Iodine, selenium, iron, and zinc intake in 5- to 10-month-old infants living in Manawatū, Aotearoa.

Mother and Infant Nutrition Investigation (MINI) Study

A thesis presented in partial fulfilment of the requirements for the degree of

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Abstract

Objective: Optimal thyroid function is essential for growth and development in early life, This study will nvestigate iodine, selenium, iron, and zinc intake in 5 to 10 month old infants living in Manawatū, Aotearoa, as they have been shown to support optimal thyroid function.

Method: This study is part of an observational longitudinal study conducted in Manawatū, Aotearoa from June 2016 – December 2017. Eighty-seven breastfed infants between 5 and 10 months old and their mothers attended a study visit at the Massey University Manawatū Campus. Fifity-one mothers recorded a three-day diet diary (3DDD) for their infants' food and fluid intake, and breastfeeding occasions. Seventy-two maternal breastmilk samples and 41 infant spot urine samples were analysed for iodine and selenium concentrations using inductively-coupled plasma mass spectrometry.

Results: Median (Q1, Q3) intake for iodine using 3DDD was 62 (30, 98) µg/day with 82% of infants below their age-specific Adequate Intake (AI). Median urinary iodine concentration (MUIC) was 107 (57.5, 198) µg/L with only 12% below 50 µg/L therefore most of the infants could be classified as iodine insufficient according to the WHO/UNICEF/ICCDD (2007) criteria. However, if MUIC is measured against higher cut-offs extrapolated from the AI, such as 125 µg/L, the iodine status of more of population could be considered suboptimal. Maternal breast milk iodine concentration (BMIC) was 59 (39, 108.5) µg/L, contributing a median 37 (6, 9) µg/day to total iodine intake in breastfed infants. Median infant selenium intake was 12 (9, 16) µg/day selenium intake, with 67% below their age-specific AI. Median urinary selenium concentration (MUSC) in infants was 11 (6, 16) µg/L. Breastmilk selenium concentration (BMSC) was 11 (9, 13) µg/L, contributing a median 7 (6, 9) µg/day to total selenium intake in breastfed infants. Median infant intake of iron was 2 (1, 5) mg/day with 78% below age specific EAR/AI. Median infant intake of zinc was 3 (2, 4) mg/day, with 31% below their age specific EAR/AI and 16% exceeding upper limit (UL) for zinc intake. In addition to complementary food, 69% of infants had only breastmilk, 23% had combination of breastmilk and infant formula, and 8% had only infant formula. One infant was not yet receiving complementary food.

Conclusion: Despite public health initiatives, this study suggests infants in Aotearoa still have suboptimal intake of iodine, zinc and iron While some infants are achieving low or adequate zinc intakes, others are consuming excessive zinc, however the associated risks are low.

Suboptimal intake of iodine, selenium, iron and zinc in the infant diet could impact thyroid function, growth, and neurodevelopment.

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Firstly, I would like to acknowledge and thank my two supervisors, Louise Brough and Jane Coad. Your collaborative support and extensive knowledge on the topic of iodine nutrition and infant feeding has truly powered this research. Thank you for encouraging and supporting me to accomplish this project independently while we navigated the challenges of remote working during a global pandemic! Special thanks to Louise for your thoughtfulness, patience, and positivity which made our many catchups over Zoom an absolute joy. I would also like to thank Ying Jin (PHD researcher) who coordinated the MINI Study, which formed the foundations for this thesis. Thank you all for your immense contribution to the field of maternal and infant nutrition in Aotearoa.

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To my partner Kurtley – making every day brighter, funnier, and choicer. Thank you for your unwavering aroha and dedication throughout the last five years.

Finally, I am dedicating this research to my new godson and nephew, Isaiah Fa'alepo Mark Frances Taei Mama, born January 7th, 2021. What a delight it is watching you grow, learn, and (of course) complementary feed!

Ngā mihi maioha ki a koutou.

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List of Abbreviations

3DDD	Three Day Diet Diary
AI	Adequate Intake
ATP	Adenosine Triphosphate
BMIC	Breast Milk Iodine Concentration
BMSC	Breast Milk Selenium Concentration
DIO	Deiodinase
EAR	Estimated Average Requirement
FFQ	Food Frequency Questionnaire
GPx	Glutathione peroxidase
GR	Goitre Rate
ICCIDD	International Council for Control of Iodine Deficiency Disorders
ID	Iodine Deficiency
IDA	Iron Deficiency Anaemia
IDD	Iodine Deficiency Disorders
MEFP	Meat, Eggs, Fish and Pulses
MINI	Mother and Infant Nutrition Investigation
MOH	Ministry of Health
MPI	Ministry For Primary Industries
MUIC	Median Urinary Iodine Concentration
MUIE	Median Urinary Iodine Excretion
MUSC	Median Urinary Selenium Concentration
NHMRC	National Health and Medical Research Council
NIS	Sodium-Iodide Symporter
NZTDS	New Zealand Total Diet Study
Q1, Q3	Quartile One, Quartile Three
RDI	Recommended Daily Intake
rT_3	Reverse Triiodothyronine
SD	Standard Deviation
T_3	Triiodothyronine
T_4	Thyroxine
TBG	Thyroglobulin Binding Protein
Tg	Thyroglobulin
TH	Thyroid Hormone
TPO	Thyroid Peroxidase
TRH	Thyrotropin Releasing Hormone
TSH	Thyroid Stimulating Hormone
UI	Urinary Iodine
UIC	Urinary Iodine Concentration
UL	Upper Limit
UNICEF	United Nations International Children's Emergency Fund
USC	Urinary Selenium Concentration
USE	Urinary Selenium Excretion

Ethical Approval

The Mother and Infant Nutrition Investigation (MINI) study was approved by the Health and Disability Ethics Committee (15/NTA/172) from December 2015. The ethics approval was registered with the Royal New Zealand Plunket Ethics Committee in June 2016. The MidCentral District Health Board also approved this study, and it was registered with the Australian New Zealand Clinical Trials Registry [ACTRN1261500102854]. The research was conducted at the Human Nutrition Research Unit at Massey University, Palmerston North, New Zealand.

1. Introduction

1.1. Background

The Ministry of Health (MOH) (2021) recommends exclusive breastfeeding until around six months of age, followed by the introduction of complementary foods with continued breastfeeding for up to two years and beyond. Maternal intake of nutrients influence the micronutrient intake and status of the breastfed infant until after complementary foods are introduced (MOH, 2006a). Infants require an adequate supply of iodine, selenium, iron and zinc from breastmilk, complementary foods and other fluids to support optimal thyroid function.

The importance of iodine and selenium for production of the human thyroid hormones (TH), thyroxine (T_4) and triiodothyronine (T_3), required for physical and neurological development in infants is well documented (World Health Organization (WHO), 2004a, Zimmermann, 2011). Aotearoa has a history of inadequate iodine and selenium intake, endemic goitre and low median iodine concentration (MUIC) in the population due to inadequate levels of both nutrients in soils resulting in low concentrations in the food supply (Thomson, 2004b). Key public health initiatives to address iodine deficiency in Aotearoa include introduction of iodised salt in the early 1900s (Hercus et al., 1925) and the mandatory use of iodised salt in commercially produced bread from September 2009 (Food Standards Australia New Zealand (FSANZ), 2008). In 2010, the government recommended a subsidised 150 µg/day iodine supplement for pregnant and lactating women (National Health and Medical Research Council (NHMRC), 2010).

Iron is required for haem-dependent thyroid peroxidase (TPO) activity which is involved in TH synthesis (Hess, 2010; Zimmermann, 2006). Poor iron status during infancy can impair physical growth and cognitive and motor development (Bouglé et al., 2000; Grantham-McGregor & Ani, 2001). Suboptimal iron intake and status among infants and toddlers in Aotearoa is also well documented (Crampton et al., 1994; Grant et al., 2007; Rive et al., 1996; Soh et al., 2004; Wham, 1996; Wilson et al., 1999). Zinc is ubiquitous throughout human cells and is thought to influence thyroid hormone production through gene expression (Beserra et

al., 2021; O'Kane et al., 2018). Zinc intake and status in Aotearoa infants is largely under investigated, and deficiency is considered rare.

1.2. Justification for the research

This thesis is part of the Mother and Infant Nutrition Investigation (MINI) Study, an observational longitudinal cohort study measuring the selenium and iodine status of 87 women and their infants in their first year after birth. There has been limited investigation into the intake and status of micronutrients that might impact thyroid function in the infant population in Aotearoa. The MINI study is unique in that it investigates several key micronutrients responsible for adequate TH synthesis concurrently, rather than in isolation. New Zealand research during the last twenty years has primarily focussed on iodine intake and status of school-aged children (Gordon et al., 2009; Jones et al., 2016; Skeaff et al., 2002), pregnant and lactating women (Brough et al., 2015; Jin et al., 2021), and non-pregnant women (Finlayson et al., 2019; Shukri et al., 2014). The most recent study examining iodine intake and status specifically in children under two years old was a community-based cross-sectional study in the South Island, which found mild iodine deficiency among breastfed infants (Skeaff et al., 2005). Suboptimal intake and status of selenium (McLachlan et al., 2004) and iron (Soh et al., 2004; Soh et al., 2002) have also been reported in this age group in Aotearoa.

This thesis provides data on infants eight years after the introduction of mandatory iodised salt in commercially made bread products in September 2009 by the New Zealand government (FSANZ, 2008), and provision for a 150 μg/day iodine supplement for all pregnant and lactating women in July 2010 (NHMRC, 2010). The most recent New Zealand Total Diet Study (NZTDS) showed iodine intake for all population cohorts has increased except in the infant population (Pearson et al., 2016). This shows the importance of public health interventions by the government and justifies further monitoring of the infant population.

Infants between the age of 5 to 10 months undergo a dietary transition from exclusive breastfeeding and/or infant formula feeding, to the introduction of complementary foods. Therefore, this study investigates the contribution of foods and fluids (other than breast milk and infant formula) to total iodine, selenium, iron, and zinc intake. The food was categorised

into fruit and vegetables, dairy, breads and cereals, and meat, eggs, fish, and pulses (MEFP). Consumption of iodine fortified commercially manufactured bread and iodised salt was also examined, as this could determine if bread intake provides a significant contribution to an infant's dietary iodine intake.

As breastmilk and/or infant formula continue to be a major part of total intake, breastfeeding patterns, and methods to estimate breastmilk volumes have been explored. Monitoring breastfeeding patterns is valuable because despite the well-established lifelong benefits for the breastfed infant (Bernardo & Cesar, 2013), exclusive breastfeeding rates in Aotearoa are low (Morton et al., 2012; National Breastfeeding Advisory Committee, 2009). Breastmilk iodine and selenium concentrations were analysed as they pertain to the impact of iodine and selenium supplementation on the intake and status of breastfeeding infants. This allowed for comparisons to be made between the micronutrient intake and status of infants who were breastfed, infant formula fed, or combination fed. Iron and zinc concentrations in the breastmilk samples were not analysed in this study.

Low intake of both iodine and selenium is a significant public health concern due to low levels in soils and food supply (Thomson, 2004b). Median urinary iodine concentration (MUIC) is typically used to measure iodine status of school-aged children (WHO/UNICEF/ICCIDD, 2007). Biological analysis of infant urine determined the iodine and selenium status of this infant cohort, which were compared with international reference ranges. Urinary concentrations of iodine and selenium have been used as a proxy measure to estimate intake. Total daily iodine and selenium excretion have been estimated using urinary iodine concentration (UIC) and urinary selenium concentration (USE), and estimated urinary excretion based on the infant body weight.

Suboptimal iodine intake and status may compromise brain growth and body development through limiting the production of TH. Deficiency in selenium impairs TH production and thyroid function which may compound the effect of iodine deficiency disorders (IDD) (Triggiani et al., 2009). Iron and zinc are also thought to influence thyroid function, and are essential for infant growth and development. Anthropometric data such as weight, head circumference, and recumbent length were collected in order to compare to micronutrient

intake and status to determine if there is any association (or consequence) related to infant growth.

Previous research concerning iodine and selenium intake and status has been carried out primarily in the South Island of Aotearoa. Due to the geographical differences concerning the iodine and selenium content of soils and food supply (Pearson et al., 2016; Thomson, 2004b), research needs to be conducted across all the whole country to monitor the issue of IDD in infants. This present study based in the Manawatū in the North Island, will add knowledge concerning iodine and selenium intake in infants throughout Aotearoa, with specific reference to the effect of the fortification of bread and provision of iodine supplementation in pregnant and lactating women.

1.3. Aim & Objectives

1.3.1. Aim

To investigate the intake of the micronutrients involved in optimal thyroid function, namely iodine, selenium, iron and zinc in 5-to 10-month-old infants in Aotearoa.

1.3.2. Objectives

i) To determine the micronutrient intake of iodine, selenium, iron, and zinc in 5-to 10-month-old infants and the relative contribution from food, breastmilk and infant formula to this intake.

ii) To estimate the iodine and selenium intake of 5-to 10-month-old infants through analysis of spot urine samples.

iii) To examine dietary patterns related to breastfeeding and formula feeding and their relationship to intake of iodine, selenium, iron and zinc.

iv) To determine if there is an association between iodine, selenium, iron and zinc intake and infant anthropometry.

1.4. Overview of the thesis

Chapter 1 introduces the study topic, providing a brief background and justification of the research before introducing the thesis aims and objectives. Chapter 2 examines the literature relating to the micronutrients involved in optimal thyroid function in 5- to 10-month-old infants, specifically iodine, selenium, iron, and zinc. The potential health consequences of deficiency of such micronutrients, particularly on thyroid hormone production and function are explored. For context, New Zealand epidemiological data related to deficiency of micronutrients relevant to thyroid function are examined, including public health interventions targeted to the general population and pregnant and lactating women. Methods for assessing status for each micronutrient in the infant population are discussed throughout the literature review. Methodologies of assessment for determining six-month-old infants' dietary intake are discussed, and finally, approaches for estimating breastmilk intake volumes are considered to determine the suitability of the methods used in this study. Chapter 3 is a research manuscript, which describes the study design, methods and materials, the procedures involved, data handling and statistical analysis. The results of the study are stated and discussed in chapter 3, including the limitations of the present research. Finally, the conclusion is presented in chapter 4, as are recommendations for future research and suggestions for improving micronutrient intake and status in infants 5-10 months old.

1.5. Research Contributors

Researchers	Contribution
Tasarla Mills-Wallis *Principal researcher*	Responsible for thesis topic and design, thesis writing, reviewing, editing and submission. Responsible for entry and analysis of diet diary, statistical analysis and interpretation.
Associate Professor Louise Brough *Primary Supervisor*	Research topic and MINI study design, funding acquisition, reviewing the thesis, ethics approval, statistical analysis and interpretation
Professor Jane Coad *Secondary Supervisor*	Research topic and MINI study design, funding acquisition. Reviewing the thesis
Ying Jin *PHD researcher*	Ethics approval, MINI study design, methodology, funding acquisition, recruitment & screening, data collection, handling of samples

2. Literature Review

2.1. Research Question

The overarching purpose of this literature review is to answer the question of what is currently known about the intake of iodine, selenium, iron, and zinc in the infant population in Aotearoa. The literature review also aims to explore role of these elements in optimal thyroid function in infants during the first year of life and explore wider public health significance of deficiencies of these micronutrients in this population. To answer these questions, it is also essential to review the literature related to methodologies for assessing dietary intake and status in infants, including breastfeeding patterns, and explore the challenges presented.

2.2. Literature Review Methods

Studies included in this review date between 1925 – 2021, although the majority are published after 2000. The primary electronic data base used to find literature for this research was Web of Science, accessed through the Massey University Discover portal. Other data bases included PubMed and Google Scholar. Key search terms are summarised in table 2.1, which were searched both independently or in combination using “and” and “or” search functions. Referenced literature was also identified through key published papers which covered the topic of iodine and selenium nutrition in Aotearoa.

Table 2.1. Key search terms used during research.

"Iodine"	"Selenium"	"Zinc"	"Infant Intake"	"Dietary analysis"
"Thyroid Function"	"Growth"	"Infant intake"	"Iron deficiency"	"Food frequency questionnaire"
"Goitre"	"Cognitive Development"	"Breastmilk Zinc"	"Toddler"	"Three-day diet record"
"Iodine deficiency disorders"	"Physical Development"	"Breastmilk Iodine"	"Weaning foods"	"24-hour recall"
"Growth"	"Thyroid Hormone"	"New Zealand"	"Breastmilk intake"	"Breastmilk Volume"
"Iodine fortification"	"Measuring Status"	"Australia"	"Measuring status"	"Dietary assessment method"
"Urinary Iodine Concentration"	"Urinary Selenium	"Weaning"	"Breastmilk Selenium"	"Infant Foods"
"Soil Iodine"	"Concentration"	"Feeding"	"Soil Selenium"	
"Thyroid Hormone Axis"	"Excretion"	"Food"	"Complementary"	
"Maternal iodine status"	"Intake"	"Supplementation"	"Toddlers"	
"Iodised Salt"	"Deficiency"	"Compliance"	"Food supply"	
	"Maternal selenium status"	"Infant formula"	"Recommendations"	
		"Feeding practices"	"human milk"	
		"Breastmilk"	"Thyroxine"	
		"Bread"	"triiodothyronine"	
			"thyroid stimulating hormone"	

Key recommendations and reviews from organisations such as the New Zealand Ministry of Health (MOH), Ministry for Primary Industries (MPI), World Health Organization (WHO) including joint consultation with United Nations International Children's Emergency Fund and the International Council for Control of Iodine Deficiency Disorders, (WHO/UNICEF/ICCIDD), and Pan American Health Organization (PAHO), and the Australian National Health and Medical Research Council (NHMRC) were also included in this review. Findings from various New Zealand Total Diet Survey/Studies (NZTDS) conducted between 1987/89 and 2016 were extensively reviewed.

2.3. Infant Dietary Intake

2.3.1. Dietary recommendations for first year of life

The MOH (2021) recommends exclusive breastfeeding until the introduction of complementary foods at around six months of age, while the WHO (2004) recommend that infants start receiving complementary foods specifically at six months of age. Clearly, maternal intake of nutrients will determine the micronutrient status of the foetus and

exclusively breastfed infant, until complementary foods are introduced (MOH, 2006a). Both organisations encourage a developmental approach to introducing appropriate complementary foods to meet infants' growing energy and micronutrient requirements, with continued breastfeeding for up to two years or longer. The nutrient reference values for intake of each iodine, seleniujm, iron and zinc for infants aged 0-6 and 7-12-months-old are summarised below (table 2.2).

Table 2.2. Nutrient Reference Values for daily intake of iodine, selenium, iron and zinc in infants

Mineral		[a] **EAR**	[b] **RDI**	[c] **UL**	[d] **AI**
Iodine	(0-6 Months)	-	-	-	90µg
	(7-12 Months)	-	-	-	110µg
Selenium	(0-6 Months)	-	-	45µg	12µg
	(7-12 Months)	-	-	60µg	15µg
Iron	(0-6 Months)	-	-	20mg	0.2mg
	(7-12 Months)	7mg	11mg	20mg	-
Zinc	(0-6 Months)	-	-	4mg	2mg
	(7-12 Months)	2.5mg	3mg	5mg	-

[a] Estimated Average Requirement
[b] Recommended Dietary Intake
[c] Upper Level of Intake
[d] Adequate intake

2.4. Thyroid Function

The thyroid gland is responsible for the formation and secretion of thyroid hormones and iodine homeostasis. Thyroxine (T_4) and triiodothyronine (T_3) are the major thyroid hormones (TH) secreted by the thyroid, as pictured below (figure 2.1). These play an important role in metabolism by regulating human metabolic rate including lipolysis, gluconeogenesis, and adenosine triphosphate (ATP) production (Chung, 2014; WHO, 2004). TH are required for

normal physical growth and maturation, including the brain and central nervous system and other target tissues such as the skeleton, particularly from the 15th week of gestation to 3 years of age (Mullur et al., 2014; Rohner et al., 2014; Segni, 2017; WHO, 2004).

Figure 2.1. Molecular structure of thyroxine, triiodothyronine and reverse triiodothyronine.

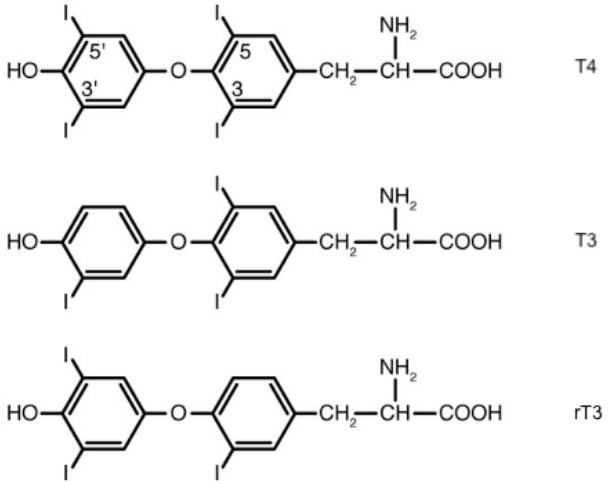

Figure 2.1 shows the molecular structures of thyroid hormones (TH) thyroxine (T_4), triiodothyronine (T_3) and reverse triiodothyronine (rT_3). Reproduced with permissions from rights-holder (Brent, 2012).

Each thyroid hormone structure is made up of protein and iodide; T_4 contains four atoms of iodide and T_3 contains three; rT_3 is the inactive reverse isomer of T_3 (Figure 2.1). Approximately 59% and 65% of the weight of T_3 and T_4 is iodine, respectively. T_4 is produced in the thyroid at greater concentrations than T_3, and almost all T_3 (99.97%) and T_4 (99.7%) is transported in the circulation bound to thyroglobulin binding protein (TBG) (Kragh-Hansen et al., 2017). Unbound thyroid hormone can enter the cell of its target tissue. Once T_4 reaches its target tissue, the iodine is removed by selenium-dependent deiodinases, converting the structure into the active T_3 form, which is then transported into the cell cytoplasm (Brent, 2012). Upon entering target tissue cell, T_3 binds to nuclear receptors, stimulating a wide range of metabolic processes. The hypothalamic-pituitary-thyroid axis is displayed below (figure 2.2).

Figure 2.2. Hypothalamic-pituitary-thyroid axis and conversion of thyroxine to triiodothyronine or reverse triiodothyronine.

