Iodine and mid-life women living in Auckland,

New Zealand who avoid bread.

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

Master of Science

In

Human Nutrition

at Massey University, Albany, Auckland,

New Zealand

Jacqueline Finlayson

2019

ABSTRACT

Aim: To investigate if avoidance of iodine fortified bread products by mid-life women results in low iodine status following mandatory fortification of bread with iodised salt in New Zealand in 2009.

Method: This cross-sectional study actively recruited women whose consumption of iodine fortified commercially baked bread was less than one slice per day. Assessment of iodine intake and status was determined via food frequency questionnaire (FFQ), three-day diet diary (3DDD) and 24-hour urine collection. Urinary iodine concentration (UIC) was determined and daily urinary iodine excretion and daily iodine intake was assessed.

Results: Forty-six mid-life women living in Auckland were recruited for assessment of dietary intake of iodine, women were aged between 40-63 years and did not have diagnosed thyroid disease. The median urinary iodine concentration was 49 (35, 78) µg/l and indicates deficiency (Zimmermann, 2011). The median urinary iodine excretion was 108 (74, 154) µg/day and based on these results, the estimated median iodine intake of 120 (82, 171) µg/day was determined. This intake is below the recommended dietary intake (RDI) of 150 µg/day. Further, 91% of participants' intake was below the estimated average requirement (EAR) of 100µg/day.

Conclusion: From this small sample, the study showed that mid-life women living in NZ who avoid bread are at risk of inadequate dietary iodine intake. This group is unable to benefit from the mandatory fortification of bread with iodised salt. This highlights the importance of continued monitoring of the iodine fortification programme within New Zealand. Further research should investigate both thyroid function and dietary habits of low bread consumers in New Zealand in a larger sample. Also an attempt to raise awareness of the best sources of iodine in the NZ diet, to improve both dietary intake and status of iodine amongst at-risk groups such as this is highly recommended.

ACKNOWLEDGEMENT

There are many people I would like to thank for their contribution to this study. This study would not have been possible without the patience and ongoing support of my trials manager, Owen Mudridge who patiently assisted me with numerous queries, from excel, survey monkey to handling of urine samples, to the interview process and data collection itself as the study's principal phlebotomist.

The collaborative support of both my supervisors; Dr Pam von Hurst; Associate Professor of the School of Exercise, Sport and Human Nutrition, Massey University and Dr Louise Brough; Senior lecturer of Massey University Institute of Food, Science and Technology, who made this research possible. Their guidance and patient support has been critical to the completion of this thesis and kept me motivated when challenges arose. Their confidence in my ability to fulfil this task was paramount to my success. The advice and assistance from all of these people was so greatly appreciated.

For the women who took part in this study I thank you wholeheartedly for without you this research would not have been possible. The generosity of both and time and task completion was unwavering. The enthusiasm for knowledge of the subject material was uplifting and inspiring.

Appreciation must be given also to the many persons who have researched this fascinating topic of iodine nutrition here in New Zealand and worldwide, without this prior knowledge there would have been no foundation on which to base my research. Locally in particular thanks to Sheila Skeaff, Christine Thomson, Louise Brough, Zheng Feei Ma, and Barbara M Thomson.

Thanks also to my family for their patience and support over the course of this research, for believing in me and encouraging me to reach this goal.

I dedicate this research to my mother, Rae Josephine Small who died while I was doing this research; a highly intelligent woman who if afforded the opportunity would have enjoyed and excelled in tertiary study.

"The highest result of education is tolerance" - Helen Keller

CONTRIBUTIONS

The principal researcher was Jacqui Finlayson, assisted by trials manager & phlebotomist, Owen Mudridge, and supervisors, Dr Pam von Hurst & Dr Louise Brough.

Research topic & study design	Jacqui Finlayson, Dr Louise Brough, Dr Pam von Hurst
Recruitment & Screening process • posters, emails, social media • data recording • data management • screening • appointment scheduling	Jacqui Finlayson
Interview • blood draw • food frequency survey • anthropometric measurements • instructions for 24hr urine collection • instructions for diet diary	Jacqui Finlayson Phlebotomist: Owen Mudridge
Handling of samples • blood samples • urine samples • transport of urine samples to Hamilton	Jacqui Finlayson Owen Mudridge
Follow up phone calls • sample return • missing information • queries	Jacqui Finlayson
Data collation, statistical analysis & interpretation	Jacqui Finlayson
Thesis writing	Jacqui Finlayson

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

EAR Estimated average requirement

FAO Food and Agriculture Organisation

FFQ Food frequency questionnaire

IDD Iodine deficiency disorder

ICCIDD International Council for Control of Iodine Deficiency Disorders

ID Iodine deficiency

IDD Iodine deficiency disorder

IQ Intelligence quotient

MPI Ministry of Primary Industries

MOH Ministry of Health

NZ New Zealand

NHANES National Health and Nutrition Examination Survey

NRV Nutrient Reference Values

NZTDS New Zealand Total Diet Study

RDI Recommended dietary intake

SAC School aged children

SCTD Subclinical thyroid disease

TDS Total diet study

TBG Thyroid binding globulin

TgAb Thyroglobulin antibodies

TPO Thyroid peroxidase

TSH Thyroid stimulating hormone

T3 Triiodothyronine

T4 Thyroxine

µg Microgram

UI Urinary iodine

UIC Urinary iodine concentration

UIE Urinary iodine excretion

UNICEF United Nations International Children Emergency Fund

WHO World Health Organization

3DDD Three-day diet diary

LIST OF APPENDICES

ETHICS

Ethics approval for this study (application 16/52) was obtained in 2016 from the Massey Human Ethics Committee (MUHEC).

1 Introduction

1.1 Background

Iodine is integral to the production of thyroid hormone which is essential to mammalian life. Metabolism, growth and cognitive function are central roles of thyroid hormone which is produced by the thyroid gland and requires iodine for its synthesis. Iodine deficiency (ID) that is severe is the greatest preventable cause of mental retardation in the world. Chronic iodine deficiency has adverse health outcomes for all ages (Zimmermann & Andersson, 2012).

New Zealand has a long history of inadequate iodine intake (Skeaff, Thomson, & Gibson, 2003). Iodine in the food supply is largely reliant on the concentration of iodine in the soil and in NZ this has typically been found to be low therefore crops and meat raised upon these soils also have low levels. This problem is not unique to NZ as iodine deficiency (ID) is a global problem (Pearce, Andersson, & Zimmermann, 2013; Thomson, 2003). From the late 1800s to the early 1900s ID was significant in NZ to the extent that endemic goitre and very low urinary iodine concentrations prevailed. The iodisation of salt, introduced in 1924 over time reduced ID and almost eradicated endemic goitre (Mann & Aitken, 2003). The use of iodophors (iodine based cleansers) by the dairy industry also helped to raise iodine intake among the NZ population and in the 1970s NZ enjoyed a period of low goitre rates. However, changes made by the dairy industry, ceasing the use of iodine based cleansers (iodophors), alongside changes in dietary patterns and other factors, saw the re-emergence of ID in the 1990s.

In response to this, in 2009, food regulations made it mandatory for all commercially made bread (except organic) to be fortified with iodised salt. This intervention was with the intent of raising iodine intake for the majority of the NZ population to adequate levels (Food Standards Australia and New Zealand, 2009). Recently, estimates from the latest NZ total diet study (TDS) has suggested the NZ diet may now be providing an adequate intake of iodine for NZ adults, as mean intakes were predicted to meet the estimated average requirement (EAR) for dietary iodine (Ministry of Primary Industries, 2016). However, central to the success of this goal to reduce ID among the NZ population is the assumption that all cohorts of the population habitually consume bread. Mid-life women are particularly vulnerable to thyroid dysfunction and ID is the leading preventable cause of thyroid disorders (Andersson, de Benoist, & Rogers, 2010; del Ghianda, Tonacchera, & Vitti, 2014). Mid-life women who do not consume bread fortified with iodised salt cannot benefit from this intervention therefore they represent an emerging at risk group for ID.

1.2 Significance of the Study

Currently there have been no studies evaluating the iodine status of mid-life women who avoid bread in New Zealand (NZ). The introduction of the mandatory fortification of commercially produced bread with iodised salt in 2009 was with the intent of addressing the re-occurrence of iodine deficiency among the NZ population (Thomson, Woodruffe, Colls, Joseph, & Doyle, 2001). However, subsets of the population who choose to avoid eating commercially made bread for a variety of reasons are unable to benefit from this public health intervention. One such group identified are mid-life women who may also be unaware of the consequences of poor iodine intake (Brough et al., 2017). Iodine is integral to the optimum function of the thyroid gland. Women at mid-life and older are also more vulnerable to thyroid dysfunction and increased risk of thyroid disease (del Ghianda et al., 2014).

Research to date has focused mainly on pregnant women and children, appropriately so as dietary requirements are higher and more immediate and severe consequences can result from insufficient intake in pregnancy, and early childhood (Gordon et al., 2009; Jones et al., 2016). However, there is a paucity of research relating to mid-life women and iodine in NZ. Studies that have investigated iodine nutrition involving mid-life women have often been as part of a larger group. Also none of these studies have specifically focused on participants who do not consume bread as part of their habitual diet (Vannoort & Thomson, 2009). Women at mid-life may also lack knowledge of the role of iodine and the importance to health and disease prevention (Charlton, Yeatman, & Houweling, 2010). The impact of iodine deficiency, even mild deficiency can have far reaching effects for the mid-life women including poorer outcomes for both the cardiovascular system and bone health (Rodondi, den Elzen, & Bauer, 2010). This Auckland study, as well as adding to the knowledge relating to iodine intake within NZ, will determine if avoiding iodine fortified bread results in an inadequate status among mid-life women subsequent to the introduction of mandatory fortification in 2009. It will also aim to identify food sources of iodine in the diet of mid-life women who avoid iodine fortified bread.

1.3 Aim & Objectives

1.3.1 Aim:

To investigate if the avoidance of iodine fortified bread products in the diet of mid-life women living in Auckland results in low iodine status following mandatory fortification of bread with iodised salt in 2009.

1.3.2 Objectives:

i) To assess the iodine status in a sample of mid-life women who avoid iodine fortified bread products subsequent to the mandatory fortification of bread with iodised salt in NZ in 2009, via iodine concentration assessment from 24-hour urine samples;

ii) To evaluate the intake of dietary iodine of mid-life women and to determine major food contributors to iodine intake;

iii) To determine if avoidance of iodine fortified bread products by mid-life women results in inadequate iodine status and/or inadequate dietary intake.

1.4 Overview of the Thesis

Chapter 1 is the introduction to the study providing a brief background along with the aim and objectives. Chapter 2 of this thesis examines the literature pertaining to iodine nutrition as it relates to women and the role of iodine and thyroid hormones are discussed. Methods of assessment for establishing iodine status are discussed in order to determine the suitability of the methods used in this study. Epidemiological data for the global and NZ issue of iodine deficiency are examined and factors contributing to the re-emergence of iodine deficiency in NZ are examined as well as past and present efforts to reduce iodine deficiency amongst the NZ population. The potential health consequences for iodine deficient mid-life women are explored, as well as research that is available relating to iodine and mid-life women. Finally, perceptions and knowledge of iodine amongst women in general is explored to highlight the broader spread of issues that hinder iodine nutrition among mid-life women. Chapter 3 describes the research study including materials and methods, the procedures involved and data handling including statistical analysis. Chapter 4 states the results of the study and in chapter 5 these are discussed. The discussion in this chapter is mostly relevant to the aims and objectives of the study but also addresses the limitations of the study. Finally, the conclusion is presented in chapter 6, as are the recommendations for future research and suggestions for improving iodine status, intake and knowledge of the NZ population.

2 Literature Review

2.1 Introduction

Iodine deficiency (ID) is a worldwide public health issue that affects many countries including New Zealand (WHO/UNICEF/ICCIDD., 2008). Iodine deficiency and iodine deficiency goitre were very common during the late 1800s and early 1900s in NZ up until 1924, when salt iodisation was introduced. However, the concentration of iodine that was used was too low and did not adequately address endemic goitre that was present at the time. It was for this reason that the level of iodine was subsequently increased in 1939. By the 1950s the iodisation of salt was deemed a successful intervention with goitre all but eradicated within the NZ population (Mann & Aitken, 2003). In the 1960s, the population's iodine status was improved further due to changes in practice by the dairy industry who commenced the use of iodine based cleansers known as iodophors. This resulted in an increase in the iodine content of milk and dairy products (Sutcliffe, 1990). However by the 1980s the dairy industry ceased using iodine based cleansers and this resulted in the reduced iodine content of dairy products in NZ (Mann & Aitken, 2003).

Surveys in both the 1960s and the early 1980s within NZ showed adequate iodine intake among the participants studied. Median urinary iodine excretion (UIE) was the method of assessment for iodine concentration and levels were found to be as high as 202µg/day in 1965 (North & Fraser, 1966) and 305µg/day in 1984 (Simpson, Thaler, Paulin, Phelan, & Cooper, 1984). This situation of adequacy amongst the NZ people continued throughout the 1980s (Mann & Aitken, 2003) however by the 1990s, iodine deficiency was found to re-emerge with median iodine intakes of iodine (based on urinary iodine excretion) of 65 to 95µg/day recorded in the adults surveyed (Thomson et al., 1997; Thomson, Woodruffe, et al., 2001). During the last two decades more studies confirmed the re-emergence of iodine deficiency in NZ with mild to moderate iodine deficiency observed throughout the NZ population (Brough et al., 2017; Skeaff et al., 2003; Thomson, 2004; Thomson, Campbell, Miller, Skeaff, & Livingstone, 2009).

Findings from the national total diet study (TDS) of 2009 estimated the mean adult dietary iodine intake to be less than the estimated average requirement (EAR) of 100 µg/d and more than half of each cohort (based on age and gender) were found to have an inadequate intake of iodine (Skeaff et al., 2003; Vannoort & Thomson, 2009). These results were consistent with the median iodine intakes from an earlier TDS (2003/04) (except for infants 6-12months), (Vannoort & Thomson, 2005).

In response to the re-emergence of iodine deficiency, mandatory fortification of all bread (except organic, parbaked and unleavened bread) with iodised salt was implemented in September, 2009 as a food regulation (Food Standards Australia and New Zealand, 2009). More recently however, results from the 2016 TDS have been published and this has shown improvements in the adult mean dietary iodine intake from the earlier findings of the TDS of 2009. The estimated mean dietary iodine intake in the 2016 TDS for adult females was 100µg/d and males 133µg/d. This is an increase of iodine intake across all cohorts since the earlier TDS of 2009, such that EAR has now been achieved or even exceeded. Results from the 2016 TDS suggest that the majority of the NZ population should now have an adequate iodine intake (Ministry of Primary Industries, 2016).

