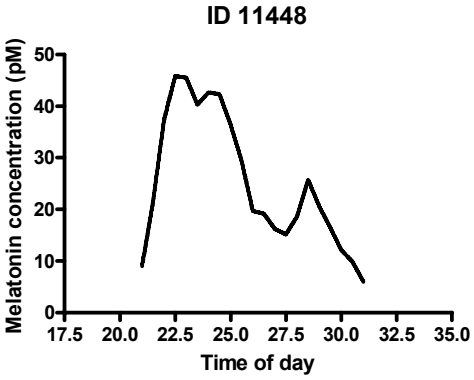
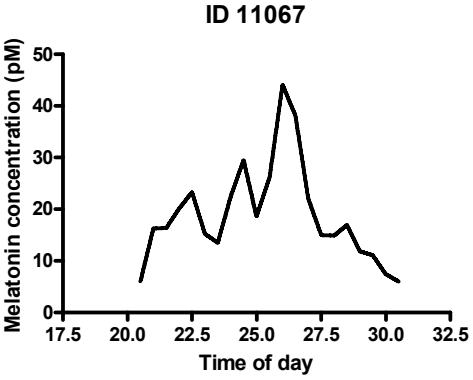
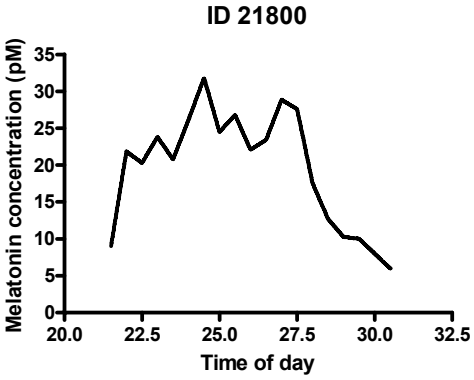


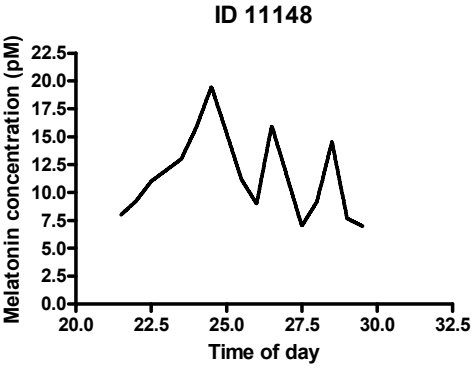
Figure 1. Examples of the LOWESS smooth procedure in GraphPad Prism software. *Raw melatonin data from one participant (ID 20697) was interpolated at one minute intervals and smoothed using the coarse (panel a), medium (panel b) and fine settings (panel c).*

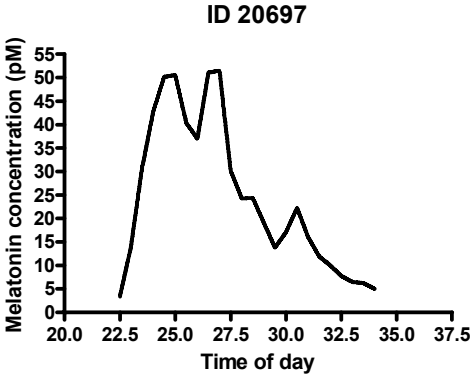
APPENDIX 24
INDIVIDUAL SMOOTHED MELATONIN PROFILES

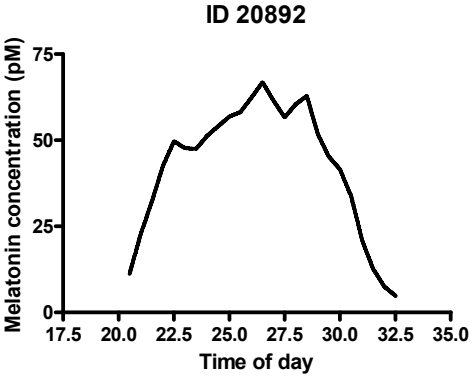


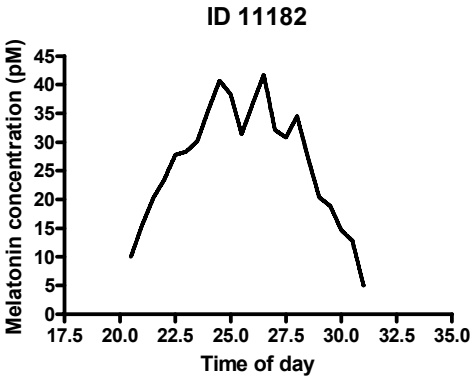


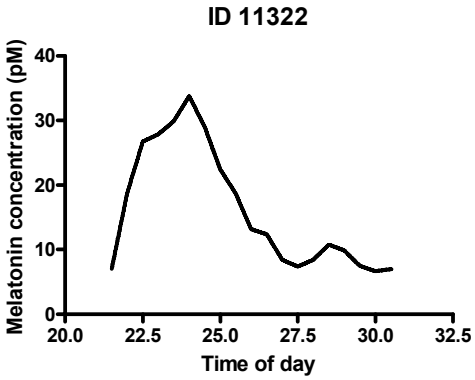


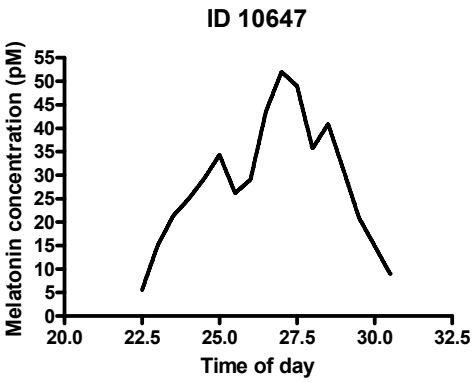


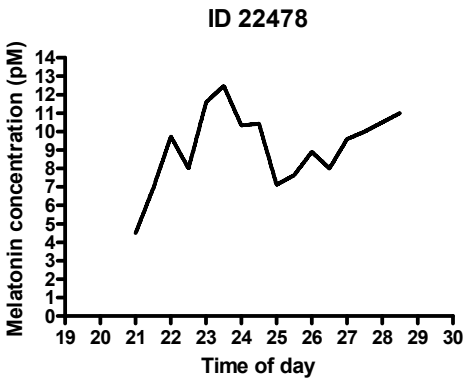





ID 11182
Melatonin concentration (pM)
0
5
10
15
20
25
30
35
40
45
17.5
20.0
22.5
25.0
27.5
30.0
32.5
35.0
Time of day


ID 11322
Melatonin concentration (pM)
0
10
20
30
40
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 10647
Melatonin concentration (pM)
0
5
10
15
20
25
30
35
40
45
50
55
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 22478
Melatonin concentration (pM)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
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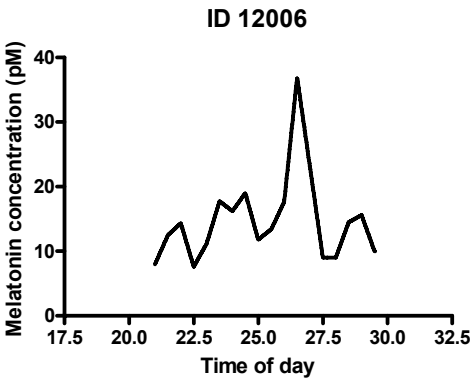
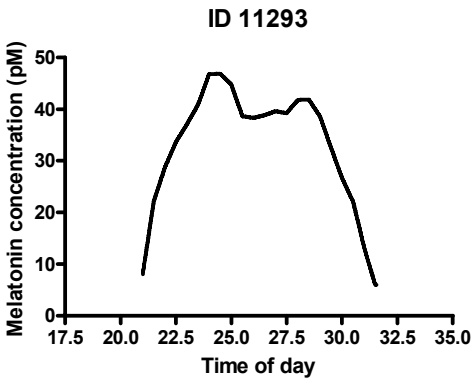
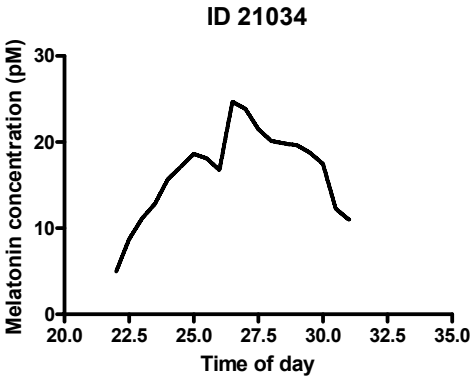
20
21
22
23
24
25
26
27
28
29
30
Time of day


ID 12006
Melatonin concentration (pM)
0
10
20
30
40
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 11293
Melatonin concentration (pM)
0
10
20
30
40
50
17.5
20.0
22.5
25.0
27.5
30.0
32.5
35.0
Time of day


ID 21034
Melatonin concentration (pM)
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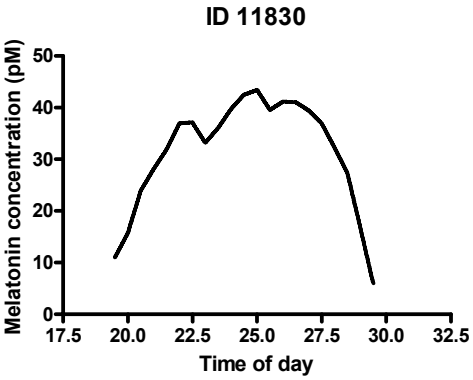
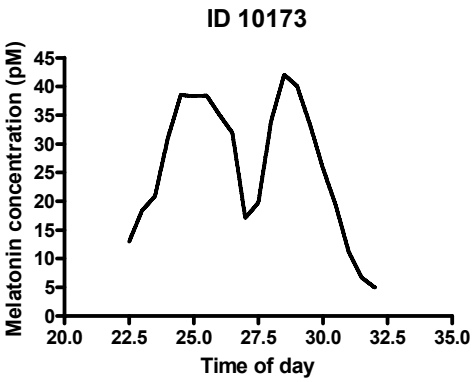
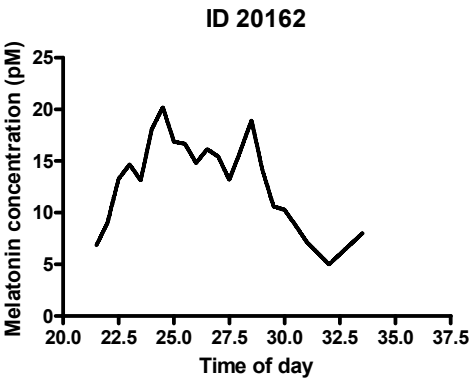
10
20
30
20.0
22.5
25.0
27.5
30.0
32.5
35.0
Time of day