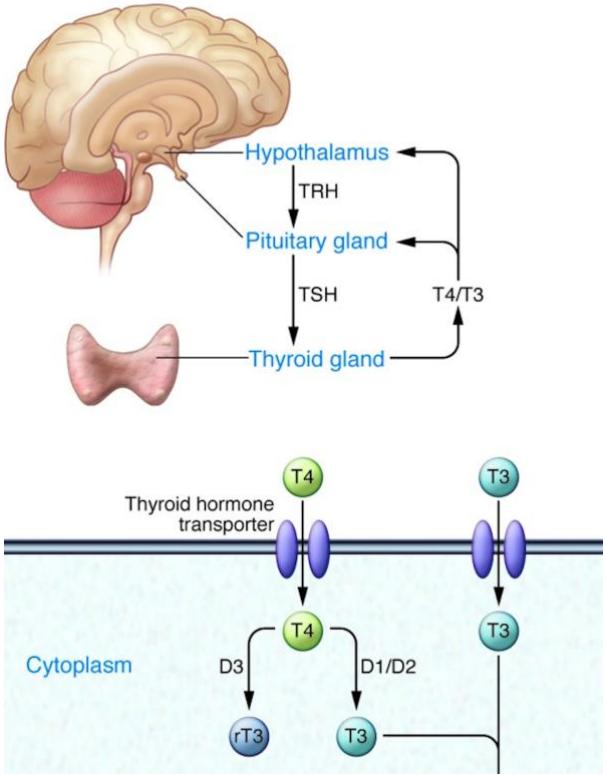

Figure 2.2. shows the key components required for thyroid hormone action and homeostasis, including the hypothalamic-pituitary-thyroid axis. Free T_3 is transported into cell directly while circulating T_4 is converted by membrane bound D3 (deiodinase 3) into metabolically active T_3 and by D1/D2 (deiodinases 1 and 2) into either T_3 or rT_3. Reproduced with permissions from rights-holder (Brent, 2012).

2.5. Micronutrients Involved in Thyroid Function

Normal thyroid metabolism is dependent on adequate levels of iodine and selenium for both synthesis and metabolism of thyroid hormones (Zimmermann & Köhrle, 2004). Iron is also important (Hess & Zimmermann, 2004; Zimmermann & Köhrle, 2004), and there is some evidence that zinc may be involved in optimal thyroid function (Beserra et al., 2021; Betsy et al., 2013). The role of other micronutrients such as vitamin A, copper and magnesium in thyroid function have also been explored (Hess, 2010). Deficiencies in one or more essential vitamins and minerals typically coexist due to similar causal factors such as poor-quality diet, malabsorption or increased physiological requirements such as periods of rapid growth and development (Hess, 2010). Deficiencies may also result from inadequate micronutrient absorption or due to infection or inflammation (Hess, 2010). Inadequate supply of TH

dependent micronutrients, especially iodine and selenium contribute to altered or disrupted thyroid function (Triggiani et al., 2009), which can impact infant growth and neurodevelopment (Zimmermann, 2011).

2.6. Iodine

2.6.1. Absorption and Utilisation

Iodine is required for production of human thyroid hormones T_4 and T_3 in the thyroid gland which are critical for the regulation of biochemical reactions, enzymatic activities and protein synthesis (Triggiani et al., 2009). Iodine in food is ingested either freely as iodide, iodate, or attached to amino acids (National Health and Medical Research Council, 2009). Iodide, which is the most common form present in food and human milk, is reduced by glutathione and nearly completely (≥90%) absorbed in the stomach and duodenum into circulation, before being taken up by the thyroid gland and kidneys (Gropper & Smith, 2012; WHO, 2004; Zimmermann, 2011). Circulating iodide enters the thyroid gland via the sodium-iodide symporter (NIS) located at the basal membrane of the thyroid follicular cell before migrating to the apical membrane. Thyroid stimulating hormone (TSH) regulates the uptake of iodide into the thyroid gland by increasing the activity of the NIS on the follicular cell membrane. Thyrotropin releasing hormone (TRH) from the hypothalamus triggers the release of TSH from the anterior pituitary gland (Zimmermann et al., 2008). This works in a feedback loop referred to as the hypothalamic-pituitary-thyroid axis.

Once iodide enters the thyroid follicle, it is oxidised by TPO and hydrogen peroxidase into iodine. It is then attached to tyrosol residues in thyroglobulin (Tg) to produce TH precursors which eventually become T_4 and T_3 in a series of enzymatic processes. Iodine released from the conversion of T_4 to T_3 at tissues is reabsorbed by the thyroid and recycled or excreted. Nearly 90% of total ingested iodine is excreted in the urine within 24-hours (Chung, 2014). Therefore, iodine status is typically assessed based on urinary iodine concentration (UIC) or excretion (UIE). In lactating women, iodine is also transferred into the breast milk via the mammary gland, with concentrations varying between 5.4 to 2170 µg/L in world-wide studies (Dorea, 2002).

2.1.2. Iodine Deficiency Disorders (IDD)

Iodine deficiency disorders (IDD) refer to the wide spectrum of adverse consequences that can occur throughout the life cycle as a result of iodine deficiency. In mild to moderate iodine deficiency, the pituitary gland secretes more TSH to increase the thyroid gland uptake of available iodine to sustain TH production (Zimmermann & Boelaert, 2015). As iodine deficiency becomes more severe, TSH rises further, increasing thyroglobulin (Tg) synthesis, TPO activity, and maximising iodine uptake and recycling at the thyroid gland (Vigone et al., 2018; Zimmermann & Boelaert, 2015). If iodine supply is exhausted, TH production declines, characterised by low levels of circulating T_4 and T_3 (Zimmermann & Boelaert, 2015). High TSH increases blood flow to the thyroid gland, stimulating hypertrophy and hyperplasia of thyroid follicular cells, which develops into a goitre (Pirahanchi et al., 2021). Goitre is rare and difficult to identify in the infant and preschool aged child population (WHO/UNICEF/ICCIDD, 2007).

An inadequate supply of iodine can interrupt neurological development of the brain and physical growth during foetal and infant development by limiting the production of T_3 and T_4 (National Health and Medical Research Council, 2009). TH modulate genes that are involved in myelination, cell migration, differentiation and maturation in the developing brain and central nervous system (Bernal, 2005). The impact of insufficient TH secondary to inadequate iodine on infant neurology may depend on the timing of deficiency during foetal and infant development (Zoeller & Rovet, 2004). Exclusively breastfed infants may be more vulnerable to iodine deficiency as they are dependent on iodine content of breastmilk, which is determined by the mothers intake and status before and during pregnancy and lactation (Andersson et al., 2007). This deficiency risk is compounded by low infant production of thyroid hormone per kilogram of weight, limited iodine stores, and increased requirements associated with rapid growth and development (Eriksen et al., 2020). Iodine deficiency was considered the single biggest contributor to preventable brain damage and mental impairment in children worldwide (Kapil, 2007; Zimmermann et al., 2008).

The most serious health consequence of iodine deficiency is cretinism which is characterised by physical abnormalities and mental impairment in children born to mothers that are severely iodine deficient in pregnancy (Skeaff, 2011). There have been no reports of cretinism

in Aotearoa, although mild-moderate iodine deficiency has been identified in non-pregnant (Finlayson et al., 2019; Shukri et al., 2014), pregnant and lactating women (Brough et al., 2015; Jin et al., 2021), children (Gordon et al., 2009; Skeaff et al., 2002) and infants and toddlers (Skeaff et al., 2005) during the last two decades.

2.1.3. Measuring Iodine Status in Infants

Historically, thyroid size and palpation has been the preferred method to assess goitre rate (GR) in populations of school-aged children, and various scales were proposed throughout the 20th century to provide an objective reference standard for goitre identification (Perez et al., 1960; WHO/UNICEF/ICCIDD, 1993; Zimmermann & Andersson, 2012). However this method lacks specificity and precision in infants (WHO, 2014) and in areas with mild iodine deficiency (Zimmermann & Andersson, 2012), where goitres are less pronounced. Iodine monitoring in populations has broadened from endemic goitre, which only looks at goitre incidence in the population, to other measures of IDD (Hetzel, 1983). The most common method to assess iodine status within infant populations is measuring iodine in the urine (WHO/UNICEF/ICCIDD, 2007). Serum or plasma levels of TH, TSH, and Tg can also be measured (WHO/UNICEF/ICCIDD, 2007), however collecting blood samples in a large population of infants may be impractical.

Almost all (>90%) of ingested iodine is excreted in the urine within a period of 24-48 hours; therefore urinary iodine (UI) is a good indication of recent iodine dietary intake (Chung, 2014; National Health and Medical Research Council, 2009; Zimmermann & Andersson, 2012). twenty-four-hour urine collection for total urinary iodine excretion (UIE; µg/day) is not effected by diurnal variation or hydration status but may beimpractical for sampling in large populations due to poor compliance. Median urinary iodine concentration (MUIC) (µg/L) is the most commonly used measure of iodine status in large populations of >300 subjects (WHO/UNICEF/ICCIDD, 2007). It is less useful for measuring individual iodine status due to day-to-day variation of iodine intake and hydration status (WHO/UNICEF/ICCIDD, 2007). In a large cohort, it has been shown that UIC estimated from spot urine samples correlate well with median 24hr UIE (µg/L) (Zimmermann, 2008; Zimmermann & Andersson, 2012), therefore UIC is often used as a practical option in infants.

Attempts to define age-sex specific UI cut-offs for identifying iodine deficiency have evolved over the years. The earliest research in Europe demonstrated high incidence of goitre in regions where total UIE was lower (17-87 μg/day), while in regions where goitre was rare or absent, UIE averaged 112-186 μg/day (Hercus et al., 1925). A Central American study (N=3000) established a correlation between estimated dietary iodine intake from creatinine and iodine excretion in goitrous areas; cited in WHO/UNICEF/ICCIDD (1993). Later, the joint Pan American Health Organization (PAHO)/WHO proposed a graded scale relating endemic goitre prevalence and severity with population UIE μg/g creatinine (grade 1; <50 μg/g creatinine, grade 2; 25-50 μg/g creatinine, grade 3; <25 μg/g creatinine) (PAHO/WHO, 1986) as cited in (WHO, 2014). In 2000, WHO recommended MUIC be used to measure the effect of salt iodisation programmes in school-aged children. The recommendations for assessing iodine nutrition used today now extrapolate spot urine sample measures to represent a MUIC (μg/L) (table 2.3).

Table 2.3. WHO/UNICEF/ICCIDD (2007) criteria for median urinary iodine concentrations (MUIC) used to categorise iodine intake of children less than 2 years old, and school aged children.

Population Group	**MUIC (μg/L)**	**Category of iodine intake**	**Comment**
Children <2 years old	<100	Insufficient	
	>100	Adequate	
School-aged Children	<20	Insufficient	Severe iodine deficiency
	20-49	Insufficient	Moderate iodine deficiency
	50-99	Insufficient	Mild iodine deficiency
	100-199	Adequate	Optimal
	200-299	Above Requirements	Likely to be adequate for pregnant/lactating women, may pose slight risk to overall population
	>300	Excessive	Risk of adverse health consequences (iodine -induced

	hyperthyroidism, autoimmune thyroid disease).

Adapted with permissions from rights holder (WHO, 2013).

The MUIC cut-off for children <2 years are extrapolated from the ranges of school-aged children, rather than epidemiological data on the iodine status of infant populations. The WHO/UNICEF/ICCIDD (2007) has used 100 µg/L as the target median, because by definition, this means 50% of the samples will be below 100 µg/L. In addition, no more than 20% should be below 50 µg/L (WHO/UNICEF/ICCIDD, 2007). However several studies have proposed higher MUIC cut-offs for the infant population to correspond with infant AI. For example Dold et al (2016) stated that the 100 µg/day cut-off may be too low for this age group, because when extrapolated to 0.5 L urine production and 90% excretion, this would require an intake of 55 µg/day, half the actual AI (7-12 months old) of 110 µg/day. The Swiss researchers suggested a higher MUIC threshold for adequacy of 125 µg/L to correlate with a higher EAR (75 µg/day), and to account for the more concentrated infant urine compared to older children (Dold et al., 2016). Similarly, Delange (2007) suggested higher MUIC range of 180 to 225 µg/L for neonates in line with optimal iodine intake of 90 µg/day. The WHO/UNICEF/ICCIDD have not renewed their current criteria.

2.1.4. Iodine status in Aotearoa

2.1.4.1. 1900 – 1950

Soils in Aotearoa are low in iodine, resulting in low iodine concentrations in locally produced food, thus predisposing the population to inadequate iodine intake (National Health and Medical Research Council, 2009). Endemic goitre in Aotearoa was first noted in several studies in the 1920s (Hercus et al., 1925; Hercus & Roberts, 1927) leading to the first introduction of iodised salt in Aotearoa (MOH, 2020). A survey comparing UIE from several parts of Aotearoa and Samoa in the mid-1930s revealed iodine intake was relatively low and goitre remained prevalent (Hercus & Purves, 1936). In order to reduce goitre rates, Hercus & Purves (1936) recommended that the median UIE in the New Zealand population would need to increase by 100 µg/day to reach 120-160 µg/day, as observed in iodine sufficient countries where goitre was rare or absent. The New Zealand Department of Health responded by increasing the level

of salt iodisation in 1938 (MOH, 2020). By the 1950s, goitre was almost eradicated in children, and median urinary iodine concentration (MUIC) for an 'adequate intake' indicated sufficient status throughout the population of Aotearoa (Thomson et al., 2001).

2.1.4.2. 1950 – 2000

The widespread use of iodine-containing iodophors for sterilising equipment in dairy factories from 1960s-1990s led to higher concentrations of iodine in New Zealand dairy products (Sutcliffe, 1990). This unintentional contamination, along with the generalised use of iodised salt by consumers and manufacturers, meant dietary iodine intake in the population of Aotearoa through this period was sufficient (Brough & Skeaff, 2020; Sutcliffe, 1990). A move away from iodophors to more affordable detergent-based cleaners in the dairy industry, coupled with a decline in the use of iodised table salt among consumers because of public health recommendations to consume less salt, is thought to have contributed to a reduction in dietary intake in the general population by the mid 1990s (Skeaff et al., 2002; Vannoort & Thomson, 2005).

NZTDS from 1997 – 2009 based on 14 day simulated diets for all age groups and genders suggested iodine intakes were inadequate (Vannoort et al., 2000; Vannoort & Thomson, 2005, 2009). Other studies during this period found mild iodine deficiency had re-emerged within various sub population groups including adults in Dunedin and Waikato (Thomson et al., 1997; Thomson et al., 2001), and pregnant women and children in Otago and Wellington (Skeaff et al., 2005; Skeaff et al., 2002), characterised by MUIC of <100 µg/L. Skeaff and colleagues studied children during this period and reported a MUIC 66 µg/L among a random sample of 8-10 year olds from two New Zealand cities; 12% presented with goitre (N=320) (Skeaff et al., 2002). The National Children's Nutrition Survey confirmed mild iodine deficiency in children aged 5-14 in Aotearoa, also finding a MUIC of 66 µg/L, with more than 28% below 50 µg/L (N=3275) (Parnell et al., 2003).

2.1.4.3. 2000 – 2020

Skeaff et al (2005) offered the first insight into the iodine content of breastmilk and iodine status of weaning infants and toddlers in Aotearoa in a cross-sectional survey of 6–24-month-

old children in three South Island cities. Suboptimal iodine status was evident among both breastfed (MUIC 44 μg/L) and weaned children (MUIC 59 μg/L), and among lactating women, with a mean iodine content of breastmilk of 22 μg/L (N=230) (Skeaff et al., 2005). Further reports of iodine deficiency among pregnant and lactating women in Aotearoa between 1995-2006 heightened concerns that intake was not adequate to meet the increased iodine requirements for optimal foetal and neonatal brain development (Mulrine et al., 2005; Thomson et al., 2001).

Two key initiatives were implemented in Aotearoa to combat this re-emergence of iodine deficiency. In September 2009, the mandatory use of iodised salt in commercially sold bread was implemented as a food regulation in New Zealand and Australia (Food Standards Australia New Zealand, 2008). It was widely accepted that while this would improve iodine intake for the general population, this measure alone would be inadequate to meet the relatively higher requirements of pregnant and lactating women (Brough & Skeaff, 2020; NHMRC, 2010). Also, fortifying only one food has implications for low/non consumers of that food. Brough et al (2015) found only 15% of pregnant (N=34) and 22% of breastfeeding (N=36) women were aware of the mandatory addition of iodised salt to bread. In addition, several studies after the introduction of bread fortification found low bread consumption among women in Aotearoa associated with low MUIC (Finlayson, 2019). On the other hand, it is common for a single food vehicle, widely consumed by the target population, to be used for food fortification programmes as this limits excessive intakes (WHO, 2006). The MOH (2021) currently recommend bread be included in the infant diet as a source of iodine once complementary feeding has been established.

In July 2010, the New Zealand Ministry of Health advised a subsidised 150 μg/day iodine supplement should be offered to all pregnant and breastfeeding women (NHMRC, 2010). Knowledge among pregnant and lactating women of the need for iodine during pregnancy and lactation has been reported as low. A pilot study in Palmerston North found only 56% of pregnant participants (N=34) and 28% breastfeeding participants (N=36) were aware of the government-subsidised iodine supplement in 2011 (Brough et al., 2015). In this study, even fewer (41% of pregnant, 19% of breastfeeding) participants took the available supplement (Brough et al., 2015). Although, 29% pregnant and 17% breastfeeding participants took an

alternative supplement containing iodine, such as Elevit or Blackmores, therefore they may have achieved acceptable iodine intakes (Brough et al., 2015). Data collected in the MINI study from 2017 found 46% were still taking it during lactation (Jin et al., 2021), therefore knowledge and adherence may have improved in Aotearoa. However, cost and inequities in access to quality healthcare in Aotearoa may still contribute to low iodine supplement adherence throughout pregnancy and lactation.

Iodine status of New Zealanders has evidently fluctuated over the last 100 years. The last three decades have seen an increased focus on iodine intake and status among pregnant and breastfeeding women, infants, and young children. The most recent study in Aotearoa examining iodine intake and status among infants was published nearly two decades ago by Skeaff et al (2005), prior to mandatory fortification of bread and introduction of the iodine supplement for pregnant and breastfeeding women.

2.2. Selenium

2.2.1. Selenium and thyroid function

Selenium (figure 2.3) is an essential micronutrient that exerts activity in the form of the amino acid selenocysteine, which is incorporated in different proteins known as selenoproteins (table 2.5) (Duntas & Benvenga, 2015; Ventura et al., 2017). Selenoproteins have a variety of antioxidant and anti-inflammatory roles throughout the body including thyroid hormone metabolism, redox reactions, DNA synthesis, reproductive and immune function (Duntas & Benvenga, 2015; Mehdi et al., 2013). The human thyroid contains the highest concentration of selenium per unit weight of all tissues, mostly incorporated into proteins of thyroid follicular cells (Triggiani et al., 2009; Ventura et al., 2017).

Figure 2.3 Selenocysteine Structure

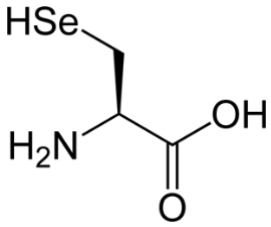

Figure 2.3 shows the molecular structure of selenocysteine. Reproduced with permissions from rights-holder (Yang & Liu, 2017).

Selenoproteins are an integral part of iodothyronine deiodinases (DIO) that regulate the synthesis and degradation of thyroid hormones (Arthur et al., 1999). There are several key types of selenocysteine-containing iodothyronine deiodinases (table 2.5) Type I (DIO 1) and II (DIO2) 5'deiodinases convert T_4 to the biologically active T_3 by removal of iodine from the 5 or 5' position (Gropper & Smith, 2012). DIO 1 catalyses this reaction within the thyroid tissue, before converted T_3 is released into the circulation, while Type III 5'deiodinases (DIO 3) inactivate TH at the target tissues (Gropper & Smith, 2012). Inadequate selenium levels in the body leads to a decline in T_4 conversion to T_3, resulting in more TSH release.

Table 2.5. Selenoproteins involved in Thyroid Function.

Selenoprotein	**Abbreviation**	**Function**
Glutathione peroxidase	GPx	Catalyses the reduction of H_2O_2 Protective against oxidative stress
Cytosolic GPx1	GPX1	Antioxidative defence
Extracellular GPx	GPx3	Anti-inflammatory action
Phospholipid GPx	GPx4	Reduces the phospholipid's hydroperoxides Regulates apoptosis
Iodothyronine deiodinase	DIO	Catalyses the conversion of T_4 and T_3
Type I DIO	DIO 1	Conversion T_4 to T_3
Type II DIO	DIO 2	Local production (intracellular) of T_3 from T_4
Type III DIO	DIO 3	Inactivating TH system, production of rT_3 from T_4, and T_2 from T_3

Adapted with permissions from rights holder (Duntas & Benvenga, 2015).

Several types of selenium-containing glutathione peroxidase (GPx) have been identified in the body including cellular GPx (GPx-1), phospholipid GP-x (GPx-2), and plasma (GPx-3) and phospholipid hydroperoxide (GPx-4) (Triggiani et al., 2009). In general, these act as antioxidants, reducing the formation of and damage caused by free radicals and limiting the oxidation of lipids (Triggiani et al., 2009; Ventura et al., 2017). GPx protects thyroid cells from damage due to excessive hydrogen peroxide (H_2O_2) generated in the synthesis of thyroid hormones (Arthur et al., 1999; Zimmermann & Köhrle, 2004). Inadequate levels of selenium may lead to an accumulation of TPO during TH production, which can damage thyroid tissue.

2.2.2. Selenium Deficiency

As GPx and DIO are key selenium-dependent enzymes, selenium deficiency may lead to accumulated peroxides which can damage the thyroid tissue, impair thyroid hormone metabolism, and exacerbate the effects of iodine deficiency (Zimmermann, 2009). In regions where endemic iodine deficiency is also present, severe selenium deficiency during late pregnancy or in the neonatal period has been associated with Kashin-Beck Disease, a cartilage condition, and myxedematous cretinism, characterised by mental impairment, short stature, goitre and hypothyroidism (Schomburg & Köhrle, 2008; Zimmermann & Köhrle, 2004). Selenium supplementation during concurrent iodine and selenium deficiency may restore selenium dependent deiodinase activity at peripheral tissues, however serum T_4 can continue to decline due to inadequate thyroid synthesis with the underlying iodine deficiency (Contempre et al., 1991).

There are few clinical manifestations associated with mild to moderate selenium deficiency (Triggiani et al., 2009; WHO, 2004). However suboptimal selenium status in pregnant and lactating women has been linked to impaired immunity and neurological and motor development in infants (Varsi et al., 2017). Infants have high requirements of selenium due to rapid growth and development (McLachlan et al., 2004). Since thyroid function is integral to the regulation of growth and metabolism, selenium is essential for infant development (Amorós et al., 2018; Polanska et al., 2016). Suboptimal intake is a concern in Aotearoa due to the low levels of both iodine and selenium in soils and food supply.

2.2.3. Measuring selenium status

Selenium status of infant populations can be measured via concentrations in blood or serum (Mehdi et al., 2013). The concentration of selenium in the blood is thought to reflect recent dietary intake (Ashton et al., 2009; Gropper & Smith, 2012). There are no established selenium cut-off levels to determine deficiency in infant populations; however a German study calculated age-specific reference intervals (0.11-1.47 µmol/L for 4-12 month old infants) (Muntau et al., 2002) which have been used in research in Aotearoa (McLachlan et al., 2004). Other blood biomarkers include measuring selenoproteins, such as GPx, which provide information on selenium function (Combs, 2015). These methods have been used in several studies in new-born infants, including three studies in Aotearoa (Darlow et al., 1995; Dolamore et al., 1992; McGuire et al., 1993). The main limitation of these methods are practicalities and the invasive process of obtaining blood samples from a large population of infants.