2.2 Iodine

Iodine is fundamental to the production of thyroid hormones in mammals. It is a trace mineral that is found in food and water, mainly in the form of iodide or iodate but with smaller amounts maybe bound organically to amino acids (Brody, 1999; Butler, Grose, Burrett, Pook, & Doyle, 2007). Though only small amounts of iodine are required by humans, a regular supply is essential to life and the production of the thyroid hormones; triiodothyronine (T3) and thyroxine (T4). For this reason, body stores of iodine are highest in the thyroid gland, some 20-50-fold higher than that found in plasma (Pearce et al., 2004). Iodine as part of thyroid hormone is essential for the biochemical processes of metabolism, growth and development and it is crucial to the optimal function of the brain and central nervous system (Brody, 1999; WHO/UNICEF/ICCIDD., 2008).

2.3 Absorption & Metabolism of Iodine

Dietary iodine ingested in foods, salt and supplements is readily absorbed in the stomach and small intestine at a proportion ≥ 90%. Iodide, is the most common form present in food and the most efficiently absorbed by the gut, whereas other organic forms of iodine such as those bound to amino acids; i.e. as part of tyrosine, are less well absorbed. Iodate, the most common form of iodine found in iodised salt, prior to absorption must first be reduced in the gut via non-enzymatic processes involving glutathione to form iodide (Zimmermann, Jooste, & Pandav, 2008).

Following absorption in the gut, iodide is released into the general circulation and is widely distributed throughout extra cellular fluids, but the primary target tissues are the thyroid gland, brain and kidneys. Renal clearance of iodine is relatively constant whereas uptake by the thyroid is highly dependent upon the level of dietary intake and the thyroid gland itself controls the rate at which it absorbs and concentrates iodine (Rohner et al., 2014; Zimmermann et al., 2008).

Once in the circulation, plasma iodide enters the thyroid gland via the sodium-iodide symporter (NIS) located at the basal membrane of the thyroid cell and then migrates to the apical membrane. Thyroid stimulating hormone (TSH) produced by the anterior pituitary gland controls the rate of entry of iodide into the thyroid gland and TSH is itself triggered by the release of thyrotropin releasing hormone (TRH) from the hypothalamus (Zimmermann et al., 2008).

Once iodide has entered the thyroid cell it is oxidized by thyroperoxidase (TPO) and hydrogen peroxidase (H_2O_2) into iodine and is attached to tyrosol residues in thyroglobulin (Tg) to produce the thyroid hormone precursors which eventually become the thyroid hormones; triiodothyronine (T4) and thyroxine (T3) essential for functions of metabolism. Thyroglobulin is a glycoprotein that is produced only in the thyroid cell. Thyroglobulin can be used to assess iodine deficiency as increased amounts of Tg are released into the general circulation in states of iodine deficiency (WHO/UNICEF/ICCIDD., 2008; Zimmermann et al., 2013).

Iodine accounts for as much as 59% of the weight of thyroxine (T3) and 65% of triiodothyronine (T4). T3 is the active form of thyroid hormone and T4 is the transportation form which is then converted into T3 via selenium dependent 5-deioinase at the site of action (Zimmermann et al., 2008).

In states of adequacy, less than 10% of absorbed iodine will be taken up by the thyroid gland, whereas ≥80% may be sequestered by the thyroid when its storage levels become chronically low, which is at levels of approximately 20µg (Rohner et al., 2014; Stanbury, Brownell, & Riggs, 1954).

Iodine is ultimately released from thyroid hormones back into the general circulation and though it can be recaptured again by the thyroid gland, turnover is slow taking approximately 1-5 days, thus over 90% of ingested iodine is eventually excreted in urine. The kidneys are the principal route of excretion for iodine, with minimal amounts lost via sweat and faeces (Zimmermann et al., 2008).

2.4 Role of thyroid hormones

Thyroid hormones are required for metabolic processes in mammals and synthesis is dependent on adequate iodine concentrations. Though it is likely that all cells are target organs for iodine, the main known function of iodine is as a component of thyroid hormones; T3 and T4. Each molecule of T3 and T4 is made up of protein and iodide, T4 contains four atoms of iodide and T3 contains three hence their respective names. Much greater amounts of T4 than T3 are produced by the thyroid gland but T4 is less potent than T3 because almost all of T4 is bound to thyroglobulin binding protein (TBG) therefore inactive. Most of both T3 (99.97%) and T4 (99.7%) are transported in the circulation bound to proteins, principally TBG, and it is only the unbound thyroid hormone that can enter the cell of its target tissue. Once T4 reaches its target tissue in the body it must be enzymatically converted to the active hormone T3 via the process of deiodination via a selenium dependent iodinase (Brent, 2012; Leung & Braverman, 2010). Thus selenium must also be adequately supplied by the diet if this process is to be efficient (Thomson, 2004). Once thyroid hormone has entered the target cell it binds to nuclear receptors stimulating a wide number of metabolic processes (Leung & Braverman, 2010).

Of the many physiological functions of thyroid hormones; essential roles relate to brain development and growth, physical growth and maturation, maintenance of basal metabolic rate and energy metabolism. The control of metabolic processes is essential to life and the role of thyroid hormone includes functions that relate to carbohydrate, fat, protein, mineral and vitamin metabolism. To illustrate, thyroid hormone regulates both glycolysis and neoglucogenesis and increases lipolysis and the production of adenosine triphosphate (ATP) (WHO/FAO, 2004). Thyroid hormone affects vital processes such as heart rate, blood pressure, body temperature and energy metabolism. Other suggested roles include reducing the risk of gastric cancer and fibrocystic breast disease and regulation of the immune response (Rohner et al., 2014).

Iodine deficiency increases the risk of abnormal thyroid function (Rohner et al., 2014). In adults with mild to moderate iodine deficiency, the risk of clinical manifestations such as hypothyroidism, diffuse goitre, nodular goitre and hyperthyroidism exist (Zimmermann & Andersson, 2012). Goitre is the term that describes enlargement of the thyroid gland and occurs due to the hyperstimulation of thyroidal tissue in response to increased secretion of thyroid stimulating hormone (TSH). The increase in synthesis of TSH is in direct response to reduced levels of T4 in the circulation (Rohner et al., 2014).

Not all iodine deficient states will produce goitre but instead manifest as abnormal thyroid function, particularly in mild to moderate iodine deficiency states and the diseases that manifest are collectively termed subclinical thyroid disease (SCTD). Subclinical thyroid disease may present as either under or overactive thyroid function i.e. subclinical hypothyroidism or subclinical hyperthyroidism. Unfortunately, what is not certain and is much debated is the clinical significance of the often subtle changes of SCTD. The determination, management and treatment of SCTD is highly controversial. This is most unfortunate as there is potential risk for the development of overt disease and reduced quality of life from undiagnosed and/or untreated SCTD (Biondi & Cooper, 2008). Iodine deficiency and associated thyroid dysfunction can also have adverse effects on other body systems, particularly the cardiovascular and musculoskeletal systems and will be discussed later.

Pregnant women, infants and children are extremely vulnerable to inadequate dietary intake, and severe iodine deficiency during pregnancy can cause irreversible mental impairment for the infant. Rapid growth occurs during the fetal and postnatal period, and iodine deficiency during this time can interrupt physical growth and maturation of deficient children and infants. Iodine deficiency during the period of rapid brain and central nervous system development can have long lasting consequences for IQ (Zimmermann et al., 2008).

While iodine deficiency is the most common cause of preventable mental impairment worldwide for the most part, for iodine deficiency to exist there must first be a situation of insufficient dietary intake (WHO/UNICEF/ICCIDD., 2008).

2.5 Effect of goitrogens on iodine uptake by the thyroid gland

Goitrogens are environmental substances that exist in some foods and drinking water that can disrupt the uptake and use of iodine by the thyroid gland. Examples of goitrogenic substances include thiocyanates found in cassava, cabbage, turnip, broccoli, brussels sprouts, bamboo shoots and cauliflower, and flavonoids found in soy and millet. Apart from foods, tobacco smoking is one of the most ubiquitous sources of goitrogens due to the inhalation of thiocyanates that occur naturally in the tobacco leaf (Brauer, Below, Kramer, Fuhrer, & Paschke, 2006).

Goitrogens exert their effect by decreasing the uptake of iodine by the thyroid gland via competitive inhibition of the sodium/iodine symporter and in states of iodine deficiency, the consumption of foods containing goitrogens can worsen iodine deficiency. However in states of iodine adequacy, there is likely little or no effect upon iodine uptake by the thyroid (Gaitan, 1990; Zimmermann et al., 2008).

2.6 Dietary requirement for iodine

People of all ages require a regular intake of dietary iodine to replace losses that occur daily and to prevent deficiency. Multiple factors determine the dietary requirement for iodine in humans and recommendations are based on daily urinary excretion of iodine; maintenance of plasma iodide levels; thyroid iodine stores; the uptake of radioactive iodine; and uptake and turnover of iodine (WHO/FAO, 2004; WHO/UNICEF/ICCIDD., 2008).

In NZ, the current EAR for adults is based on information from studies showing iodine balance being achieved at intakes greater than 100µg/day but not less than 40µg/day, and results from a NZ study that related urinary iodide to thyroid volume. The latter study showed physiological requirements for iodine of 85-100µg/day therefore 100µg/day was accepted as the EAR (Ministry of Health & National Health and Medical Research Council, 2006; Thomson et al., 2001).

The NZ recommended dietary intake (RDI) for healthy adults is currently 150µg day. This is based on the EAR of 100µg/day with an assumption of a Hill variation of 20% that has been rounded upward to allow for the potential inhibitory effect of dietary goitrogens (Knudsen et al., 2000; National Health and Medical Research Council & New Zealand Ministry of Health, 2006). The NZ RDI is in accordance with World Health Organization (WHO) recommended dietary allowance of 150µg day (WHO/UNICEF/ICCIDD., 2008). Pregnant and lactating women require more, with an RDI of 220µg and 270µg per day respectively. The upper limit for iodine intake in adults is 1100µg/day and is not recommended as a daily intake due to the risk of adverse health consequences (National Health and Medical Research Council & New Zealand Ministry of Health, 2006). Table 2.1 displays the current nutrient reference values for New Zealand and Australia (Ministry of Health & National Health and Medical Research Council, 2006).

Table 2.1 Nutrient Reference Values across the Life Span*

Infants: Adequate intake only has been established at 90µg/d for 0-6 months & 110µg/d for 7-12 months		
AGE	**EAR (µg/day)**	**RDI (µg/day)**
1-8 years	65	90
9-13 years	75	120
14-18 years	95	150
Adults *19 to ≥70 years*	100	150
Pregnancy	160	220
Lactation	190	270

* Adapted from Nutrient Reference Values for Australia and New Zealand (National Health and Medical Research Council & New Zealand Ministry of Health, 2006).

The Total Diet Study (TDS) is a nationwide survey conducted by the NZ Ministry of Primary Industries (MPI) once every 5 years. The aim of the TDS is to assess the population's exposure to agricultural compounds, contaminants, and nutrients from a range of foods that are typically consumed in the NZ diet. The 2009 TDS reported the mean dietary intake of iodine of adult females to be 63µg/day, well below the EAR of 100µg/day and reflected an inadequate intake for more than half of the group (Vannoort & Thomson, 2009). The most recent TDS (2016) has reported mean dietary intake of iodine for adult females now at 100µg/d, this shows marked improvement from the earlier TDS of 2009 where EAR was not achieved (Ministry of Primary Industries, 2016; Vannoort & Thomson, 2009).

2.7 Food Sources of iodine

Diet provides the main source of iodine for humans. Iodine is an essential nutrient because it must be obtained from exogenous sources and due to its role as part of thyroid hormone. It occurs naturally in foods or is added to foods often as iodised salt. Iodine occurring in foods is mostly in the form of iodide but concentration is highly dependent on soil levels. However, soil content is variable within and across different geographic regions due to the effects of environmental processes such as glaciation, flooding and erosion which leach iodine from the soil into the sea. As a result most of the earth's iodide is found in the ocean whereas inland mountainous regions soils have a low content (WHO/UNICEF/ICCIDD., 2008; Zimmermann, 2010).

This cyclic process that results in iodine eventually being deposited in the soil involves oxidation of iodide from seawater with subsequent release into the earth's atmosphere where it is then returned to the land through rain and snow. However, this ecological cycle is slow and fragmented resulting in soil and water that is depleted in iodine. Low soil and water content of iodine results in plants and animals that also have a low iodine concentration and consequently so too the food supply which humans are dependent upon for iodine intake (Zimmermann, 2010).

For this reason, the naturally occurring iodine content of most foods is low with the exception of foods derived from the ocean. These marine origin foods have a high iodine content because ocean plants and animals concentrate iodine from seawater. Therefore foods such as seaweed, fish and shellfish have a high concentration of iodine and when consumed provide an excellent source of iodine in the diet (Haldimann, Alt, Blanc, & Blondeau, 2005; Zimmermann, 2010). In many parts of the world milk and eggs are a valuable source of iodine in the diet and this is largely because of their frequent consumption, as they contain only moderate amounts of iodine compared to marine derived food. However, the iodine content of meat is highly variable due to varied methods of feeding i.e. whether the animals are grazed on soil depleted of iodine or fed supplemental iodine through fortified food, which can vary by season (Haldimann et al., 2005).

2.7.1 Food sources of iodine in New Zealand

New Zealand has low levels of iodine in the soil therefore foods such as meat and crops that are grown in these soils also have low iodine content. In NZ, milk and eggs are considered a good source of iodine in the diet and they are also consumed frequently (Vannoort & Thomson, 2009). In 2009, prior to the mandatory fortification of bread, the NZ TDS showed the main contributors of iodine in the NZ diet in descending order of contribution were; dairy foods (36%), eggs, mussels, fresh fish and oysters (26%), takeaways (15%), and grains (11%), (Vannoort & Thomson, 2009). However, the recent TDS of 2016 has shown cereal-grain based foods now contribute the most iodine in the diet of NZ adults. Traditionally dairy products have been the largest source of iodine in the NZ diet but bread is now the primary source according to the 2016 TDS, with meat, chicken, fish, and eggs the second highest followed by dairy products (Ministry of Primary Industries, 2016).