ID 11830
Melatonin concentration (pM)
0
10
20
30
40
50
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 10173
Melatonin concentration (pM)
0
5
10
15
20
25
30
35
40
45
20.0
22.5
25.0
27.5
30.0
32.5
35.0
Time of day


ID 20162
Melatonin concentration (pM)
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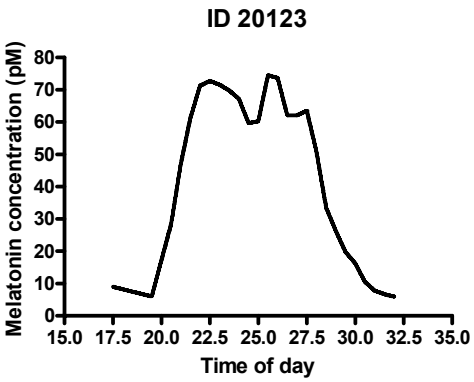
5
10
15
20
25
20.0
22.5
25.0
27.5
30.0
32.5
35.0
37.5
Time of day


ID 20123
Melatonin concentration (pM)
0
10
20
30
40
50
60
70
80
15.0
17.5
20.0
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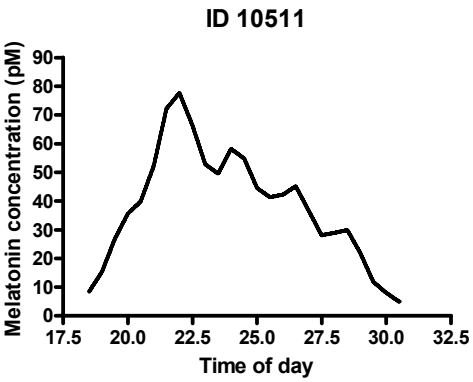
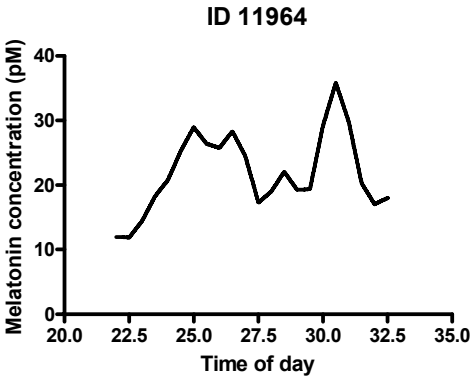
25.0
27.5
30.0
32.5
35.0
Time of day


ID 10511
Melatonin concentration (pM)
0
10
20
30
40
50
60
70
80
90
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 11964
Melatonin concentration (pM)
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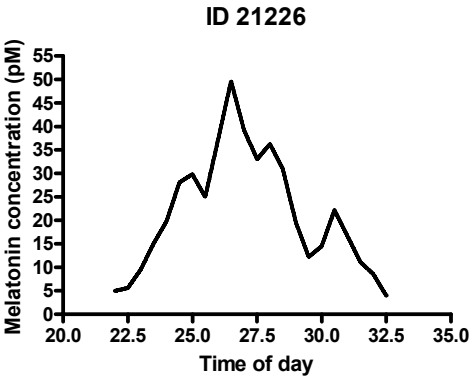
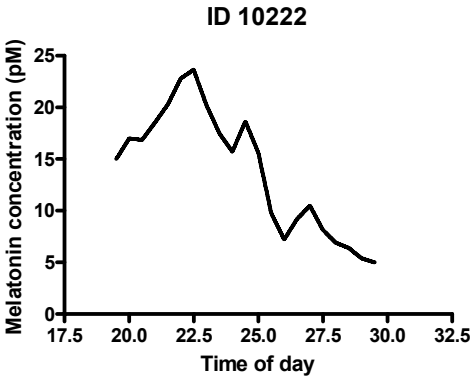
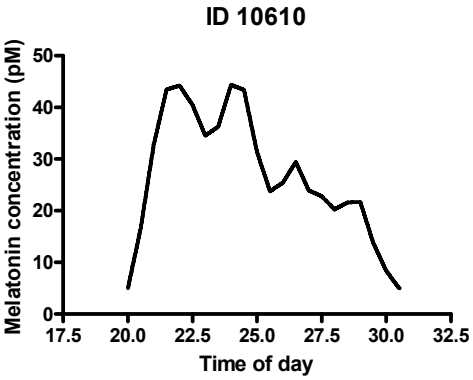
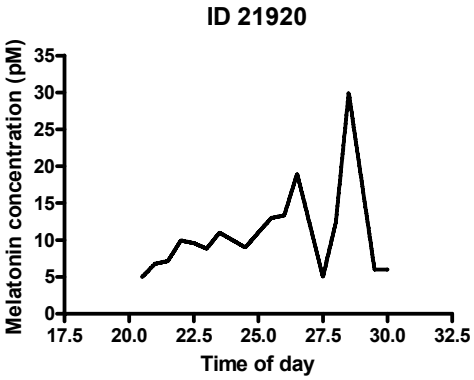
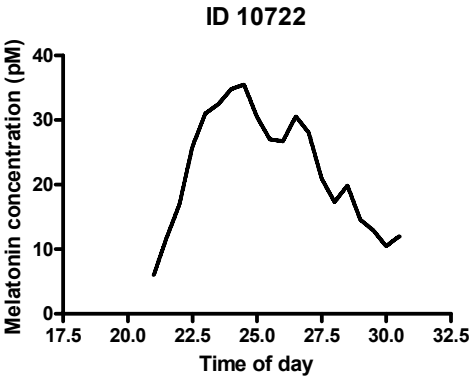
10
20
30
40
20.0
22.5
25.0
27.5
30.0
32.5
35.0
Time of day


ID 21226
Melatonin concentration (pM)
0
5
10
15
20
25
30
35
40
45
50
55
20.0
22.5
25.0
27.5
30.0
32.5
35.0
Time of day


ID 10222
Melatonin concentration (pM)
0
5
10
15
20
25
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 10610
Melatonin concentration (pM)
0
10
20
30
40
50
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 21920
Melatonin concentration (pM)
0
5
10
15
20
25
30
35
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 10722
Melatonin concentration (pM)
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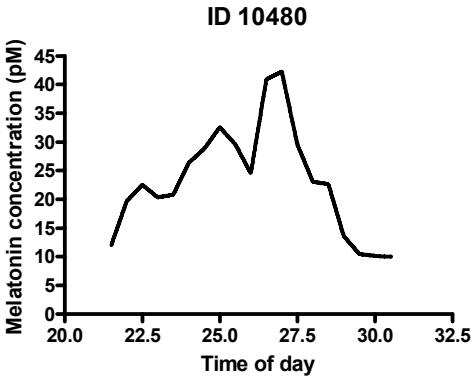
10
20
30
40
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 10480
Melatonin concentration (pM)
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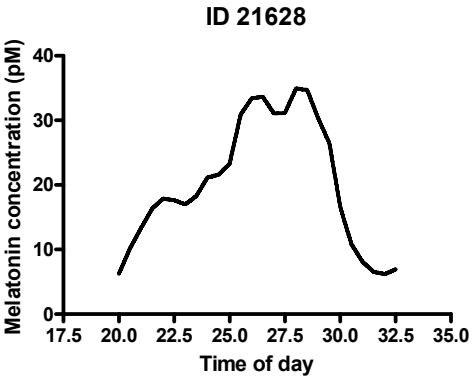
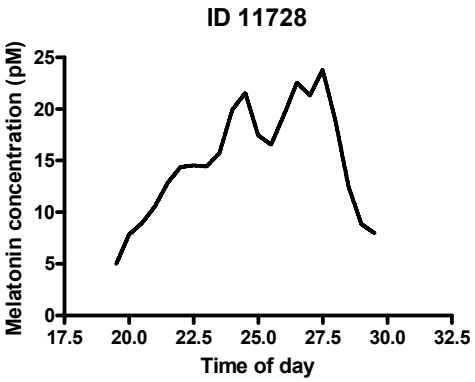
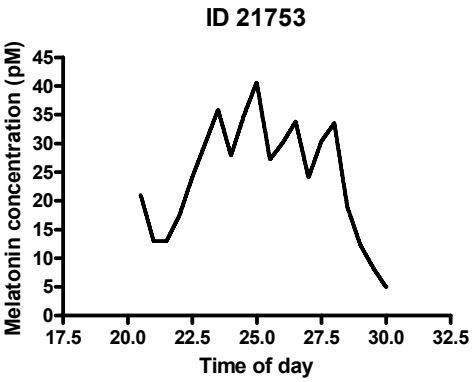
5
10
15
20
25
30
35
40
45
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 21628
Melatonin concentration (pM)
0
10
20
30
40
17.5
20.0
22.5
25.0
27.5
30.0
32.5
35.0
Time of day


ID 11728
Melatonin concentration (pM)
0
5
10
15
20
25
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day


ID 21753
Melatonin concentration (pM)
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5
10
15
20
25
30
35
40
45
17.5
20.0
22.5
25.0
27.5
30.0
32.5
Time of day