Some epidemiological studies have found analysis of hair and toenail clippings correlates reasonably well with blood/plasma selenium concentrations and therefore could be used as a measure of long-term selenium status (Combs, 2015; Longnecker et al., 1996; Thomson, 2004a). However, these biological samples are not responsive to dynamic changes in circulating selenium measured in urine or blood, and the method has not been validated in infants.

Selenium homeostasis is maintained through urinary selenium excretion (USE) which represents 50-60% of total selenium losses (Gropper & Smith, 2012). USE is closely associated with plasma selenium concentration and is proportional to dietary intake. Around 55% of consumed selenium is excreted in the urine, hence total dietary intake can be estimated as nearly twice the daily USE (Thomson, 2004a). USE can be used as a proxy measure for intake to an indication of selenium status, particularly in populations living in selenium-poor areas (Griffiths & Thomson, 1974; Thomson, 2004a). Urinary selenium is normally expressed as a concentration (µg/L) or as total excretion (µg/day) (Combs, 2015; Jin et al., 2019). Twenty-four-hour urinary collection is preferable because selenium excretion is dependent on individual hydration status, time of day and recent selenium intake, however this is less practical for larger studies (Gibson, 2005). Spot urine selenium concentrations are a

convenient, non-invasive and cost-effective option for obtaining median urinary selenium concentrations (MUSC) in large populations of infants or children.

2.2.4. Selenium in Aotearoa

The interaction between selenium and iodine and thyroid hormone synthesis is of particular concern in Aotearoa due to dietary insufficiency of both selenium and iodine. As with iodine, the selenium content of soil varies geographically, impacting the selenium content of the food supply. The selenium content of soil is especially low in the South Island (Pearson et al., 2016; Thomson et al., 2007). Low levels in the soil affect the entire food system, as both plants and animal feed will be low in selenium and impact the dietary intake of those living in affected areas. Soil selenium content is influenced by soil type and texture, organic matter content, and rainfall (Mehdi et al., 2013). Soil concentrations can range from 0.01 – 1000 mg/kg and plant food selenium content generally correspond to this range (Mehdi et al., 2013; Vannoort & Thomson, 2009).

An early study in children aged 5-13 years in Auckland, Dunedin and Tapanui (South Island) highlighted geographical differences in selenium status, with the highest blood selenium concentrations detected in the North Island and lowest in Tapanui, which had particularly low soil selenium content (McKenzie et al., 1978). The importation of Australian wheat for flour and breadmaking in the North Island and domestically grown grain used in the South Island under low selenium soil conditions has further contributed to the regional variation in selenium intake (Pearson et al., 2016; Thomson et al., 2007; Vannoort & Thomson, 2009). White and mixed grain bread sampled for the 2016 NZTDS showed North Island varieties had a mean selenium content 0.075 – 0.093 mg/kg, compared to <0.020 – 0.025 mg/kg in South Island products (Pearson, 2016).

The limited data on infants in Aotearoa include an early study that found low levels of blood selenium (36 µg/L) and GPx in infants and children (N=107) (McKenzie et al., 1978). A 1992 study based in Christchurch showed plasma selenium in breastfed 12 month-old-infants had not increased with the introduction of complementary foods, as seen in selenium replete areas overseas, indicating suboptimal selenium intake as a result of low levels in the diet (N=70) (Dolamore et al., 1992). Interestingly, levels in formula fed infants were half that of

breastfed infants, which correlated with the low levels of selenium in infant formula at the time (3.9 µg/mL in formula compared to 13.4 µg/ml in breastmilk samples) (Dolamore et al., 1992). Blood selenium and GPx did not rise in the breastfed infants until complementary food was introduced. Two other studies in Aotearoa also explored selenium supplementation in formula-fed infants with suboptimal intake which improved selenium status (Darlow et al., 1995; McGuire et al., 1993). An Australian study also found selenium supplemented formula increased blood selenium levels and USC compared to breastfed and supplemented groups (Daniels et al., 2008). The minimum selenium level in infant formula was later increased to 10.7-13.4 µg/L to be consistent with breastmilk concentrations reported by Dolamore (1992) and Daniels (2008) (Food Standards Australia New Zealand, 2016).

In 2004, a community based cross-sectional survey in the South Island found much lower selenium intake and blood selenium in pregnant women (N=302), infants and toddlers (N=136) compared to international levels (McLachlan et al., 2004). Selenium status did not differ between formula-fed and breastfed infants. However commercially produced infant foods (including infant formula) contributed little to total selenium intake of non-breastfeeding infants, compared to the intake from bakery products, cereals, dairy and eggs (McLachlan et al., 2004). The NZTDS published between 1999-2005 estimated selenium intake was sufficient for most New Zealanders compared to earlier surveys, due to increased imported foods (Vannoort et al., 2000; Vannoort & Thomson, 2005). The most recent NZTDS (2016) also estimated sufficient intakes of selenium for all population groups (Pearson et al., 2016). However, low selenium intakes have been reported in other studies in Aotearoa women of childbearing age (Shukri et al., 2014) and among post-menopausal women (Brough et al., 2017). There is inconsistency between published literature and NZTDS findings regarding population selenium intake and status. Low levels in the food supply continue to be a public health concern because requirements for selenium increase significantly during pregnancy and lactation to support the growing foetus and newborn (MOH, 2006b).

2.3. Iron

2.3.1. Iron overview and requirements during infancy

Iron is essential for human health because of its capacity to participate in redox reactions and its role in transporting oxygen around the body (Hess, 2010). Iron deficiency remains the most prevalent nutrient deficiency and public health problem world-wide, affecting an estimated 33% of non-pregnant women, 40% pregnant women and 42% of children (WHO, 2020). Iron deficiency and iron deficiency anaemia (IDA) have adverse effects on cognitive and psychomotor development in infants (Michaelsen et al., 1995) and children (Grantham-McGregor & Ani, 2001; Pala et al., 2010), immune function and pregnancy outcomes (WHO, 2020). The prevalence of suboptimal iron status among children aged 6-24 months in Aotearoa is well documented, with rates of iron deficiency in study samples ranging from 18-51% (Grant et al., 2007; Soh et al., 2004) and IDA ranging from 5-34% (Crampton et al., 1994; Rive et al., 1996; Wham, 1996; Wilson et al., 1999). Exclusively breastfed infants that are breastfed for longer than six months are at increased risk of deficiency due to depleted stores and inadequacy of breastmilk iron to meet growing demands (Calvo et al., 1992; Grant et al., 2007). This has led to increased attention to the quality of complementary food at 6 months to meet infant nutritional requirements for iron.

2.3.2. Iron and Thyroid Function

The association between iron status and thyroid function has been reported in several studies. Early animal studies focussed on thermoregulation and TH metabolism in iron-deficient rodents (Beard et al., 1982; Dillman et al., 1980; Tang et al., 1988). Cold exposure induced a reduction in plasma T_3 and T_4 concentrations, increased TSH, and while overall TH production was upregulated, this was to a lesser extent in iron-deficient rats compared to controls (Beard et al., 1982; Dillman et al., 1980; Tang et al., 1988). Beard et al (1982) and Tang et al (1988) suggested iron deficiency reduced activity of DIO and was associated with impaired conversion of T_4 to T_3. Infusion of T_3 in cold exposed, anaemic rats improved the ability to maintain body temperature while T_4 infusion had little effect, which suggests iron acts as a 'limiting reagent' in the TH pathway (Beard et al., 1982). Iron deficiency may also reduce TPO activity in the thyroid, impairing initial production of the thyroid hormone (Zimmermann et al., 2000b).

Iron deficiency and IDA may blunt the benefits of iodine treatment, and iron supplementation improve the efficacy of iodine treatment in children who have suboptimal iodine and iron status. A trial of iodised oil supplementation in children (aged 6-12 years) in a region of endemic goitre in West Africa found thyroid volume and TSH status significantly improved after treatment for goitrous children with adequate iron status (Hb >120g/L) (N=53) compared to children with IDA (N=56) (Zimmermann et al., 2000b). TSH remained high and goitre persisted in children with poor iron status (Zimmermann et al., 2000b). The study identified a strong correlation between the percentage decrease of thyroid volume and haemoglobin concentration in anaemic children, indicating iron deficiency impaired the response to iodine therapy (Zimmermann et al., 2000b). A follow-up intervention trial in the same region found that iron supplementation in addition to iodised oil improved iron status, thyroid hormone levels and further decreased mean thyroid volume in anaemic children compared to controls (Zimmermann et al., 2000a). However another study in children with IDA showed normal thyroid function before and after iron treatment compared to healthy control children, although thyroid size was not measured (Tienboon & Unachak, 2003). More evidence is needed to determine the impact of iron status on thyroid function in infants, especially in the New Zealand context where suboptimal iron and iodine status may coexist.

2.4. Zinc

2.4.1. Zinc overview

Zinc is an essential trace mineral that is found throughout all organs, tissues and body fluids (Gropper & Smith, 2012). It is a component of various enzymes that help maintain structural integrity of proteins and regulate gene expression (MOH, 2006b). Zinc is vital for enzyme function, DNA and RNA metabolism, protein synthesis, gene expression, cell growth and differentiation, and cell-mediated immunity cell growth, cell membrane integrity, and cell replication in tissue and bone formation (Gropper & Smith, 2012; Lowe et al., 2009; Roohani et al., 2013; Wieringa et al., 2015).

There are challenges to reliable measurement of zinc status, and there is no single, specific biochemical index of zinc status for populations of infants. At present, the most reliable method for diagnosing mild deficiency is a positive response to zinc supplementation (Simon-Hettich et al., 2001). Severe deficiency may cause stunted growth, immune dysfunction, hypogonadism, anorexia, and poor wound healing (Prasad, 1991). In infants, it has also been associated with diarrhoea, alopecia and behavioural changes (Dassoni et al., 2014). Mild to moderate zinc deficiency is estimated to affect 17% of the world's population (Wessells & Brown, 2012). However lack of consensus on appropriate indicators for measuring zinc status in populations has hindered efforts to document the prevalence of deficiency (Caulfield & Black, 2004). Zinc intake and status in Aotearoa infants is largely under investigated.

2.4.2. Zinc and Thyroid Function

Zinc is thought to play a role in normal thyroid function via several mechanisms. Beserra et al (2021) suggest zinc participates in the synthesis of TRH in the hypothalamus, as well as TSH in the pituitary gland. Zinc is involved in gene transcription, and therefore may influence the expression of proteins involved in the production of thyroid hormones via a homeostatic mechanism. Along with selenium, zinc is also a cofactor for type (I) and (II) DIO, making it essential for the conversion of T_4 to metabolically active T_3 (Beserra et al., 2021; O'Kane et al., 2018). Like other nuclear receptors, T_3 receptors contain nuclear zinc-binding proteins, which suggest zinc is important in the biological function of T_3 within cells (Mahmoodianfard et al., 2015).

Most of the research available includes factors that influence zinc status or thyroid response. For example, a decrease in TH and basal metabolic rate has been observed in individuals receiving a zinc restricted diet (Maxwell & Volpe, 2007). Zinc supplementation increases TH concentration in zinc deficient individuals (Beserra et al., 2021). Zinc deficiency has been observed at higher rates in patients with nodular goitre (Kravchenko et al., 2020), thyroid disease and hypothyroidism (Mahmoodianfard et al., 2015; Talebi et al., 2020), and among smokers (Jain, 2014), compared to controls. Mild zinc deficiency can occur in response to stress, acute trauma, and infection (MOH, 2006b), therefore, findings in states of disease and existing thyroid dysfunction may not be applicable to the general population, particularly

healthy infants. The role of zinc nutrition in infants in Aotearoa and the relationship to optimal thyroid function needs further investigation.

2.4.3. Zinc requirements during infancy.

Infants have high requirements due to their high growth rate and so are also at increased risk of deficiency (Roohani et al., 2013). Suboptimal zinc status in young children is widely reported, including studies in Aotearoa (Bouglé et al., 2000; Daniels et al., 2018; Han et al., 2011; Morgan et al., 2010). Zinc depletion in children and infants has been associated with stunting and failure to thrive, while zinc supplementation improves growth in underweight children (Park et al., 2017). The New Zealand reference ranges requirements for infants are calculated by multiplying the average intake of breastmilk per day (0.78 L) by average zinc concentrations of breastmilk. The average breastmilk zinc concentrations decline during the first six months (Krebs et al., 1995), therefore complementary foods become an important zinc source early on. This demonstrates the need for further investigation into zinc intake and status of infants in Aotearoa during this period of rapid growth and development in the first year of life.

The key studies from the last 30 years that have examined the intake of iodine, selenium, zinc and iron in infants and toddlers in Aotearoa are as summarised (table 2.6).

Table 2.6. Dietary intake of iodine, selenium, zinc and iron in infants and toddlers aged 0-3 years in Aotearoa (1992-2016)

Reference	N	Age	Dietary Assessment method	Iodine (µg/day)	Selenium (µg/day)	Zinc (mg/day)	Iron (mg/day)	Comments
(Dolamore et al., 1992)	70	0-12 m			10.05			Selenium status of infant reflected diet, with 3.9-5.2 µg/mL formula, and 13.4 µg/mL breastmilk. Intake based on breastmilk intake 750 mL/day.
(Hannah et al., 1994)	*	1-3 y	*	100	27	6.8	5.9	1987/89 New Zealand Total Diet Study (NZTDS) shows selenium intake low. Iodine intake adequate across age-sex diets, reduction of adequate discretionary iodised salt without concern for resurgence of endemic goitre. Concern for groups with increased requirement maintained, i.e. pregnant women. Zinc and iron adequate.
(Hannah et al., 1995)	*	1-3 y	*	62		6.1	6.6	Selenium not analysed in 1990/91 NZTDS. Notable drop in iodine intake compared to 1987/89 NZTDS, report highlighted need to monitor food sources as iodine with decline in iodine content of dairy products (less industrial iodophor use) and decline in discretionary iodised salt use.
(Watson et al., 2001)	183	12-36 m	24-hour recall		25.7 [f] 27.7 [m]	6.6 [f] 7.6 [m]	7.7 [f] 7.9 [m]	Findings part of the New Zealand Children's Nutrition Survey (Pilot).
			24-hour assisted		27.3 [f] 23.6 [m]	6.9 [f] 7.6 [m]	8.9 [f] 7.9 [m]	

			dietary recall					
			4-day Weighed food record		22.6 [f] 23.2 [m]	6.4 [f] 6.5 [m]	8 [f] 6.8 [m]	
(Soh et al., 2002)	226	6-24 m	3-day weighed food record				8.6 [f] 8.3 [m]	Results suggested iron intake in 6-24 month-old infants were low.
(McLachlan et al., 2004)	42	6-12 m	3-day weighed food record		7.9			Excluded breastfed infants and toddlers. Selenium intake estimated to be 4.4 µg/day, from complementary foods only, with breastmilk excluded. Intake including breastmilk estimated to be 7.9 ± 6.2 µg/day. Lower selenium levels observed in South Island compared to North Island, however no association between selenium intake and status. No significant difference seen in breastmilk vs formula fed infants.
(Vannoort & Thomson, 2005)	*	6-12 m	¤	47	16		7.1	First NZTDS to analyse 6-12 month age group. zinc not analysed in 2003/04 NZTDS.
(Skeaff et al., 2005)	230	6-24 m	3-day diet record	18				Iodine intakes calculated based on mean conc breastmilk 22 µg/L and average breastmilk intake 750 mL/day, correlation between BM iodine, and UC in children *p*=0.0073 (N=29). Iodine status suboptimal (MUIC).
(Vannoort & Thomson, 2009)	*	6-12 m	*	49	16			Infant weaning foods contribute the highest proportion of iodine, selenium. Iron and zinc not analysed.

(Morgan et al., 2010)		12-20 m	3-day food records			4.9 - 5.4		Results from week 0 for placebo and intervention groups.
(Watson, 2013)	188	12-24 m	5-day weighed food record, 24-hour recall			4.2	5.8	
(Pearson et al., 2016)	*	6-12 m	*	83	24	5.8	7.6	All age-sex groups except infants exceeding RDI for iodine. Zinc and selenium recommended daily intake (RDI) met by all age-sex groups. Infant weaning food contributed the highest proportion to intake of iodine, selenium and zinc.

* Total diet survey determine concentrations of selected nutrient elements in commonly eaten foods, estimating intake for selected age-sex groups in a simulated 14 day "typical" diet.

[f] Female

[m] Male

2.5. Dietary Assessment in Infants

In general, there are four types of dietary methods available to collect information on food and nutrient intakes (table 2.7), each with their own strengths and weaknesses. While accurate measurement of dietary intake in all age groups is challenging, measuring infant intake has some unique challenges. All methods rely on information gathered by the caregiver, who is usually familiar enough with infant feeding practices to accurately report normal dietary intake (Gibson, 2005). They may, on the other hand, modify feeding regimes in children to present a perceived healthier diet, or for ease of recording (Dwyer, 1988; Shim et al., 2014). However, this may be less important for infants receiving very basic introductory foods. Estimating food intake and associated plate waste, spills and regurgitation for infants who are developing their feeding skills is an additional challenge. The difficulty of capturing usual intake in infants is a further problem for researchers because dietary patterns rapidly evolve through the first 12 months of life.

Problems associated with all dietary assessment methods include time commitment from researchers and/or participants (Shim et al., 2014). Finally, because caregivers who are completing food records are likely to be dedicated, motivated and literate, the findings may not be representative of the general population (Dwyer, 1988; Shim et al., 2014).

A diet history combines multiple dietary assessment methods together to provide accurate information on habitual intake (table 2.7), however it is rarely used in its entirety in modern research (National Research Council (US) Committee on Diet and Health, 1989). Food frequency questionnaires (FFQ) may miss key nutrients in foods not listed, and often focus on food groups rather than specific foods (Gibson, 2005). A food record, such as a three day diet diary (3DDD), is preferred because it can be recorded in real time, rather than relying on memory (Gibson, 2005). Currently, the collection of multiple weighed food records (WFR) is considered the most accurate method to estimate usual dietary intake (Boushey et al., 2001). Calibrated weighing equipment needs to be supplied to participants.

Table 2.7. Dietary Assessment Methods

Method	Description
Food Record	All food and beverages consumed are weighed or estimated for 3-7 consecutive days. Requires the use of kitchen scales or estimations using household portion sizes, such as 1 cup or grams. Self-administered - detailed descriptions include the type of food, brand name, preparation method, and portion sizes are recorded.
24 Hour Recall	Structured interview intended to capture detailed information on all foods and beverages consumed in the previous 24 hours or a defined 24-hour period. Three phases includes (1) collating a list of all foods and beverages consumed, (2) gathering further details including brands, portion sizes and preparation cooking methods (Gibson, 2005). Finally (3), record is reviewed to ensure all food and beverages have been accurately recorded (Gibson, 2005).
Food Frequency Questionnaire	Frequency of consumption of certain foods and beverages presented on a list within a certain timeframe, for example, one month (Gibson, 2005). This method is often self-administered in a survey format (Gibson, 2005).
Diet History	Interviewer obtains health habits and patterns of eating including quantities and varieties using a 3 day food diary, a 24 hour food record and an FFQ (Gibson, 2005; National Research Council (US) Committee on Diet and Health, 1989).

2.6. Estimating Breastmilk Volume

Another key challenge for dietary assessment in infants, which applies to all assessment methods, is estimating breastmilk intake. The Estimated Average Requirement (EAR) for fluid in infants from birth to 6 months is 700 mL per day of total fluid from breastmilk and/or formula (MOH, 2021b). At 7-12 months, total fluid intake increases to approximately 800 mL, assuming 600 mL from breastmilk and formula, and the remaining from water or other beverages (MOH, 2021b). Most estimates predict intake to average 750-800 mL/day in the first 4-5 months; however this can range from 450 - 1,200 mL/day (Institute of Medicine (US) Committee on Nutritional Status During Pregnancy and Lactation, 1991). Breastfeeding is a complex activity which demands coordination between the rhythmic processes of sucking, swallowing, and breathing (Goldfield et al., 2006; Moral et al., 2010). Several factors influence this process including the infant's age, time of day, hunger, mouth position on the breast, sucking time and pressure, fatigue, satiation and milk flow (Moral et al., 2010). The amount of milk transferred from the mother to the infant in a single feed can vary.

The most widely accepted method for measuring milk intake is test weighing, a procedure in which the infant is weighed before and after each feed (Institute of Medicine (US) Committee on Nutritional Status During Pregnancy and Lactation, 1991). This method is reported to underestimate actual volume of intake by 1-5% due to the evaporative water loss from infants between weighing (Brown et al., 1982; Institute of Medicine (US) Committee on Nutritional Status During Pregnancy and Lactation, 1991). This method inconvenient and may be disruptive and stressful for both mother and infant, which can affect infant breastmilk intake. Modern techniques to measure infant breastmilk intake involve measuring turnover of stable isotopes ingested by the mother, passed through to the infant via breastmilk, and measured in saliva or urine (Da Costa et al., 2010; Slater et al., 2019). While these methods are easy to administer with participants, materials can be costly and may be impractical for large scale epidemiological studies (Johnson & Coward-McKenzie, 2001)

A cross-sectional study by Kent et al (2006) in Western Australia collected data from mothers and their infants (aged 1-6 months) to investigate the volume and pattern of milk intake. Infants had 11 ± 3 breastfeeds per day (range 6-18), with intervals of 2 hours 18 minutes ± 43

minutes (Kent et al., 2006). Milk volume at each feed was measured using the weighing method, which showed infants took 76 ± 12.6 g (range 0 – 240 g) at each breastfeed, and that there was an inverse relationship between the number of breastfeeds per day and average breastmilk volume (r^2=0.442; p=0.001; N=142 breasts). Breastfeed volumes also related to whether the infant fed from one or both productive breasts during the breastfeed (Kent et al., 2006).

In a later study, Kent et al (2013) measured longitudinal changes in breastfeeding patterns from 1-6 months of lactation (N=17). While total daily breastmilk intake was relatively constant throughout 1-6 months, the frequency and duration of feeds changed (Kent et al., 2013). Infants (1-3 months) had large, less frequent breastfeeds (7.6 feeds per day; duration 36 minutes), while towards 6 months of age, breastfeeds decreased in duration and increased in frequency (Kent et al., 2013). Overall, the research suggested a median duration of 32.5 minutes per feed (SD=10.1), a median milk volume of 121 mL per feed (SD=27), and a total 24 hr milk volume of 797mL (SD=169), which is consistent with the estimated average intake of 750 mL/day breastmilk cited by WHO (2004) and MOH (2006) (Kent et al., 2013). The challenge of measuring breastmilk volumes is not straight forward and is a continuing area of research.