The NZ Ministry of health (MOH) recommends the use of iodised salt instead of non-iodised salt but (since many local foods have a low iodine content) the TDS does not include the discretionary use of iodised salt so the contribution made to total iodine intake from this source is unknown. However, it is recognised that the assessment of discretionary salt use is prone to error not least due to issues with reliability of estimation; i.e. how much salt is added at either the table or in cooking.

Though seaweed is a rich source of iodine, it or products containing seaweed prior to 2016 had not been included in the TDS. More recently sushi has become popular in the NZ diet and this was assessed by Edmonds et al (2016), though found it contributed minimal amounts at less than 1% of total iodine intake. The most recent TDS (2016) included sushi, (the first time in the history of the TDS), but similar to Edmonds et al (2016) found it was not a significant source of iodine in the NZ diet. It did however find sushi to contain appreciable iodine content, with ranges higher than that found in fresh fish and this is largely due to the nori sheets used as wraps in sushi, which are natural iodine accumulators (Edmonds, McLean, Williams, & Skeaff, 2016; Ministry of Primary Industries, 2016).

The estimation of dietary intake of iodine for mid-life or older adults, either male or female is not well represented by the TDS. Assessment uses a diet simulation model based on 19-24 year. old males and females and though this may be an efficient method for a nationwide survey it is much less accurate for assessment of an older person's dietary intake (Vannoort & Thomson, 2009). This is an anomaly that presents a gap in iodine knowledge for this age group.

Since 2009, in response to the re-emergence of iodine deficiency in NZ, it became mandatory to use iodised salt instead of non-iodised salt in all commercially made bread, except for organic. Thus, providing an additional source of iodine in the NZ diet and the impact of this will be discussed subsequently (Food Standards Australia and New Zealand, 2009). According to the NZTDS of 2016 this intervention has been successful in raising the mean dietary iodine intake of adults within NZ (Ministry of Primary Industries, 2016).

2.8 Assessment of iodine intake and status

The assessment of iodine nutrition within a population is important and regular monitoring allows the opportunity for both recognition and correction of any iodine deficiency found. Without this knowledge iodine deficiency disorders within a population may manifest but not be recognised until much later when disease occurs. However, the methods of assessment for iodine status are not without their limitations and methodological challenges. Assessment is determined by the use of biomarkers of exposure such as urinary iodine concentration (UIC) and functional biomarkers such as thyroid hormones and thyroid volume, the latter being more appropriate when deficiency is chronic and enlargement of the thyroid gland or even goitre has developed (Zimmermann & Andersson, 2012). The specific biomarkers for assessment of iodine status within a population include; urinary iodine (UI), urinary iodine excretion (UIE), urinary iodine concentration (UIC), dried whole-blood spot (or serum) thyroglobulin, thyroid volume and thyroid stimulating hormone (TSH) (WHO/UNICEF/ICCIDD., 2008). Each method has its own merits and disadvantages and will be discussed.

2.8.1 Urinary iodine excretion

As it is thought that almost all dietary iodine is concentrated (>90%) and eventually excreted in the urine of healthy adults within a period of 24 hours, urinary iodine concentration (UIC) can be used as a biomarker for measuring iodine nutrition. To determine the iodine status of a population the WHO recommends collecting a spot sample of urine from a sufficiently large population (WHO/UNICEF/ICCIDD., 2008). This is well validated as a method of assessment for iodine deficiency of a population, however it is not a reliable method for the measurement of individual iodine status. There are some limitations to its use as it only measures recent exposure to dietary iodine so does not reflect habitual dietary iodine intake; it does not allow for day to day and within day variations of iodine intake within an individual; and it does not reflect changes in hydration status which influence the urinary output and excretion of iodine. However, it is thought that the effect of these variations will even out at the population level of assessment (Pearce & Caldwell, 2016; WHO/UNICEF/ICCIDD., 2008).

24-hour urine samples can also be used to measure iodine status and remove the effects of hydration status and diurnal variation. However, they still have the same problems with day to day variation. They are also impractical for large studies. The reliability of using spot samples over 24 hr urine collections is also supported by earlier studies. In these studies, it was found that if enough spot urine samples are assessed, then median UIC from the spot samples was significantly correlated with the median concentration from 24 hr urine samples (König, Andersson, Hotz, Aeberli, & Zimmermann, 2011; Thomson et al., 1997). UIC is the most common method of assessment of iodine deficiency of a population (WHO/UNICEF/ICCIDD., 2008).

Urinary iodine concentrations can be expressed and measured in different ways; 24-hr urinary iodine excretion (UIE; µg/day); urinary iodine concentration (UIC; µg/l); or in relation to creatinine excretion (µg iodine/g creatinine) (Rohner et al., 2014; Vejbjerg et al., 2009). The median UIC of a group is the value most often used to indicate the iodine status of a population. The median value best reflects the measure of central tendency in a population because generally the frequency of distribution for UIC value in a group does not follow a normal distribution.

Cut off points to determine iodine status are according to median UIC values (μg/l) and have been determined for different age groups by the World Health Organization (WHO) and are outlined in table 2.2 below (WHO/UNICEF/ICCIDD., 2008). Based on current guidelines from the WHO, iodine status within a population is deemed adequate if the median UIC of children and non-pregnant women is between 100ug/l and 299ug/l, with no more than 20% of all samples below 50μg/l. If the median UIC of a population is between 50ug/l and 99ug/l this reflects mild iodine deficiency; if between 20ug/l and 49ug/l moderate iodine deficiency and <20ug/l this reflects severe iodine deficiency (WHO/UNICEF/ICCIDD., 2008).

Table 2.2 Epidemiological indicators and criteria for assessing and determining iodine deficiency based on urinary iodine concentration

Median UIC	**Iodine Intake**	**Iodine Nutrition Status**
Criteria and Population cohort		
Median UIC for school aged children (≥6yrs) (µg/l)		
<20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Mild iodine deficiency
100-199	Adequate	Adequate iodine nutrition
200-299	More than requirements	More than adequate dietary intake with slight risk for the general population
≥300	Excessive	Higher risk of adverse health outcomes

Adapted from (WHO/UNICEF/ICCIDD., 2008).

Some researchers use the UIC cut off which was developed for school-age children (SAC) in adults. However, adults typically produce greater volumes of urine compared to SAC this results in the potential for overestimation of iodine deficiency among adults. The average volume of urine produced per day for SAC is typically only 1L vs 1.5L for adults, so there has been much debate whether it is appropriate to use these cut-off values based on SAC for the assessment of iodine deficiency in adults (Zimmermann & Andersson, 2012).

Based on the higher volume of 1.5l/day for adults, it is proposed that the cut-off for iodine deficiency in adults is more likely 60-70µg/l rather than 100µg/l based on results from SAC. This lower cut-off value (60-70µg/l) for adults is supported by results from a large study of young women prior to the introduction of iodine prophylaxis in Slovakia. Approximately 10,000 women with goitre (goitre size was assessed) and a further 2500 women provided a spot urine sample for assessment of UIC. There was no evidence of increased goitre rate when mean UIC was >60ug/l, suggesting possible iodine sufficiency at mean levels less than 100µg/l (Langer, 1980). Other methods support this rationale also, such as the EAR cut point approach which is used to estimate iodine intake in populations. Rather than using a single mean or median intake from an individual this method uses the distribution of population intake (Murphy, Barr, & Poos, 2002).

2.8.2 Thyroid size

Historically, palpation of the thyroid gland has been widely used as a practical method for determining the prevalence of iodine deficiency disease in a population. This method however lacks specificity and sensitivity as it is subjective and prone to inter observer error. Also as the thyroid gland is slow to respond to changes in iodine intake this results in a long lag time before the effect of iodine deficiency on thyroid function is obvious and potential delay in diagnosis of disease. Palpation of goitre size is therefore more useful as a baseline measure only to determine the severity of iodine deficiency disease within a population (Rohner et al., 2014; Zimmermann & Andersson, 2012). Ultrasound examination of the thyroid gland is a tool that can be used also and has advantages over manual palpation to measure thyroid volume, however it is an expensive method and subject to inter observer error so it is not a common method used for monitoring of a population's iodine status (WHO/UNICEF/ICCIDD., 2008).

2.8.3 Thyroid stimulating hormone

Thyroid stimulating hormone (TSH) is released by the pituitary gland in response to low circulating iodine levels which in turn controls the release of thyroid hormones; T4 and T3 (Brent, 2012). TSH concentration in blood or serum is useful for measuring iodine deficiency in neonates only and to test for congenital hypothyroidism but not as a method of assessment for adults and school age children (SAC). Measuring TSH to assess iodine nutrition in a population of adults and SAC lacks accuracy and is unreliable as the test lacks sensitivity; i.e. it can be raised in states of iodine deficiency but still remain within normal range (Rohner et al., 2014; WHO/UNICEF/ICCIDD., 2008).

2.8.4 Thyroid hormones

Thyroid hormones; triiodothyronine (T3) and thyroxine (T4) are secreted by the thyroid gland in response to increased circulating levels of TSH. These hormones have a vital and varied physiological role in the body, including regulation of metabolism, physical growth and maturation and brain function as described (Brent, 2012). The thyroid hormones; T3 and T4 directly reflect thyroid function, however their usefulness as indicators of population iodine status is very much limited to that of severe deficiency states. This is because in an iodine deficient population serum T3/T4 may increase or remain unchanged, but often stays within the normal range and as such is an insensitive method for assessing iodine status of a population (Rohner et al., 2014).

2.8.5 Thyroglobulin

Thyroglobulin (Tg) can be detected in both blood or serum and is a precursor protein needed for the synthesis of thyroid hormone. Tg is synthesized only in the thyroid and is the most abundant protein within the thyroid gland. In states of iodine sufficiency small amounts of Tg are released into the bloodstream but in iodine deficiency Tg is released in greater amounts (Spencer & Wang, 1995; WHO/UNICEF/ICCIDD., 2008). Serum Tg concentration can also increase with age, alcohol, smoking, in the presence of thyroid disorders and it has also been found to be raised in populations with exposure to excessive iodine intake (Demers & Spencer, 2003)

Unlike urinary iodine concentration which measures recent (days-weeks) iodine status, Tg reflects chronic iodine status (weeks to months), and is thought to be a more sensitive indicator of improvements in iodine status in populations found to be mildly deficient (Ma & Skeaff, 2014; Zimmermann & Andersson, 2012).

There are advantages in using Tg as a biomarker of iodine deficiency in adults, however there are also limitations. If antithyroglobulin (TgAb) and Tg are not measured concurrently the potential for underestimation of Tg exists, though the prevalence of TgAb in iodine deficiency is not yet clear. In addition, there are issues with interassay variability and reproducibility and it is not known whether iodine prophylaxis precipitates TgAb synthesis. Further understanding of these issues is needed (Rohner et al., 2014).

Also, while median cut-off values for Tg have been determined in school aged children, until recently validation of cut-offs for adults had not been confirmed. Studies in school aged children have suggested that iodine is adequate if the median Tg is <13 µg/l and/or <3% of the population have Tg concentrations >40µg/l but whether this can be applied equally to determine iodine adequacy in adults is less well known due to the lack of observational and intervention studies to confirm (Ma & Skeaff, 2014; Zimmermann et al., 2013).

Although, recently a randomised, double blind, placebo controlled study of mildly iodine deficient NZ adults (n=116) who were supplemented with 150µg/day for 24 weeks were found to have improvements in iodine status (as assessed by UIC) which was associated with a concomitant decrease in Tg concentrations. At 24 weeks the median Tg in the intervention group had reduced to 13µg/l from 19.5µg/l at baseline (P<0.001) whereas the median Tg of the placebo group showed little change (Ma, Venn, Manning, Cameron, & Skeaff, 2016).

The outcome, the first study of its kind in a group of NZ adults showed that the cut-off of <13µg/l previously determined by Zimmermann et al (2009) to determine adequate iodine status in school aged children can also be used as an index for assessing adequate iodine status in adults and as such is a useful biomarker (Ma et al., 2016).

However, at this time spot UIC remains the most popular method for assessment of iodine status in a population and has the most evidence to support its use.

2.8.6 Estimation of dietary iodine intake

The assessment of iodine intake via dietary assessment has a number of limitations and as such is not recommended to be used as a stand-alone tool but to support other methods such as UIC or Tg (Subar et al., 2012; Thompson & Subar, 2008).

The use of food frequency questionnaires (FFQs) to determine consumption patterns of iodine-rich foods provides qualitative rather than quantitative data and recording of information in diet diaries is well known to be subject to participant error. Often, there are problems with accuracy; i.e. estimation of portion size and errors in recording foods eaten (Thompson & Subar, 2008). Also there is the unique issue relating to the discretionary use of iodised salt and the difficulty of reliably quantifying the amount used in cooking and at the time of eating.

Another issue with estimation of iodine intake from foods is that it relies on information contained within food composition databases. These databases do not always offer a reliable estimation of the iodine content of food, particularly if these are not kept updated or values from other countries (such as the UK or USA) are used. There are several reasons for this; iodine content of food is naturally highly variable within foods and also across different seasons and there may be no allowance made by food composition databases when determining the specific iodine content of foods. In addition, while the salt content of processed foods is often included in food composition databases, seldom does it differentiate between the types of salt used, i.e. whether the salt is iodised or uniodised (Carriquiry et al., 2016; Rohner et al., 2014).

The current method of assessment for iodine nutrition, in particular UIC is suitable for determining population status but further evidence to support the proposed cut-off limits for defining adequacy in adults not school age children will be beneficial. More research should provide support for using Tg as an accurate biomarker of iodine nutrition in addition to UIC.

2.9 Iodine deficiency disorders

Iodine deficiency is a common micronutrient deficiency that affects humans at all stages of life and has multiple adverse effects on health. Collectively these effects are termed iodine deficiency disorders (IDD) (WHO/UNICEF/ICCIDD., 2008; Zimmermann, 2009). For iodine deficiency to exist, there must first be an inadequate intake of dietary iodine which results in less iodine available for use by the thyroid gland. If iodine deficiency persists then the production of thyroid hormone eventually decreases and so too thyroid hormone concentration, resulting in hypothyroidism and/or goitre (Leung & Braverman, 2010). The effects of iodine deficiency are diverse across different age groups and depend too on the severity of deficiency (Zimmermann, 2009). The WHO, the United nations international children's education fund (UNICEF) and the International council for control of iodine deficiency disorders (ICCIDD) refer to IDD as "all of the consequences of iodine deficiency in a population that can be prevented by ensuring that the population has an adequate intake of iodine" (WHO/UNICEF/ICCIDD., 2008).