APPENDIX 25
AVERAGED SLEEP PARAMETERS

Table 1. Averaged sleep parameters for the whole group and by chronotype

	Whole group		M-types		E-types		M vs. E-types		
All 14d	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*t*	*df*	*p*-value
SlpSt	*23:09	1:31	22:46	0:23	23:55	0:45			0.0002
SlpMid	3:10	0:51	2:31	0:28	3:48	0:38	-6.086	26	<0.0001
SlpEnd	6:59	0:59	6:16	0:43	7:41	0:38	-5.610	26	<0.0001
Weekdays									
SlpSt	23:12	0:48	22:37	0:21	23:47	0:41	-5.698	26	<0.0001
SlpMid	2:54	0:48	2:17	0:24	3:31	0:35	-6.404	26	<0.0001
SlpEnd	6:33	0:55	5:57	0:42	7:14	0:35	-5.280	26	<0.0001
Weekends									
SlpSt	23:41	1:04	23:07	0:41	0:14	1:06	-3.251	26	0.0032
SlpMid	3:51	1:11	3:06	0:47	4:35	1:01	-4.331	26	0.0002
SlpEnd	8:01	1:25	7:04	1:02	8:57	1:06	-4.620	26	<0.0001
Last week									
SlpSt	*22:59	1:46	22:38	0:34	*00:13	2:09			0.0002
SlpMid	3:13	0:59	2:30	0:32	3:56	0:45	-5.778	26	<0.0001
SlpEnd	7:08	1:04	6:23	0:42	7:54	0:47	-5.387	26	<0.0001
Last 5d									
SlpSt	23:05	0:57	22:24	0:33	23:46	0:44	-5.618	26	<0.0001
SlpMid	3:00	0:54	2:19	0:29	3:41	0:40	-6.158	26	<0.0001
SlpEnd	6:54	1:00	6:13	0:42	7:35	0:47	-4.823	26	<0.0001
Final night									
SlpSt	23:04	1:24	22:14	0:53	23:55	1:19	-3.862	24	0.0007
SlpMid	3:36	1:18	2:45	0:56	4:28	1:02	-4.403	24	0.0002
SlpEnd	8:08	1:34	7:17	1:23	9:00	1:14	-3.347	24	0.0027

Note. * Median and IQR presented for non-normal data and Wilcoxon Mann-Whitney *U* non-parametric test for differences between Morning and Evening-types

APPENDIX 26
CORRELATIONS BETWEEN MELATONIN PHASE MARKERS AND ACTUAL SLEEP TIMING

Table 1. Univariate relationships between melatonin onset phase markers and mean sleep timing

	DLMO		DLMO25		DLMO50	
All 14d	*r*	*p*-value	*r*	*p*-value	*r*	*p*-value
SlpSt	0.535	0.0034	0.437	0.0201	0.091	0.6446
SlpMid	0.582	0.0012	0.490	0.0081	0.137	0.4885
SlpEnd	0.565	0.0017	0.488	0.0085	0.162	0.4114
Weekdays						
SlpSt	0.559	0.0020	0.496	0.0073	0.147	0.4549
SlpMid	0.603	0.0007	0.525	0.0041	0.151	0.4439
SlpEnd	0.567	0.0017	0.487	0.0086	0.135	0.4919
Weekends						
SlpSt	0.410	0.0303	0.263	0.1764	-0.025	0.8995
SlpMid	0.465	0.0127	0.357	0.0620	0.078	0.6948
SlpEnd	0.464	0.0128	0.396	0.0371	0.147	0.4542
Last week						
SlpSt	0.528	0.0039	0.402	0.0339	0.024	0.9039
SlpMid	0.628	0.0003	0.511	0.0055	0.124	0.5301
SlpEnd	0.658	0.0001	0.560	0.0019	0.204	0.2989
Last 5d						
SlpSt	0.572	0.0015	0.485	0.0089	0.091	0.6464
SlpMid	0.660	0.0001	0.556	0.0021	0.150	0.4456
SlpEnd	0.649	0.0002	0.544	0.0028	0.184	0.3477
Final night						
SlpSt	0.491	0.0108	0.443	0.0235	0.079	0.7028
SlpMid	0.569	0.0024	0.502	0.0090	0.144	0.4831
SlpEnd	0.513	0.0074	0.444	0.0232	0.170	0.4052

Table 2. Univariate relationships between melatonin offset phase markers and mean sleep timing

	DLMOff [a]		DLMOff25		DLMOff50	
All 14d	*r*	*p*-value	*r*	*p*-value	*r*	*p*-value
SlpSt	0.279	0.1507	0.173	0.3795	-0.081	0.6814
SlpMid	0.420	0.0259	0.263	0.1756	-0.009	0.9648
SlpEnd	0.473	0.0109	0.314	0.1031	0.054	0.7868
Weekdays						
SlpSt	0.268	0.1679	0.181	0.3572	-0.088	0.6571
SlpMid	0.407	0.0315	0.272	0.1618	-0.037	0.8511
SlpEnd	0.434	0.0209	0.319	0.0985	0.012	0.9521
Weekends						
SlpSt	0.212	0.2779	0.135	0.4932	-0.048	0.8066
SlpMid	0.351	0.0667	0.224	0.2527	0.040	0.8382
SlpEnd	0.361	0.0594	0.270	0.1649	0.103	0.6008
Last week						
SlpSt	0.279	0.1507	0.176	0.3702	-0.068	0.7308
SlpMid	0.433	0.0214	0.311	0.1072	0.054	0.7857
SlpEnd	0.532	0.0036	0.404	0.0329	0.161	0.4138
Last 5d						
SlpSt	0.329	0.0879	0.195	0.3205	-0.071	0.7214
SlpMid	0.402	0.0340	0.329	0.0875	0.051	0.7972
SlpEnd	0.527	0.0040	0.408	0.0311	0.157	0.4258
Final night						
SlpSt	0.433	0.0272	0.262	0.1967	0.070	0.7342
SlpMid	0.503	0.0088	0.315	0.1167	0.119	0.5640
SlpEnd	0.454	0.0198	0.293	0.1460	0.136	0.5084

Note. [a] Spearman rank correlations calculated for non-normal data

Table 3. Univariate relationships between melatonin midpoint, peak, first and last detectable samples and mean sleep timing

	Midpoint		Peak		MelStart		MelEnd	
All 14d	*r*	*p*-value	*r*	*p*-value	*r*	*p*-value	*r*	*p*-value
SlpSt	0.006	0.9767	0.090	0.6477	0.473	0.011	0.417	0.0271
SlpMid	0.075	0.7050	0.134	0.4967	0.521	0.0044	0.483	0.0092
SlpEnd	0.126	0.5226	0.158	0.4224	0.511	0.0054	0.491	0.0079
Weekdays								
SlpSt	0.035	0.8606	0.128	0.5151	0.497	0.0071	0.401	0.0343
SlpMid	0.067	0.7366	0.139	0.4796	0.520	0.0046	0.484	0.0091
SlpEnd	0.086	0.6622	0.132	0.5034	0.477	0.0103	0.497	0.0071
Weekends								
SlpSt	-0.043	0.8276	0.011	0.9545	0.359	0.0608	0.396	0.0369
SlpMid	0.069	0.7265	0.105	0.5949	0.452	0.0158	0.435	0.0206
SlpEnd	0.147	0.4553	0.166	0.3994	0.481	0.0095	0.426	0.0239
Last week								
SlpSt	-0.026	0.8958	0.074	0.7078	0.449	0.0165	0.417	0.0275
SlpMid	0.104	0.5979	0.176	0.3693	0.551	0.0024	0.505	0.0062
SlpEnd	0.214	0.2751	0.253	0.1941	0.589	0.0010	0.535	0.0033
Last 5d								
SlpSt	0.012	0.9527	0.122	0.5375	0.495	0.0074	0.404	0.0329
SlpMid	0.118	0.5503	0.198	0.3113	0.572	0.0015	0.474	0.0109
SlpEnd	0.200	0.3075	0.242	0.2153	0.561	0.0019	0.473	0.0111
Final night								
SlpSt	0.087	0.6733	0.198	0.3334	0.424	0.0307	0.451	0.0207
SlpMid	0.153	0.4544	0.234	0.2505	0.510	0.0077	0.468	0.0159
SlpEnd	0.179	0.3819	0.214	0.2934	0.474	0.0144	0.379	0.0559

Table 4. Regression parameters (y=ax + b) for the relationship between DLMO and mean sleep timing, and correlation coefficients for the whole group

	Regression		Correlation	
All 14d	*a*	*b*	*r*	*p*-value
SlpSt	0.650	6.260	0.535	0.0034
SlpMid	0.685	2.816	0.582	0.0012
SlpEnd	0.582	3.404	0.565	0.0017
Weekdays				
SlpSt	0.703	5.109	0.559	0.0020
SlpMid	0.758	1.030	0.603	0.0007
SlpEnd	0.627	2.251	0.567	0.0017
Weekends				
SlpSt	0.389	12.230	0.410	0.0303
SlpMid	0.398	10.360	0.465	0.0127
SlpEnd	0.329	10.888	0.464	0.0128
Last week				
SlpSt	0.542	8.804	0.528	0.0039
SlpMid	0.653	3.646	0.628	0.0003
SlpEnd	0.623	2.019	0.658	0.0001
Last 5d				
SlpSt	0.611	7.331	0.572	0.0015
SlpMid	0.736	1.565	0.660	0.0001
SlpEnd	0.651	1.313	0.649	0.0002
Final night				
SlpSt	0.366	12.966	0.491	0.0108
SlpMid	0.454	8.879	0.569	0.0024
SlpEnd	0.342	10.415	0.513	0.0074

Table 5. Correlation coefficients for the relationship between melatonin phase markers and mean sleep timing for morning-types