2.7. Conclusion

Infants transition from exclusive breastfeeding or formula feeding and complementary feeding to meet their growing nutritional needs at around six months of age. Adequate intake of iodine and selenium is necessary for optimal thyroid function and production of thyroid hormones, required for infant growth and neurodevelopment. Aotearoa has a history of poor iodine and selenium intake in the general population due to low levels in soil and food supply. Iron intakes of infants are often low in this age group, and there is little known about their zinc requirements, or the impact zinc and iron have on thyroid function in infants. Iodine status in adults, pregnant and lactating women, and children has improved with government initiatives, however the intake and status of infants is unknown. Accurately assessing dietary intake and estimating breastmilk intake in infants is challenging but important for monitoring

the nutritional adequacy of the infant population in Aotearoa in relation to optimal thyroid function.

3. Manuscript: Intake of micronutrients involved in optimal thyroid function in in 5- to 10-month-old infants in Aotearoa: iodine, selenium, iron and zinc. Mother and Infant Nutrition Investigation (MINI Study)

This chapter has been formatted for the MDPI Open Access Journal *Nutrients*

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3.1. Abstract

Thyroid function and synthesis of thyroid hormone relies on adequate intake of a number of micronutrients. Inadequate intake of iodine and selenium can disrupt normal thyroid hormone production, which may have adverse effects on physical and cognitive development in infants. Iron and zinc also contribute to optimal thyroid hormone function. This study investigated the intake and status of iodine, selenium, zinc and iron in five-to ten-month-old infants living in Manawatū, Aotearoa (June 2016 – December 2017). Mothers completed a three-day diet diary for their infants including all breastfeeding occasions (recorded in minutes), complementary foods and fluids (N=51). Breastmilk samples (N=72) and infant spot urine samples (N=41) were obtained to measure iodine and selenium concentration using inductively coupled plasma mass spectrometry. Median (Q1, Q3) intake for iodine was 62 (30, 98) µg/day with 82% below the Adequate Intake (AI), and 12 (9, 16) µg/day for selenium, with 67% below the AI. Median urinary iodine concentration (MUIC) was 107 µg/L and median urinary selenium concentration (MUSC) was 11 (6, 15.5) µg/day. Median intake of zinc was 3 (2, 4) mg/day, with 31% below EAR, and median intake of iron was 2 (1, 5) mg/day with 78% below EAR. Findings suggest that despite public health initiatives to combat iodine deficiency, infants in Aotearoa are at risk of suboptimal intake of iodine along with selenium and iron. Zinc intakes are adequate, or potentially excessive. MUIC of this population is categorised as

sufficient according to the WHO/UNICEF/ICCIDD (2007) criteria. However, it is low if compared against alternative cut-offs, proposed by other researchers, and iodine status of this population needs continued monitoring due to low iodine intake. More surveillance of this dietary transition period of complementary feeding of infants is needed to determine the impact of suboptimal intake and status of key minerals on growth and development.

3.2. Introduction

Adequate functioning of the thyroid and synthesis of thyroid hormones (TH), thyroxine (T_4) and triiodothyronine (T_3), relies on adequate iodine intake. TH are critical for the control of metabolic processes, growth and development, especially the brain and central nervous system (World Health Organization, WHO, 2004a). Iodine deficiency disorders (IDD) refers to the range of adverse physiological consequences that can occur throughout the lifecycle as a result of inadequate dietary supply of iodine (Kapil, 2007). Deficiency during infant development may irreversibly impair brain development and increase infant mortality risk (Cao et al., 1994). Selenium supports optimal thyroid function and production of adequate concentrations of TH through its role as an antioxidant and in selenium-dependent enzymes (Schomburg & Köhrle, 2008). Selenium deficiency can impair the conversion of T_4 to metabolically active T_3, leading to thyroid tissue damage, and exacerbate the impact of iodine deficiency on thyroid metabolism (Triggiani et al., 2009).

Another two micronutrients which impact thyroid function are iron and zinc. Iron deficiency can impair thyroid hormone synthesis by reducing activity of haem-dependent thyroid peroxidase (TPO) (Zimmermann & Köhrle, 2004). Infants over 6-months old have high iron requirements for growth, often coinciding with depleted body iron stores during a period where dietary patterns are not yet established, and breastmilk alone no longer meets requirements (Calvo et al., 1992; Michaelsen et al., 1995). The prevalence of suboptimal iron status among children aged 6-24 months in Aotearoa is well documented, with rates of iron depletion in studies ranging from 18-51% (Grant et al., 2007; Soh et al., 2004) and iron deficiency anaemia (IDA) ranging from 5-34% (Crampton et al., 1994; Rive et al., 1996; Wham, 1996; Wilson et al., 1999). Poor iron status during infancy can impair physical growth and

cognitive and motor development (Bouglé et al., 2000; Grantham-McGregor & Ani, 2001). Zinc is ubiquitous throughout body cells and is a component of various enzymes and proteins (Gropper & Smith, 2012). Zinc is thought to influence thyroid hormone production through gene expression (Beserra et al., 2021; O'Kane et al., 2018), however the mechanisms are not clear.

Aotearoa has a history of dietary insufficiency of iodine and selenium due to low levels of both minerals in soils and the local food supply. Endemic goitre was seen throughout Aotearoa during the early 20th century (Hercus et al., 1925; Jones, 1928). A significant reduction in goitre rate was seen by the 1950s following the introduction of iodised salt, however a number of studies during 1990s identified re-emergence of poor iodine intake and status among pregnant and breastfeeding women (Mulrine et al., 2010; Thomson et al., 2001), breastfed infants and toddlers (Skeaff et al., 2005). To improve the iodine status of the population, the New Zealand government introduced the mandatory fortification of bread with iodised salt (2009) and subsidised an iodine supplement (150 µg/day) for all pregnant and breastfeeding women (2010).

Iodine status of child populations has typically been measured via median urinary iodine concentration (MUIC) (WHO/UNICEF/ICCIDD, 2007). Both iodine and selenium status of infants has been measured using this method (Kazi et al., 2010; Skeaff et al., 2005; Thomson et al., 1996; Wang et al., 2009). Iodine and selenium concentrations in breastmilk (BMIC and BMSC) have been used as a proxy measure for iodine and selenium intake in infants (Azizi & Smyth, 2009; Brough et al., 2015; Skeaff et al., 2005).

This study applies secondary analysis of data from the Mother and Infant Nutrition Investigation (MINI) Study. It aims to investigate the infant intake of iodine, selenium, zinc and iron from breastmilk and/or infant formula, and complementary foods. The study also aims to estimate iodine and selenium intake based on urinary excretion, and compare with dietary intakes from diet diaries.

3.3. Material and Methods

3.3.1. Overview

The Mother and Infant Nutrition Investigation (MINI) study is an observational longitudinal cohort study of breastfeeding women and their infants, living in Manawatū, Aotearoa, spanning the first year postpartum. The first visit for participants took place at 3 months postpartum, and two follow-up assessments took place at approximately 6 and 12 months postpartum. Data analysed for the present study were obtained at the second visit (6 months), and dietary data was reported when infants were aged between 5 to 10 months old.

MINI Study Visit 2: Infants are aged 6 months (N=87)

- Maternal breastmilk samples (N=72)
- Infant spot urine samples (N=41)
- Infant anthropometry (N=87)
    - Weight (kg)
    - Head circumferance (cm)
    - Recumbent length (cm)
- Three-day-diet diary (N=51) (data collected 5-10 months)

3.3.2. Study population

Healthy breastfeeding mothers aged over sixteen years and their healthy singleton infants were recruited via local health professionals who work closely with pregnant and breastfeeding women. Women of any ethnic and socioeconomic status were eligible to participate, who were living within the Manawatū region and able to attend Massey University for scheduled visits. Mother-infant pairs were excluded if they developed significant health problems such as metabolic diseases or medical complications during the pregnancy or birth. Potential participants responded by recording an expression of interest online or via telephone or email. They were then supplied with a study information sheet. Those interested then completed a screening questionnaire to ensure eligibility. After providing consent, they were each provided with an identifier code and scheduled for their first visit.

3.3.4. Ethics

The Mother and Infant Nutrition Investigation (MINI study) was approved by the Health and Disability Ethics Committee (15/NTA/172) from December 2015. The ethics approval was registered with the Royal New Zealand Plunket Ethics Committee in June 2016. The MINI study was approved by the MidCentral District Health Board and was registered with the Australian New Zealand Clinical Trials Registry [ACTRN1261500102854]. The research was conducted at the Human Nutrition Research Unit at Massey University, Palmerston North, New Zealand.

3.3.5. Questionnaire

Mothers answered general questions at the first visit to determine demographic information including age, ethnicity, educational attainment, household size and income. Other health related information obtained in this initial questionnaire that has been used in this study includes breastfeeding patterns, gestational age at birth (weeks), method of infant delivery and birth weight.

3.3.6. Anthropometric data

Infant recumbent length was measured crown to heel using an infant length board and recorded to the nearest millimetre (Jin et al., 2020). Infant weight without clothing and diapers was measured, using a baby weighing scale (Nagata Scale CO. LTD, Happy Pig, Taiwan), and recorded to the nearest 10 g (Jin et al., 2020). Infant head circumference was measured over the most prominent part of the head (occiput) and just above eye brows (supraorbital ridges) by using a flexible, non-stretch tape, and recorded to the nearest millimetre (Gibson, 2005).

3.3.7. Dietary data collection

Mothers were asked to complete a three-day estimated food diary (3DDD) for their infant's intake at around the introduction of complementary foods. Mothers were provided full instructions for how to estimate portion size of foods offered to infants and were asked to record as much information as possible including the type of food, product brands, and cooking methods. 3DDD were analysed using Foodworks 10 Professional (Xyris Software,

Brisbane, Australia) and the New Zealand FOODfiles (2016; Version 01) (New Zealand Food Composition Database (NZFCD), 2016). When foods were not listed in the New Zealand FOODfiles, new food items or recipes were created based on manufacturers information and adapted using information from the most recent New Zealand Total Diet Study (NZTDS) (Pearson et al., 2016). If a suitable same or equivalent item was available in the Australian database, was used, with micronutrients compared against a similar item from New Zealand FOODfiles or the 2016 NZTDS. Unless specified, non-iodised table salt was recorded in recipes as listed. All milk and breads were reported as either generic or "Lower North Island" varieties. Foodworks does not contain the current iodine concentrations for all breads, thus estimates for iodine concentrations for categories of bread were based on data from Ministry for Primary Industries (MPI) (Table 5.1) (MPI, 2014).

All breastfeeding occasions were recorded in the 3DDD by mothers in minutes. A standardised volume was applied to infants based on age and known fluid volume intakes adapted from Briefel et al (2010), (0-6 months (780 ml); 6-12 months (600 ml); Table 5.2). Known consumed fluid volumes of infant formula, expressed breastmilk and other milks were subtracted from this total for each infant. This data was entered into each food record in Foodworks 10.

All foods and fluids, including estimated breastmilk volumes and infant formula feeds were entered into Foodworks in succession to obtain an average intake from each component of the diet. This meant intakes from breastmilk, formula, and food could be analysed in isolation as well as together as a total. Breastmilk iodine and selenium concentrations (mg/kg) from biological analysis were multiplied by estimated breastmilk volumes, corrected for fluid density using the gram weight obtained from Foodworks, and incorporated into final analysis.

All diaries were also collated into one record, to obtain information on the average percentage contributions of each food group to total iron, zinc, iodine, and selenium intake for the infant group. Food groups included (1) breastmilk, (2) infant formula, (3) meat, eggs, fish, and pulses (MEFP), (4) breads and cereals, (5) fruit and vegetables, (6) dairy, and (7) other.

Each infant's 3DDD was analysed for overall adequacy by comparing it against their estimated energy (kcal) and protein (g) requirements calculated from body weight (kg), gender and age (months). Diets were also compared to age-specific AI for carbohydrate (g), fat (g), sugar (g), and sodium (mg). Criteria for calculations were obtained from the National Health and Medical Research Council and New Zealand Ministry of Health (2006) Nutrient Reference Values for Australia and New Zealand.

3.3.8. Sample collection and analysis of infant urine and maternal breastmilk

Spot urine samples were collected from infants using a paediatric urine bag (EMURIC, 100 ml), placed inside the diaper and checked every 10 minutes (Jin et al., 2020). The collected urine was frozen and stored at -20°C for later analysis of iodine and selenium. Lactating mothers were asked to provide a breastmilk sample (approximately 30 - 50 ml) using an electric breast pump (Unimon Allegro, Korea) if required (Jin et al., 2020). All breastmilk samples were collected before 12 pm (noon) on the visit day; timing of breastmilk collection was not standardised. Iodine and selenium concentration in infant spot urine samples and breastmilk samples were determined by an accredited commercial laboratory (Hill Laboratories, Hamilton, New Zealand) using inductively coupled plasma mass spectrometry (ICPMS) (Fetcher et al., 1998). Measures of quality control include analysis of blank samples, analytical repeats, and certified reference material (CRM) to ensure accuracy and precision (Jin et al., 2020). Breastmilk iodine and selenium concentrations were incorporated into dietary analysis of the infant. Infant urine production in the first year is approximately 2 ml/kg/hour (Hazinkski, 1992), which was used to calculate total daily iodine and selenium excretion in the urine.

3.3.9. Statistical analysis

Statistical analysis of all data was conducted using IBM SPSS statistics version 27. Percentages and frequencies were used to describe all categorical variables, and mean, median, standard deviation (SD), percentiles (Q1, Q3) were used to described continuous variables. Continuous variables were tested for normality using Kolmogorov-Smirnov and Shapiro-Wilk statistics analysis. Most of the data were not normally distributed. Non-parametric data were expressed as a median (Q1, Q3, percentile) and parametric data expressed as a mean (± SD).

The relationships between continuous variables with non-parametric data were explored using the Mann-Whitney U test, and correlations were examined using the non-parametric Spearman's Rho Correlation. Multiple linear regression was used to determine predictors of total urinary iodine excretion (UIE). Predictor variables considered were estimated dietary intake of iodine (µg) from breastmilk, infant formula, bread, and all other food. Reporting of statistical significance was at a level of p=<0.05, unless otherwise stated. Effect size calculated as r=Z/√n.

3.4. Results

3.4.1. Descriptive Characteristics

A total of 91 mother infant pairs were recruited however 4 pairs were excluded in final analysis due to missing data, giving a total of 87 mother-infant pairs. The remaining mothers' age ranged from 22 to 41 years old. The ethnicities were New Zealand Pakeha (79%), Asian (10%), Māori (8%), Pacifika (3%) and 'Other' ethnicities (3%). The majority (78%) were tertiary educated, and 42% of the infants were the mother's first child. Thirty-two percent (24/75) of infants were exclusive breastfed until 6 months of age, while the majority 68% (51/75) were partially breastfeeding by 6 months.

Table 3.1. Descriptive characteristics of mother-infant pairs (N=87)

Maternal Characteristics	**N**	**%**
Age (Mean ± SD)	32 ± 4.2	
Tertiary Education	68	78
Ethnicity (Pakeha)	69	79
Ethnicity (Asian)	9	10
Ethnicity (European)	8	9
Ethnicity (Māori)	7	8
Ethnicity (Pacifika)	3	3
[a] Ethnicity (Other)	3	3
Smoker	3	3
[b] Annual household income (above average household)	33	38
Infant Characteristics		

First Child	38	42
[c] Female	35	36
[c] Male	56	62
[c] Gestation at birth (weeks) (Mean ± SD)	39 ± 1.5	-
Caesarean Delivery	20	22.0
[c] Birth weight (kg) (Mean ± SD)	3.6 ± 0.6	-
[d] Age of infants (weeks) (Mean ± SD)	32 ± 5	-
[e] Weight (kg) (Mean ± SD)	7.7 ± 1	-
[e] Recumbent length (cm) (Mean ± SD)	67 ± 3	-
[e] Head circumference (cm) (Mean ± SD)	43 ± 1.5	-
[f] Exclusive Breastfeeding Six Months	24	32
[f] Partial Breastfeeding Six Months	51	68

[a] Australian, Latin American
[b] Average annual household income based on Statistics New Zealand NZD $100,103 for the year that ended 2017, at time of data collection.
[c] Infant gender, birth weight N=91.
[d] Eligible infants (5- to 10 months old) who provided 3DDD N=51.
[e] Anthropometric characteristics of infants at second visit 5-10 months old N=79
[f] Breastfeeding practices as reported by mothers in online questionnaire

3.4.2. Milk feeding patterns

In addition to complementary food, 69% (35/51) of infants had only breastmilk, 12% (23/51) had a combination of breastmilk and formula while the remaining 8% (4/51) were provided only infant formula (Table 3.2). Breastfed infants spent a median 75 (54, 95) minutes per day contact breastfeeding. Infants who were formula fed had a mean intake of 444 ± 254 mL/day, and those given expressed breastmilk were provided a median of 160 (100, 285) mL per day in addition to breastfeeding and/or formula feeding.

Table 3.2. Feeding patterns in infants at 5-10 months (N=51)

	N	**%**
[a] Breastfed	35	69
Infant Formula	4	8
[b] Combination Breastmilk and Infant Formula	12	23
[c] Total daily minutes breastfeeding (Median (Q1, Q2)	75 (54, 95)	

[d] Estimated daily volume breastmilk (mL/day) Median (Q1, Q2)	600 (600, 600)
[e] Volume Expressed Breastmilk (mL/day) Median (Q1, Q2)	160 (100, 285)
[f] Volume Infant Formula (mL/day) Mean ± SD	444 ± 254

[a] Six infants provided expressed breastmilk in addition to direct breastfeeding
[b] Two infants provided expressed breastmilk in addition to infant formula bottle feeding, remaining infants directly breastfed in addition to infant formula bottle feeding.
[c] Mean calculated from 121 food record days with breastfeed occasions recorded in minutes.
[d] Volumes estimated using age specific guideline (Briefel et al, 2010). Mean based off 136 food record days with breastfeeding occasions recorded. Five 3DDD did not include breastfeeding minutes (total 15 food record days). Five infants were assigned 780ml baseline volume; seventy-eight infants assigned 600ml baseline volume.
[e] Calculated from 71 food record days in which known volumes of expressed breastmilk provided.
[f] Calculated from 51 food record days in which known volumes infant formula provided.

3.4.3. Concentrations of iodine, selenium, iron and zinc in breastmilk and infant formula

Assuming an average breastmilk intake of 750 ml/day, median intakes of iodine for the exclusively breastfed infant would be 44.3 µg/day, which is below the Adequate Intake (AI) of 90 µg/day iodine for infants 0-6 months old (Ministry of Health (MOH), 2006b). Similarly, daily selenium intake based exclusively on 750 mL/day breastmilk is estimated as 8.2 µg/day, below the Adequate Intake (AI) of 12 µg/day for infants 0-6 months (MOH, 2006b). Based on the age-assigned estimated breastmilk volume used in this study, median iodine from breastmilk alone (not including any other food) was estimated to be 37 (22, 64) µg/day and selenium from breastmilk alone was around 7 (6, 9) µg/day, in addition to complementary food.

Table 3.3. Breastmilk iodine and selenium concentration 5-10 months postpartum (N=72)

	Median (Q1, Q2)
Breastmilk iodine concentration (BMIC), µg/L	59 (39, 109)
Breastmilk selenium concentration (BMSC), µg/L	11 (9, 13)
[a] Breastmilk iron concentration, mg/L	0.7
[a] Breastmilk zinc concentration, mg/L	3
Infant formula iodine concentration, µg/L	140 (100, 150)
Infant formula selenium concentration, µg/L	20 (16, 20)
Infant formula iron concentration, mg/L	6 (5, 6)
Infant formula zinc concentration, mg/L	9 (8, 10)

[a] Mean concentration accordingly to the New Zealand FOODfiles (2016).

3.4.4. Dietary intake of micronutrients involved in thyroid function

3.4.4.1. Iodine

Median total iodine intake from all foods, breastmilk, and/or infant formula among infants was calculated as 62 (30, 98) µg/day. Eighty-two percent were below their age specific Adequate Intake (AI) for iodine [90 µg/day (0-6 months), 110 µg/day (7-12 months)]. Twenty-eight percent (13/51) consumed commercially manufactured bread fortified with iodine on 1 to 4 occasions over the three days. For bread consumers, iodine from bread contributed a median of 35% (19, 66) towards total iodine intake. Estimated total iodine intake was higher among bread consumers (79 (63, 99) µg/day) than non-bread consumers (39 (26, 85) µg /day; *p*=0.016, N=51, R=-0.3). Estimated intake of iodine from complementary food overall was higher among bread consumers (14 (10, 23) µg/day) compared to non-bread consumers (2 (1, 6) µg/day; *p*=<0.001, N=50, R=-0.6). This indicates that bread consumption had a medium to large effect on estimated total iodine intake and on iodine intake from solely complementary food sources. However, no statistically significant difference was detected between infant UIC (µg/L) when comparing bread consumers to non-bread consumers.

3.4.4.2. Selenium

Median selenium intake was 12 (9, 16) µg/day and 69% (35/51) of infants' intakes did not achieve their age specific AI [12 µg/day (0-6 months); 15 µg/day (7-12 months)]. Selenium intake was slightly high among bread consumers 16 (12, 25) µg/day) than non-bread consumers 12 (8, 15) µg/day; *p*=0.004, N=51, R=-0.4). Bread contributed a median of 7 (3, 16) % towards total selenium intake among bread consumers. Selenium intakes were slightly lower among breastfed infants (11 (9, 15) µg/day) than in infants who drank infant formula 14 (11, 22) µg/day), however this was not significant. Selenium intakes were weakly correlated with urinary selenium concentration (USC, µg/L) (R=0.375, *p*=0.05).

3.4.4.3. Iron

The median intake of iron was 2.4 (1, 5) mg/day and 78% (40/51) did not achieve their age specific AI/Estimated Adequate Requirement (EAR) for iron [0.2 mg/day (AI, 0 to 6 months); 7 mg/day (EAR, 7-12 months)]. Overall, food alone contributed a median of 1 (1, 3) mg/day

to total iron intake, higher compared to breastmilk (0.4 (0.3, 0.4) mg/day), but lower than formula (4 (1, 6) mg/day). Median iron intake was higher in formula/combination fed infants (6, (4, 8) mg/day compared to breastfed infants (2, (1, 3) mg/day; *p*=>0.000, N=51, R=-0.68).

3.4.4.4. Zinc

Median zinc intake was 3 (2, 4) mg/day, with 31% (16/51) below AI/EAR for zinc [2mg/day (AI, 0 to 6 months), 2.5 mg/day (EAR, 7 to 12 months)]. Interestingly, 16% (8/51) exceeded their age specific Upper Limit (UL) for zinc intake [4 mg (0-6 month olds) and 5 mg (7-12 months)], putting them at risk of toxicity. Food alone contributed a median of 1 (0, 2) mg/day to total zinc intake. Median intake from breastmilk was (2 (2, 2) mg/day), similar to infant formula (2 (2, 2) mg/day) overall, however median zinc intake was higher among infant formula fed infants (5 (4, 6) mg/day) compared to breastfed infants (2 (1, 3) mg/day; *p*=>0.000, N=51, R=-0.5).