Severe iodine deficiency results in goitre and is likely to occur when iodine intake has been chronically low, at amounts less than 50μg/day, or with a median UIC of <20μg/l in a given population and can affect all ages. Severe iodine deficiency may cause goitre, hypothyroidism, and intellectual and developmental impairment and in pregnancy and young children this may be irreversible. While most organ systems are affected and indeed damaged by severe iodine deficiency the most vulnerable is the human brain (Hetzel, 1983; Li & Eastman, 2012; WHO/UNICEF/ICCIDD., 2008). However, the worldwide use of iodized salt has almost eradicated severe iodine deficiency, therefore focus is now directed more towards studying the consequences of mild to moderate iodine deficiency in both children and adults (WHO/UNICEF/ICCIDD., 2008).

Knowledge of goitre is well known, but the understanding and classifying of mild to moderate iodine deficiency and its manifestations is less so. Most information has been obtained from observational studies so is less robust than randomized controlled studies. The classification for the severity of iodine deficiency, including mild to moderate deficiency, was originally based upon epidemiological goitre surveys in school age children. Due to the inherent inaccuracies with this method this was replaced with determination by UIC and this method is still in use today (Li & Eastman, 2012). Chronic insufficient intakes of iodine in adults results in adverse changes in thyroid function that can result in goitre, thyroid dysfunction and mental impairment and the risk of thyroid cancer and/or thyroid disease is also increased (Bath, Steer, Golding, Emmett, & Rayman, 2013; Canaris, Manowitz, Mayor, & Ridgway, 2000; Hollowell et al., 2002).

Unfortunately, there is a paucity of information relating to the adverse effects of mild to moderate iodine deficiency in adults however thyroid dysfunction and cognitive effects are the known to be the most profound manifestations. Table 2.3 shows the possible health consequences of iodine deficiency disorders across the lifespan (WHO/UNICEF/ICCIDD., 2008).

Table 2.3 Iodine Deficiency Disorders according to Life Stage

Life Stage	Iodine deficiency disorder
All ages	*Goitre* *Hypothyroidism* *Increased vulnerability to radiation*
Adults	*Impaired mental ability* *Hyperthyroidism (iodine induced)* *Goitre*
Children and adolescent	*Impaired mental ability* *Physical developmental delays* *Hyperthyroidism (iodine induced)*
Neonates	*Infant mortality* *Severe mental and physical developmental defects* *Infant hypothyroidism*
Fetus	*Still birth* *Spontaneous abortion* *Congenital abnormalities* *Perinatal mortality* *Irreversible mental retardation*

*Adapted from Hetzel., B. S, 1983 & WHO/UNICEF/ICCIDD, 2008.

2.10 Epidemiology of iodine deficiency

2.10.1 Global iodine Deficiency

Iodine deficiency remains one of the most common global nutrient deficiencies to affect humans but it is also one of the easiest to prevent with sufficient dietary intake of iodine. At the population level iodine deficiency can result in the loss of 10-15 IQ points and throughout the world it is the greatest single cause of preventable brain damage (Delange, 2001). Over the last two decades salt iodisation has been in place in over two thirds of the world as an attempt to reduce the global burden of iodine deficiency (Zimmermann, 2014).

Global organizations such as the WHO and the Iodine global network (formerly the ICCIDD) continuously monitor iodine nutrition throughout the world and have been since work first began in 1960. At this time, the WHO estimated that iodine deficiency affected as much as 20-60% of the world's population. Since then and particularly over the last two decades the global burden of iodine deficiency has steadily decreased due to influences such as the implementation of salt iodisation and improved monitoring and fortification strategies at both the global and national level (Andersson, Karumbunathan, & Zimmermann, 2012; Pearce et al., 2013).

Global statistics for iodine deficiency are based on surveys involving SAC. The reasons for using SAC rather than adults is mainly due to the participant burden of collecting urine samples and because samples are easier to obtain from children in school environments than community living adults. In 2016 it was estimated that only 15 countries had insufficient iodine intake; 102 were sufficient and 10 countries were reported to have excessive intakes. This was based upon surveys conducted between 2002 and 2016. Among the 15 countries found to have insufficient intake 2 were classified as moderately deficient and the other 13 mildly deficient. This is in contrast to 32 countries with insufficient intake in 2011 (Andersson et al., 2012; The Iodine Global Network, 2016). However while improvements in global iodine nutrition have been made, there is concern that progress may now be slowing (Andersson et al., 2012). Though results from the latest TDS (2016) has estimated the dietary intake of the NZ population to be adequate some groups within the population may still be at risk and past history has shown NZ was listed as one of the 13 countries classified as mildly deficient (Ministry of Primary Industries, 2016; Thomson, Vannoort, & Haslemore, 2008; Thomson et al., 1997; Vannoort & Thomson, 2009).

2.10.2 Iodine Excess

While iodine deficiency is of concern so too is iodine excess. Iodine excess occurs when intake is too high and the median UIC of a population is ≥300µg/l. Ten countries were reported to have excess iodine intake in 2016, likely due to over-iodisation of salt or poor quality control of this process and/or intakes being too high from food and water sources (Delange, de Benoist, Pretell, & Dunn, 2001). Prolonged intake of excess iodine in a population can result in iodine toxicity and iodine induced hyperthyroidism, particularly in vulnerable groups and in populations that have more recently undergone iodine repletion (Laurberg, Cerqueira, Ovesen, Rasmussen, Perrild, Andersen, Pedersen, & Carlé, 2010).

Though the benefits of correcting iodine deficiency far exceed the possible health risks from excess intakes, the optimal intake of iodine falls within a narrow range, and intakes above and below this level in a population will result in more disease (Laurberg, Cerqueira, Ovesen, Rasmussen, Perrild, Andersen, Pedersen, & Carlé, 2010). It is therefore imperative that regular monitoring of population iodine status, salt iodisation or fortification programs takes place to ensure optimal intakes of iodine that are neither too high nor too low and are able to provide current information about dietary sources of iodine.

2.10.3 Re-emergence of iodine deficiency in New Zealand

New Zealand has low levels of iodine in the soil therefore foods that are grown or raised upon these soils such as meat and crops also have low iodine content. As iodine intake is largely determined from dietary sources, there has been a long history of iodine deficiency amongst the NZ people and this trend continued well into the last decade (Vannoort & Thomson, 2009).

Attempts were made to address this situation with the introduction of salt iodisation in NZ in 1930s and by the 1950s it was found to be effective in reducing goitre rates and the incidence of goitre was almost eradicated. However, by the 1990s goitre and iodine deficiency among the NZ people had re-emerged (Hercus, Benson, & Carter, 1925; Thomson, Woodruffe, et al., 2001;

Vannoort & Thomson, 2009). Since this time more studies have confirmed mild to moderate iodine deficiency among participants with many finding median UIC to be less than the 60-70 µg/l suggested by Zimmermann (Skeaff, Thomson, & Eastman, 2009; Thomson, 2004)

Low iodine intake was reported in all of the total diet studies between 1982 and 2009 across all ages and genders, except infants 6-12 months. The TDS of 2007/08 showed the estimated mean dietary intake of adults failed to meet the EAR of 100µg/day and more than half of each cohort (age and gender) were estimated to have an inadequate intake of iodine (Skeaff et al., 2003; Vannoort & Thomson, 2009). These results were consistent with the estimated median iodine intakes from the earlier total diet survey (2003/04) (Vannoort & Thomson, 2005).

For these reasons the mandatory fortification of all bread (excepting organic, parbaked and unleavened bread) with iodised salt was implemented as a food regulation within NZ (and Australia) in September, 2009 (Food Standards Australia and New Zealand, 2009). Studies since this time have shown varying results.

One such study of postmenopausal women (n=97) from 3 cities in the North Island investigated both iodine and selenium status and intake, and was conducted post mandatory fortification of bread with iodised salt. In this study, the median UIC was found to be 57µg/l indicating mild iodine deficiency. Also, the estimated median iodine intake based on UIC was below the RDI of 150µg/day (with 25% below the EAR of 100µg/day) at 138µg/day (Brough et al., 2017).

The most recent NZTDS (2016) estimated the mean dietary intake of adults 25yrs+ at or above the EAR of 100µg/d. However, the lowest levels of iodine intake were estimated to be amongst the dietary model for adult females (Ministry of Primary Industries, 2016). All estimates in the TDS are based upon a diet simulation model that includes the consumption of bread fortified with iodised salt.

2.11 Factors contributing to the re-emergence of iodine deficiency in New Zealand

Changes in both dietary patterns and commercial food processing have contributed to low dietary exposure to iodine and consequently low iodine status of the NZ population (Sutcliffe, 1990; Thomson, 2004).

The dairy industry's use of iodophors (iodine based disinfectants) commenced in 1962 and increased the iodine concentration of dairy based foods within NZ for the subsequent two decades. However between 1978 and 1988 the use of iodophors by the industry ceased and as a result significant decreases in the concentration of iodine in milk were reported, from 87µg/200ml in 1978 to 24µg/200ml in 1988 (Sutcliffe, 1990; Thomson, 2003). This decline in iodine concentration in milk is consistent with reports at the time and subsequently that showed low iodine status and low urinary iodine excretion (Thomson et al., 1997; Thomson, Woodruffe, et al., 2001), and is suggested to be a potential contributor to deficiency.

Despite the changes made by the dairy industry to the use of non-iodine based cleansers, dairy products have been, and continue to be, a significant contributor to the total iodine content of the NZ diet (Edmonds et al., 2016; Vannoort & Thomson, 2009). However, it is noted that prior to the 1987/1988 NZ TDS, information for sources of iodine in the diet for individual foods were not obtained (Thomson et al., 2008).

Consumer exposure to convenience foods that contain non-iodised salt and the increased consumption of these foods has also contributed to the decreased intake of iodine (Thomson et al., 2008). Though often a significant source of salt, commercially prepared foods typically lack salt that is iodised and the choice of using either iodised salt or non-iodised salt in NZ is solely at the discretion of the manufacturer. Although consumer information regulations require clear labelling information, lack of public awareness of the importance of iodised salt and its inherent lack in convenience foods is a significant problem. Consumers purchasing convenience foods containing non-iodised salt may be unaware of this issue (Charlton et al., 2010). Conversely, it may be unwise for all convenience foods to contain salt that is iodised due to the potential for excessive dietary intakes and risk of toxicity.

Much debate and conflict about public health recommendations for reducing salt intake throughout the world including NZ exists i.e. the reduction of salt intake has long been promoted due to the potential for increased risk of cardiovascular disease such as hypertension. However, simultaneously an increase in iodine intake is desired and this presents a dilemma because the principal fortification vehicle for delivery of iodine is via the use of iodised salt. To compound this, public knowledge of the importance of iodine for health is likely to be the lesser known of the two public health recommendations (Charlton et al., 2010; Tayie & Jourdan, 2010). Thus, salt reduction programmes may have indirectly reduced dietary exposure to iodine and adversely affected population iodine status (Tayie & Jourdan, 2010).

The trend for using non-iodised specialty, mineral or flavoured salts is problematic as their use is at the expense of iodised salt, though there are few studies to confirm the extent of their use. That these salts contain negligible amounts of iodine may also be poorly understood. Loose labelling requirements may further compromise this lack of awareness and a general decline in awareness of the importance of choosing iodised salt persists (Charlton et al., 2010; Yeatman, Player, & Charlton, 2010).

All of these factors have contributed to the decline in iodine status of the NZ population over the last 3-4 decades.

2.12 Efforts to reduce iodine deficiency in New Zealand

2.12.1 Salt iodisation

Throughout the world salt iodisation has been an effective strategy to reduce the burden of iodine deficiency (WHO/UNICEF/ICCIDD., 2008). In an attempt to address the wide spread iodine deficiency and goitre found amongst the NZ people early last century, the fortification of salt with iodine was introduced in 1924. However the level of iodine that was added was deemed too low as it was not effective in reducing endemic goitre rates of the time and for this reason, by the late 1930s the concentration was raised (Mann & Aitken, 2003) . Today current Australian and NZ legislation stipulates that salt sold under the banner of "iodised" must contain not less than

25mg/kg and not more than 65mg/kg of potassium iodide or iodate (Food Standards Australia and New Zealand, 2016).

In general it would appear that these levels are adhered too, as shown by a study in 2009, which analysed a range of table salts and found a mean concentration of iodine of 32-64mg/kg across the samples included. As part of the same study, a variety of other "uniodised" salts such as sea, rock and low sodium salts were tested and as expected, were found to contain very low concentrations of iodine at 1-5mg/kg, confirming their negligible contribution to overall iodine intake (Thomson, 2009).

2.12.2 Mandatory fortification of bread with iodised salt

In response to the re-emergence of iodine deficiency in NZ, mandatory fortification of all commercially made bread (except organic) with iodised salt was introduced and implemented in 2009. This has been effective in raising the iodine status of school aged children (SAC), however determining the success of mandatory fortification in raising the iodine status of adults is less clear (Edmonds et al., 2016; Jones et al., 2016; Skeaff & Lonsdale-Cooper, 2013; Thomson et al., 2008).

To be effective, fortification programs must reach all groups within a population and be routinely monitored to ensure the levels of fortification are both adequate and appropriate to ensure neither deficiency or excess states occur (Zimmermann, 2004). Monitoring iodine status in a population is via measurements of UIC (often from SAC), and is the method most commonly employed in NZ. Whereas monitoring the appropriate level of iodine fortification in food, (i.e. in this case bread) is via estimates of dietary intake of iodine and testing samples of food as part of the NZ total diet study (Vannoort & Thomson, 2009).

In 2012, in order to assess the impact of mandatory fortification, the iodine intake and status of 301 NZ adults aged 18-64yrs was investigated in a cross-sectional study. While improvements in iodine status were noted; i.e. median UIC increased from 53μg/l (reported in the 2008/09 adult nutrition survey) to 73μg/l, the levels of iodine previously predicted were not achieved (Edmonds et al., 2016). Although this is below the 100 μg/L cut-off it is well within the 60-70 μg/L cut-off suggested by Zimmerman to represent adequacy. A significant difference (10μg/l) between the median UIC of females compared to males (P<0.043) was found, with females having a lower UIC (Edmonds et al., 2016; WHO/UNICEF/ICCIDD., 2008). Though this latter result is not unexpected as males typically consume more food than females., i.e. the NZ total diet study shows females typically consume less bread than men (Vannoort & Thomson, 2009).