	DLMO	DLMO25	DLMO50	DLMOff [a]	DLMOff25	DLMOff50	Midpoint	Peak	MelStart	MelEnd
All 14d										
SlpSt	-0.1174	-0.227	-0.302	0.237	0.114	-0.104	-0.243	-0.017	-0.289	0.111
SlpMid	-0.100	-0.257	-0.416	0.404	0.069	-0.202	-0.364	-0.241	-0.232	0.305
SlpEnd	-0.068	-0.215	-0.383	0.415	0.029	-0.210	-0.347	-0.308	-0.148	0.342
Weekdays										
SlpSt	0.063	-0.077	-0.137	0.124	0.151	-0.040	-0.107	0.168	-0.262	0.020
SlpMid	0.007	-0.184	-0.405	0.486	0.117	-0.227	-0.370	-0.226	-0.253	0.366
SlpEnd	0.039	-0.178	-0.407	0.401	0.061	-0.246	-0.381	-0.351	-0.165	0.420
Weekends										
SlpSt	-0.149	-0.348	-0.420	0.107	0.028	-0.154	-0.343	-0.250	-0.235	0.193
SlpMid	-0.195	-0.291	-0.350	0.184	0.000	-0.125	-0.284	-0.206	-0.140	0.168
SlpEnd	-0.198	-0.215	-0.258	0.065	-0.018	-0.089	-0.208	-0.149	-0.059	0.129
Last week										
SlpSt	0.115	-0.152	-0.380	-0.006	-0.095	-0.376	-0.486	-0.365	-0.069	-0.031
SlpMid	-0.006	-0.216	-0.440	0.314	0.020	-0.251	-0.404	-0.251	-0.195	0.219
SlpEnd	0.149	-0.031	-0.293	0.398	0.100	-0.122	-0.247	-0.194	0.003	0.331
Last 5d										
SlpSt	-0.128	-0.212	-0.316	0.138	0.080	-0.207	-0.304	-0.032	-0.303	0.033
SlpMid	0.088	-0.082	-0.377	0.325	0.095	-0.204	-0.341	-0.151	-0.159	0.208
SlpEnd	0.226	0.054	-0.274	0.480*	0.069	-0.123	-0.234	-0.184	0.016	0.263
Final night										
SlpSt	-0.077	-0.099	-0.032	0.528*	0.285	0.108	0.034	0.220	-0.233	0.494
SlpMid	-0.019	-0.026	-0.088	0.639**	0.138	-0.046	-0.078	0.061	-0.119	0.330
SlpEnd	0.023	0.027	-0.099	0.367	0.006	-0.130	-0.127	-0.057	-0.013	0.134

Note. [a] Spearman rank correlations calculated for non-normal data. * p <0.100 ** p <0.05 *** p <0.01

Table 6. Correlation coefficients for the relationships between melatonin phase markers and mean sleep timing for evening-types

	DLMO	DLMO25	DLMO50	DLMOff [a]	DLMOff25	DLMOff50	Midpoint	Peak	MelStart	MelEnd
All 14d										
SlpSt	0.302	0.056	-0.267	0.203	-0.014	-0.305	-0.347	-0.239	0.302	0.238
SlpMid	0.402	0.172	-0.076	0.223	0.172	-0.148	-0.142	-0.056	0.402	0.279
SlpEnd	0.457	0.282	0.162	0.387	0.367	0.062	0.123	0.171	0.457	0.283
Weekdays										
SlpSt	0.287	0.088	-0.280	0.078	-0.024	-0.373	-0.402	-0.275	0.287	0.219
SlpMid	0.359	0.200	-0.084	0.120	0.168	-0.219	-0.197	-0.074	0.359	0.244
SlpEnd	0.385	0.298	0.155	0.262	0.364	-0.006	0.071	0.170	0.385	0.236
Weekends										
SlpSt	0.272	-0.001	-0.200	0.014	0.010	-0.134	-0.193	-0.131	0.272	0.249
SlpMid	0.314	0.039	-0.100	0.206	0.148	-0.016	-0.060	-0.030	0.314	0.292
SlpEnd	0.312	0.074	0.013	0.273	0.265	0.104	0.080	0.074	0.312	0.295
Last week										
SlpSt	0.349	0.112	-0.196	0.184	0.015	-0.231	-0.213	-0.117	0.349	0.257
SlpMid	0.524	0.245	-0.066	0.337	0.299	0.037	-0.006	0.081	0.524*	0.390
SlpEnd	0.571**	0.357	0.153	0.552*	0.500*	0.250	0.253	0.305	0.571**	0.415
Last 5d										
SlpSt	0.444	0.185	-0.273	0.234	0.021	-0.271	-0.326	-0.206	0.444	0.2441
SlpMid	0.541**	0.272	-0.074	0.276	0.312	-0.004	-0.039	0.057	0.541**	0.310
SlpEnd	0.516*	0.296	0.127	0.440	0.518*	0.246	0.237	0.291	0.516*	0.308
Final night										
SlpSt	0.306	0.179	-0.356	0.234	0.146	-0.070	-0.223	-0.091	0.306	0.251
SlpMid	0.478	0.250	-0.187	0.493*	0.324	0.110	-0.013	0.062	0.478*	0.370
SlpEnd	0.477	0.229	0.064	0.450	0.388	0.258	0.214	0.200	0.477*	0.354

Note. [a] Spearman rank correlations calculated for non-normal data. * p <0.100 ** p <0.05 *** p <0.01

APPENDIX 27
THE 1840 TREATY OF WAITANGI

There are three copies of the Treaty here:

- The English version as signed: taken from the first schedule to the Treaty of Waitangi Act 1975
- The Māori version as signed: taken from the first schedule to the Treaty of Waitangi Act 1975
- A modern English translation of the Māori version (translated by Sir Hugh Kawharu).

English Text of the Treaty

Source: **http://www.waitangi-tribunal.govt.nz/treaty/english.asp**

Preamble

HER MAJESTY VICTORIA Queen of the United Kingdom of Great Britain and Ireland regarding with Her Royal favour the Native Chiefs and Tribes of New Zealand and anxious to protect their just Rights and Property and to secure to them the enjoyment of Peace and Good Order has deemed it necessary in consequence of the great number of Her Majesty's Subjects who have already settled in New Zealand and the rapid extension of Emigration both from Europe and Australia which is still in progress to constitute and appoint a functionary properly authorised to treat with the Aborigines of New Zealand for the recognition of Her Majesty's Sovereign authority over the whole or any part of those islands - Her Majesty therefore being desirous to establish a settled form of Civil Government with a view to avert the evil consequences which must result from the absence of the necessary Laws and Institutions alike to the native population and to Her subjects has been graciously pleased to empower and to authorise me William Hobson a Captain in Her Majesty's Royal Navy Consul and Lieutenant Governor of such parts of New Zealand as may be or hereafter shall be ceded to her Majesty to invite the confederated and independent Chiefs of New Zealand to concur in the following Articles and Conditions.

Article the First

The Chiefs of the Confederation of the United Tribes of New Zealand and the separate and independent Chiefs who have not become members of the Confederation cede to Her Majesty the Queen of England absolutely and without reservation all the rights and powers of Sovereignty which the said Confederation or Individual Chiefs respectively exercise or possess,

or may be supposed to exercise or to possess over their respective Territories as the sole Sovereigns thereof.

Article the Second

Her Majesty the Queen of England confirms and guarantees to the Chiefs and Tribes of New Zealand and to the respective families and individuals thereof the full exclusive and undisturbed possession of their Lands and Estates Forests Fisheries and other properties which they may collectively or individually possess so long as it is their wish and desire to retain the same in their possession; but the Chiefs of the United Tribes and the individual Chiefs yield to Her Majesty the exclusive right of Preemption over such lands as the proprietors thereof may be disposed to alienate at such prices as may be agreed upon between the respective Proprietors and persons appointed by Her Majesty to treat with them in that behalf.

Article the Third

In consideration thereof Her Majesty the Queen of England extends to the Natives of New Zealand Her royal protection and imparts to them all the Rights and Privileges of British Subjects.

W HOBSON Lieutenant Governor.

Now therefore We the Chiefs of the Confederation of the United Tribes of New Zealand being assembled in Congress at Victoria in Waitangi and We the Separate and Independent Chiefs of New Zealand claiming authority over the Tribes and Territories which are specified after our respective names, having been made fully to understand the Provisions of the foregoing Treaty, accept and enter into the same in the full spirit and meaning thereof: in witness of which we have attached our signatures or marks at the places and the dates respectively specified.

Done at Waitangi this Sixth day of February in the year of Our Lord One thousand eight hundred and forty.

[Here follow signatures, dates, etc.]

The Māori version of the Treaty

Source: http://www.waitangi-tribunal.govt.nz/treaty/english.asp

Preamble

KO WIKITORIA, te Kuini o Ingarani, i tana mahara atawai ki nga Rangatira me nga Hapū o Nu Tirani i tana hiahia hoki kia tohungia ki a ratou o ratou rangatiratanga, me to ratou wenua, a kia mau tonu hoki te Rongo ki a ratou me te Atanoho hoki kua wakaaro ia he mea tika kia tukua mai tetahi Rangatira hei kai wakarite ki nga Tangata Māori o Nu Tirani-kia wakaaetia e nga

Rangatira Māori te Kawanatanga o te Kuini ki nga wahikatoa o te Wenua nei me nga Motu-na te mea hoki he tokomaha ke nga tangata o tona Iwi Kua noho ki tenei wenua, a e haere mai nei. Na ko te Kuini e hiahia ana kia wakaritea te Kawanatanga kia kaua ai nga kino e puta mai ki te tangata Māori ki te Pākehā e noho ture kore ana. Na, kua pai te Kuini kia tukua a hau a Wiremu Hopihona he Kapitana i te Roiara Nawi hei Kawana mo nga wahi katoa o Nu Tirani e tukua aianei, amua atu ki te Kuini e mea atu ana ia ki nga Rangatira o te wakaminenga o nga Hapū o Nu Tirani me era Rangatira atu enei ture ka korerotia nei.