3.4.5. Contribution of food groups to iodine, selenium, iron and zinc

Both breastmilk and infant formula contribute to a large proportion to total iodine, selenium, zinc and iron to the infant populations' diet (table 3.5). The measures of contribution to the total infant diet are partially attributed to higher rates of breastfeeding (68%) and combination feeding (23%) compared to infant formula feeding (8%), and the relative average concentrations in breastmilk compared to infant formula. For example, infant formula contains higher concentrations of iodine (140 (100, 150) µg/L) and selenium (20 (16, 20) µg/L) compared to the breastmilk concentrations measured in this study (59 (39, 109) µg/L iodine, 11 (9, 13) µg/L), but breastmilk still contributes higher when assessing the whole group because most infants in this sample were breastfed. Similarly, infant formula concentrations of iron (6 (5, 6) mg/L), and zinc (9 (8, 10) mg/L) were also higher than the respected concentrations of iron (0.7 mg/L) and zinc (3mg/L) (NZFCD, 2016) in breastmilk used in this analysis. The discrepancy is largest for iron, therefore iron from breastmilk contributed the least (11%) to total intake compared with the three other minerals. However, is well

documented that although concentrations are lower in breastmilk the bioavailability is high, therefore intake does not necessarily predict status (Friel et al., 2018).

Table 3.5. Contribution to total intake of Iron, Zinc, Iodine and Selenium by food group in the infant diet. (N=51)

Food Group	Iodine %	Selenium %	Iron %	Zinc %
Breastmilk	53	42	11	45
Infant Formula	31	16	47	21
Meat, Eggs, Fish and Pulses	6	24	10	14
Breads and Cereals	5	7	17	6
Fruit and Vegetables	2	4	10	8
Dairy	1	2	1	2
[a] Other	4	4	5	6

[a] Includes some commercially prepared infant foods

Milk, eggs, fish and pulses (MEFP) are a good source of source of selenium (24%), iodine (6%) zinc (14%). Breads and cereals also contribute relatively highly to total iron intake (18%) due to levels present in iron fortified infant cereals. Breads and cereals contributed less (5%) to iodine across the total population diet because only 28% of infants in this study consumed iodine fortified bread. Iodised table salt contributed less than 1% of the total iodine intake across the infant diet. Fruit and vegetables are poor sources of iodine (2%), selenium (4%) compared to iron (10%) and zinc (8%).

The relationship between variables suggest that dietary contributors to total intake of iodine, selenium, iron and zinc are similar (table 5.5, supplementary results). Selenium intake (µg/day) was strongly correlated with zinc intake (mg/day) (R=0.738, *p*=0.04), iron intake (mg/day) (0.663, *p*=0.>001), and moderately correlated with iodine intake (µg/day) (R=0.428 N=51, *p*=0.002; table 5.5). Iron intake (mg/day) was also strongly associated with zinc intake (mg/day) (R=0.867*, p*=>0.001), and weakly correlated with iodine intake (µg/day) (R=0.391, *p*=0.01; table 5.5). However, there was no relationship between iodine (µg/day) and zinc intake (mg/day).

3.4.6. Iodine and selenium status

Median urinary iodine concentration (MUIC) in the infants aged 5-10 months of age was 107 (58, 198) µg/L. 2% (1/41) had a UIC below 20 µg/L and 12% (5/41) had a UIC below 50 µg/L. Infant UIC (µg/L) was strongly positively correlated with total iodine intake (µg/day: R=0.78, *p*=<0.001) and BMIC (µg/L: R=0.603, *p*=<0.001; table 5.5). UIC was negatively correlated with anthropometric measures taken at 5-10 months, including infant weight (kg) (R=-0.35. *p*=0.03) and head circumference (cm) (R=-0.354, *p*=0.06). Urinary iodine concentration (UIC) was lower in breastfed (102 (54, 190) µg/L) compared to infant-formula fed/combination fed infants (159 (104, 248) µg/L; *p*=0.04, N=28, R=-0.4). MUIC was higher among bread consumers (186 (66, 260) µg/L compared to non-bread consumers (107 (63, 198) µg/L), but the difference was not significant.

Estimated mean 24-hour infant urine excretion based on infant weight was 368 ± 43.3 mL/day and estimated median 24-hour urinary iodine excretion (UIE) was 46 (23, 75) µg/day. Approximately 90% of iodine intake is excreted within a 24-hour period, therefore median iodine intake based on UIE in this study was calculated to be 51 (26, 84) µg/day, with 89% (24/27) below their age specific AI for iodine.

Median urinary selenium concentration (MUSC) was 11 (3, 15.5) µg/L, with urinary selenium concentration (USC) lower among breastfed (10 (6, 19) µg/L) compared to infant formula/combination fed infants (13, 11, 22) µg/L; however, the difference was not significant. Twenty-four-hour urinary selenium excretion (USE) was 4 (2, 6) µg/day. There is no universally accepted standard reference range for selenium status based on USC, however kidneys account for around 50-60% of excreted selenium which can be used as a proxy measure for intake. Median intake based on USE was 8 (5, 11) µg/day, with 93% (25/27) below their age specific AI for selenium

Table 3.6. Iodine and Selenium status based on UIC and USC at 5-10 months of age.

	N	**Median(Q1, Q2)**
MUIC µg/L	41	107 (58, 198)
UIC <20 µg/L (N, %)	41	1, 2%

UIC < 50 µg/L (N, %)	41	5, 12%
UIC <125 µg/L (N, %)	41	24, 59%
[a] UIE µg/day	40	46 (23, 75)
[b] UIE µg/day	40	54 (29, 99)
[c] Estimated iodine intake	40	51 (26, 84)
MUSC µg/L	41	11 (6, 16)
MUSE µg/day	40	4 (2, 6)
[d] Estimated Selenium intake	40	8 (5, 11)

[a] Based on average urinary excretion 2mL/kg/day
[b] Based on urinary excretion 0.5L/day
[c] Estimated intake based on 90% iodine excretion
[d] Estimated intake based on 55% selenium excretion

Multiple linear regression for the model included isolated iodine contribution (µg) from breastmilk, infant formula, bread, and all other food as predictors of urinary iodine excretion (µg/day). The model was close to significance (*p*=0.097*)* for predicting 10% of the variance (adjusted R^2=0.104), however was not significant at the 5% level (*p*=<0.05). UIE was significantly predicted by breastmilk; *b=0.549, p*=0.037 and infant formula; *b*=0.416, *p*=0.034, however the iodine contribution from bread and all other food did not. Multiple linear regression comprising selenium contribution (µg) from breastmilk, infant formula, bread and all other food as predictors of urinary selenium excretion (µg/day) was not significant (*p*=0.953).

Table 3.7. Multiple linear regression for predictors of urinary iodine excretion (UIE)

	Beta	**Standard Error Beta**	***b***	***p***
Constant	1.030	0.258		0.00
[a] Infant formula	0.263	0.121	0.416	0.037
[a] Breastmilk	0.316	0.143	0.549	0.034
[a] Bread	0.266	0.266	0.189	0.323
[a] All other food	-0.161	0.167	-0.191	0.341

[a] Log10 transformed data

3.4.7. Adequacy of the infant dietary intake

Infants estimated dietary intake was compared against calculated requirements (summarised in Table 5.4, supplementary results); 51% (26/51) and 28% (16/51) of infants did not meet their estimated daily requirements for energy (Kj) and protein (g) based on body weight. Fifty-five percent (28/51) of infants' intakes were below their age-specific AI for dietary fat, 63% (31/51) were below age-specific AI for carbohydrate and 18% (18/51) below age-specific AI for sodium.

3.5. Discussion

The current research shows the majority (82%) of infants had iodine intakes below the age specific AI for iodine, with median iodine intake estimated to be 62 (30,98) µg/day based on dietary analysis. This is not dissimilar to estimated intake extrapolated from UIC of 51 (25, 83) µg/day, of which 85% were below the AI. It indicates that this group of infants are at risk of suboptimal iodine intake, however more evidence is needed beyond the use of AI which should be interpreted with more caution. NZTDS have identified the steady decline in iodine intake in infants and children over the past few decades. For example, intakes in toddlers (aged 1-3 years) declined from 100 µg/day in 1988/89 to 49 µg/day in 2002/04, primarily due to the decreased iodine content of dairy products, which were previously a good source of iodine in the New Zealand diet through adventitious contamination by iodophors (Hannah et al., 1994; Vannoort & Thomson, 2005). Skeaff et al (2005) also showed iodine intakes in exclusively breastfed 6 month old infants in the South averaged 18 µg/day based on mean breastmilk concentration 22 ± 4 µg/L and an estimated breast milk volume 850 ml/day, much lower than results in the present study.

One of the key government initiatives to improve iodine intake of the population was fortification of commercially sold bread in 2009. The 2016 NZTDS noted an increased contribution to iodine intake from grain products in adult and child cohorts, however as infants and toddlers consume less grain-based foods, mandatory fortification of bread was predicted to have less influence on dietary intakes of this cohort (Pearson et al., 2016). In our study, 28% of these infants consumed small amounts of bread, which contributed a median of 35% (19, 66) of their total dietary iodine intake. As median iodine intake and status were

significantly higher among bread consumers than non-bread consumers (P=0.016), fortification can evidently have an impact on infants if the food is consumed.

Iodine in the urine was also analysed by adjusting UIC with a 24-hour urine excretion based on infant from body weight. The multiple linear regression model analysis showed that the iodine in breastmilk and infant formula were significant predicters of UIE, while iodine from complementary food and bread were not. This is consistent with the dietary analysis which showed higher proportion of iodine contribution from breastmilk and iodine compared to food. Although it was hypothesised that iodine from bread may also be a significant predictor of iodine in the urine, the model was limited by low rates of bread consumption within a relatively small sample size.

Median BMIC in the present study was 59 (39, 109) µg/L, an improvement from early data collected in goitrous (28 µg/L, N=14) and non-goitrous (43 µg/L; N=14) regions of Aotearoa, prior to the introduction of iodised salt in Aotearoa (Hercus & Roberts, 1927). The present findings reflect a marginal increase from mean breastmilk iodine measured in breastfeeding women living in the same region of the Manawatū in 2009 (55 ± 48 µg/L; N=32), prior to government initiatives similar to estimates reported by Brough et al in 2011 after supplementation was introduced (63 ± 44 µg/L; N=36) (Brough et al., 2015). Brough et al (2015) found only 14% of participants mothers took the iodine containing supplements during lactation in 2009, increasing to 36% of lactating women in 2011 after the provision of iodine supplements. Data from the MINI study showed 46% of mothers took an iodine supplement (Jin et al., 2021). This suggests awareness and compliance has slightly improved, however accessibility and cost associated with GP visits after 6 weeks postpartum may be a barrier for some women. Consequently, the breastfed infants of non-supplementing mothers may be at higher risk of insufficient iodine intake.

In the present study, the MUIC of 107 (58, 198) µg/L is an improvement compared to a South Island study, prior to government initiatives, which found MUIC 67 µg/L in infants, with 37% UIC below 50 µg/day (Skeaff et al., 2005). This is considered adequate according to WHO/UNICEF/ICCIDD (2007) criteria; MUIC >100 µg/L. However, Dold et al (2016) emphasised that the 100 µg/day cut-off may be too low for the infant population, because

when extrapolated to 0.5 L urine production and 90% excretion, this would require an intake of 55 μg/day, half the actual AI (7-12 months old) of 110 μg/day. The Swiss researchers suggested a higher MUIC threshold for adequacy of 125 μg/L which aligns with a higher EAR (75 μg/day) and to account for the more concentrated infant urine compared to older children (Dold et al., 2016). The present study MUIC of 107 μg/L is below this alternative higher threshold, indicating suboptimal iodine status of this infant population if assessed against these higher thresholds.

Median selenium intake of infants in this study was 12 (9, 16) μg/day based on dietary analysis and BMSC, with 69% below their age specific AI for selenium. Intake extrapolated from USC was even lower 8 (5, 11) μg/day, with 93% below their age specific AI. This is lower than previous studies in Aotearoa, including Watson *et al.* (2001) who estimated median selenium intake in 1- to 3-year-old New Zealand children of 25 μg/day (N=181). A South Island study by McLachlan *et al.* (2004) estimated mean selenium intake from complementary foods in infants between 6 to 11.9 months old was 4.4 μg/day, excluding breastmilk, as breastmilk intakes were not determined. The present study estimated intakes from complementary food only to be around 3 (1, 7) μg/day. While bread intake was low in this group, it was predicted that selenium intakes in this study could be higher due to the importation of flour from Australia for breadmaking in the North Island, which has a higher selenium content (Pearson et al., 2016).

The current findings are also inconsistent with NZTDS of the past decades which estimated selenium intakes of 6-12 month old infants of 16 μg/day (Vannoort & Thomson, 2005, 2009), and later 24 μg/day (Pearson et al., 2016). The NZTDS showed most selenium and iodine is sourced from infant foods including infant formula and cereal, custard, fruit and savoury-based weaning foods. However, the NZTDS does not differentiate between complementary food and infant formula, so it is difficult to determine the proportion from complementary foods. Also, the NZTDS does not include breastmilk which contains lower selenium (11 (9, 13) μg/L) than infant formula (20 (16, 20) μg/L), which could be a further factor for the lower selenium intakes found in the present study.

Breastmilk contributed a large proportion (42%) of selenium to the total diet of infants in this study, with breastfed infants receiving a median 7 (6, 9) μg/day from breastmilk alone, a median 7 (3, 12) μg/day from infant formula, and a median 3 (1, 7) μg/day from complementary food. BMSC in the present study was 11 (9, 13) μg/L, lower than results reported in the South Island in 1992 (13.4 μg/L, N=70) (Dolamore et al., 1992). Two other studies have examined BMSC from lactating women living in the same region in Manawatū. The first collected in 2009-2011 found similar median concentration to the current study (11.3 μg/L, N=68) (Jin et al., 2019); the second in 2017 (14 μg/L, N=78) which was slightly higher (Butts et al., 2018). Total dietary selenium intake in our study and was strongly correlated with infant USC, therefore maternal selenium intake and status can clearly influence the selenium status of the breastfed infant.

Thiocyanate from first and second-hand tobacco smoke is known to impact iodine and selenium status (Brauer et al., 2006). Maternal tobacco smoking can reduce iodine content in breastmilk, increasing risk of iodine deficiency in the breastfed infant (Laurberg et al., 2004; Laurberg et al., 2009; Oliveira et al., 2009). Rates of tobacco smoking are higher in the wider population (10.9%) (MOH, 2021a), compared the rate in the present study (4%). The most recent New Zealand data show the rate is higher among females compared to males (1.13, 95% CI 0.98 – 1.3), and among Māori compared to non-Māori (2.94, 95% CI 2.61 – 3.31). The effect of tobacco smoking on iodine and selenium status within the wider population requires further investigation.

Median iron intake among infants was 3 (1, 6) mg/day with 78% below the AI/EAR. Low dietary iron intake in this age group is consistent with the 2016 NZTDS which indicated infants aged 6-12 months old were achieving a median intake of 7.6 mg/day (Pearson et al., 2016). Breastmilk is generally unable to meet the increasing iron requirements as children transition away from exclusive breastfeeding when complementary foods are introduced at around six months (Calvo et al., 1992; Grant et al., 2007). As a result, suboptimal iron status is particularly common in the 6-24 month age group, with some studies finding as many as half of subjects iron deficient (Wham, 1996; Wilson et al., 1999). Iron deficiency is one of the most common micronutrient deficiencies around the world, therefore both local and international governing bodies recommend the introduction of iron rich foods to infants as soon as weaning

commences in order to meet their requirements during this period of high growth (MOH, 2006b). The bioavailability of iron is variable due to many dietary factors influencing absorption (Hurrell & Egli, 2010), and breastmilk contains lactoferrin, a highly bioavailable source of iron (Friel et al., 2018). Alternatively, inhibitors of iron absorption, such as phytates mean that intake does not always equate with status.

Median zinc intake was 3 (2, 4) mg/L and majority of infants had sufficient intakes. Interestingly 29% and 18% of the infants' total zinc intake exceeded the UL of 4 mg (0-6 months) and 5 mg (infants 7-12 months), respectively. Excess zinc is associated with impaired copper metabolism which is the basis for the UL (MOH, 2006b). There is clearly low risk of deficiency in this age group, although there are potentially issues related to toxicity if concentrations are unnecessarily like high in fortified infant foods such as infant formula. In this study, intake was significantly higher in infant-formula fed infants compared to breastfed infants.

3.5.1. Strengths of the study

This study examines dietary intake of iodine, selenium, iron, and zinc concurrently rather than in isolation for infants aged 5-to 10-months, during a critical period of dietary transition. Although the sample size is relatively small, the dietary analysis is in-depth and comprehensive adds to our understanding of the nutritional adequacy of the key components in the infant diet in Aotearoa.

3.5.2. Limitations of the study

Dietary analysis is notoriously difficult during the transition period in which complementary foods are introduced into the infant diet. Accurate recording dietary intake of infants is especially challenging while feeding skills are developing. It relies on time commitment and memory for caregivers to complete the food diary accurately. It is equally challenging for researchers to interpret and analyse the food diaries. Breastmilk intake also cannot be precisely measured without weighing before and after feeds, which is an impractical method for large epidemiological studies. It is unsurprising that some infants did not meet their requirements for energy (55%) and protein (28%) as calculated from body weight (kg), as

dietary intake may have been underestimated. This may mean intake of iodine, selenium, iron and zinc have also been underestimated. While every effort was made to ensure the accuracy of dietary analysis, this study highlights the methodological challenges with dietary assessment in infants, and the need for better food recording methods for both mothers and researchers.

This relatively small, sample does not represent the ethnic, socio-economic status and education level of all mothers and their infants in Aotearoa. The majority of mothers recruited are Pakeha (79%), tertiary educated (78%), and many participated in the study with their first child (42%). Additionally, 42% of participants' annual household income exceeded the national median for 2017, at the time of data collection (Statistics New Zealand, 2018). The average annual household income measures all New Zealand households (with and without children), however the median income for households with young children is lower, and often dependent on a single income (Statistics New Zealand, 2021). Therefore, participants in this study appear to be of relatively high socioeconomic status compared to the range seen in Aotearoa. While information was gathered about maternal birth country and ethnicity, this was not gathered for the infant's ethnicity which may differ. The lack of representation is a significant limitation of this study, because research shows nutritional deficiencies and the associated health consequences are more common among tamariki Māori, Pacifika children, and infants living in low-income families (Gerritsen et al., 2020). Therefore, infants in this study may have better nutritional status than the range seen across Aotearoa.

This study is a secondary analysis of data from the MINI study. The sample size of this study is relatively small, and due to non-compliance, parts of the data were incomplete and smaller again. For example, more than one third of participating mothers did not provide a 3DDD for their infant, and MUIC of a population would ideally have more than urine samples from more than 100 individuals, which is a limitation of the present study. Therefore results should be interpreted with caution. Finally, the study was limited to the Manawatū region and therefore the conclusions may not apply to other geographical regions in Aotearoa where levels of iodine and selenium in the soil and food supply may be lower, such as in the South Island.

3.6. Conclusions

The findings suggest that public health interventions have had limited impact on the intake of iodine in infants aged 5 to 10 months in Aotearoa, and iodine intake continues to be low. Insufficient selenium and iron intake in infants continues to be of concern, while intake of zinc appears to be adequate, with possibly some excessive intakes. Further research is required to assess the impact of iodine, selenium, zinc and iron intake and status on thyroid function by measuring biomarkers such as thyroid hormones and selenoproteins along with physical growth and cognitive development in the first year of life. It is also important to monitor larger population groups of all socio-economic and ethnic backgrounds.

4. Conclusions and Recommendations

4.1. Conclusion

The results from this relatively small sample of infants aged 5-to 10-months-old suggest that they may not be consuming enough iodine, selenium, and iron, while most infants were consuming zinc in adequate or possibly excessive amounts. This is consistent with literature which has shown poor intake of iodine, selenium and iron among infants and toddlers in Aotearoa. Zinc intake among infants in Aotearoa is largely under-investigated, however low zinc intake is likely uncommon.

Breastmilk contributes more to total iodine intake in this cohort than complementary food for the breastfed infant. Complementary foods may still have limited contribution to iodine intake in infants due to low levels in New Zealand soils and food supply (Vannoort & Thomson, 2009). Pearson et al (2016) reported iodine intakes had improved in all population cohorts in response to bread iodine-fortification from 2009, except among infants where bread consumption was predictably low. Twenty-eight percent of infants in this study consumed bread, which contributed a median 35 (19, 66) percent to total iodine intake. Bread consumption evidently improves iodine intake for those who consume it. Only two participants had iodised salt noted in their three-day food diary (3DDD), which is unsurprising as discretionary salt use is not recommended in this age group (Ministry of Health (MOH), 2021). It is therefore clear that public health interventions targeted at the general population have limited impact on infants who remain vulnerable to iodine inadequacy.

Adequate infant iodine status was observed in this study using the World Health Organization/United Nations International Children's Emergency Fund/International Council for Control of Iodine Deficiency Disorders (WHO/UNICEF/ICCIDD) (2007) criteria. However calculated intakes based on excretion were low, with many not achieving their age-specific AI, which reinforced the low intakes measured in the diet. Several studies have proposed higher median urinary iodine concentration (MUIC) cut-offs for infants in order to achieve AI, for example 125 µg/L (Dold et al., 2016), and 180 to 225 µg/L (Delange, 2007). The MUIC of 107 (58, 198) µg/L seen in the current study would suggest iodine status in this infant cohort

is suboptimal, and that a review of the international criteria for measuring MUIC in infant populations in developed countries is necessary. MUIC needs to be compared to markers of thyroid function in the infant population. Furthermore, if intake falls below AI, it is difficult to comment on adequacy of intake as more research is needed.

Most of the selenium in the infant diet was sourced from breastmilk or infant formula, which each contributed similarly to the total intake depending on breastfeeding status. The strong correlation of total dietary intake and breastmilk concentrations with urinary selenium concentration (USC), suggests optimising maternal intake and status is vital to sustain adequate intake and status in the breastfed infant. However due to the lack of international criteria measuring infant selenium status based on selenium excreted in the urine, little can be concluded. Further research is required to investigate the consequences of this on optimal thyroid function, infant growth, and brain development.

Low iron intake in infants is prevalent both in Aotearoa and internationally, so it is unsurprising that the majority (78%) did not achieve estimated average requirements (EAR). Iron was mainly sourced from complementary foods, specifically meat, eggs, fish, and pulses (MEFP), iron-fortified cereals and, for non-breastfed infants, infant formula. Iron intakes were lower among infants who were only breastfed compared to non-breastfed infants. This was expected as the levels of iron in breastmilk are lower compared to levels found in commercial infant formula (Dewey & Chaparro, 2007; Friel et al., 2018), although the iron absorption from breastmilk is superior (Lönnerdal et al., 2015). Therefore, while total intakes of iron may have been higher among infant formula fed infants compared to breastfed, this may not result in higher iron status.