More recently, findings from the 2016 TDS showed that bread has now become the major contributor of iodine in the NZ diet (Ministry of Primary Industries, 2016). Dairy products had previously contributed the most iodine, so this is a notable change since the introduction of mandatory fortification of bread with iodised salt. In addition, the TDS showed that dietary intake of iodine is now sufficient to meet the nutritional needs of all cohorts within the NZ population excepting infants, a situation that had not been reported since the early 1990s. Based on these results, mandatory fortification of bread with iodised salt looks to be an effective policy for improving iodine nutrition in the NZ population (Ministry of Primary Industries, 2016). However, women living in NZ who do not consume bread in their diet cannot benefit from this policy and are likely at risk of iodine deficiency.

Factors that influence the success of fortification programs aimed at preventing iodine deficiency are unpredictable, but may include changes in government policy, issues that relate to the commercial manufacture of food that is to be fortified, and choice of target group. Bread is considered a universal food eaten by many, hence the vehicle of choice for mandatory fortification of food with iodine in NZ. However dietary trends come and go and human dietary behaviour is unpredictable and fortification is only effective if it is able to reach all groups within a population.

It is well known that specific groups of a population are more at risk from the adverse consequences of iodine deficiency, including pregnant women, infants and young children due to the high requirement this life stage demands. However, subsets of the population who adhere to specific diets such as veganism, vegetarianism, low-salt, non-dairy, non-fish, low carbohydrate, gluten or wheat free are not well identified or studied. An at-risk group to emerge since the 2009 fortification of commercial bread products with iodised salt in NZ are those who choose to avoid commercially prepared bread. Also, as mentioned females typically eat less bread than males

(Vannoort & Thomson, 2009). Therefore, women at mid-life who choose to adhere to a low carbohydrate diet or for health reasons may choose to reduce or avoid the consumption of bread altogether, are unlikely to benefit from this method of iodine fortification (Fardet, 2015; Giugliano, Maiorino, Bellastella, & Esposito, 2018; Janssen, Busch, Rodiger, & Hamm, 2016). To date there have been no studies investigating the iodine status of adults, particularly mid-life women in NZ who do not eat bread subsequent to mandatory fortification.

Iodine deficiency is the main cause of subclinical hypothyroidism and women at mid-life are at increased risk of thyroid dysfunction. It is therefore important that this subset of the population are more closely monitored for iodine deficiency (Biondi & Cooper, 2008; Hollowell et al., 2002; Rodondi et al., 2010). It is essential that the iodine status of all New Zealand people is monitored but there exists a real lack of research relating to women, in particular mid-life women and iodine nutrition.

2.13 Health consequences for the iodine deficient midlife women

Iodine deficiency can result in irreversible and severe consequences for the developing foetus and adverse effects on brain development and mental ability in children. Appropriately, therefore, much research has been focussed upon iodine deficiency in this highly vulnerable group of pregnant women and children (Zimmermann et al., 2008). However, there has been much less investigation of the chronic effects of mild to moderate iodine deficiency in the mature female. We do know that the most common cause of subclinical (SCH) and clinical hypothyroidism (CH) is iodine deficiency and that there is a higher incidence of hypothyroidism with advanced age, particularly in females (Canaris et al., 2000; Hollowell et al., 2002; Zimmermann & Andersson, 2012). The alterations to thyroid function may be partly explained by the resulting prolonged hyperactivity of the thyroid gland in response to iodine deficiency causing thyroid tissue growth (Biondi & Cooper, 2008; Knudsen et al., 2000). Subclinical thyroid disease (SCTD) is defined by the presence of abnormal serum TSH levels in the presence of free T3 and T4 within the accepted reference ranges (Biondi & Cooper, 2008).

Abnormal thyroid function has wide spread implications for women at mid-life, but few studies have investigated dietary iodine intake or iodine status in association with thyroid dysfunction for older women. There have been several large population based studies that have involved older women showing them to be at greater risk for thyroid dysfunction and SCTD, (Canaris et al., 2000), (Hollowell et al., 2002) but not all investigated iodine status in association with thyroid abnormality.

Amongst the large cohort (n=25,862) of participants in the Colorado Thyroid Disease Prevalence Study, thyroid dysfunction was found to be common, almost 10% had a functional abnormality of the thyroid gland which was possibly also unknown to them. Elevated TSH concentrations in the presence of normal T3 and T4 levels confirmed subclinical hypothyroidism to be more common among women for every decade of age, with statistical significance shown at ≤34 years; ($P<.01$), and the oldest participants reported the highest TSH levels indicating a labouring thyroid gland (Canaris et al., 2000).

This was not a population study, but self-selected cross-sectional study with both female and male participants recruited from a state-wide health fair, (18yrs to >74yrs), therefore its generalisation to the wider population is not appropriate. Nonetheless, this was a large cohort and the outcome is in support of other findings, in particular the increased prevalence of hypothyroidism amongst older women (Hollowell et al., 2002; Vanderpump et al., 1995). Dietary iodine intake of participants was not evaluated, nor was their iodine status so no association can be made between iodine status and thyroid function.

The National Health and Nutrition Examination Survey (NHANES), a large (n=17,353) population-based survey also found older women (≥50 to ≤70yr), significantly more likely to have SCH or CH than males ($P<0.01$) but found no significant relationship between raised TSH and low iodine intake (Hollowell et al., 2002). Thyroid disease and or use of thyroid medication in this study was self-reported.

The Dan Thyr study was conducted prior to the implementation of the national iodisation programme in Denmark in 2001. Female and male participants (n=4649), aged 18-65yr from Copenhagen and Alborg, (areas known to be either mild or moderately deficient) were evaluated for thyroid abnormalities. Thyroid gland enlargement was found in approximately 24% of the women participants ≤40 years and the prevalence of thyroid abnormality was reported as more common amongst females than males. Goitre was more common in Alborg which is not surprising as this area was more severely deficient than Copenhagen (Knudsen et al., 2000; Laurberg et al., 2006).

For the most part these studies highlight issues relating to iodine deficiency and thyroid dysfunction, and it is recognized that iodine status alone is not a direct indication of thyroid function however it still remains that the most common cause of hypothyroidism worldwide is iodine deficiency (Laurberg, Cerqueira, Ovesen, Rasmussen, Perrild, Andersen, Pedersen, & Carle, 2010). Iodine deficiency can have far reaching consequences beyond the immediate effects on the thyroid gland. Though it would be difficult to show iodine deficiency as a direct cause of either osteoporosis or cardiovascular disease, because thyroid hormone is central to all metabolic functions other body systems are adversely affected by abnormal thyroid function and will be discussed.

Subclinical hypothyroidism has been associated with increased risk of osteoporosis, hypercholesterolemia and atherosclerosis but outcomes from large prospective cohort studies for cardiovascular disease (CVD) and mortality have been conflicting, some suggesting no relationship and others showing positive outcomes (Hak, Pols, van Hemert, Hofman, & Witteman, 2000; Hollowell et al., 2002; Razvi, Weaver, Vanderpump, & Pearce, 2010; Tseng et al., 2012).

2.13.1 Iodine deficiency, the thyroid and heart

One of the major target organs for the actions of thyroid hormone is the heart. Thyroid hormone is essential to the regulation of cardiac metabolism having the ability to act upon cardiac myocytes, endothelial cells and vascular smooth muscle (Dillmann, 2002). Profound changes in cardiac function occur in both hypothyroid and hyperthyroid states either directly or indirectly. Clinical manifestations affecting the cardiovascular system and heart due to hypothyroidism include; bradycardia, reduced cardiac output, an increase in diastolic blood pressure, and peripheral vasoconstriction whereas the effects of hyperthyroidism include; increased systolic blood pressure, venous resistance, cardiac output and cardiac mass; tachycardia and atrial arrhythmia’s; and patient symptoms include; palpitations, dyspnoea and chest pain (Kahaly & Dillmann, 2005).

Randomised clinical trials investigating clinical outcomes between SCH and risk of CVD are lacking. However, SCH is a common finding in the older person, occurring in 10-15% among those ≥ 65 years. An association between SCH and increased risk of coronary heart disease (CHD) events and mortality in adults with higher TSH levels has been found (Rodondi & Bauer, 2013; Rodondi et al., 2010).

The Whickham study observed a large group (n=2779) of women for over 20 years and similar to the NHANES study found the prevalence of SCH to be increased in women and with age (Hollowell et al., 2002; Vanderpump et al., 1995). The original findings showed no association between vascular events and thyroid dysfunction. However the study was found to be at odds with other's findings and subsequently a re-analysis was conducted which reported an association between IHD events and IHD-related mortality with subclinical hypothyroidism (Razvi et al., 2010; Vanderpump et al., 1995).

The Rotterdam study (n=1149) found elevated TSH levels indicative of SCH in 11.8% of the older (≥ 55yrs) females who participated. Additionally an association between SCH and atherosclerosis (odds ratio 1.7; 95% confidence interval (CI), 1.1-2.6)) and the prevalence of myocardial infarction (MI) (odds ratio, 2.3; 95% CI, 1.3-4) was found (Hak & Pols, 2000).

Aoki et al (2010) in their review of 11 prospective cohort studies (n=55,287) assessed SCH with risk of coronary heart disease (CHD) and total mortality. A significant trend for increased risk of CHD events ($P<0.001$) and CHD death ($P<0.005$) but not total mortality in adults with higher TSH levels was found (Aoki et al., 2008).

Unlike the finding above by Aoki et al (2010), amongst Taiwanese adults (n=115746) a significant association was found between relative risk (95% CI) for all cause and CVD mortality (1.08; 1.22, $P<0.005$) in participants <65yrs with SCH. In general, the risk was further increased for those ≥65yrs, and in females (Arab, Tseng, Ang, & Jardack, 2011).

Even fewer studies have gone one step further and investigated iodine status in association with CVD risk and SCH. However, a randomised controlled trial of iodine supplementation of 200ug/day for 6 months was found to decrease hypercholesterolemia in iodine deficient overweight women (n=163). The outcome on total cholesterol levels was significant only for those in the intervention group (receiving the iodine) that had elevated cholesterol at baseline (>5mmol/L), showing reduction of 11% by the trial end (P=0.034). Iodine increased significantly, with median UIC at baseline 38ug/l (95% CI: 34,45) increasing to 77ug/L (95% CI:59,89) and by trial end, TSH was found to be 33% lower in the intervention group than in the placebo group (P=0.024), (Herter-Aeberli et al., 2015).

It is known that iodine supplementation can lower elevated TSH concentrations in women who are moderately to severely iodine deficient, however these findings further suggest that overweight women with moderate to severe iodine deficiency are at increased risk of an adverse atherogenic profile. All participants were overweight and/or obese, and compared to normal-weight women these women are already at increased risk of SCH and dyslipidaemia, therefore generalization of the findings to women with different metabolic profiles and varying iodine status cannot be made at this time (Herter-Aeberli et al., 2015).

Sub-clinical hypothyroidism and sub-clinical hyperthyroidism are more common amongst women 50+ years and this presents different risks for mature women. Though there is much debate about the clinical significance of both, thyroid dysfunction in any form still exerts detrimental effects upon both the cardiovascular system and bone (Biondi & Cooper, 2008; Rodondi et al., 2010).

2.13.2 Iodine deficiency, thyroid function and effects upon bone

In adults, thyroid hormones are key regulators for the maintenance of bone and as such exert a multitude of effects upon bone metabolism. Therefore, any change in thyroid function can result in severe consequences for bone health. In hypothyroidism, decreased function of both osteoblasts and osteoclasts results in a decline in the metabolism and remodelling of bone. However, there is little evidence to show the long term effect of hypothyroidism upon bone health. This is because the process of bone remodelling itself is very slow and investigation would involve long term prospective data involving untreated hypothyroid patients and measurements of bone mineral density (Williams & Bassett, 2018). This is neither ethical nor feasible. The effects of sub-clinical hypothyroidism on bone mineral density and risk of fracture also lacks extensive investigation.

Conversely, in hyperthyroidism osteoblasts and osteoclasts are overstimulated resulting in a shortened bone remodelling cycle. Thus, hyperthyroidism causes an increase in the rate of bone turnover and as a result accelerates net bone loss by as much as 10% within one cycle of bone remodelling. Over time this causes significant bone loss that leads to osteoporosis and increased vulnerability to fracture (Bours et al., 2011; Williams & Bassett, 2018). Undiagnosed hyperthyroidism is a recognised risk factor for secondary bone loss and osteoporosis in hospital patients admitted with fracture and population based studies have suggested this risk is also greater for post-menopausal women (Patel et al., 2014; Wirth et al., 2014).

Though there is much evidence to suggest diverse and increased health risks for the older women from poor iodine intake and status, it is also recognised that proving direct association between some of the secondary health risks and iodine status is difficult. The reason for this is perhaps due to the lengthy processes involved in manifesting of disease or that the paradigm is too complex at this time. However, that iodine deficiency is the most common cause of thyroid disease is well established.

2.14 Research relating to iodine and the midlife women

It is well accepted that women in the post-menopausal phase of life have increased risk of CVD and thyroid dysfunction, particularly SCH which has been found to be associated with increased risk of osteoporosis and poorer outcomes for cardiovascular health in older women (del Ghianda et al., 2014). However, despite the known association between thyroid dysfunction and iodine deficiency (Zimmermann & Andersson, 2012) there is paucity of research investigating the iodine status of older women, or more specifically women at midlife. The following discusses mostly NZ research relating to iodine nutrition and mid-life/older women.

Of the 12 intervention studies that Ristic-Medic et al (2009) systematically reviewed with the aim of assessing the usefulness of biomarkers of iodine status in humans, none included women older than 44 years of age (Ristic-Medic et al., 2009). Though it is noted that the author's selection criteria was limited to include only those studies that showed an outcome of altered iodine status and whether a varied selection criteria would have seen more studies including older women is unknown. However, this is yet another example of the lack of research involving the health of older women.

A Dunedin based study, involving 100 older men and women (60-80 years) assessed the effect of 12 weeks of iodine supplementation on thyroid function. At baseline, this double-blind, randomised, placebo-controlled trial found median urinary iodine concentration (UIC) to be indicative of iodine deficiency (median UIC was 48ug/L). Following supplementation with iodine, a significant increase in UIC (P=0.0014) was found with median UIC of 68ug/L recorded. There was also a significant improvement in thyroglobulin concentrations, reducing as much as 24% by week 12 in the supplemented group (P=0.009), (Thomson et al., 2009). This study was conducted prior to the introduction of mandatory fortification of bread and dietary intake of foods was determined by an iodine specific FFQ (Skeaff, McLean, Mann, & Williams., 2013).