Ko te Tuatahi

Ko nga Rangatira o te Wakaminenga me nga Rangatira katoa hoki ki hai i uru ki taua wakaminenga ka tuku rawa atu ki te Kuini o Ingarani ake tonu atu-te Kawanatanga katoa o o ratou wenua.

Ko te Tuarua

Ko te Kuini o Ingarani ka wakarite ka wakaae ki nga Rangitira ki nga Hapū-ki nga tangata katoa o Nu Tirani te tino rangtiratanga o o ratou wenua o ratou kainga me o ratou taonga katoa. Otiia ko nga Rangatira o te Wakaminenga me nga Rangatira katoa atu ka tuku ki te Kuini te hokonga o era wahi wenua e pai ai te tangata nona te Wenua-ki te ritenga o te utu e wakaritea ai e ratou ko te kai hoko e meatia nei e te Kuini hei kai hoko mona.

Ko te Tuatoru

Hei wakaritenga mai hoki tenei mo te wakaaetanga ki te Kawanatanga o te Kuini-Ka tiakina e te Kuini o Ingarani nga tangata Māori katoa o Nu Tirani ka tukua ki a ratou nga tikanga katoa rite tahi ki ana mea ki nga tangata o Ingarani.

(Signed) WILLIAM HOBSON,

Consul and Lieutenant-Governor.

Na ko matou ko nga Rangatira o te Wakaminenga o nga Hapū o Nu Tirani ka huihui nei ki Waitangi ko matou hoki ko nga Rangatira o Nu Tirani ka kite nei i te ritenga o enei kupu, ka tangohia ka wakaaetia katoatia e matou, koia ka tohungia ai o matou ingoa o matou tohu. Ka meatia tenei ki Waiangi i te ono o nga ra o Pepueri i te tau kotahi mano, e waru rau e wa te kau o to tatou Ariki. *Ko nga Rangatira o te wakaminenga.*

An English translation of the Māori text

Source: Appendix 3b in (Ramsden, 2002)

Victoria, The Queen of England, in her concern to protect the chiefs and subtribes of New Zealand and in her desire to preserve their chieftainship and their lands to them and to maintain

peace and good order considers it just to appoint an administrator one who will negotiate with the people of New Zealand to the end that their chiefs will agree to the Queen's Government being established over all parts of this land and (adjoining) islands and also because there are many of her subjects already living on this land and others yet to come.

So the Queen desires to establish a government so that no evil will come to Māori and European living in a state of lawlessness.

So the Queen has appointed me, William Hobson a captain in the Royal Navy to be Governor for all parts of New Zealand (both those) shortly to be received by the Queen and (those) to be received hereafter and presents to the chiefs of the Confederation chiefs of the subtribes of New Zealand and other chiefs these laws set out here.

The First

The Chiefs of the Confederation and all the chiefs who have not joined that Confederation give absolutely to the Queen of England for ever the complete government over their land.

The Second

The Queen of England agrees to protect the Chiefs, the subtribes and all the people of New Zealand in the unqualified exercise of their chieftainship over their lands, villages and all their treasures. But on the other hand the Chiefs of the Confederation and all the Chiefs will sell land to the Queen at a price agreed to by the person owning it and by the person buying it (the latter being) appointed by the Queen as her purchase agent.

The Third

For this agreed arrangement therefore concerning the Government of the Queen, the Queen of England will protect all the ordinary people of New Zealand and will give them the same rights and duties of citizenship as the people of England.

(signed) William Hobson

Consul and Lieutenant –Governor

So we, the Chiefs of the Confederation and the subtribes of New Zealand meeting here at Waitangi having seen the shape of these words which we accept and agree to record our names and mark thus. Was done at Waitangi on the sixth day of February in the year of our Lord 1840. The Chiefs of the Confederation

APPENDIX 28
THE MATAATUA DECLARATION ON CULTURAL AND INTELLECTUAL PROPERTY RIGHTS OF INDIGENOUS PEOPLES

In recognition that 1993 is the United Nations International Year for the World's Indigenous Peoples;

The Nine Tribes of Mataatua in the Bay of Plenty Region of Aotearoa New Zealand convened the First International Conference on the Cultural and Intellectual Property Rights of Indigenous Peoples. (12-18 June 1993, Whakatane).

Over 150 delegates from fourteen countries attended, including indigenous representatives from Ainu (Japan), Australia, Cook Islands, Fiji, India, Panama, Peru, Philippines, Surinam, USA, and Aotearoa.

The Conference met over six days to consider a range of significant issues, including; the value of indigenous knowledge, biodiversity and biotechnology, customary environmental management, arts, music, language and other physical and spiritual cultural forms. On the final day, the following Declaration was passed by the Plenary.

PREAMBLE

Recognising that 1993 is the United Nations International Year for the World's Indigenous Peoples;

Reaffirming the undertaking of United Nations Member States to-

"Adopt or strengthen appropriate policies and/or legal instruments that will protect indigenous intellectual and cultural property and the right to preserve customary and administrative systems and practices." - United Nations Conference on Environmental Development; UNCED Agenda 21 (26.4b);

Noting the Working principles that emerged from the United Nations Technical Conference on Indigenous Peoples and the Environment in Santiago. Chile from 18 - 22 May 1992 (E/CN.4/Sub. 2/1992131);

Endorsing the recommendations on Culture and Science from the World Conference of Indigenous Peoples on Territory, Environment and Development Kari-Oca, Brazil, 25 - 30 May' 1992;

***WE*:**

Declare that Indigenous Peoples of the world have the right to self determination and in exercising that right must be recognised as the exclusive owners Of their cultural and intellectual property

Acknowledge that Indigenous Peoples have a commonality of experiences relating to the exploitation of their cultural and intellectual property'

Affirm that the knowledge of the Indigenous Peoples of the world is of benefit to ail humanity;

Recognise that Indigenous Peoples are capable of managing their traditional knowledge themselves, but are willing to offer it to all humanity provided their fundamental rights to define and control this knowledge are protected by the international community'

Insist that the first beneficiaries of indigenous knowledge (cultural and intellectual property rights) must be the direct indigenous descendants of such knowledge;

Declare that all forms of discrimination and exploitation of indigenous peoples, indigenous knowledge and indigenous cultural and intellectual property rights must cease.

1.0 RECOMMENDATIONS TO INDIGENOUS PEOPLES

In the development of policies and practices, indigenous peoples should:

1.1 Define for themselves their own intellectual and cultural property.

1.2 Note that existing protection mechanisms are insufficient for the protection of Indigenous Peoples Intellectual and Cultural Property Rights.

1.3 Develop a code of ethics which external users must observe when recording (visual, audio, written) their traditional and customary knowledge.

1.4 Prioritise the establishment of indigenous education, research and training centres to promote their knowledge of customary environmental and cultural practices.

1.5 Reacquire traditional indigenous lands for the purpose of promoting customary agricultural production.

1.6 Develop and maintain their traditional practices and sanctions for the protection, preservation and revitalization of their traditional intellectual and cultural properties.

1.7 Assess existing legislation with respect to the protection of antiquities.

1.8 Establish an appropriate body with appropriate mechanisms to:

a) preserve and monitor the commercialism or otherwise of indigenous cultural properties in the public domain

b) generally advise and encourage indigenous peoples to take steps protect their cultural heritage

c) allow a mandatory consultative process with respect to any new legislation affecting indigenous peoples cultural and intellectual property rights.

1.9 Establish international indigenous information centres and networks.

1.10 Convene a Second International Conference (Hui) on the Cultural and intellectual Property Rights of Indigenous Peoples to be hosted by the Coordinating Body for the Indigenous Peoples Organisations of the Amazon Basin (COICA).

2.0 RECOMMENDATIONS TO STATES, NATIONAL AND INTERNATIONAL AGENCIES

In the development of policies and practices, States, National and International Agencies must

2.1 Recognise that indigenous peoples are the guardians of their customary knowledge and have the right to protect and control dissemination of that knowledge.

2.2 Recognise that indigenous peoples also have the right to create new knowledge based on cultural traditions.

2.3 Note that existing protection mechanisms are insufficient for the protection of Indigenous Peoples Cultural and Intellectual Property Rights.

2.4 Accept that the cultural and intellectual property rights of indigenous peoples are vested with those who created them.

2.5 Develop in full co-operation with indigenous peoples an additional cultural and intellectual property rights regime incorporating the following:

- collective (as well as individual) ownership and origin
- retroactive coverage of historical as well as contemporary works
- protection against debasement of culturally significant items
- cooperative rather than competitive framework

- first beneficiaries to be the direct descendants of the traditional guardians of that knowledge
- multi-generational coverage span

BIODIVERSITY AND CUSTOMARY ENVIRONMENTAL MANAGEMENT

2.6 Indigenous flora and fauna is inextricably bound to the territories of indigenous communities and any property right claims must recognise their traditional guardianship.

2.7 Commercialization of any traditional plants and medicines of Indigenous Peoples, must be managed by the indigenous peoples who have inherited such knowledge.

2.8 A moratorium on any further commercialisation of indigenous medicinal plants and human genetic materials must be declared until indigenous communities have developed appropriate protection mechanisms.

2.9 Companies, institutions both governmental and private must not undertake experiments or commercialisation of any biogenetic resources without the consent of the appropriate indigenous peoples.

2.10 Prioritise settlement of any outstanding land and natural resources claims of indigenous peoples for the purpose of promoting customary, agricultural and marine production.

2.11 Ensure current scientific environmental research is strengthened by increasing the involvement of indigenous communities and of customary environmental knowledge.