The majority (69%) of infants had only breast milk in addition to complementary foods while the remainder were either formula fed (8%) or had a combination of breastmilk and infant formula (23%). Iodine levels in the breast milk showed marginal increases compared to previous literature, which suggests that the provision of a 150 µg/day iodine supplement may have improved iodine status among some lactating women in Aotearoa since 2010. However, this research suggests adherence to supplementation recommendations is limited, so further

work is needed to raise awareness of the value of the iodine supplement, and to reduce barriers to its availability among pregnant and lactating women.

Optimal thyroid function is essential for neurodevelopment and growth among infants. Infant anthropometric data, including weight (kg), recumbent length (cm) and head circumference (cm) were measured and compared against estimated micronutrient intake and status. There was no significant association identified between micronutrient intake and status and infant anthropometry.

Overall, infants between the age of 5 and 10 months present vulnerabilities for low intake of iodine, selenium and iron during the complementary feeding transition. Zinc intakes appear to be adequate. Studies to date support the importance of adequate iodine, selenium and iron intake and status to support infants' growth and neurodevelopment, which enables children to reach their optimal cognitive potential and academic performance in later years. Micronutrient intake between 5-10 months of age is multifactorial with varying amounts obtained from complementary foods, infant foods including infant formula and/or breastmilk. Breastfeeding rates vary enourmously throughout New Zealand. Therefore, the nutritional intake and status of this group requires monitoring and consideration of public health interventions to support optimal intakes.

4.2. Strengths of the study

This is the first study to explore the intake of four micronutrients, iodine, selenium, iron, and zinc concurrently rather than in isolation as pertaining to optimal thyroid function and infant growth in Aotearoa. It is the first study to report on infant iodine nutrition after the introduction of mandatory iodine fortification of bread in 2009 and the provision of a subsidised iodine supplement for pregnant and breastfeeding women in 2010. The study examines intake and status of these key minerals in infants aged between 5-to 10-months-old, during a transition period from exclusive to partial breastfeeding or infant formula feeding. The contribution of each micronutrient from the major components of the infant diet are explored, including complementary foods, breastmilk, and infant formula. In doing so, this study contributes to current literature related to complementary feeding and breastfeeding

practices in Aotearoa. Assessment of iodine and selenium in the infants' urine and in maternal breastmilk provides valuable data that can be evaluated against local and international figures.

4.3. Limitations of the study

A limitation of the study is that intake was measured for iodine, selenium, iron and zinc, but not status. The findings need to be corroborated with measures of status in the infant population to determine if inadequate status of these micronutrients is a problem. Zinc is of particular interest because there is little existing research. It is important to see how well intakes are associated with status, explore clinical manifestations on thyroid function look like in the infant population.

Although a weighed multi-day diet diary is considered the most reliable and practical option for large studies, measuring infant intake has unique challenges. A limitation, therefore, of this study relates to accuracy of the three-day diet diaries (3DDD). Mothers in this study were encouraged to weigh or estimate food consumed, which required both time commitment and precision for accurate recording. Measuring the actual amount of food consumed relative to plate waste, spills, or regurgitation while infants' feeding skills are developing will inevitably introduce error. Foods are likely to be missed, or are under or over reported.

A significant limitation of this study was estimating the breastmilk intakes of infants. The most precise method is to weigh before and after feeds to obtain an approximate volume (Institute of Medicine (US) Committee on Nutritional Status During Pregnancy and Lactation, 1991). However, this method may disrupt both mother and infants, and affect breastmilk intake. Doubly labelled water could also be used estimate the volume of breastmilk consumed by the infant (Da Costa et al., 2010; Slater et al., 2019), however it is costly (Johnson & Coward-McKenzie, 2001). Both methods are impractical for large studies; in the present study, the duration of breastfeeds were recorded. Due to the limited methodology available for estimating breastmilk intake volume from length of time of the breastfeed, a total daily volume was assigned based on an age-specific criteria proposed by Briefel et al, (2010). These volumes were used to calculate total dietary intake, including from iodine and selenium based

on BMIC and BMSC respectively. While every effort was made to ensure the accuracy of dietary analysis, intakes from food or breastmilk may be under or over estimated. Therefore, results need to be interpreted with caution.

Other limitations of the study include the relatively small sample size compared to large epidemiological studies. Selection bias is a limitation because majority of participants were predominantly well-educated, Pakeha, from relatively high income-earning household, and are clearly not representative of the wider population of Aotearoa. Those volunteering to participate in a mother-infant nutrition study may be more health conscious than the general population or have pre-existing knowledge of iodine nutrition. Furthermore, the likelihood of initiating breastfeeding and continue breastfeeding for longer than six months is increased in older, tertiary educated mothers, and decreased in Māori, Pacifika, and Asian women (Castro et al., 2017). Whānau socioeconomic characteristics such as education, ethnicity, and household income are strong predictors of nutritional health in infants in Aotearoa (Gerritsen et al., 2020), therefore the findings of suboptimal micronutrient intake among infants are likely to be far more widespread in Aotearoa then what has been illustrated in the present study.

Finally, the iodine and selenium concentrations in the soil and food supply vary geographically across Aotearoa (Pearson et al., 2016; Thomson, 2004b), while the present study population is based in Manawatū, in the North Island. A limitation of this is that the data do not capture regional variation, and inadequate intakes may be more prevalent. This also raises the challenge of determining the geographical source of foods consumed. Future research is recommended to have a larger sample size of mothers and their infants over a larger geographic region of Aotearoa to capture the variability in iodine and selenium intake and status.

4.4. Research Recommendations

It is highly recommended that further studies involve larger groups of infants to assess the intake and status of iodine, selenium, iron and zinc as related to optimal thyroid function. More research is needed to determine how measures of status compare to measures of

thyroid function. Therefore, other indicators of thyroid function, such as levels of thyroid stimulating hormone (TSH) or thyroglobulin (Tg) from blood samples, needs to be incorporated into these studies. Specific investigation is needed to provide greater understanding of the role of iron and zinc intake in infant thyroid function, and to further define what the adequate intake and status levels for this age group should be.

As adequate thyroid hormone production is required for supporting optimal neurodevelopment, future studies should investigate iodine, selenium, iron and zinc intake and status on neurodevelopment during the first year. Specific measures of cognitive development, memory and learning should be explored. Optimal thyroid function is also thought to influence the physical development of infants, therefore larger studies should focus on changes in growth parameters in the first two years of life, along with other physical development progress.

More research needed to clarify optimal cut-offs for MUIC for iodine adequacy in infant populations. Research is required to establish reference ranges for MUSC as a measure of infant selenium status. Such research could incorporate other measures such as selenium in the blood. Collecting blood from infants can be problematic in research, so there is a need to investigate non-invasive measures for assessing selenium and zinc, such as hair and nails.

As the present study has highlighted vulnerability for achieving optimal intake of iodine, selenium and iron, further mandatory food fortification strategies need to be considered that will target the infant population. For example, fortification of a commonly consumed infant weaning food, such as cereal or fruit puree.

In addition, further research is needed in relation to public perception and knowledge about the micronutrients pertaining to optimal thyroid function in infants. This could inform public health promotion strategies related to optimising thyroid health in infants. This could include raising awareness among pregnant and breastfeeding women around the benefits of taking the iodine supplement to optimise breastmilk concentrations.

Finally, for more comprehensive nutrition screening of the population in Aotearoa, future research should prioritise expanding the ethnic and socioeconomic diversity of participants through alternative recruitment channels, such as Māori Health Providers.

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Appendices

Appendix A. Mini Study Ethics Approval

Health and Disability Ethics Committees

Health and Disability Ethics Committees
Ministry of Health
Freyberg Building
20 Aitken Street
PO Box 5013
Wellington
6011

0800 4 ETHICS
hdecs@moh.govt.nz

15 December 2015

Ms Ying Jin
School oF Food and Nutriton
Massey University
Private Bag 11222
Palmerston North 4442

Dear Ms Jin

Re:	Ethics ref:	15/NTA/172
	Study title:	Mother and Infant Nutrition Investigation

I am pleased to advise that this application has been *approved* by the Northern A Health and Disability Ethics Committee. This decision was made through the HDEC-Full Review pathway.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Northern A Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.

2. Before the study commences at *a given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

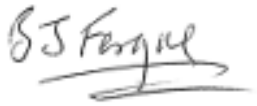
Your next progress report is due by 15 December 2016.

Participant access to ACC

The Northern A Health and Disability Ethics Committee is satisfied that your study is not a clinical trial that is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Participants injured as a result of treatment received as part of your study may therefore be eligible for publicly-funded compensation through the Accident Compensation Corporation (ACC).

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,



Dr Brian Fergus
Chairperson
Northern A Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Health and Disability Ethics Committees

Health and Disability Ethics Committees
Ministry of Health
Freyberg Building
20 Aitken Street
PO Box 5013
Wellington
6011

04 816 3985
hdecs@moh.govt.nz

04 May 2016

Ms Ying Jin
School oF Food and Nutriton
Massey University
Private Bag 11222
Palmerston North 4442

Dear Ms Jin

Re:	Ethics ref:	15/NTA/172/AM01
	Study title:	Mother and Infant Nutrition Investigation

I am pleased to advise that this amendment has been *approved* by the Northern A Health and Disability Ethics Committee. This decision was made through the HDEC Expedited Review pathway.

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Dr Brian Fergus
Chairperson
Northern A Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix B. MINI Study MDHB Locality Approval

MidCentral District Health Board

MDHB APPROVAL FORM FOR RESEARCH ACTIVITY

Research Practice Title: Mother and Infant Nutrition Investigation (MINI) Study : A cohort of postpartum women
Principal Investigator: Ying Jin
Designation : PHD Candidate Service Area: Womens Health
Research Practice Experience : _____
Other Researchers Involved: Lovise Brough (Massey) Jane Coad (Massey)

Brief description of research study purpose, methodology and reporting:

Purpose:

After the birth of their baby, most women continue to see their health care professionals. However, the focus is often on the infant's health. Only limited attention is given to the mother's mental health. This study will monitor the mothers' health by assessing her nutrient status, thyroid function and mental health. The thyroid is a small butterfly-shaped gland at the base of the neck which produces hormones. How a mother's health status might affect her baby's development during early life is important. The three nutrients we are studying are iodine, selenium, and iron. Understanding these nutrients will help to provide better health care to future mothers. This leads to greater knowledge about the health and wellbeing of both the mothers and their infants.

Methodology:

Advertisements and posters place at selected sites where preganat or post partum women frequently attend. Potential participants will record an expression of interest online or via telephones.Prospective participants will be sent an appropriate study information sheet. Once they indicate their willingness to participate, the researcher will conduct a screening questionnaire to ensure participants are eligible to take part in the study. Informed consent will be obtained. The target number of study participants is 180. Taking

Progress and final reporting:

Section A : Initial Registration and Approval of Research Practice

Documented evidence :

- ☐ Research purpose and parameters
- ☐ Consultation with all MDHB involved parties
- ☐ Risk and indemnity cover
- ☐ Resources required (*eg, staff, equipment, other service involvement*)
- ☐ Approved research budget

Operations Director signature to proceed : Date:

Professional approval

☑ Yes ☐ No ☐ Not applicable

Designation:	Signature:	Date:
ACTING CLINICAL DIRECTOR		14/9/16
CHARGE MIDWIFE	DHNRST	15/9/16

MidCentral District Health Board

MDHB APPROVAL FORM FOR RESEARCH ACTIVITY

External approval *(eg, HDEC, Educational Institution)*

☑ Yes ☐ No ☐ Not applicable

State where from : HDEC

Documented evidence (where applicable):

☐ National application form for ethical review of a research project *(NAF- 2005- 01)*

☐ 'Participants who are unable to give informed consent to participate' form *(NAF- Part 7)*

☑ Locality assessment form

☐ 'Use of human tissue' form *(NAF- Part 5)*

☐ 'Genetic research' form *(NAF - Part 6)*

Section B : Operations Director's Endorsement to Proceed

Proposed start/end dates of research: _____

Operations Director signature _____

Service Line : Women Health Date: 15.9.16.

This submission has been considered to meet ethical and professional requirements, and clearly demonstrate potential clinical, professional and/or strategic benefit to the organisation.

Clinical Board Acknowledgement of Registration

Signed: _____ Designation: CHO/Chair Date: 22/9/16

Copy to be retained by Chief Medical Officer's office and details entered onto Register.

To be completed by the Principal Investigator and Operations Director. The Operations Director is to forward a copy of the form to the MidCentral Health Clinical Board, via Quality & Clinical Risk. All relevant supporting documentation is to be included.

Locality Assessment Sign Off for Approval of Research/Clinical Trials

Full project title:	Mother and Infant Nutrition Investigation
Short project title:	MINI

1. Declaration by Principal Investigator

The information supplied in this application is, to the best of my knowledge and belief, accurate. I have considered the potential ethical, resource and cultural issues involved in this research and believe that I have adequately addressed them for this locality.

A formal letter of consultation was sent to the Maori Health Unit on the __/__/__ (date)

Maori Consultation with Dr Maureen Holdaway, Massey University

Name of Principal Investigator (please print):	Ying Jin
Signature of Principal Investigator:	Ying Jin
Date:	25 July 2016

2. Declaration by Clinical Leader of Service/Department in which the Principal Investigator is located

I have read the application, and it is appropriate for this research to be conducted in this department. I give my consent for this locality to be included in the ethics committee application.

Name (please print):	Steven Grant		
Signature:		Institution:	Palmerston North Hospital/MCH
Date:	14/9/16	Designation:	Acting C.D.

- Where the Clinical Leader is also one of the investigators, the Clinical Leader declaration must be signed by the Clinical Executive Director.

MidCentral District Health Board
Te Pae Hauora o Ruahine o Tararua

3. If the application is for a student project, the supervisor should sign the declaration.

I have read the application, and it is appropriate for this research to be conducted under my supervision. I give my consent for this locality to be included in the ethics committee application.

Name (please print): LOUISE BROUGH

Signature: L. Brough

Institution: ~~Palmerston North Hospital/MCH~~ MASSEY UNIVERSITY

Date: 26/7/16

Designation: SENIOR LECTURER.

4. Declaration by relevant Operations Director

I have read the application, and it is appropriate for this research to be conducted in this department. I give my consent for this locality to be included in the ethics committee application.

Name (please print): NICHOLAS GROBB

Signature:

Institution: Palmerston North Hospital/MCH

Date: 23.9.16

Designation: Ops Director

Appendix C. MINI Study ANZCTR Registration

Dear Ying Jin,

Re: Mother and Infant Nutrition Investigation - Investigating micronutrient intake and status in mothers and babies, and their possible effects on thyroid function

Thank you for submitting the above trial for inclusion in the Australian New Zealand Clinical Trials Registry (ANZCTR).

Your trial has now been successfully registered and allocated the ACTRN: ACTRN12615001028594

Web address of your trial: http://www.ANZCTR.org.au/ACTRN12615001028594.aspx
Date submitted: 15/09/2015 1:15:17 PM
Date registered: 1/10/2015 10:29:21 AM
Registered by: Ying Jin

If you have already obtained Ethics approval for your trial, could you please send the ANZCTR a copy of at least one Ethics Committee approval letter? A copy of the letter can be sent to info@actr.org.au (by email) OR (61 2) 9565 1863, attention to ANZCTR (by fax).

Please be reminded that the quality and accuracy of the trial information submitted for registration is the responsibility of the trial's Primary Sponsor or their representative (the Registrant).
The ANZCTR allows you to update trial data, but please note that the original data lodged at the time of trial registration and the tracked history of any changes made will remain publicly available.

The ANZCTR is recognised as an ICMJE acceptable registry (http://www.icmje.org/faq.pdf) and a Primary Registry in the WHO registry network (http://www.who.int/ictrp/network/primary/en/index.html).

If you have any enquiries please send a message to info@actr.org.au or telephone +61 2 9562 5333.

Kind regards,
ANZCTR Staff
T: +61 2 9562 5333
F: +61 2 9565 1863
E: info@actr.org.au
W: www.ANZCTR.org.au

Appendix D. MINI Study Poster

MINI Study –
Mother and Infant Nutrition Investigation

Would you like to find out more about your dietary intake and nutrient status and its effect on both you and your new-born baby?

If you are a healthy woman aged 16 or older
Either in the late stage of pregnancy
Or have recently given birth
We would like to hear from you

What would be involved if joining this study?

- Three Visits to the Human Nutrition Research Unit at Massey University
- Complete questionnaires about food intake, use of supplements, general health
- Complete a Child Development Questionnaire when your baby reaches 4, 8 and 12 months old
- We will measure your body composition and thyroid gland size
- Collect a small urine, blood and/or breastmilk samples and toenail clippings from you
- Collect a small urine sample and nail clippings from your child

We will continue to follow you and your baby's nutritional health until your child is 12 months old

This project has been reviewed and approved by the Health and Disability Ethics Committee: 15NTA172.

Please contact:
Ms Ying Jin (PhD Scholar) through mini@massey.ac.nz
Or Go to www.massey.ac.nz/ministudy

School of Food and Nutrition, Massey University, 027 399 4138/06-951-7556

TE KURA HAUORA TANGATA
MASSEY UNIVERSITY
COLLEGE OF HEALTH

Appendix E. MINI Study Health Screening Questionnaire

Health Screening Questionnaire

Thank you volunteering to take part in this study. I would like to ask you a few questions to check that you are a suitable subject and provide you with an opportunity to ask any questions that you may have about the study.

What is your age?

Are you currently breastfeeding?

When was your baby born?

Do you have any contagious blood borne disease, e.g. Hepatitis A or HIV?

Do you currently have any medical conditions?

Have you ever been diagnosed with thyroid disease such as thyroid enlargement or goiter/ hyperthyroidism/ hypothyroidism?

If yes, are you currently receiving any treatment or consuming medication containing iodine? Or, are you now fully recovered?

Are you taking iodine contain supplements due to other reasons rather than pregnancy or lactation?

Are you taking any other medication? *If yes, can you please indicate the type or name of the medication(s) that you are taking?*

Does your baby have any health complications, e.g. Preterm?

Appendix F. MINI Study Participant Information Sheet

Study title:	**[MINI - Mother and Infant Nutrition Investigation]**	
Locality:	**Palmerston North**	Ethics committee ref: **15/NTA/172**
Lead investigator:	**Ying Jin**	Contact **email**: **mini@massey.ac.nz** **Register your interest – www.massey.ac.nz/ministudy** **Phone: +64 (06) 9517556** **027 399 4138**

Would you like to help us?

We invite you to take part in a research study: Mother and Infant Nutrition Investigation (MINI). This sheet gives detailed information about the study. Please read it carefully before deciding whether you wish to join our study.

We need mothers and their infants to take part. It is important that you understand why we are doing this research, and what it may involve for you. Please take time to read the sheet carefully. Feel free to discuss it with other people, such as your family, whānau, friends, or your health care providers. Please ask us questions if anything seems unclear, or if you wish to know more details.

Introducing the researchers

This research is led by PhD scholar Ms Ying Jin. Ying's supervisors are Dr Louise Brough and Professor Jane Coad. They are human nutritionists in the School of Food and Nutrition, Massey University, Palmerston North. Anne Broomfield, research officer, will also assist in the study.

What is the purpose of this study?

After the birth of their baby, most women continue to see their health care professionals. However, the focus is often on the infant's health. Only limited attention is given to the mother's mental health. This study will monitor the mothers' health by assessing her nutrient status, thyroid function and mental health. The thyroid is a small butterfly-shaped gland at the base of the neck which produces hormones. How a mother's health status might affect her baby's development during early life is important. The three nutrients we are studying are iodine, selenium, and iron. Understanding these nutrients will help to provide better health care to future mothers. This leads to greater knowledge about the health and wellbeing of both the mothers and their infants.

Do I have to take part?

No. It is entirely up to you to decide whether you wish to take part. If you do agree, you will be asked to sign a Consent Form. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

Should you change your mind about being in the study, you are free to withdraw from the study at any time without giving any reason.

What would your participation involve?

If you are interested in taking part in the study, please phone or email us. You can also enter your details on this study's "Express of Interest" webpage. We will reply immediately and arrange a brief telephone conversation. We will ask you some questions to ensure that you are eligible. You must feel totally comfortable about taking part in the study.

Soon after, we shall make an appointment for you and your baby to come into the Human Nutrition Research Unit at Massey University. If this is not possible, we may visit you either at home, at a local community Centre, or at a health professionals' clinic.

During the first visit, we shall

ask you some questions about your nutrient supplement use, and your nutrition knowledge. We will also ask you about your health, diet and some personal information;

- measure your weight, height, and body composition;
- ask you to provide small samples of urine and breastmilk which we will use to assess your nutrient status;
- measure your baby's weight, length and head circumference.
- collect a small urine sample from your baby to assess his/her nutrient status.
- Your first visit should take no more than two hours.

After the first visit, you will be given

- two small paper bags for you to collect nail clippings from yourself and from your baby to assess selenium status.
- a 4-day food record diary to measure your nutrient intake.

Within a month after your first visit, at a convenient time, we will collect the samples and food diary from you at home.

The 2nd visit will be when your baby is 6 months old. The 3rd visit will be when your baby is 12 months old. We will ask you to complete questionnaires to assess your child's development at 4, 8 and 12 months. A Flow Chart is included in this Information Sheet.

How would the required samples be collected?

A clear detailed instruction of how to collect infant or adult nail clippings would be given at the first visit. Infant urine samples will be collected by placing a pad inside the nappy, checking every 10 minutes until wet, and then urine aspirated (extracted) with a syringe. Blood samples will be drawn by experienced phlebotomist. The collected biological samples will be frozen, labelled with a unique code (no personal information will be displayed on the samples), and then stored for 10 years to allow a number of analyses to take place. After 10 years, the samples will be properly disposed in biohazard bags to be incinerated (burned) by a professional company who specialise in destroying biological samples. We acknowledge that the use and storage of tissue is a cultural concern for some Māori people. We are unable to return body fluids such as blood, urine and breastmilk due to safety (microbiological) issues. However, if you wish, the nail clippings, after analysis, will be returned to you if you request this in advance.

What are the possible risks to you?

There are small risks when taking blood samples such as discomfort, bruising, infection or fainting. To minimise any risk, your blood will only be taken by experienced and fully trained research staff.

Any risks involved in this study are very minor. All of the checks are routinely made. If you have any concerns during the study, you may discuss these with any of the study team.

Any complaints you may make will be fully investigated. If you have any concerns about any aspect of this study, you should speak immediately to a member of the study team. They will do their best to answer all of your questions fully.

What are the advantages of taking part in the study?

Your thyroid gland size, thyroid function and iron status will be monitored during the study. These are not normally covered by primary health care services;

Repeated monitoring of your wellbeing during the first year after delivering a baby;

Based on your food diary, you will receive feedback on your intake of nutrients within a month after we receive the dietary diary. This will be compared to New Zealand standard dietary guidelines.