To investigate the impact of mandatory fortification upon the iodine status of the NZ population, a cross sectional study was conducted by the NZ Ministry of Primary Industries (MPI) in 2012 as part of their ongoing monitoring of iodine status. When compared with findings from the adult nutrition survey of 2008/09, this study reported improvements in iodine status. Median UIC of 69 (43,105) µg/l as determined by 24hr urine collection indicated mild iodine deficiency among the participants (according to the criteria set by ICCIDD/UNICEF/WHO for SAC) and 71% were below the EAR cut off of 100µg/l. However, as discussed previously, when basing the adequacy of iodine status of adults upon the criteria as recommended by the ICCIDD/UNICEF/WHO, which is determined by the urine volume of 1l of SAC there is potential for underestimation of the proportion of adults with adequate iodine status. In this study the mean volume of urine excretion amongst the adult participants was 2 litres. This issue is widespread and is not unique to NZ as validated cut-offs for adults, allowing for their higher volume of urine, have not been determined worldwide (Edmonds et al., 2016; Skeaff et al., 2013). This study of 300 men and women included 58 older females (45-64yrs), but did not specifically look at the iodine status of women who avoid bread (Skeaff et al., 2013; Vannoort & Thomson, 2009).

Another NZ based study that investigated the iodine and selenium intakes of postmenopausal women (n=97) ranging in age from 50-70yrs following mandatory fortification of bread found the median UIC to be 57µg/l. This level indicates mild iodine deficiency as it is lower than the 60-70µg/l recommended by Zimmermann for adults. The median intake of bread was also found to be low at 1.8 serves/day and 25% of participants reported consuming ≤ 1 serve/day (Brough et al., 2017; Zimmermann & Andersson, 2012).

The iodine status of much older (median age; 85yrs) men and women, all residents of a long term residential care facility was investigated (n=309) following fortification of bread with iodised salt in NZ. A median UIC of 72µg/l was reported, with 29% < 50µg/l, and although indicates mild iodine deficiency according to the WHO/UNICEF/ICCIDD criteria, is sufficient according to recommended levels for adults as proposed by Zimmermann of 60-70µg/l (Miller et al., 2016; WHO/UNICEF/ICCIDD., 2008; Zimmermann & Andersson, 2012). Though median Tg concentration was also suggestive of iodine insufficiency at 18ng/ml and 26% had an elevated Tg concentration (>40ng/ml). Though this study was strengthened by the use of two biomarkers of assessment for iodine, (Tg and UIC), it noted its own limitations or those beyond control; lack of validation for cut-offs for adults for median UIC and others that relate to the advanced age of this group such as renal insufficiency, high prevalence of disease, multiple medication use; including the use of diuretics, all of which have the potential to affect outcomes (Miller et al., 2016).

A NZ randomised placebo controlled trial that investigated iodine supplementation and Tg concentrations found all participants (n=112) at baseline to have inadequate iodine status. Iodine status was assessed by UIC (<100 µg/day) and Tg concentrations. At baseline median UIC was found to be 69µg/l and 64µg/l (P<0.001) respectively for the intervention and placebo group and amongst the whole cohort Tg concentrations were 16.6µl/l with 8% of the cohort having a Tg >40µg/l (Ma et al., 2016). Zimmermann et al (2013) recommends that median Tg concentrations <13µg/l and/or 3% of the population with Tg concentration >40µg/l indicates iodine sufficiency in a group of children.

These are important findings by Ma et al (2016) as they show that the cut-off for Tg as recommended by Zimmermann et al (2013) can be applied to adults as well as children, previously unknown. Though both groups included more females than males (n=112; & <13 males in each), any differences in iodine status between gender were not investigated. Older women were not included, with the upper age range limited to 40 years (Ma et al., 2016).

There are few studies investigating the dietary intake of iodine and/or the iodine status of mid-life to older women living in NZ and no studies investigating the iodine status of NZ women who avoid commercially made bread.

2.15 Perceptions & Knowledge of Iodine

Adequate public health knowledge for the role of iodine in promoting health is vital to eradicating iodine deficiency, however few studies have investigated this aspect of iodine nutrition. To date, studies investigating knowledge and/or perceptions of the importance of iodine and its role in health among the NZ people is lacking. Some information from other countries such as Australia, the UK, Ireland, Tehran and South Africa is available and will be discussed.

Prior to the introduction of mandatory fortification of bread with iodised salt in Australia, a small (n=20) Wollongong based study investigated perceptions relating to iodine fortification. It was found among the women participants, (20-49yrs) that there was little knowledge of the role of iodine in health, other than its use as an antiseptic (Yeatman, Player, & Charlton, 2010).

Similarly, another Wollongong based study revealed poor knowledge of iodine amongst non-pregnant women (n=78, age range: 20-55yrs; 36 % were 45yrs+), with only 49 % being able to relate low iodine status with adverse pregnancy outcomes and as few as 24 % were aware that iodine was lacking in the Australian diet. Apart from approximately 76% being aware that fish and seafood were sources of iodine to the diet, knowledge of food sources of iodine was poor (Charlton et al., 2010).

Both studies recognize the limitations of generalizing these outcomes to the wider population as they were small groups including mostly well educated women from one region of Australia, nevertheless these studies highlight the lack of knowledge relating to iodine and are among the few studies of their kind to investigate this.

An UK and Ireland based study assessed iodine knowledge and its association with iodine intake amongst women of childbearing age (18-45yrs; n = 520), and found poor knowledge of iodine, with only one third being able to accurately cite pregnancy as a critical stage for iodine adequacy and 41 % unable to acknowledge a health problem related to iodine deficiency. Greater iodine knowledge was positively associated with higher iodine intake (r 0.107; P =0.016) and almost half (46 %) also did not meet the adequate dietary requirement of 140 μg/d (O'Kane et al., 2016). The assessment of iodine intake was determined by a food frequency questionnaire so limitations of this method such as reporting bias and inaccuracies in the determination of iodine in foods can occur. Ideally this would have been supported by other biomarkers such as UIC or Tg however similar to the Australian studies it highlights the lack of knowledge regarding the importance of iodine.

Family members with poor knowledge of iodine who make the major choices regarding food and nutrition may unknowingly affect the iodine status of their family. An observational study in Tehran explored this aspect by conducting a series of interviews with adult family members (n=290). To be included, at least one of the family members had to be identified as being in the role of "the mother" (mean age 44.3yrs (SD 11.2)) of the family who assumed responsibility for all major food choices. The association between urinary iodine concentration with knowledge, attitude and behavior as it related to iodine intake, practice and dietary iodine status was evaluated. However, only "the mothers" who took part in the study had their knowledge, attitude and behavior assessed via completion of an iodine specific questionnaire.

Knowledge of iodine was explored using questions related to signs of iodine deficiency disorders, the use of iodized salt in cooking and preservation conditions of iodised salt. The concept of attitude was evaluated via questions that related to the importance of consuming both iodine and iodised salt. Behavior was explored using questions related to iodised salt and included its use, preservation, timing of addition to cooking and considerations when purchasing iodised salt. Significant correlations were found between median 24hr urine concentration and dietary iodine intake of family members and "the mother's" attitude (r=0.17,p=0.003, r=0.20, p=0.001) and behavior (r= 0.15, p=0.008, r= 0.008, p<0.001) respectively (Nazeri, 2015). In particular, the behavior of "the mother" in the study was found to contribute to the suboptimal iodine status of her adult family members.

However, as single rather than multiple 24hr urine collections were analysed for iodine this does not confirm habitual dietary intake of iodine nor allow for variations in diet. As well, there was no assessment of iodine from food sources (which could have offered more to these findings), though Tehran's main source of iodine is iodized salt and considering most of the behavioral questions related specifically to the use of this, these findings do add to the paucity of research regarding knowledge of iodine nutrition among mid-life women.

Similarly, public knowledge of iodine nutrition was found to be poor as assessed via survey in South Africa (Jooste, Upson, N., & Charlton, 2005). One adult from each house (n=2164) was surveyed with 65.7 % unable to identify the main source of dietary iodine and of these, 43.2 % did not know what iodine was. Socio-economic status was also found to be a factor in both the latter two studies (Jooste, Upson, & Charlton, 2005).

Studies investigating knowledge of iodine nutrition, dietary sources and outcomes of deficiency among women are lacking, and even less are those investigating women's knowledge who are past their reproductive years. The most recent and closest surveys were both based in Australia immediately prior to the introduction of the mandatory fortification of bread with iodised salt in NZ and Australia. Lack of awareness regarding the importance of iodine nutrition and dietary sources is a potential risk factor contributing to inadequate iodine intake and status of all the NZ population. More research to address this gap is needed.

2.16 Conclusion

It is well recognized that the food supply in NZ contains low levels of iodine and this has resulted in the local population having a long history of inadequate iodine intake. Although steps to improve iodine intake through mandatory fortification of bread are welcomed, and recently considered successful, it can only enhance the status of those who consume the fortified food product, i.e. bread. Therefore, mid-life women who do not eat bread are representative of a group who are at increased risk of the serious health implications which can occur both indirectly and directly from inadequate intake of iodine.

Iodine is integral to the optimal function of the thyroid gland and though it is able to compensate for a low intake of iodine in the short term, if this state is allowed to continue then it is more likely that adverse biological and functional changes occur. Controversy relating to diagnostic parameters and long lag time before symptoms manifest can result in diagnosis of thyroid disease due to iodine deficiency, slow and unreliable. Changes in the function of the thyroid gland are also more likely with advanced age and female gender.

Lack of awareness about the role of iodine in health and poor knowledge about food sources rich in iodine may also be a contributing factor to poor iodine status of a population, however currently there is no research involving mid-life women living in NZ to confirm this suspicion.

To date there has been no research exploring the dietary intake of iodine or the iodine status of NZ women at mid-life women who avoid the consumption of iodine fortified bread. Women at mid-life are particularly vulnerable to inadequate intake of iodine therefore it is unfortunate that it also appears that this subset of the population lack priority within scientific research.

3 Materials and Methods

3.1 Study Design

This study was a cross sectional study that included quantitative data. The study was given an acronym of "Wombi" which stood for women, bread and iodine. Written and verbal consent was obtained prior to completion of the food frequency questionnaire (FFQ), the three day diet diary (3DDD) and the 24 hour urine collection. Dietary information was collected via an online iodine specific food frequency questionnaire (FFQ) which was completed at the research unit and a three day diet diary, to be returned later by post. Each participant was then asked to collect a 24-hour urine sample for analysis of iodine concentration. Lastly, a 20 ml blood sample was requested from each participant for analysis of thyroid biomarkers. Full explanation was provided by the principal researcher prior to completion of all information and any sample collection.

3.2 Study Sample

Forty women living in Auckland, New Zealand (NZ) aged between 40 to 65 years of age who did not eat more than one slice of bread per day were sought for participation in the study. Participants were excluded if they had thyroid, kidney or cardiovascular disease, smoked cigarettes, took iodine supplements, thyroid medication, medication containing >10µg iodine, lithium, hormone replacement therapy and/or consumed more than one slice of bread containing iodised salt per day. We used a derived (Edmonds et al., 2016) population standard deviation (UIC) of 40 µg/l, and an effect size of 30 µg/l with 95% confidence interval and significance at 0.05, resulting in a recommended sample size of 29. However, as measures of UIC are known to be highly variable the sample size was increased to accommodate this and 40 women were sought (Zimmermann & Andersson, 2012).

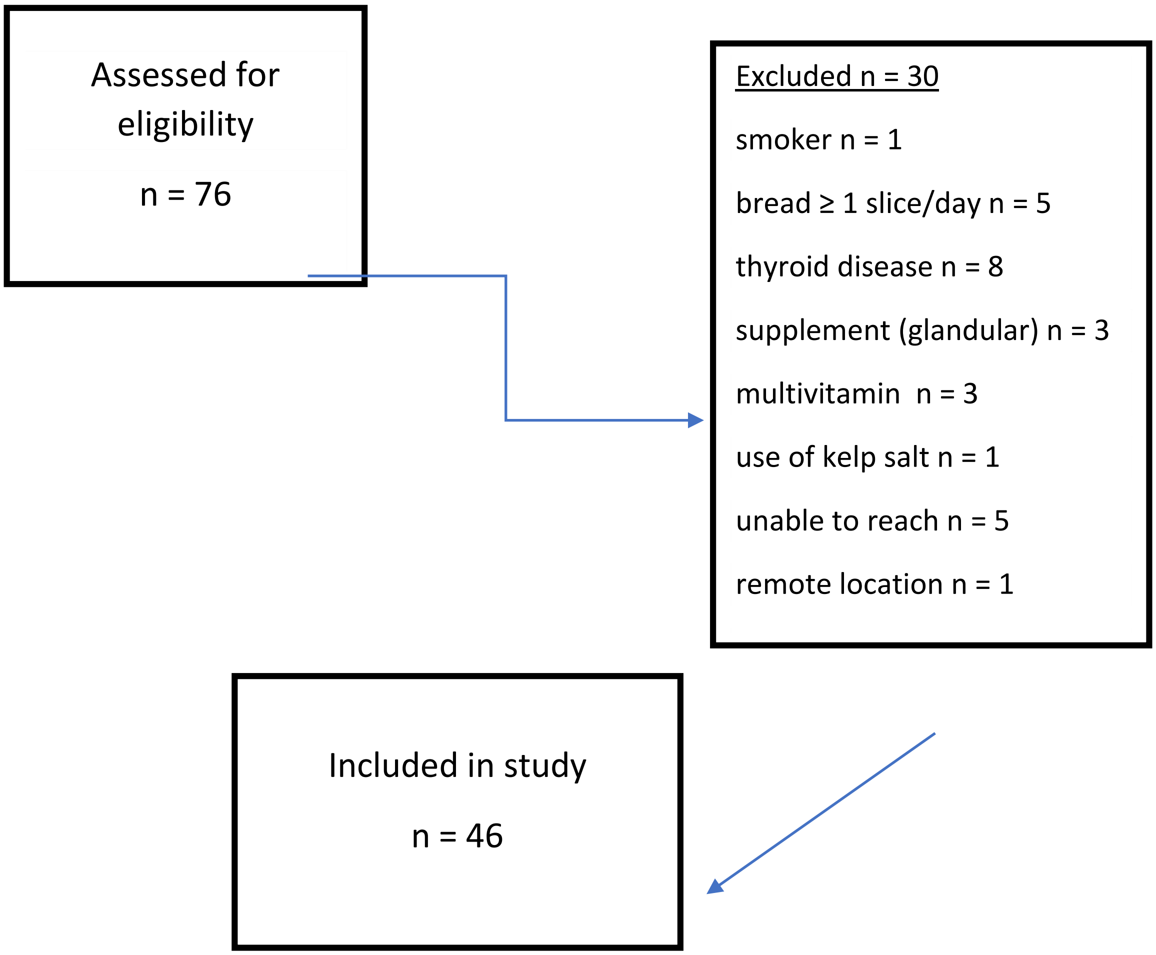
3.3 Recruitment of Participants

Posters (Appendix 1) were placed at surrounding gyms, the Massey university campus, Albany and the South Pacific College of Natural Medicine. An advertisement (Appendix 2) was circulated via email to Massey university staff and students and two posts were made via Massey University's social media (Facebook) page (Appendix 3) and one further media release via a larger research group within Auckland (Facebook) (Appendix 4). Potential participants were asked to express their interest by registration on the Massey university's research page and this was followed up with an information sheet (Appendix 5) sent via email. Subsequent to this, the researcher made contact by phone to assess eligibility using a screening questionnaire (Appendix 6) and that participants understood the requirements of the study as per the information sheet. At this time the participant burden was also outlined to each potential recruit and it was confirmed that all personal details and responses would be kept private and confidential.