CULTURAL OBJECTS

2.12 All human remains and burial objects of indigenous peoples held by museums and other institutions must be returned to their traditional areas in a culturally appropriate manner.

2.13 Museums and other institutions must provide, to the country and indigenous peoples concerned, an inventory of any indigenous cultural objects still held in their possession.

2.14 Indigenous cultural objects held in museums and other institutions must be offered back to their traditional owners.

3.0 RECOMMENDATIONS TO THE UNITED NATIONS

In respect for the rights of indigenous peoples, the United Nations should:

3.1 Ensure the process of participation of indigenous peoples in United Nations fora is strengthened so their views are fairly represented.

3.2 Incorporate the Mataatua Declaration in its entirety in the United Nations Study on Cultural and Intellectual Property of Indigenous Peoples.

3.3 Monitor and take action against any States whose persistent policies and activities damage the cultural and intellectual property rights of indigenous peoples.

3.4 Ensure that indigenous peoples actively contribute to the way in which indigenous cultures are incorporated into the 1995 United Nations International Year of Culture.

3.5 Call for an immediate halt to the ongoing 'Human Genome Diversity Project' (HUGO) until its moral, ethical, socio-economic, physical and political implications have been thoroughly discussed, understood and approved by indigenous peoples.

4.0 CONCLUSION

4.1 The United Nations, International and National Agencies and States must provide additional funding to indigenous communities in order to implement these recommendations.

APPENDIX 29
RECOMMENDATIONS ON GENETIC MODIFICATION

The following recommendations on genetic modification were endorsed at the Royal Commission on Genetic Modification national hui at Turangawaewae marae (Source: Appendix 3, Section 4.1 (Eichelbaum et al., 2002)).

On Sunday 8 April the National Hui attendees considered and passed a resolution of support for 16 recommendations on genetic modification

(1) That the Crown honour Te Tiriti o Waitangi

(2) That a process for implementing constitutional change is negotiated between Māori and the Crown which includes a revision of all legislation inconsistent with Te Tiriti o Waitangi including the Hazardous Substances and New Organisms act 1996

(3) That following such a process, any constitutional change implemented reflects a basis in tikanga Māori and acknowledges that following constitutional documents as the foundation for such process:

- Declaration of Independence
- Te Tiriti o Waitangi
- Draft Declaration of Indigenous Rights
- Mataatua Declaration
- An Aotearoa (New Zealand) Constitution

(4) That the Crown fund a parallel process which seeks Māori knowledge and opinions on genetic modification (GM) sourced from kaupapa Māori processes and contexts immediately

(5) That a moratorium be placed upon all activities related to GM and GMOs immediately

(6) That we outlaw the patenting of any life forms

(7) That an inventory on GMAs and GM activity in Aotearoa be completed by Māori and the Crown. Such an inventory must cover all GMOs and GM research, outputs and activities to date

(8) That Māori in negotiation with the Crown commence immediately an environmental, spiritual and cultural GMO impact assessment, followed by a cultural, spiritual and environmental clean up

(9) That the Crown stops free-trade negotiations and stops biotechnology multinationals from entering Aotearoa to conduct GM experiments

(10) That Māori in negotiation with the Crown develop separate standards from the current ANZFA and other food standards that label GM foods

(11) That Māori in negotiation with the Crown label all GM foods

(12) That Māori in negotiation with the Crown halt the import of GM foods for the future

(13) That the Crown fund sustainable organic agricultural practices and implement processes that will ensure that Aotearoa is an organic nation by 2020

(14) We declare that Aotearoa should be an independent, nuclear- and GE-free nation

(15) That the Royal Commission include the resolutions from the National Māori Hui held 6-8 April 2001 in their final report, and to the New Zealand government

(16) National Hui held at Turangawaewae acknowledged and support the recommendations presented by Nga Wāhine Tiaki o te ao and other whānau, hapū and iwi, and Māori submissions that were received and delivered.

APPENDIX 30
FOCUS GROUP STUDY PACK

<Date>

Te Rōpū Rangahau Hauora a Eru Pōmare
Wellington School of Medicine
University of Otago
Private Bag 7343
Wellington South

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai
Massey University
Private Box 756
Wellington

katoa
21 Reuben Avenue
Brooklyn
Wellington

Kia ora ……..

He mihi nui ki a koe.

Thank-you for your interest in our discussion on our hopes and concerns, as Māori, of genetics & research.

I would like to invite you to attend a small group discussion on this issue to be held on **<Date>** at **<Time>.** Please be aware that this date may be postponed further if I am unable to recruit enough participants. In this instance I will contact you by phone to let you know of the alternative arrangements.

This meeting will be held at the Research School of Public Health (the No Names Building Recyclers building), 102 Adelaide Road, Newtown, Wellington.

If you enter the building from Adelaide Road, please take the elevator or stairs to Level 2.

Car parking is available on the roof of this building which you can access from King Street, using the ramp at the back of the building. There is a door on the roof which will take you to Level 2.

I will ring you the day before to remind you of this meeting and to answer any more questions you may have. If your circumstances have changed since our last telephone call and you cannot make this time or date, please call me and I will try and fit you into another discussion group (ph: 801 5799 extn 6039).

Thank-you again for agreeing to take part in our discussion. I value your involvement.

Noho ora mai rā,
nā

Paine.

Sarah-Jane Paine.
PhD Student

Developing guidelines for the use of Māori biological samples in research

PARTICIPANT INFORMATION SHEET

Te Rōpū Rangahau Hauora a Eru Pōmare
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Brooklyn
Wellington

Kia ora……

The researchers, Sarah-Jane Paine (Tuhoe), Fiona Cram (Ngati Kahungunu) and Papaarangi Reid (Te Rarawa, Te Aupouri) initiated this study in response to a growing concern that there are currently no formal guidelines for researchers who collect DNA/genetic samples from Māori. The research group acknowledges that there are specific issues for Māori, concerning the collection of blood, body fluids and tissue samples, who uses them, where they are kept and who will have access to the information, now, and in the future. We are interested in hearing from Māori what these issues may be and discussing what can be done to ensure that these issues are addressed. We invite you to take part in this research.

Participant recruitment:

This study is part of the PhD work of Sarah-Jane Paine, which also involves looking at sleep patterns in New Zealand and whether you are an "early bird" or a "night owl". Initially, your name was randomly selected from the electoral roll as part of a sample of 5,000 people in the Wellington region aged 30-50 years. The researcher asked you to fill out a blue questionnaire about your sleep habits and also asked you to consider taking part in further studies looking at your sleep and to indicate your willingness to participate by completing a consent form, and leaving your contact phone number.

This study presents an opportunity for Māori to determine research that uses Māori DNA. We are interested in talking to:

- 20 Māori participants who agreed to take part in further sleep studies.
- 20 Māori participants who declined to take part in the sleep studies, but who agreed to be contacted by a researcher to discuss their reasons.

We would like to hear from both groups of people to ensure that we consider a range of views.

What does it involve?

This phase of the project involves a group discussion which will take 1-2 hours of your time. As a member of the discussion group you will be asked questions about your hopes and dreams for genetic research and also your fears or concerns.

With your consent the interview will be audiotaped. These recordings will be kept on a secure computer at Massey University which can only be accessed by members of the research team. In addition, the reporting of the results of the research will not include anything that could identify you personally.

The discussion groups will be held on **Tuesday 2nd November 2004** at The Research School of Public Health, 102 Adelaide Road, Newtown.

If you are interested in joining our discussion please contact me directly by calling 801-5799 extension 6039.

If you would like to participate but you are unable to meet at this time, please feel free to call me and I will organise a time where we can discuss the issues one to one.

What are the outcomes of the study?

- You will have an opportunity to read the transcripts from your interview and make changes or editions as you see fit
- A draft report will be sent to you for your comments.
- A summary of the findings of the study will be prepared for publication in a peer-reviewed journal
- The findings of this study will be presented in the PhD thesis of Sarah-Jane Paine

Important points:
You are under no obligation to accept this invitation. If you decide to participate, you have the right to:

- decline to answer any particular question;
- withdraw from the study up to two days before the discussion group is held
- ask any questions about the study at any time

This project has been reviewed and approved by the Massey University Human Ethics Committee, WGTN Protocol 03/149. If you have any concerns about the conduct of this research, please contact Mr Jeremy Hubbard (Acting Chair) Massey University Campus Human Ethics Committee: Wellington, telephone 04 801 2794 x6358, email humanethicswn@massey.ac.nz

Please be aware that confidentiality cannot be ensured entirely as this is a group discussion. However, group members will be asked to respect others views and to keep the discussion confidential.

We thank-you for your time and for sharing your views with us. If you have any further questions regarding this evaluation or any concerns, feel free to contact Sarah-Jane Paine (tel. (04) 801 5799 x 6039) during working hours.

Sarah-Jane Paine
Sleep/Wake Research Centre

Papaarangi Reid
Te Rōpū Rangahau Hauora a Eru Pōmare

Fiona Cram
Katoa Ltd.

Developing guidelines for the use of Māori biological samples in research

PARTICIPANT CONSENT FORM

Te Rōpū Rangahau Hauora a Eru Pōmare
Wellington School of Medicine
University of Otago
Private Bag 7343
Wellington South

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai
Massey University
Private Box 756
Wellington

katoa
21 Reuben Avenue
Brooklyn
Wellington

- I have read and I understand the participant information sheet.
- I understand that the information I share will be kept in the utmost confidentiality and only be used for this specific evaluation
- I understand that participation in this study is confidential and that no material, which could identify me, will be used in any reports on this study.
- I agree to not disclose anything discussed in the focus group
- I have had the opportunity to discuss this study. I am satisfied with the answers I have been given, and understand that I may ask further questions at any time.
- I understand that participation in this study is voluntary and that I may withdraw from the study at any time.
- I have had sufficient time to consider whether to take part.
- I know whom to contact if I have any questions about the study.
- I give my consent for this interview to be audio-taped.
- I give my consent for my comments to be included in the research

Please print your full name here _____

Signature _____ Date _____

Researcher: Sarah-Jane Paine

Contact phone number: 801 5799 x 6039
(Weekdays, 9am to 5pm)

APPENDIX 31
FOCUS GROUP FACILITATOR GUIDE

Introduction

(1) Mihi whakatau

(2) Introduce staff present

(3) Purpose of the discussion

Each of you were contacted by the Sleep/Wake Research Centre about taking part in some of our research projects and you indicated to us that you were/were not interested in taking part. What I'd like to do tonight is hear your views on genetic research and what informs our decisions about this type of research. Our hope is that through talking with Māori about some of the issues we can work towards developing guidelines that will inform researchers who want to work with Māori.