You will also receive information about your child's development assessments at 4, 8 and 12 months.

Will my participation in the study be kept confidential?

Yes. All information collected about you and your baby during the study will be kept strictly confidential. Each mother will be given a unique code which will be used on all data collected. No identifying details will be recorded on the interview sheets or other records. When the study results are presented, you will not be named or recognised from any of the information given. All information will be entered into a protected database at Massey University. Information collected about you and your baby will be kept strictly confidential and secure in a locked filing cabinet. All electronic files on computers will have passwords and restricted access. Only the named members of research team will have access to detailed personal information.

Massey University maintains a central record of all research projects undertaken. This does not include personal information about those who take part. The data (without containing personal information) will be held for 10 years after the youngest person in the study has reached the age of consent or 16 years old.

What will happen to the results?

Should you wish, you will receive all the results about you and your baby. Should your results be, in any way, unusual, you will be encouraged to contact your general practitioner and seek appropriate medical advice. Once the whole study has ended, we can send you a summary of the study results, should you wish to have it. The results will also be presented at scientific meetings or published in peer reviewed journals. This ensures that a wider community, including health professionals, can know and read about the findings. You and your baby will not be identified by any of these publications or presentations.

What would happen if you were injured in the study?

If you were injured in this study, which is unlikely, you would be eligible for compensation from ACC. This would be the same as if you were injured in an accident at work or at home.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study will not in any way affect your cover.

Who has reviewed the study?

This project has been reviewed and approved by the Northern A Health and Disability Ethics Committee through the full review pathway.

Contact for further information:

If you have any further questions or if you have any concerns whilst taking part in the study then please contact:

Ms Ying Jin, Lead Investigator/PhD Scholar

Email: mini@massey.ac.nz, or go to www.massey.ac.nz/ministudy
Cell phone: 027 399 4138
Telephone: +64 (06) 9517556

Dr. Louise Brough, Principle Supervisor/Senior Lecturer
Telephone: +64 (06) 356 9099 ext. 84575
Email: L.Brough@massey.ac.nz

Where can you go for more information about the study, or to raise concerns or complaints?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Ms Anne Broomfield, Research Technical Officer
Human Nutrition Research Unit
Massey Institute of Food Science and Technology
Telephone: +64 (06) 356 9099 ext. 84566
Email: A.M.Broomfield@massey.ac.nz

If you want to talk to someone who is not involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

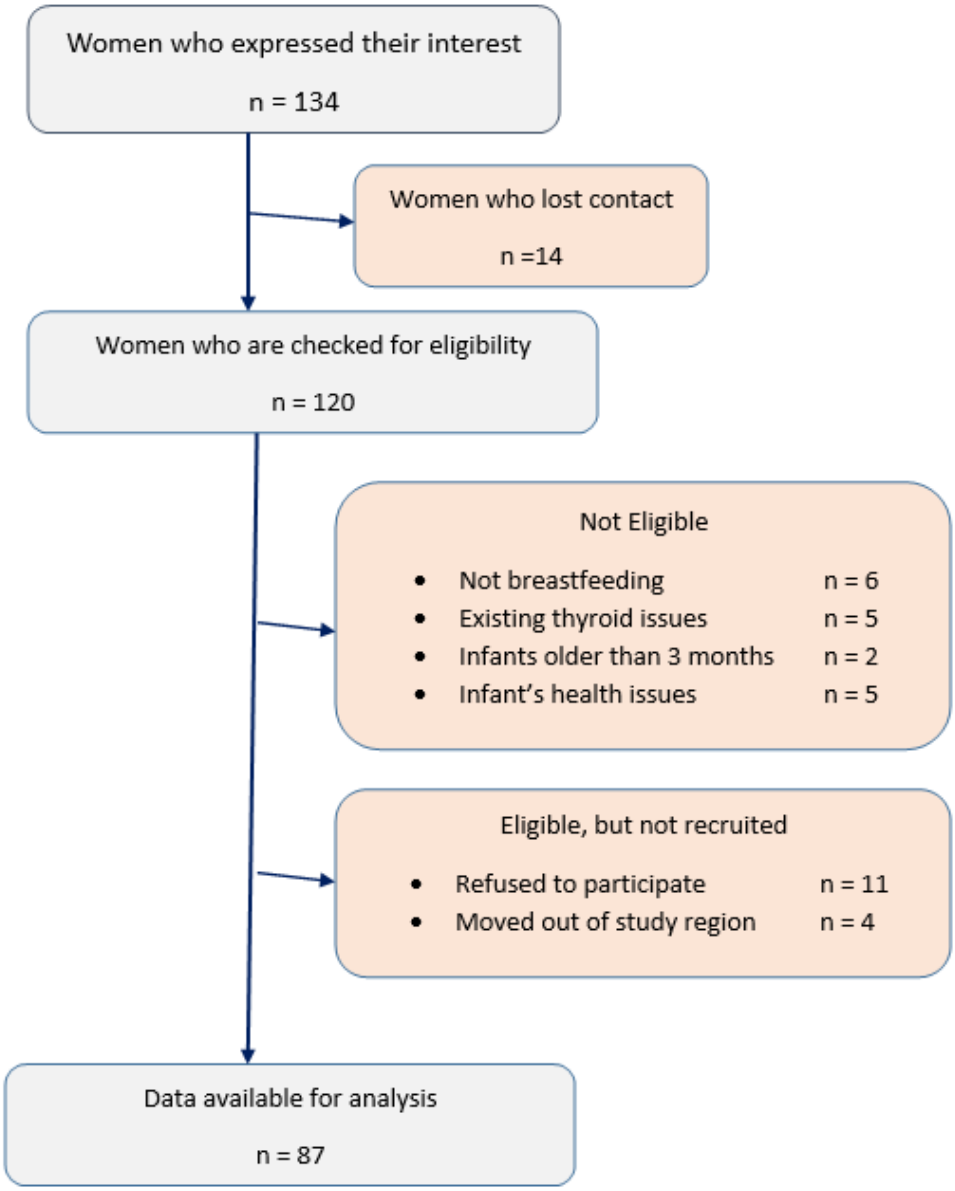
If you feel you would like to talk to a Māori health support person, please contact:

Dr Maureen Holdaway
Associate Director, Research Centre for Maori Health & Development
Telephone: +64 (06) 356 9099 ext. 85092
Email: M.A.Holdaway@massey.ac.nz

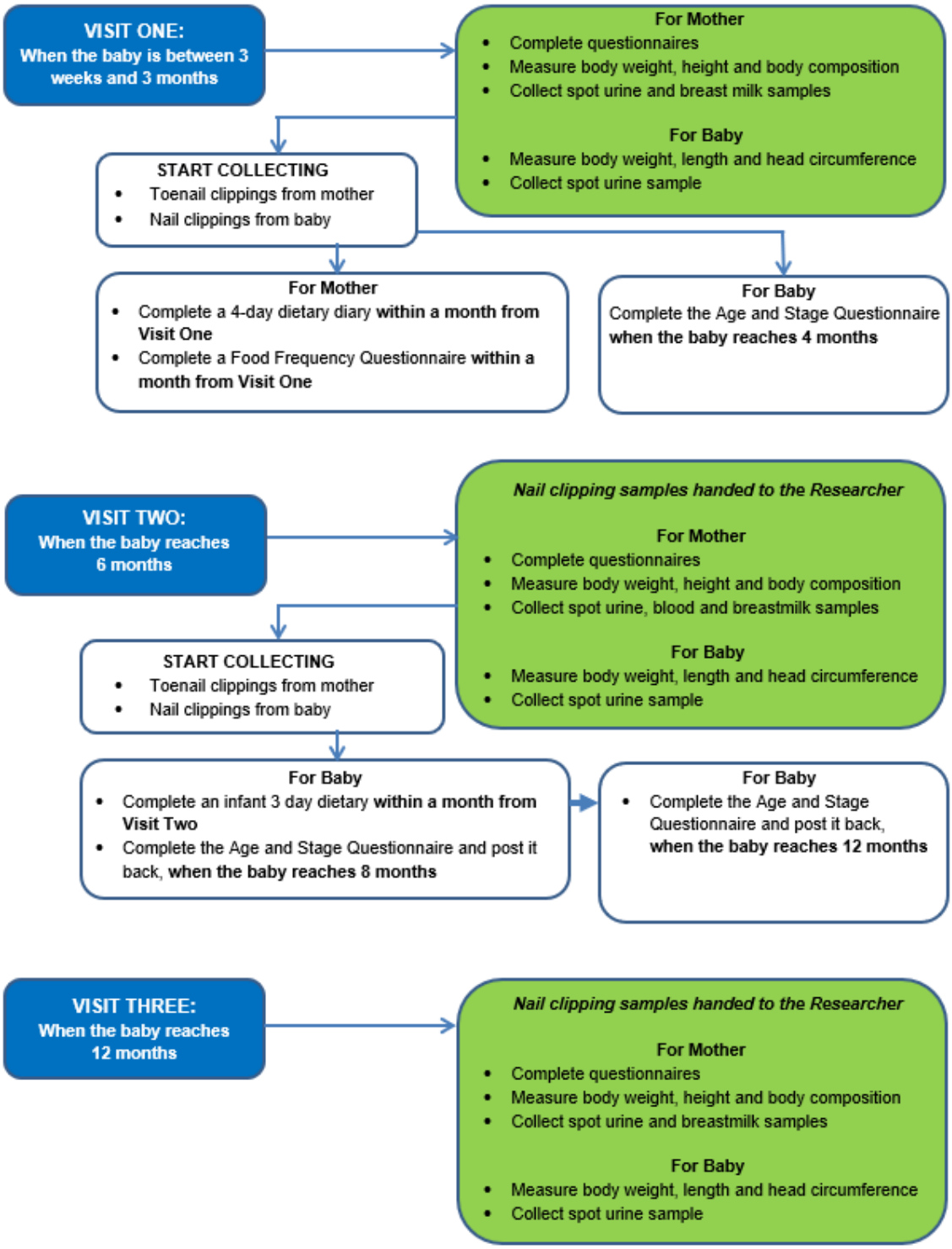
You can also contact the health and disability ethics committee (HDEC) that approval this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Appendix G. MINI Study Recruitment Flow Chart



Appendix H. MINI Study Flow Chart



Appendix I. MINI Study Consent Form

Please tick to indicate you consent to the following		
I have been given sufficient time to consider whether or not to participate in this study.		
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.		
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.		
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.		
I consent to the research staff collecting and processing my information, including information about my health.		
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.	Yes ☐	No ☐
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.		
I know who to contact if I have any questions about the study in general.		
I wish the nail clippings to be returned to me after analysis	Yes ☐	No ☐
I wish to receive a summary of the results from the study.	Yes ☐	No ☐

Declaration by participant:

Participant's name: _____

Signature: _____ Date: _____

Declaration by a member of the research team:

I have given a verbal explanation of the research project to the participant and have answered fully any of the participant's questions concerning this study.

I believe that the participant fully understands the details of this study and has given informed consent to participate.

Researcher's name: _____

Signature: _____ Date: _____

Appendix J. MINI Study General Questionnaire – Baseline

Date of visit: _____ Day_____ Month_____ Year

General Questionnaire – when your baby is born

I would like to ask you about what you usually eat and your meal preparation.

1. Do you add any **SALT** to your food (either AT THE TABLE or in COOKING)?

☐ No (**go to Q 4**)
☐ Yes

2. Do you add **SALT** to your food AT THE TABLE?

☐ No (**go to Q3)**
☐ Yes

2a. If yes, what type of SALT do you mainly use (more than 60%)?

☐ Plain table salt
☐ Iodised salt **(go to Q2b.)**
☐ Other mineral salt (rock, sea salt)
☐ Others_____

2b. Considering only **IODISED SALT** added AT THE TABLE, please indicate the average amount of your individual portion used DAILY.

☐ Less than 1/4 teaspoon
☐1/4 teaspoon
☐ 1/2 teaspoon
☐ 1 teaspoon
☐ More than 1 teaspoon

3. Do you add **SALT** to your food in COOKING?

☐ No **(go to Q4)**
☐ Yes

3a. If yes, what type of SALT do you mainly use (more than 60%)?

☐ Plain table salt
☐ Iodised salt **(go to Q3b.)**
☐ Other mineral salt (rock, sea salt)
☐ Others_____

3b. Considering only **IODISED SALT** added in COOKING please indicate the average amount of your individual portion used DAILY.

☐ Less than 1/4 teaspoon
☐1/4 teaspoon
☐ 1/2 teaspoon
☐ 1 teaspoon
☐ More than 1 teaspoon

4. Which of the following foods do you EXCLUDE from your usual diet? *(Tick all that apply)*

☐ Eggs
☐ Dairy
☐ Fish
☐ Seafood
☐ Chicken
☐ Beef
☐ Lamb
☐ Pork
☐ Other meat or animal products

I would like to ask you what you know about nutrition.

5. Which part of the body needs IODINE to produce hormones?

☐ Brain
☐ Heart
☐ Bone
☐ Thyroid gland
☐ Do not know

6. What health issues are associated with inadequate intake of IODINE? *(tick all that apply)*

☐ Neural Tube Defects
☐ Goiter
☐ Birth defects
☐ Weak bone and teeth
☐ Mental retardation
☐ Impaired physical development during childhood
☐ Blindness
☐ Do not know

7. Do you think there is currently a problem with IODINE deficiency in New Zealand?

☐ No
☐ Yes
☐ Do not know

8. From your knowledge, which of the following describes the current fortification in the manufacture of bread in New Zealand? *(Tick all that apply)*

☐ Producers must add iodised salt (mandatory fortification)
☐ Producers must add folic acid (mandatory fortification)
☐ Producers may add or may not add iodised salt (voluntary fortification)
☐ Producers may add or may not add folic acid (voluntary fortification)
☐ Do not know

9. Since 2010, which target population groups routinely are recommended to take an IODINE supplement? *(Tick all that apply)*

☐ Pregnant women
☐ Breastfeeding women
☐ All women of childbearing age
☐ All babies
☐ Do not know

10. From your knowledge, which of the following foods contribute good sources of IODINE?

	Good source	Poor source	Do not know
Milk	☐	☐	☐
Potatoes	☐	☐	☐
Fish	☐	☐	☐
Carrots	☐	☐	☐
Bread (excluding organic)	☐	☐	☐
Organic bread	☐	☐	☐
Beef	☐	☐	☐
Seaweed	☐	☐	☐
Lettuce	☐	☐	☐
Eggs	☐	☐	☐
Sea salt	☐	☐	☐
Rock salt	☐	☐	☐

I would like to ask about your supplement usage DURING REGNANCY.

11. Did you take any supplements?

☐ Yes **(go to Q13)**

☐ No

11a. If no, which if the following statements are the reasons for not taking any supplements?

(Tick all that apply)

☐ I was not advised to take them by doctor/nurse practitioner/mid-wife
☐ I could not tolerate them because of nausea (or any other side effects)
☐ I could not afford to purchase them
☐ I did not feel the need to as my health is good
☐ I believed that I could obtain adequate nutrients from my diet
☐ Others _____

12. Please complete the following table with details of any supplements you took.

Brand name (manufacture)	GPs or Midwife's prescription	Start date	Stop date	Frequency Times per week							Dosage each time
				7	6	5	4	3	2	1	
Eg.Blackmores Pregnancy and breastfeeding gold capsule	**Yes**	**12/04/2015**	**12/08/2015**					**√**			**2 tablets**

I would like to ask about your CURRENT supplement usage SINCE THE BABY WAS BORN 13.

Are you taking any supplements?

☐ Yes **(go to Q 14)**

☐ No

13a. If no, which if the following statements are the reasons for not taking any supplements?

(Tick all that apply)

☐ I was not advised to take them by my doctor/nurse practitioner/mid-wife

☐ I could not tolerate them because of nausea (or any other side effects)

☐ I could not afford to purchase them

☐ I did not feel the need to as my health is good

☐ I believed that I could obtain adequate nutrients from my overall diet

☐ Others _____

14. Please complete the following table with details of any supplements you are taking now.

Brand name (manufacture)	GPs or Midwife's prescription	Start date	Stop date	Frequency Times per week							Dosage each time
				7	6	5	4	3	2	1	
Eg. Blackmores Pregnancy and breastfeeding gold capsule	**Yes**	**12/04/2015**	**12/08/2015**					**√**			**2 tablets**

Note to the interviewer: If the participant is not able to remember details please ask them to send us an email later with details. (Email requested ☐ Email received☐)
I will now ask you some questions about your smoking habits SINCE YOUR BABY WAS BORN.

15. Have you ever smoked a total of more than 100 cigarettes in your entire life?

☐ No **(go to Q18)**

☐ Yes

16. Did you smoke regularly during **THIS** pregnancy?

☐ No **(go to Q17)**
☐ Yes

16a. If yes, on average, how many cigarettes did you smoke each day?

☐ Less than 1 per day
☐ 1-5 per day
☐ 6-10 per day
☐ 11-15 per day
☐ 16-20 per day
☐ 21-25 per day
☐ 26-30 per day
☐ 31 or more a day

17. Now, after the delivery of your baby, do you continue to smoke?

☐ No **(go to Q18)**

☐ Yes

17a.If yes, on average, how many cigarettes do you now smoke each day?

☐ Less than 1 per day
☐ 1-5 per day
☐ 6-10 per day
☐ 11-15 per day
☐ 16-20 per day
☐ 21-25 per day
☐ 26-30 per day
☐ 31 or more a day

18. Are you regularly exposed to secondhand smoke; for example, does someone smoke around you, or in your house or a house you visit often?

☐ No
☐ Yes

18a. If yes, how many hours per day are you exposed to the smoking of others?

_____Hours

I will now ask you some questions about your use of alcoholic drinks SINCE YOUR BABY WAS BORN.

19. Have you had a drink containing alcohol?

☐ No **(go to Q 20)**

☐ Yes

19a. If yes, how often have you had a drink containing alcohol?

☐ Monthly or less
☐ Up to 4 times a month
☐ Up to 3 times a week
☐ 4 or more times a week

Appendix K. MINI Study General Questionnaire – Six Months Old

Date of visit: _____ Day_____ Month_____ Year

Questionnaire – when your child is around 6 months old

1. Which of the following foods do you EXCLUDE from your usual diet? *(Tick all that apply)*
   - ☐ Eggs
   - ☐ Dairy
   - ☐ Fish
   - ☐ Seafood
   - ☐ Chicken
   - ☐ Beef
   - ☐ Lamb
   - ☐ Pork
   - ☐ Other meat or animal products
2. How often do you eat red meat?
   - ☐ Never
   - ☐ Less than once a week
   - ☐ 1-2 times per week
   - ☐ 3-4 times per week
   - ☐ 5-6 times per week
   - ☐ 7+ times per day
3. How often do you use a cast-iron fry pan, wok or pot when preparing your meals?
   - ☐ Never or less than once a month
   - ☐ 1-3 times per month
   - ☐ Once a week
   - ☐ 2-3 times per week
   - ☐ 4-6 times per week
   - ☐ Once a day
   - ☐ 2-3 times per day
   - ☐ 4+ times per day
4. Some foods and drinks have iron added to them (eg. Some breakfast cereals) when you are choosing foods and drinks, how often do you choose the product with added iron instead of the product without?
   - ☐ Whenever I can
   - ☐ Usually
   - ☐ Sometimes
   - ☐ Never
   - ☐ I do not know
   - ☐ I do not consider whether the product has iron added
5. On average, how many slices of bread/toast or bread rolls do you eat per day?
   - ☐ None, I do not eat bread or toast
   - ☐ Less than one per day
   - ☐ 1-2 per day
   - ☐ 3-4 per day

☐ 5-6 per day
☐ 7+ per day

6. Have you had any of the following symptoms since the baby was born? If you know symptoms are due to allergy and not infection, do not check. Please check the correct answer: **(**Carr Infection Symptom Checklist)

0=No symptoms 1=Mild symptoms 2=Moderate symptoms

	0	**1**	**2**	**3**	**4**
Cold sores					
Canker sores					
Nasal stuffiness					
Sore throat					
Sinus drainage					
Sinus pain/pressure					
Swollen glands					
Diarrhea					
Abdominal cramps					
Burning on urination					
Dark, smelly urine					
Earache					
Hoarseness					
Styes					
Runny nose					
Skin infections					
Acne					
Red eyes					
Vaginal itching					
Vaginal yeast infection					
Vaginal herpes					
Fever					
Fingernail infection					
Wheezing					
Cough					
Shingles					
Generalized flu-like					
Breast infection					
Episiotomy infection					
Dental abscess					

3=Strong symptoms 4=Severe symptoms

7. Apart from when you were in hospital immediately after having your baby, have you

	Never	Rarely	Occasionally	Often
Extreme tiredness/exhaustion				
More frequent coughs/colds/minor illness than usual				
Severe headache or migraines				
Lower back pain				
Upper back pain				
Painful perineum				
Pain from caesarean section wound				
constipation				
hemorrhoids				
Breast problems				
Pelvic pain				

experienced any of the following?