3.3.1 Inclusion criteria

A total of 76 women registered for the study, 46 were entered and 30 were excluded. The reasons for exclusion were as follows; eating more than one slice of bread per day (5), smoking (1), taking thyroid medication/thyroid disease (8), other (3), taking supplements containing more than 10µg iodine (3), remote location (1), using kelp (contains iodine) salt on a daily basis (1), unable to contact or could not complete interview (5) and the use of porcine derived thyroid extract (3). One potential participant was excluded only after interest in the study prompted a visit to her General practitioner who subsequently diagnosed thyroid disease.

Figure 3.1 Flow Chart for Participant Inclusion



3.4 Ethics

The study was approved by the Massey University Human Ethics committee (MUHEC); application number 16/52 in 2017. Identification numbers (IDN) were assigned to participants at the first interview and participants were informed that records would be kept in a locked filing cabinet for five years, subsequently transferred to an official secure archive and after ten years destroyed upon the approval of the research supervisor. Data stored electronically on the principal researcher's computer was password protected at all times. Participants' written consent (Appendix 7) was obtained prior to participation in the study. Anthropometric data was collected by the principal female researcher and participants remained fully clothed throughout the collection of this information.

3.5 Development of Questionnaire

Both a food frequency questionnaire (FFQ) (Appendix 8) and a separate three day diet diary (3DDD) with full instructions (Appendix 9 & 10) were used to collect information from participants. The iodine specific food frequency questionnaire was adapted from a validated FFQ used in previous studies (Hine, Zhao, Begley, Skeaff, & Sherriff, 2018; Jorgensen, O'Leary, James, Skeaff, & Sherriff, 2016) and contained a mix of closed and open ended questions relating to 22 foods known to be contributors of iodine in the diet. As our study focused on mid-life women (40-65 years), a small number of questions were modified to suit the study sample. The three day diet diary contained detailed instructions and examples regarding completion.

3.5.1 Demographic information

The first part of the FFQ (Q1-9) sought to obtain information regarding date of birth/age, reproductive and smoking status, known thyroid disease, medication and dietary supplement use.

3.5.2 Dietary iodine intake

The second part of the FFQ was designed to collect information about the participants' main sources of dietary iodine for the previous 2 months (Appendix 8). For each food item, participants were asked about frequency and portion size for the preceding 2 months (Q11-Q51). There were seven frequency categories ranging from *2 or more times per day, once a day, 5-6 times per week, 2-4 times per week, once per week, 1-3 times per month, less than once per month and never*. A total of 22 foods known to be potential sources of iodine were identified in the FFQ and included fish, shellfish, eggs, milk, ice cream/yoghurt, cheese, eggs and iodised salt. Portion sizes were specific to the food item, i.e. nuts and seeds eaten as a snack, a choice of ½, ¼ or 1/8 cup was given and eggs; a choice of size 5, 6 or 7.

Q34-36 asked specifically about the frequency (< or > one slice per day) and type of bread products consumed. The last part of the FFQ (Q52-56) sought information about salt use, including questions relating to amount, type (iodised, uniodised, flakey, rock), frequency and occasion (in cooking or at the table).

3.5.3 Three day diet diary (3DDD)

Each participant was asked to complete and return an estimated three day diet diary (Appendix 9 & 10) to record food eaten during this period. Participants were asked to estimate portion size and to record as much information as possible regarding brand, method of cooking, and type of food. Clear instructions for the food diary was provided with examples given.

3.6 Data collection

Eligible participants visited the nutrition research unit at the Oteha rohe campus of Massey University, at Albany, Auckland for a 30-45 minute session to facilitate data collection. At this appointment an explanation was given regarding the FFQ, the 3DDD, the urine collection procedure, and the both the blood draw and anthropometric measurements were obtained.

3.6.1 Food Frequency Questionnaire (FFQ)

The iodine specific FFQ was delivered online via SurveyMonkey (www.surveymonkey.com) and participants completed this whilst at the nutrition unit using a local computer The principal researcher was available during this time to provide clarification for questions. Questions about dietary intake related to the frequency of consumption and portion size for foods known to contain iodine in the NZ diet for the 2 months prior to inclusion in the study (Skeaff & Lonsdale-Cooper, 2013). Though all of these foods contained iodine, there was a wide range of iodine concentration for the foods ranging from low to high.

3.6.2 Anthropometric Data

Participants' height was determined using a stadiometer (Seca 213). Weight was recorded to the nearest gram using bio-impedance equipment; Inbody230 Body composition analyser (Inbody Co, Seoul, Korea). BMI was calculated using weight (kg) / height (m^2). Participants were asked to remove bulky clothing and shoes prior to measurements being taken.

3.6.3 Blood samples

A blood draw of 20 ml was taken from each participants' forearm by the study's qualified phlebotomist at the research unit. The aim of taking the blood sample was to establish thyroid biomarkers however at this stage this has not been completed due to budget restraints.

3.6.4 Three day diet diary (3DDD)

Instructions and documents containing both text and images for completing the three day diet diary were provided (appendices 9 & 10). Participants were given a self-addressed and pre-stamped envelope for return of the completed diet diary.

3.6.5 Urine collection procedure

At the appointment participants were provided with all the necessary equipment to collect a 24 hour urine sample and a thorough explanation was given. Insulated cooler bags, frozen silica pads, funnel and four by one L urine collection bottles, previously labelled with the participants' identification number were provided. Clear instruction sheets were provided (Appendix 11) explaining the procedure for collection of the 24 hour urine sample which were:

- Collection day 1: participants were asked to void the first morning urine specimen into the toilet (i.e. not retain this specimen) and record the time. This was recorded as the collection start time.
- All urine voided after this time and for the next 24 hours was retained and poured into the collection bottles provided and kept cool. Participants were also instructed to retain any urine voided during a bowel motion.
- Collection day 2: the following day at the same time as the first urine void of the previous day the final and only sample for that day was collected. This was recorded as the time of completion.

Participants were requested to keep the sample cool at all times in the cooler bags provided. Upon completion and on the same day participants transported the specimens to the Food and Nutrition unit where the samples were processed without delay.

3.6.6 Urine sample processing

On receipt of the samples at the research unit the entire urine sample from each participant (i.e. either 1, 2, 3 or 4 bottles) was poured into large measuring cylinder and the total urine was measured and recorded to the nearest ml. 60ml was retained from each sample and this was then poured into 2 x 30ml sterile and labelled sample tubes with the date and participants' identification number. The remaining urine sample was discarded. Samples were then transferred to the laboratory freezer, and stored in batches at -20^0 C until analysis. All of the urine samples were sent in two batches to Hills Laboratory (Hamilton, NZ) for analysis of iodine using inductive-coupled mass spectrometry (ICP-MS). Quality control measures included analysis of blanks, analytical repeats and spiked samples in order to ensure accuracy and precision. On very run calibration standards and checks were undertaken with the limit of detection at 0.001 mg/kg for iodine. Each batch of samples was analysed together with an external reference standard (Seronorm Trace Elements Urine, SeroAs, Norway) giving a mean (SD) iodine concentration of 283 (13) µg/L (published value: 297 µg/L) with a coefficient of variance (CV) of 4.8% (n=12). The ICP-MS method is considered the gold-standard technique for measuring iodide concentration and therefore the most accurate for urinary iodine concentration (Jooste & Strydom, 2010; Vanderpas, 2006). No participants reported missing a urine sample during the 24-hour collection.

3.7 Handling of Data

Qualitative data was taken directly from the questionnaire via survey monkey online and recorded into an Excel data sheet. This data was then converted into numerical data where possible and entered into SPSS (Statistics Package for the Social Sciences) version 24 for windows data files as codes (IBM Corp, 2016). Quantitative data was recorded into an Excel data sheet, converted into a comprehensible format, coded accordingly and then entered into SPSS data files.

3.7.1 Semi-quantitative food frequency questionnaire

To enable calculation of participant total iodine intake and iodine contribution from food, data from the semi-quantitative FFQ was first entered into an Excel data sheet, and later SPSS for statistical analysis (IBM Corp, 2016). The iodine content of food, frequency of consumption and usual portion size formed the basis of these calculations. The semi-quantitative FFQ used a broad range of frequencies (day/week/month), thus to make data comprehensible, all frequencies were entered as frequency per week and numerical values were given to represent how many times per week the item was consumed (Table 3.1). Where appropriate, if the frequency from the original FFQ was described as a range then either the mid-range or lowest value was used i.e. 2-4 times per week was given a score of 3, but 2 or more times per day was given a score of 14, denoting the minimum possible frequency of twice daily. Any frequency of less than once per week was given a score of 0.

Table 3.1 Frequencies of consumption of iodine rich food from semi-quantitative FFQ

Frequency	**Numerical Score**
(from FFQ)	(entered into SPSS)
Never	0
< *Once per month*	0
One to three times per month	0
Once per week	1
Two to four times per week	3
Five to six times per week	5
Once per day	7
Two or more times per day	14

Next, an iodine factor (iodine content in µg/100gram) for each food item was determined. This was based upon information contained in the NZ food composition database, Foodfiles™, 2014 (The New Zealand Institute for Plant and Food Research, 2014). The specific values for iodine content for each food are contained in Appendix 12. Since the mandatory fortification of bread with iodised salt, the iodine content has not been determined for all commercially made bread in New Zealand. The Ministry for Primary Industries has estimated iodine concentrations for categories of bread (e.g., white, fibre white, fruited, mixed grain etc.) and these were entered into Foodworks (Ministry of Primary Industries, 2014).

In addition, for each food, the participants' usual serving size (in grams) according to frequency per week was multiplied by the pre-determined iodine factor. This allowed calculation of iodine content for each food/per participant and then a sum total of iodine content for each food for all participants (n=46). The value that was derived then represented the total iodine contribution made by each food item per week and a further calculation (division by 7) converted this to a daily score. Finally, the individual iodine intake for each participant/day was calculated by summing up the iodine content of all foods (listed in the FFQ) consumed by each participant and dividing by 7.

3.7.2 Three-day diet diary

Information from each participants' 3DDD was entered into the food composition database; Foodworks professional package version 8.0.3553 for windows (Xyris software (Australia) Pty Ltd, 2015) using the standard database for New Zealand (NZ foodfiles 2014). Each participants' nutrient and daily iodine intake was then determined by Foodworks and subsequently entered into SPSS for statistical analysis (IBM Corp, 2016).

3.7.3 Adjustment for the use of iodised salt

Participants who indicated that they used iodised salt at least once per day in the 3DDD had their total iodine intake scores adjusted by 49.3µg of iodine per day which was based upon the addition of 1g of iodised salt per day (Xyris software (Australia) Pty Ltd, 2015). This adjustment was made to both scores for the dietary intake of iodine; i.e. derived from data from the 3DDD and the FFQ.

3.7.4 Urine sample results

Iodine concentration in urine was reported as both µg/L (UIC) and µg/day. Daily iodine intake was estimated by extrapolation of 24-hour excretion based on 90% of dietary intake being excreted via urine. The excretion of iodine in a 24 hour urine sample is estimated to represent approximately 90 % of total dietary intake of iodine for the preceding 24 hours (Zimmermann, 2008).

3.8 Statistical Analysis

Statistical analysis of all data, questionnaires and urinary iodine concentration were made using SPSS Version 24 for windows (IBM Corp, 2016). Percentages and frequencies were used to describe all categorical variables and frequencies, distribution as well as the mean, median, standard deviation, percentiles (25^{th}, 75th) and ranges were determined from continuous variables. The continuous variables were tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilk statistical analysis and these were not all normally distributed. To describe the relationship between the continuous variables for non-parametric data was therefore made using

Spearman's rank order correlation, in particular UIC, 24-hour iodine excretion, and iodine intake estimated from the FFQ, 24-hour iodine excretion and the 3DDD. The median UIC was compared with the WHO/UNICEF/ICCIDD criteria to determine the iodine status of this study group. Reporting of statistical significance for all data was set at a level of $P < 0.05$.

4 Results

4.1 Characteristics of Participants

The participants (n=46) were all mid-life women between the age of 40 and 63 years (mean age: 50.1 yrs.), and lived in Auckland. All participants avoided bread or consumed less than one slice per day, and mean consumption was 0.3 slices per day.

The participants' mean body mass index (BMI) was 27.3 and the mean height and weight were 163.8cm and 73.6kg respectively. No information regarding level of education, ethnicity, employment or living situation were obtained as they were not the purpose of this study. One participant declined the measurement of weight. Participant characteristics are shown in table 4.1 below.

Table 4.1 Participant Characteristics

Age groups	**n**	**Percentage of total (%)**
40-44	9	20
45-49	13	28
50-54	11	24
55-59	8	17
60-65	5	11
BMI (kg/m2)		
18-25	21	46
25-30	15	33
≥ 30	9	20
Missing	1	-

4.2 Dietary patterns, salt use and type

4.2.1 Food frequency questionnaire

Foods included in the FFQ were all known to contribute iodine in the diet but the iodine content of each food is known to vary. Of these foods, the food least frequently consumed was soy milk, with 96 % of respondents either not consuming soy milk at all or less than once per week. Similarly, 94 % of respondents consumed no tofu or less than once per week. Better sources of iodine but consumed infrequently (less than once per week or not at all) were shellfish (78 %) and sushi (85 %) and almost a third (28 %) of respondents reported eating no fish at all during the 2 months prior. The pattern for foods least consumed are outlined in table 4.2 below.