(4) Information sheets and consent forms

Read through, take questions, and complete before we start the discussion.

(5) Format for the discussion

This is how I see our time together panning out. I'm here today to listen to you and your thoughts and experiences, so I'll try not to do too much talking. I'm going to be taking notes, and writing something's on the white board. I have set up microphones so that we can record our talk today, everyone should have a pen and paper so that you can write things down if you want to. We'll have a quick break after about an hour and then come back together to continue our discussion.

(6) Housekeeping

Bathrooms are down the hallway to the right, and we have tea/coffee and cold drinks at the back so please help yourself if need something to drink.

(7) Warm-up (5 minutes)

Participant introduction ("I am here tonight/today because……..")

Session 1: Hopes and Dreams (90 minutes).

There has been a lot of talk lately, about research and genetics and the technology that is used. There are lots of different groups around in our communities talking about the issues, and we hear about it in the media all the time. There seems to be quite a wide range of views on this topic, from people who are totally against any sort of research and technology that involves genetics, to people who feel that they want to embrace it all. I've gathered you all here today to hear your thoughts on genetic research

To start with I'd like us to talk about our hopes and dreams for genetic research? (40-45 minutes)

In pairs I want you to write down on the paper in front of you, what your hopes and dreams are for genetic research (3-5 minutes).

Now can one person from each group read out what you've written down and I'll put them up here on the whiteboard.

OK, let's talk about this first one…….

Break for kai

Session 2: Fears and concerns

Now the next thing I want to talk about is our fears and concerns for genetic research? (40-45 minutes).

This time in your pairs, can you try and think of your fears and concerns and at the end I'll write them all up and the board and we can talk about those (3-5 minutes).

OK, let's talk about this first one…….

Summary (25 minutes)

What I'd like us to do now is to think about how these things that we've talked about today fit together. I've summarised our discussion today into themes and made a list of them on the board. Next to it I've drawn a noughts and crosses grid. Along this direction I have written benefits and in this direction I have written risks. The way the grid works is that up in this corner we will put those issues which we think bring about the greatest benefits at little risk, where as down here, these are the issues that we see as bringing little benefit to us, and are extremely risky.

I'd like each of you to try and put these points into the grid. I've numbered each point to hopefully make it a bit easier to manage. (5 minutes).

OK, (first group) tell me where you put each point and I'll put them in the grid. Next, group, can you read out your points.

OK, so let's talk about why you put these things in here……

Final words

Before we finish up tonight/today I'd like to go around the table one last time. I really appreciate all of the information you have each shared today, and I want to acknowledge the fact that this information comes from your own experiences and lives outside of this room. So this time I want you to describe your thoughts tonight in terms of your personal life journey. How have your opinions and thoughts about genetic research been informed by your experiences as a mother or father, your occupation, your own cultural, religious or spiritual beliefs, what you've heard on the t.v. or radio or in the newspapers.

And then to finish I'd like you to tell us "one thing I liked about tonight/today was……"

Thanks and koha

APPENDIX 32
LETTER FOR TRANSCRIPTS

<Date>

<First> <Surname>
<Addr1>
<Addr2>
<Addr3>

Te Rōpū Rangahau Hauora a Eru Pōmare
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Private Bag 7343
Wellington South

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai
Massey University
Private Box 756
Wellington

katoa
21 Reuben Avenue
Brooklyn
Wellington

Tēnā koe <First>,

Thank-you for coming to our discussion group on genetics and research.

Please find enclosed a transcript of our discussion for you to keep. I have gone through the transcript and highlighted all of your comments from the discussion.

I would appreciate it if you could find the time to carefully read through it and make changes if you believe that your input from that day has been incorrectly recorded or if you would like to add any final comments for inclusion in our report. I would like to remind you that the group was conducted with the understanding that our conversations would be kept confidential and so I would ask that you do not share this transcript with anyone else.

I have also enclosed an envelope for you to return the transcript if you have any comments to make. Because of our own deadlines I would ask that you please send in your comments or changes by **<Date>**. However, any changes or suggestions that I receive after this date will still be gratefully accepted.

He mihi tenei naku mo tōu manaaki i ahau. Nō reira, nga mihi aroha ki a koe me tōu whanau whanui huri noa te motu.

Nāku nā,

Sarah-Jane Paine
PhD Student
Sleep/Wake Research Centre
Massey University
WELLINGTON

s.j.paine@massey.ac.nz
04 801 5799 x6039

APPENDIX 33
LETTER FOR THEMATIC ANALYSIS

<Date>

Te Rōpū Rangahau Hauora a Eru Pōmare
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katoa
21 Reuben Avenue
Brooklyn
Wellington

Kia ora ……..

He mihi tēnei nāku ki a koe mō te tau hou. I hope you have had an enjoyable Christmas and New Year.

Enclosed with this letter is a copy of the **first** stage of analysis from our focus group discussions on genetic research that you kindly took part in during 2004.

Please take the time to read through this report. I would like to point out that this is a **draft** of the report and more changes will be made before the final report is written-up. This is your opportunity to look at what I have written and make any comments or suggestions, especially if you believe that I have not accurately captured your thoughts or feelings around genetic research.

Finally, I would like to extend an invitation to you to participate in a **final** discussion around this report and the project in general. During this session I would value your feedback in terms of the themes which I have identified in this report and also your thoughts on the project itself, the methods we have used and the way it has been conducted. At the end of this letter I have included a form for you to complete indicating whether or not you would be interested in coming along to this feedback session. Please fill it out and send it back in the envelope I have provided.

Thank-you for your participation in this study. Please feel free to contact me directly if you have any questions or concerns

Noho ora mai,
nā

Sarah-Jane Paine.
PhD Student
Sleep/Wake Research Centre
Massey University
Private Box 756
WELLINGTON
Ph: 04 801-5799

Please return this form to Sarah-Jane Paine by
Friday 11th February

Te Rōpū Rangahau Hauora a Eru Pōmare
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University of Otago
Private Bag 7343
Wellington South

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai
Massey University
Private Box 756
Wellington

katoa
21 Reuben Avenue
Brooklyn
Wellington

Name: _____

Home address: _____

_____

I **am** able to join in the feedback session (please tick) ☐

I **am** able to come to the following session times (please tick):

Tuesday 15th February 6:30-8:30pm ☐

Wednesday 16th February 6:30-8:30pm ☐

Thursday 17th February 6:30-8:30pm ☐

Monday 21st February 6:30-8:30pm ☐

I **am not** able to join in the feedback session (please tick) ☐

Contact details:

Home phone: _____

Cell phone: _____

Email address: _____

Please note that filling in this form does not mean that you consent to participate in the study. It only allows us to contact you to discuss the study further.

Sarah-Jane Paine will contact you at the phone number(s) you have provided to confirm the feedback session time and to organise your transport if necessary.

Kia ora.

APPENDIX 34
KEY-INFORMANT STUDY PACK

Te Rōpū Rangahau Hauora a Eru Pōmare
Wellington School of Medicine
University of Otago
Private Bag 7343
Wellington South

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai
Massey University
Private Box 756
Wellington

katoa
21 Reuben Avenue
Brooklyn
Wellington

02 February 2005

E te rangatira, tēnā koe,

My name is Sarah-Jane Paine and I am a PhD Student at the Sleep/Wake Research Centre, Massey University. My research interests include the control of sleeping patterns by the circadian clock, kaupapa Māori research methodologies and the development of Māori ethical frameworks.

One of my PhD studies is in collaboration with Drs. Papaarangi Reid and Fiona Cram. This study has been kindly funded by Ngā Pae o te Māramatanga and utilises a kaupapa Māori framework and qualitative methods to discuss our hopes and fears of genetic research, with a hope that this information may be used to formulate ethical guidelines for the research use of Māori biological samples.

In 2004 I held a short series of focus-group discussions with Māori participants from one of my concurrent sleep studies. During February I am hoping to hold key-informant discussions with Māori involved in research or Māori end-users of this information.

I would like to extend an invitation to you to take part in one of these discussions.

In these meetings I would present a summary of the themes which arose from the focus groups and follow this with a discussion around the familiarity of these themes from your experience as a Māori researcher involved with Māori communities. To finish the meeting I would welcome your evaluation of our methods and processes that we have used during this study.

If you would be available to contribute to this study please contact me directly with suggestions of dates and times in which I could visit and meet with you. The meeting would take approximate 1-1.5 hours of your time; however I am more than happy to accommodate your other commitments, so please also indicate your availability and I will work around this.

Thank-you for your time and consideration, I look forward to hearing from you.

Noho ora mai,
nā,

Sarah-Jane Paine
Sleep/Wake Research Centre
Massey University
WELLINGTON

04 801 5799 extn 6039
s.j.paine@massey.ac.nz

KEY-INFORMANT INFORMATION FORM

Developing guidelines for the research use of Māori biological samples

Te Rōpū Rangahau Hauora a Eru Pōmare
Wellington School of Medicine
University of Otago
Private Bag 7343
Wellington South

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai
Massey University
Private Box 756
Wellington

katoa ltd
21 Reuben Avenue
Brooklyn
Wellington

E ngā waka, e ngā mana, e ngā reo,
e ngā karangatanga maha o ngā hau e whā
ko tēnei te mihi atu ki a koutou.
Tēnā koutou hoki i roto i ngā āhuatanga o tēnei wā.
Nō reira, tēnā koutou, tēnā koutou, tēnā koutou katoa.