8. Overall, how would you describe your physical health at the moment?
   ☐ Excellent
   ☐ Very good
   ☐ Good
   ☐ Fair
   ☐ Poor

9. Do you take or have taken cod liver oil, vitamins or other dietary supplements since the previous questionnaire?
   ☐ No

   ☐ Yes

   9a. If yes, which product, when did you take it and how often (one line for each product)

Brand name (manufacture)	GPs or Midwife's prescription	Start date	Stop date	Frequency Times per week							Dosage each time
				7	6	5	4	3	2	1	
Eg. Blackmores Pregnancy and breastfeeding gold capsule	**Yes**	**12/04/2015**	**12/08/2015**					**√**			**2 tablets**

10. How often are you physically active at present?

	Never	1-3 times a month	Once a week	Twice a week	Three times or more a week
walking					
brisk walking					
running/jogging/orienteering					
cycling					
training studio/weight training					
special gymnastics/aerobics for women					
aerobics/gymnastics/dancing without running and jumping					
aerobics/gymnastics/dancing with running and jumping					
dancing (swing, rock, folk)					
skiing					
ball sport					
swimming					
riding					
other					

11. Have you ever suffered from low iron stores, iron deficiency or iron deficiency anemia?

☐ No

Diagnosis date	Diagnosed by	Any further details

☐ Yes

Type of treatment	Duration	Any further details

12. Have you ever been treated for iron deficiency or iron deficiency anemia?

13. Have you had a severe blood loss during delivering your baby?

☐ No

☐ Yes

14. Do you have or have you had any medical condition which has resulted in blood loss?

If yes, please describe it and give approximate date_____

15. Have you had a blood donation during the last 6 months?
    ☐ No
    ☐ Yes
    15a. If yes, how many times did you donate your blood? _____.
16. Have you had a blood transfusion during the last 12 months?
    ☐ No
    ☐ Yes
    16a. If yes, do you know why you received the blood transfusion _____
17. Have you noticed any form of blood loss during the last 6 months?
    ☐ Not at all
    ☐ Yes, in stools
    ☐ Yes, in urine
    ☐ Yes, when brushing my teeth
    ☐ Yes, from a wound

18. Are you pregnant at the moment?
    ☐ No
    ☐ Yes
    18a. If yes, how many weeks have you been pregnant? _____.

19. Has your period started again?
    ☐ No
    ☐ Yes
    19a.If yes, please give an approximate date _____.

About your child

20. How old was your baby when you stopped breastfeeding?
    ☐ _____months_____ weeks_____ days
    ☐ I continue to breastfeed (**go to Q 22**)
21. Tick the reason (s) you chose not to breastfeed or stop breastfeeding your baby *(Tick all that apply)*
    ☐ Have breastfed long enough
    ☐ Baby had trouble latching on
    ☐ Did not have enough milk
    ☐ Breastmilk alone did not seem to satisfy my baby
    ☐ Painful breast
    ☐ Baby not gaining enough weight
    ☐ Baby lost interest/self-weaned
    ☐ I wanted/needed someone else to feed the baby
    ☐ Went back to work and expressing breastmilk was not convenient/possible
    ☐ New pregnancy
    ☐ Baby was old enough that the difference between breastmilk and formula was minimal
    ☐ Others _____
22. Including times of weaning, what is the total time your baby was breastfed?
    ☐ Weeks
    ☐ Months
    ☐ Less than one week
23. At what age was your baby first given infant formula regularly?
    _____Weeks _____ Months
24. At what age was your baby first given solid food regularly?
    _____Weeks _____ Months

	Never /seldom	1-3 times/week	4-6 times/week	At least once a day
Breastmilk				
Pasteurised Cow's milk				
Pasteurised Goat's milk				
Evaporated milk				
Organic milk products (milk, yoghurt)				
Standard infant formula/formula milk				
Standard formula milk with Omega-3				
Hypoallergenic formula				
Water				
Gripe water				
Sugar water				
Cold flavored milk drinks				
Fizzy (carbonated) drinks				
Squash, artificially sweetened				
Baby cordial, artificially sweetened				
Fruit juice				
Herbal drinks				
Tea/Coffee				
Others _____				

25. How often do you give your child the following to drink at the moment?

26. Do you give your child cod liver oil, vitamins, iron or any other dietary supplements?

☐ No

☐ Yes

26a. if yes, specify

Name of product	How many teaspoons/time	How often	How old was your child at first time consumption (months)

27. Has your child had the following health problems?

	Has your child had health problems		Number of times	Did you visit a doctor/clinic		Has your child been admitted to hospital for this	
Common cold	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
Throat infection	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
Ear infection	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
Bronchitis pneumonia	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
Diarrhea	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
wheezing	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
vomiting	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
High temperature	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
Urinary tract infection	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
Colic	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
Nappy rash	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No
An accident	☐ Yes	☐ No		☐ Yes	☐ No	☐ Yes	☐ No

28. How would you describe the health of your baby now:

    ☐ Very healthy

    ☐ Healthy, but a few minor problems

    ☐ Sometimes quite ill

    ☐ Almost always unwell

29. Since your last visit, have you changed your smoking habits?

    ☐ No

    ☐ Yes, specify _____.

30. Since your last visit, have you changed your drinking habits?

    ☐ No

    ☐ Yes, specify _____.

Thanks for completing this questionnaire

Appendix L. MINI Study Maternal and Infant Data Collection Sheets

Date of visit: _____ Day_____ Month_____ Year

Maternal Data		
DOB:	**Age:**	**Weeks after giving birth:**

Prior to Pregnancy: Estimated usual body weight _____ kg

Pregnancy: Blood hemoglobin _____

Any complications:

Maternal delivery Information	
Date of delivery:	_____ Day _____ Month
Time of delivery:	_____
Method of delivery:	_____
Usage of iodine containing sanitizer:	_____
Any severe blood loss	_____
Pain relief used	_____
Baby's summary	
Gestation:	_____ weeks
Gender:	_____
Apgar score at 1 minute	_____
Apgar score at 5 minutes	_____
Birth weight: _____ kg	Head circumference: _____ cm
Body length:_____ cm	
Guthrie test :	_____(positive or negative)

Have you given birth to any other children?

Yes=1/ No=0

Number	**Gender**	**Age**	**Method delivery**	**Method of feeding** *(probe duration of bf)*

Anthropometric measurement - Visit One

Body weight _____kg Average _____ kg

_____ kg

_____ kg

Body height _____ cm Average _____ cm

_____ cm

_____ cm

BMI _____

BIA results

BodPod Results

Anthropometric measurement - Visit Two

Body weight _____ kg Average _____ kg

_____ kg

_____ kg

Body height _____ cm Average _____ cm

_____ cm

_____ cm

BMI _____

BIA results

BodPod Results

Anthropometric measurement - Visit Three

Body weight _____ kg Average _____ kg

_____ kg

_____ kg

Body height _____ cm Average _____ cm

_____ cm

_____ cm

BMI _____

BIA results

BodPod Results

Infant Data

Infant Anthropometric measurement – Visit One

Body weight: _____ kg

_____ kg

_____ kg Average _____ kg

Body length: _____ cm

_____ cm

_____ cm Average _____ cm

Head circumference: _____ cm

_____ cm

_____ cm Average _____ cm

Infant Anthropometric measurement – Visit Two

Body weight: _____ kg

_____ kg

_____ kg Average _____ kg

Body length: _____ cm

_____ cm

_____ cm Average _____ cm

Head circumference: _____ cm

_____ cm

_____ cm Average _____ cm

Infant Anthropometric measurement – Visit Three

Body weight: _____ kg

_____ kg

_____ kg Average _____ kg

Body length: _____ cm

_____ cm

_____ cm Average _____ cm

Head circumference: _____cm

_____cm

_____cm Average _____ cm

First week	
Body weight: _____ kg	
2-4 weeks	
Body weight: _____ kg	Head circumference: _____cm
4-6 weeks	
Body weight: _____ kg	Head circumference_____ cm
Body length: _____ cm	
8-10 weeks	
Body weight: _____ kg	Head circumference_____ cm
Body length: _____ cm	
3-4 months	
Body weight: _____ kg	Development
5-7 months	
Body weight: _____ kg	Development
9-12 months	
Body weight: _____ kg	Body length: _____ cm
Development	

(Notes taken from the Well Child Book)

	Beer, cider and RTDs	Wine	Spirits
			
	330ml glass	100ml glass	30 ml short
How many			

19b. How many units do you have on **A TYPICAL DAY** when you are drinking alcohol?

About your child

20. What did you give your child to drink routinely during <u>the FIRST WEEK</u> of life? (*Tick all that apply)*

☐ Breastmilk
☐ Water
☐ Sugar water
☐ Infant formula/milk formula
☐ Pasteurized/bottled cow's milk
☐ Soy formula
☐ Hypoallergenic formula
☐ Fruit juices/water down juice/cordial
☐ Herbal drinks
☐ Tea/coffee
☐ Fizzy drinks
☐ Other, specify: _____

21. Do you add sugar to your child's drink?

☐ No
☐ Yes

22. Since the baby was born, have you been breastfeeding your baby, including feeding expressed milk?

☐ No **(go to Q 26)**
☐ Yes

22a. If yes, which of the choices below most describes your breastfeeding pattern?

☐ Exclusive (100%) breastfeeding
☐ Medium (50-80%) breastfeeding
☐ Partial (less than 50%) breastfeeding

☐ Artificial (less than 10%) breastfeeding

23. On average, how many times a day (during the 24hour period) do you currently breastfeed our baby?

    _____ Times

24. On average, how long does it take for each breastfeed?

    _____ minutes _____ hours

25. How old was your baby when you stopped breastfeeding?

    ☐ _____months_____ weeks_____ days

    ☐ I continue to breastfeed (**go to Q 27**)

26. Tick the reason (s) you chose not to breastfeed, or to stop breastfeeding your baby:

    (Tick all that apply)

    ☐ Have breastfed long enough
    ☐ Baby had trouble latching on
    ☐ Did not have enough milk
    ☐ Breastmilk alone did not seem to satisfy my baby
    ☐ Painful breast
    ☐ Baby not gaining enough weight
    ☐ Baby lost interest/self-weaned
    ☐ I wanted/needed someone else to feed the baby
    ☐ Went back to work and expressing breastmilk was not convenient/possible
    ☐ New pregnancy
    ☐ Baby was old enough that the difference between breastmilk and formula was minimal
    ☐ Other, specify: _____

27. How often do you give your child the following to drink at the moment?

Type of drinks	Never (seldom)	1-3 times/ week	4-6 times/ week	More than once a day
Breastmilk	☐	☐	☐	☐
Pasteurized/bottled cow's milk	☐	☐	☐	☐
Regular Infant formula/milk formula	☐	☐	☐	☐
Hypoallergenic formula	☐	☐	☐	☐
Soy formula	☐	☐	☐	☐
Water	☐	☐	☐	☐
Gripe water	☐	☐	☐	☐
Sugar water	☐	☐	☐	☐
Fruit juices/water down juice/cordial	☐	☐	☐	☐
Herbal drinks	☐	☐	☐	☐
Tea/coffee	☐	☐	☐	☐
Other	☐	☐	☐	☐

Now I am going to ask a few questions about you and your current living situation. The answers to these questions help us to check that we have selected a representative sample of New Zealanders to participate in this survey.

28. Which country were you born in?

☐ New Zealand
☐ Australia
☐ England
☐ Scotland
☐ China (People's Republic of China)
☐ India
☐ South Africa
☐ Samoa
☐ Cook Islands
☐ Other (specify) _____

29. What is your first language? _____.

30. Which ethnic group or groups do you identify with? *(tick all that apply)*

☐ NZ European
☐ Maori
☐ Samoan
☐ Cook Island Maori
☐ Tongan
☐ Niuean
☐ Chinese
☐ Indian
☐ Other (specify) _____

31. If from overseas, in what year did you arrive to live in New Zealand? _____Year
32. What is your date of birth?

_____ Year _____ Month (range Jan-Dec) _____ Day (range 1-31)

33. How old are you?

☐ <20
☐ 20-24
☐ 25-29
☐ 30-34
☐ 35-39
☐ 40-45
☐ >45

34. What is your highest completed qualification?

☐ School
☐ Trade Certificate
☐ Diploma/Bachelor/Tertiary education
☐ Postgraduate qualification
☐ Other (specify) _____

35. Who do you live with? *(Tick all that apply)*

☐ Husband/partner
☐ Other Children (not including new baby)
☐ My siblings
☐ My parents
☐ Parents in laws
☐ Other relatives
☐ On my own (with my baby)
☐ Others, specify _____

36. What is the total income of your household from all sources, before tax or any other deductions, in the last 12 months?

☐ Loss
☐ Zero income
☐ $1 – $5,000
☐ $5,001 – $10,000
☐ $10,001 – $15,000
☐ $15,001 – $20,000
☐ $20,001 – $25,000
☐ $25,001 – $30,000
☐ $30,001 – $35,000
☐ $35,001 – $40,000
☐ $40,001 – $50,000
☐ $50,001 – $60,000
☐ $60,001 – $70,000
☐ $70,001 – $100,000
☐ $100,001 – $150,000
☐ $150,001 or more

Thanks for completing this questionnaire

Appendix M. MINI Study Instructions for infant 3-Day Diet Diary

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MINI Study - Mother and Infant Nutrition Investigation

Date of visit: _____ Day_____ Month_____ Year

PLEASE READ THROUGH THESE PAGES BEFORE STARTING YOUR DIARY

We would like you to record in this diary everything your child eats and drinks, at meal times and in between, day and night for **3 DAYS**. Please include all food and drink consumed at home and outside the home.

When to fill in the diary

Please record the food as you go, **does not list from memory** at the end of the day. Use written notes on a notepad if you forget to take your diary with you. Each diary day covers a 24 hour period, so please include any food or drinks that your child may have had through the night. Remember to include foods and drinks between meals (snacks) including water.

Home-made dishes

Please record the name of the recipe, ingredients with amounts (including water and other fluids) for the whole recipe, the cooking method; record how much your child individually has eaten.

Take-away and eating out

If your child has eaten take-away or made up dishes not prepared at home such as at a cafe or friend's house, please record as much detail about the ingredients as you can e.g. spaghetti with mince, onion and tomato sauce.

Brand name

Please note the brand name (if known). Most packed foods will list a brand name, e.g. Watties, Heinz, Karicare. Labels/Wrappers Labels are an important source of information for us. It helps us a great deal if you enclose, in the plastic bag provided, labels from already prepared meals, labels from foods of lesser known brands.

Portion sizes

We would like to know the quantity or portion size you served your child and the quantity of food or drink leftover. Please record in the quantity served and quantity leftover columns. If there are no leftovers, please enter 'NONE' in the quantity leftover column. For foods, quantity can be described using:

- household measure e.g. one level teaspoon of sugar, two thick slices of bread, 4 heaped tbsp of peas, ¼ pint of gravy. Be careful when describing amounts in spoons that you are referring to the correct spoon size. Compare the spoons you use with the photos in **pg.25.**
- weights from labels - use the weight marked on canned or packet foods, e.g. quarter of a 420g tin of baked beans, one 60g pot of yoghurt.
- number of items, e.g. 1 baby rice cake, 2 fish fingers, 2 pieces of chicken nuggets, 1 regular size jam filled doughnut, 10 peas.
- fruit - indicate whether the piece of fruit is small, medium or large and portion size of the fruit eaten e.g. 1 segment of a large orange, ½ a medium banana.

For drinks, quantity can be described using:

- the volume (e.g. 150ml) or size of cup (e.g. large).
- volumes from labels (e.g. 200ml Readymade milk).

For breast milk, quantity can be described as:

The duration in minutes or the volume if the milk has been expressed. Where breast milk has been expressed please record 'E' at the side of the volume.

At the end of each recording day, you will be prompted to tell us Was it a typical day?

After each day of recording you will be prompted to tell us if this was a typical day and if there were any reasons why your child consumed more or less than usual.

Did you take any supplements?

At the end of each recording day there is a section for providing information about any supplements your child took. Brand name, full name of supplement, strength and the amount taken should be recorded.

See the next page for the pictures of variety of spoons.

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Thank you for your time- we really appreciate it!

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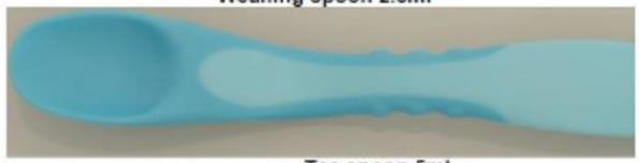
Weaning spoon 2.5ml

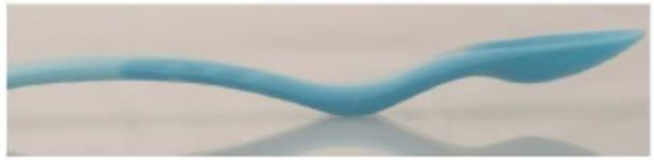


Tea spoon 5ml

Dessert spoon 10ml

Table spoon 15ml

Weaning spoon 2.5mls



Tea spoon 5mls

Dessert spoon 10mls

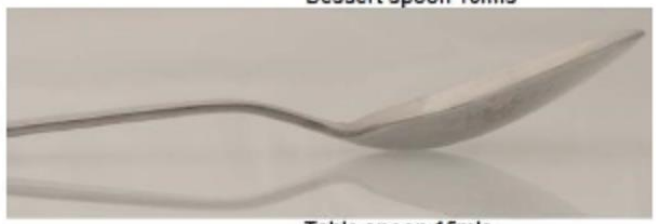


Table spoon 15mls

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Code: _____

MINI Study - Mother and Infant Nutrition Investigation

Date of recording: _____ Day_____ Month_____ Year

Day 1

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Code: _____

DAY 1		**Date: _____Day _____Month_____Year**			
Time	**Where**	**Food/drink description & preparation**	**Brand name**	**Quantity served**	**Quantity leftover** If no leftovers enter '**NONE**'
6am to 9am					
9am to 12noon					

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Code: _____

Time	Where	Food/drink description & preparation	Brand name	Quantity served	Quantity leftover If no leftovers enter 'NONE'
12noon to 2pm					
2pm to 5pm					

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Code: _____

Time	Where	Food/drink description & preparation	Brand name	Quantity served	Quantity leftover If no leftovers enter 'NONE'
5pm to 8pm					
8pm to 10pm					
10pm to 6am					

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Code: _____

Please record the details of any recipes or (if not already described) ingredients of made up dishes or take-away dishes

Write in recipes or ingredients of made-up dishes or take-away dishes			
Name of Dish:		Serves:	
Ingredients	Amount	Ingredients	Amount
Brief description of cooking method:			

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Code: _____

1. Was the amount of **food** that your child had today about what you usually have, less than usual, or more than usual?

   ☐ Yes, usual

   ☐ No, **less** than usual.

Please tell us why your child had less than usual

   ☐ No, **more** than usual

Please tell us why your child had more than usual

2. Was the amount your child had to **drink** today, including water, tea, and soft drinks (and alcohol), about what he/she usually has, less than usual, or more than usual?

   ☐ Yes, usual

   ☐ No, **less** than usual

Please tell us why your child had less than usual

   ☐ No, **more** than usual

Please tell us why your child had more than usual

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Code: _____

3. Did your child finish all the food and drink that you recorded in the diary today?

   ☐ Yes ☐ No

   If no, please **go back to the diary and make a note of any leftovers**

4. Did your child take any **vitamins, minerals or other food supplements** today?

   ☐ Yes ☐ No

   If yes, **please describe the supplements your child took below**

Brand	Name (in full) including strength	Number of pills, capsules, teaspoons
Example Thomson's	Vitamin D	1 tablet

Appendix N. Supplementary Methods

Table 5.1. Median iodine concentrations (µg/100g) in breads used in Foodworks analysis.

Bread or Bread Product Category	N	Median Iodine (µg/100g bread, 95% CI)
Mixed Grain	45	40.0 (36.6, 44.8)
White	51	41.3 (37.4, 45.3)
Wholemeal	48	38.8 (35.1, 44.9)
Bread rolls, mixed grain	6	41.1 (34.2, 86.1)
Pita breads	24	27.7 (25.7, 31)

Adapted from (MPI, 2014)

Table 5.2. Estimated Breastmilk Volumes.

Infant Age	Daily Volume
<6 months	780mL/day
6-12 months	600ml/day
Per feed	*90mL

*If the total volume of measured expressed breastmilk, formula or other milks exceeds the daily volume listed for infant, 90mL per feed is applied to each feed occasion listed instead (Briefel et al., 2010).

Appendix O. Supplementary Results

Table 5.3. Median intake iodine, selenium, iron and zinc food, infant formula, and breastmilk.

		Median (Q1, Q2)
Iodine (µg/day)	**Total Intake**	**62 (30, 98)**
	[a] Food	4 (1, 13)
	[b] Infant Formula	50 (19, 84)
	[d] Breastmilk	37 (22, 64)
Selenium (µg/day)	**Total Intake**	**12 (9, 16)**
	[a] Food	3 (1, 7)
	[b] Infant Formula	7 (3, 12)
	[d] Breastmilk	7 (6, 9)
Zinc (mg/day)	**Total Intake**	**3 (2, 4)**
	[a] Food	1 (0.3, 2)
	[b] Infant Formula	2 (1, 4)
	[c] Breastmilk	2 (1.5, 2)
Iron (mg/day)	**Total Intake**	**2 (1, 5)**
	[a] Food	1 (1, 3)
	[b] Infant Formula	4 (2, 6)
	[c] Breastmilk	0.4 (0.3, 0.4)

[a] Median intake of each micronutrient from food portion of the diet was calculated from Foodworks average daily intake (N=51)

[b] Median each micronutrient from infant formula portion of the diet was calculated from Foodworks average daily intake (N=16)

[c] Median intake of Iron and Zinc from breastmilk portion of the diet calculated from Foodworks average daily intake (N=46)

[d] Median intake of iodine and selenium calculated from BMIC and BMSC and estimated daily breastmilk intake (N=66).

Table 5.4. Total daily dietary Intake of infants based on 3DDD analysis

	Median (Q1, Q3)
Energy (kj)	2608 (2149, 3070)
[a]N (%) below calculated energy requirements	26 (51%)
Protein (g)	16 (10, 21)
[a]N (%) below calculated protein requirements	14 (28%)
Dietary Fat (g)	29 (27, 36)
[a]N % below AI for age	28 (55%)
Saturated Fat (g)	13 (11, 16)
Carbohydrate (g)	63 (54, 85)
[a]N % below AI for age	31 (63%)
Sugar (g)	51 (46, 58)
Sodium (mg)	194 (116, 362)
[a]N % below AI for age	18 (35%)

[a] National Health and Medical Research Council and New Zealand Ministry of Health, Nutrient Reference Values for Australia and New Zealand (2006).

Table 5.5. Spearman's Correlation Matrix													
		Infant Urinary Iodine Concentration (µg/L)	Infant Urinary Selenium Concentration (µg/L)	Total Iodine intake (µg/day)	Total Selenium intake (µg/day)	Breastmilk Iodine Concentration (µg/L)	Breastmilk Selenium Concentration (µg/L)	Infant Weight (kg)	Infant Length (cm)	Infant Head circumference (cm)	Infant Age (months)	Total Zinc Intake (mg/day)	Total Iron Intake (mg/day)
Infant Urinary Iodine Concentration (µg/L)	R												
	p												
	n												
Infant Urinary Selenium Concentration (µg/L)	R	.721**											
	p	.000											
	n	41											
Total Iodine intake (µg/day)	R	.780**	.543**										
	p	.000	.003										
	n	28	28										
Total Selenium intake (µg/day)	R	NS	.375*	.428**									
	p		.049	.002									
	n		28	51									
Breastmilk Iodine Concentration (µg/L)	R	.603**	.281	.758**	NS								
	p	.000	.083	.000									
	n	39	39	47									
Breastmilk Selenium Concentration (µg/L)	R	.320*	.426**	.303*	.346*	.263*							
	p	.047	.007	.038	.017	.026							
	N	39	39	47	47	72							
Infant Weight (kg)	R	-.354*	NS	NS	NS	NS	NS						
	p	.025											
	n	40											
Infant Length (cm)	R	NS	NS	NS	NS	NS	NS	.610**					
	p							.000					
	n							79					

Infant Head Circumference (cm)	R	NS	NS	NS	NS	NS	NS	.567**	.413**				
	p							.000	.000				
	n							79	79				
Infant Age (months)	R	NS	NS	NS	.293*	NS	NS	NS	NS	.381**			
	p				.037					.007			
	n				51					49			
Total Zinc Intake (mg/day)	R	NS	NS	NS	.738**	NS	NS	NS	NS	NS	NS		
	p				.000								
	n				51								
Total Iron Intake (mg/day)	R	NS	.502**	.391**	.664**	NS	NS	NS	NS	NS	.296*	.867**	
	p		.006	.005	.000						.035	.000	
	n		28	51	51						51	51	

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).
R. Correlation Coefficient
p. Significance level
n. Number of subjects compared