What is this study about?

The researcher, Sarah-Jane Paine (Ngāi Tuhoe, Ngāti Rongo), is based at the Sleep/Wake Research Centre, Massey University in Wellington. This study is part of a larger project looking at sleep patterns and whether a person is an "early bird" or a "night owl".

As part of this project we have asked people if they would be prepared to come to the Sleep/Wake Research Centre, and provide saliva samples, which will be used and analysed by the research group.

The research group acknowledges that there are specific issues for Māori, concerning taking samples of body fluids and tissues, who uses them, where they are kept and who will have access to the information, now, and in the future. We are interested in hearing from Māori what these issues may be, with a particular focus on genetic samples, and discussing what can be done to ensure that these issues are addressed. From the discussions we will produce a report that will be presented to Māori and all of the material produced from this study will also be included in the PhD thesis of Ms. Paine.

What are the outcomes of the study?

- You will have an opportunity to read the transcriptions from your interview and make changes or editions as you see fit.
- A draft report will be sent to you for your comments.
- You will receive a summary of the findings of the study.
- Information from this study will be described and submitted for publication in national and international journals.
- Dissemination of the study findings to the wider Māori community will be achieved through the media and hui where possible.
- Finally, one of the key objectives of this project is to inform and direct policy through the National Māori Ethics Working Group. It is hoped that this key-group of people will be able to co-ordinate this framework and advocate for it's inclusion in the policy nationwide.

What does this involve?

If you choose to take part you will be asked some questions and this will take 1 to 1/12 hours of your time. You will be asked questions about

- Your views on the themes that have been identified through our focus group discussions with Māori in the Wellington community.
- Your views on the risks and benefits of research that uses human tissues and fluids.
- Your views on the acceptability of this type of research.

With your consent the interview will be audiotaped. The tapes will be locked in a filing cabinet at Massey University and only the researchers will have access to it.

Important points

- You have the right to answer or to pass on any question, and you may choose to withdraw from the interview.
- This project has been reviewed and approved by the Massey University Human Ethics Committee, WGTN Protocol 03/149. If you have any concerns about the conduct of this research, please contact the following person:

Mr Jeremy Hubbard, Acting Chair
Massey Human Ethics Committee
Massey University Wellington
Private Box 756
Wellington

Telephone: 04 801 2794 x 6358
E-Mail: J.J.Hubbard@massey.ac.nz

- Your name and details will be kept confidential at all times. There is no way that you will be able to be identified in any reports on the study.

What do I do now?

- Please read and complete the consent form. Only the names of those who agree to participate will be retained.
- Your participation is entirely voluntary. If you do agree to take part you are free to withdraw from the study at any time without having to give a reason.

Thank-you for your time and for sharing your views with us. Any of the following members of the research team would be happy to answer questions you may have about this study. Kia ora.

Researchers:
Sarah-Jane Paine
PhD Student
Sleep/Wake Research Centre
Massey University
Ph: (04) 801 5799 ext. 6039.

Dr. Fiona Cram
Director
Katoa Ltd.

KEY INFORMANT CONSENT FORM

Developing guidelines for the research use of Māori biological samples

Te Rōpū Rangahau Hauora a Eru Pōmare
Wellington School of Medicine
University of Otago
Private Bag 7343
Wellington South

SLEEP / WAKE RESEARCH CENTRE
Moe Tika, Moe Pai
Massey University
Private Box 756
Wellington

katoa
21 Reuben Avenue
Brooklyn
Wellington

- I have read and I understand the information sheet
- I understand that the information I share will be kept in the utmost confidentiality and only be used for this specific evaluation
- I have had the opportunity to discuss this study. I am satisfied with the answers I have been given, and understand that I may ask further questions at any time.
- I understand that participation in this study is voluntary and that I may withdraw from the study at any time.
- I understand that participation in this study is confidential and that no material, which could identify me, will be used in any reports on this study.
- I have had sufficient time to consider whether to take part.
- I know whom to contact if I have any questions about the study.
- I give my consent for this interview to be audio-taped.
- I give my consent for my comments to be included in the research

Please print your full name here _____

Signature _____ Date _____

Researcher: Sarah-Jane Paine
Contact phone number: (04) 801 5799 x 6039

APPENDIX 35
FOCUS GROUP THEMATIC ANALYSIS

Findings: Our Hopes and Dreams for Genetic Research

Within each focus group our hopes and dreams for genetic research were discussed first, in case talking about our concerns discouraged any of the informants from raising their hopes later in the session. Despite this approach, it became evident that the issues surrounding this new technology are not clearly delineated, and as one key informant observed

> *…the hopes are based around essentially the same things as the fears, the same concepts; it is just a different expression around the process...*
>
> ***Key-informant, MH1***

Some participants formulated their hopes in response to a discussion around a particular fear for genetic research. As a key-informant explains

> *…you should call that* [theme] *research practices as well, cos that is a really good way of illustrating the positive and negative of the same thing, cos it's not a separate thing, and that actually demonstrates the element of trust that Māori put into going along with a research project now, because it is one of their major concerns, and yet they know it is also one of the ways that they can benefit…*
>
> ***Key-informant, MH1***

The participants' hopes and dreams for genetic research were broader in nature providing a rich description and analysis of research that is relevant for Māori facing this 'new frontier' in science. Within the discussion of our hopes for genetic research, three major themes were identified which encompassed the topics raised by the focus group participants (see Table 1)

The first theme is called **social enhancement** which endeavours to capture the hope that genetic research would be used for the good and wellbeing of our communities. During the construction of this theme each focus-group undertook their own risk/benefit analysis where potential benefits, such as developments in medicine and production of food crops, were weighed up against the perceived risks to society such as their long-term efficacy and safety. It was clear that this analytical approach largely involved the consideration of their personal beliefs and tikanga as criteria against which they could judge the acceptability, or not, of the technology or research agenda.

The second theme is called **governance**. This theme attempts to describe the talk that genetics and research will be controlled and monitored for the protection of people and environment. It was clear that the informants spoke to the characteristics of 'good' governance and an analysis of the current structures that exist to regulate and control genetic research in the public interest.

The final theme was entitled **research practices**. Within the discussion of our hopes for genetic research, the informants described how acceptance of research by Māori could be facilitated by research practices that acknowledge a Māori worldview. In these conversations, the participants evaluated research as they know it and made suggestions as to how this experience could be improved.

Table 1. Māori hopes and dreams for genetic research in Aotearoa New Zealand

Social Enhancement	Research Practices
Finding cures for diseases including genetic screening, prolonging and enhancing life, prevent suffering, fertility	What is the kaupapa? Take a broader focus to genetic research, provide public with good reasons to do the research
Development and production of new medicines and technologies to identify 'sick' genes	Community benefits: whānau, hapū and iwi development
DNA technology: a passive alternative to blood testing	Community benefits: informed decision through better research
DNA technology: genealogical tracing, libraries of information at our finger tips	The research experience: kaupapa Māori research methodology enables empowerment of communities, ethics, cultural safety and tikanga
Food/crops production: aid for Third-World countries	The research experience: Allow for more active participant involvement
Food/crops: increase yield and availability while decreasing cost to consumer	**Governance**
Public information and education: balanced information around genetics	Control: continual and strict regulation and monitoring of research
Communication: public and scientists	Control: public vs. private sector interests
Communication: Māori and scientists	Control: community interests inform decision making
Enhanced understanding and awareness of te āo Māori and tikanga	Protection: take burden from the community
	Protection of individual and community interests and rights
	Complex issues requiring high skill and knowledge base
	Objectivity, transparency and accountability

Findings: Our Fears and Concerns for Genetic Research

Although talking about our fears and concerns for genetic research was reserved for the second half of focus group sessions they often featured throughout each discussion as the informants would articulate their concerns when considering their hopes genetic research. Three major themes were identified within the discussion of our fears and concerns for genetic research (See Table 2).

The first theme was entitled **morality and ethics** which broadly encompassed the belief that the continued development of genetic research will challenge the moral and ethical boundaries that protect our society. Morality was discussed in terms of the research itself and of the people involved, while our talk around ethics often focused on recent examples of unsafe research that has occurred both locally and abroad.

The second theme was called **research processes** which examined the methods used in research and the way in which the knowledge gained can be used against the community. It also describes the uncertainty that exist within our communities regarding a future that involves genetic research. This theme talks about the unknowns, including possible consequences to our health and our land.

The third theme was called **power** which describes the talk around power-relationships hegemony within research and society. This theme was born from the participants' fears and concerns that genetic research involves ideologies of control, power, marginalisation and racism.

Table 2. Māori fears and concerns for genetic research in Aotearoa/New Zealand

Morality	Power
Scientists playing God: prolonging/altering natural life courses, loss of individuality and wairua	Control and access: power, wealth, large corporations
Moral disagreement including cloning, designer babies, embryo screening, xenotransplants. Who has the right to decide and where do we stop?	Speed of genetic research silences the community
Gap between scientific knowledge and Mātauranga Māori	Economic drivers: relationship with governments, multi-national companies, U.S
Is it a necessity or desire: health outcomes are glamorised?	Racism: unequal benefit, access and control.
Research Practices	Marginalisation and oppression: Western knowledge and genetic research silences marginalised communities
Unwanted outcomes: research can't provide any assurances	
Research practices disempower communities. Outcomes don't reflect our realities	
Victim-blaming: the framing of research highlight issues as 'Māori' issues	
Research-myopia: short-term benefits may cause long term problems	