Table 4.2 Foods least frequently consumed from FFQ information (n=46)

Foods least consumed	nil or < once per week)
Soy milk	96 %
Tofu	94 %
Snack bars	93.5 %
Muffins	89 %
Sausages	89 %
Beer	89 %
Sushi	85 %
Shellfish	78 %
Cake	74 %

The most frequently consumed foods from the iodine specific FFQ were fruit and milk with 59 % of respondents reporting eating one or more serves per day, followed by nuts and seeds (41 %) and leafy green vegetables (30 %). Almost a quarter (24 %) of the respondents ate ice cream and/or yoghurt one or more times per day. Though only 6.5 % of participants reported consuming eggs one or more times per day, over half (52 %) reported eating eggs, a rich source of iodine three times per week. Table 4.3 outlines the foods most frequently consumed.

Table 4.3 Foods most frequently consumed from FFQ information (n=46)

Food	**≥ 1 serve/day**
Fruit	59 %
Milk	59 %
Nuts/Seeds	41 %
Leafy green vegetables	30 %
Ice cream/yoghurt	24 %
Cheese	15 %
Meat (beef/lamb/pork)	8.6 %
Eggs	6.5 %
Poultry	2.2 %

4.2.1.1 Use of salt

Participants were asked about their use of salt within the FFQ; i.e. type (iodised, un-iodised, rock or flakey), usage and serving size and the responses given are shown in table 4.4 below. Response to the use of iodised salt in the FFQ was low, with only 6 of the 46 respondents (13%) definitively reporting the use of iodised salt, one participant did not use salt at all and another reported only using uniodised flakey salt. Rock salt was used most with over half (54%) of the participants reporting using this type of salt. Overall responses to the questions about frequency of iodised salt use however were considered ambiguous. A number of respondents answered yes to the "use of iodised salt" but in the subsequent question; "how often do you use iodised salt", they responded with "never", similarly where respondents had indicated the "use of rock salt", in the subsequent question, asking "how often do you use iodised salt", they responded "yes" to the use of iodised salt. This meant that an additional 10 participants may or may not have used iodised salt, or used both on daily basis. However, the use of iodised salt on a daily basis could only be considered accurate for 6 of the participants. For this reason, the use of iodised salt on a daily basis was only included for a total of 6 participants.

Table 4.4 Salt use according to type and frequency

Total (n)	Salt type	Frequency (n)	Percentage (%)
46	No salt	1	2
46	Iodised salt	6*	13
46	Rock salt	25	54
46	Uniodised salt	3	7
46	Flakey salt	1	2
46	Unsure*	10	22

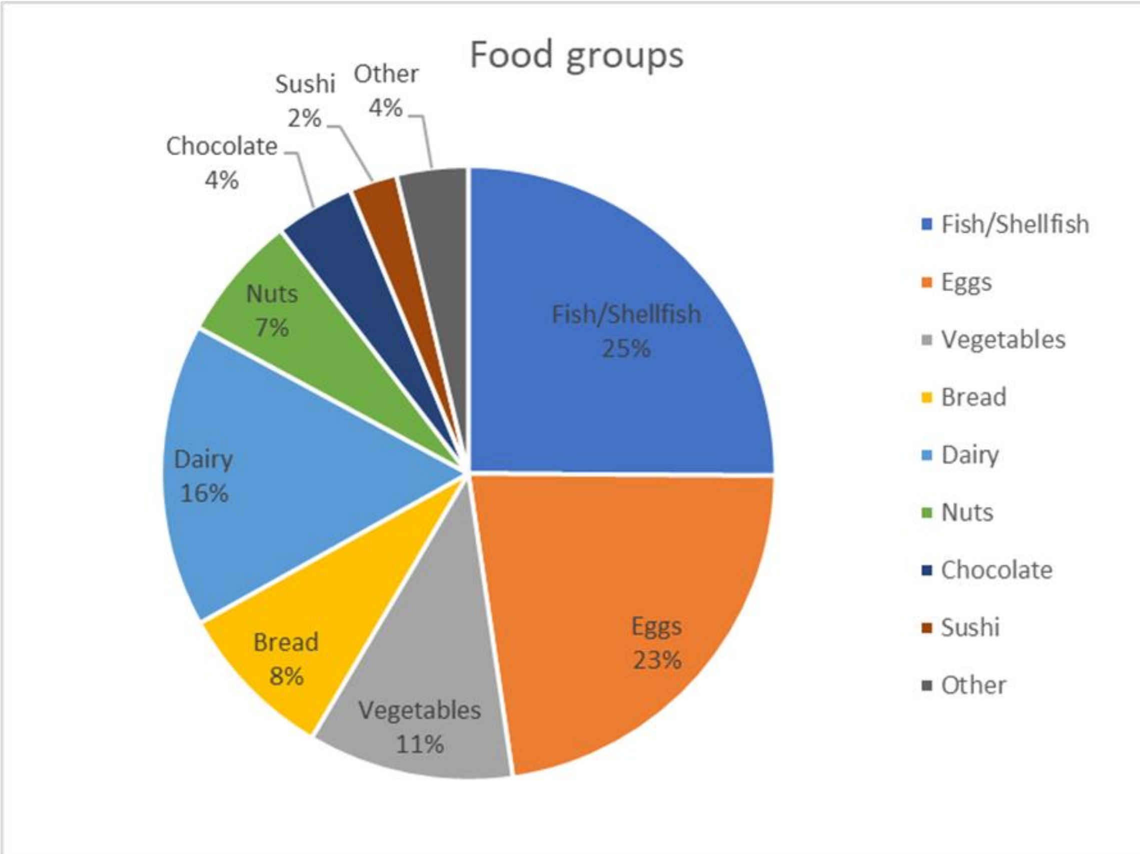
*** Responses to the use of iodised salt use were considered ambiguous in 10 participants**

4.2.2 Foods as contributors to dietary iodine intake

Analysis of the FFQ showed fish and shellfish to contribute the most iodine in the diet of the women studied, providing 24 %, almost one quarter of daily intake, with fish alone contributing the most at 18 % and shellfish somewhat less at 6 % of total daily intake (Figure 4.1). Eggs contributed almost as much to the diet as the combined fish/shellfish group at an estimated 23 % of the daily iodine intake. Though, the consumption of eggs on a daily basis was found to be low (6.5 %), over half (52 %) of the participants recorded eating eggs three or more times per week.

Though fruit and milk were reported as the most frequently consumed of all foods surveyed, fruit did not contribute significantly to total iodine intake, as these are poor sources of iodine. When milk, cheese, yoghurt and ice cream were combined as one food group; i.e. dairy, as in many other similar studies, then their contribution to total iodine intake ranked third highest behind the fish/shellfish group and eggs. As expected, bread consumption was low and this ranked 5th at 8 % after dark green leafy vegetables at 11 % for contribution to iodine intake. Other foods including soy milk, tofu, meat, poultry, cake, muffins, fruit, and beer were found to provide negligible amounts of iodine to the overall intake so for this reason where combined as one group.

Figure 4.1 Contribution to iodine intake by food from the FFQ*



**** dairy includes yoghurt, ice cream, cheese and milk and the other group includes meat, poultry, snack bars, cake, beer, fruit, tofu, soy milk, cake and muffins which have been grouped together due to their negligible contribution to overall iodine intake.***

4.3 Estimate of dietary iodine intake

Dietary iodine intake (µg/day) was estimated using three methods, measurement of iodine excretion in 24-hour urine sample (UIE), and estimate of iodine intake based on responses to the iodine specific semi-quantitative FFQ matched to values from the NZ food composition database and also the three-day diet diary.

4.3.1 Estimate of iodine intake from food frequency questionnaire

Based on data from the FFQ, the median (25^{th}, 75^{th} percentiles) intake of iodine for all participants was estimated to be 47 (33, 68) µg/day (Table 4.6). The majority (91.3 %) of all participants' iodine intake was estimated to be below the EAR of 100 µg/day. None of the participants' estimated iodine intake achieved the RDI of 150 µg/day and only a minority (8.7 %) had values between the EAR and RDI of between 100 and 149 µg/day (Ministry of Health & National Health and Medical Research Council, 2006).

As expected, responses from the FFQ showed that all participants reported eating bread less than once daily, however when analysed further the participants either ate bread three times per week (37 %), once weekly (21.7 %) or not at all or less than once per week (34.8 %) as shown in table 4.5. Thus mean consumption of bread was 0.3 slices per day. As previously outlined an auto correction was made for the iodised salt content of any bread (excluding homemade or organic) consumption and recorded in the 3DDD.

Table 4.5 Frequency of consumption of iodine fortified bread per week

Participant frequency of bread serves/week	n	Percentage (%)
Nil to once	16	34.8
Once	10	21.7
Three	17	37
Four	1	2.2
Five	2	4.3
Total	46	100

4.3.2 Estimate of iodine intake from three-day diet diary (3DDD)

Based on data from the 3DDD the median (25^{th}, 75^{th} percentiles) iodine intake was estimated to be 63 (46, 82) µg/day (Table 4.6). One diet diary was lost in transit and not found, therefore data for 45 of the 46 participants only, was available and included. It was noted that one participant consumed a concentrated protein shake containing 33µg of iodine per/day which would have added to their overall iodine intake. None of the participants were taking multivitamin or other supplements containing iodine and none reported the use of kelp or kelp salt in their diet. There was no evidence of large intakes of goitrogenous (inhibitors of iodine uptake by the thyroid) foods such as cassava or cruciferous vegetables within the 3DDD information supplied by the participants.

For all the participants who had recorded the daily use of iodised salt clearly in the FFQ a correction was made to their total iodine score for both the FFQ and the 3DDD (and entered into Foodworks). This meant that 49.3 µg of iodine per day (based on 1g of salt) was added to a total of six participants' total iodine intake.

4.3.3 Estimate of iodine intake from UIE

Urinary iodine excretion from a 24-hour urine sample can be used to estimate daily iodine intake due to approximately 90 % of iodine intake being excreted within this same period the median urinary iodine excretion (25^{th}, 75^{th} percentiles) in this study was 108 (74, 154) µg/day (Table 4.6). Therefore, based on this, the estimated median iodine intake was 120 (82, 171) µg/day, below the RDI of 150 µg/day, with 41 % also below the EAR of 100 µg/day and suggesting dietary inadequacy.

4.4 Iodine status

No participants reported missing the collection of any of the urine samples within the 24-hour period and all samples were returned on the final collection day in the cooler bags provided. The mean urine volume collected was 2.18 (SD = 0.81) L.

The median UIC (25th, 75th percentiles) of all participants (aged 40-63 years) was 49 (34.8, 78) µg/l which indicates iodine deficiency according to the WHO/UNICEF/ICCIDD criteria and still indicates iodine deficiency when based on the alternative values for adults of 60-70 µg/l as recommended by Zimmermann (Zimmermann & Andersson, 2012). The WHO/UNICEF/ICCIDD recommends that no more than 20 % of the population has a UIC of <50µg/. This study found 50 % of participants to have a UIC <50µg/l.

Table 4.6 Urinary iodine excretion and estimated daily iodine intake

Biomarker	**Assessment method**	**Median (25^{th,} 75th percentiles)**	**Mean ± SD**
Dietary Iodine Intake (µg/day)	Estimated from UIE	120 (82, 171)	128 ± 62
	Estimated from 3DDD (including iodised salt)	63 (46, 82)	69 ± 33
	Estimated from FFQ (including iodised salt)	47 (33, 68)	53 ± 27
24-hour urinary Iodine samples	UIC (µg/l)	49 (35, 78)	58 ± 30
	UIE (µg/day)	108 (74, 154)	115 ± 56

4.4.1 Associations between iodine variables

There were no correlations found when comparing iodine intake as estimated from the iodine specific FFQ and the 24-hour UIE and also none found between the 3DDD and the UIE. However, a moderate correlation (0.423, p=0.04, n= 45) was found between iodine intake as assessed via the FFQ and iodine intake assessed via the 3DDD. It is possible that the ambiguity in responses to the questions about iodised salt use in the FFQ has contributed to the low association between UIE and the 3DDD and FFQ.

5 Discussion

5.1 Introduction

The primary aim of this study was to assess iodine status in mid-life women who avoided iodine fortified bread, following the mandatory fortification of bread with iodised salt in NZ in 2009. Despite the implementation of mandatory fortification of bread with iodised salt this group of mid-life women were found to be iodine deficient according to both WHO/ICCIDD/UNICEF and EAR cut point definitions for iodine sufficiency. Also, even if using the more conservative cut-off levels as suggested by Zimmermann (2012) to reflect the greater urine volume of adults, the women participants of this study would still be classified as iodine deficient (Zimmermann & Andersson, 2012).

5.2 Participants' demographic background

The participants were all women aged between 46-63 years and were from the greater Auckland region, mostly the North Shore who all avoided the consumption of bread on a daily basis. The women did not smoke, therefore it was not likely that this would have been a significant cause for concern in terms of effect from goitrogenic substances such as thiocyanate, however as an analysis of other goitrogenic foods was not made any larger effect from this source is not known (Aggarwal, Keluskar, Goyal, & Dahiya, 2013). If participants ate large quantities of cruciferous vegetables and/or cassava, known to be goitrogenic then this could further impact poor iodine status however this was not evident from the information contained within the 3DDD (Braganza et al., 2015; Gaitan, 1990).

As no information regarding ethnicity was gathered an analysis of iodine status by ethnicity cannot be determined. This was a small sample of mid-life women (n=46) recruited via associations with tertiary institutions and mostly from the North Shore of Auckland which is considered a high demographic area. For these reasons the results cannot be generalized to all New Zealand women of differing ethnicity, age, socio-economic status or education level.

5.3 Iodine status and intake of participants

5.3.1 Iodine status determined by urinary iodine excretion

According to the most recent TDS (2016) the mandatory fortification of bread has been shown to have improved iodine levels within the general population (Ministry of Primary Industries, 2016). However, this is in contrast to the results from this study of mid-life women who avoid bread. According to the international criteria for assessing iodine deficiency (WHO/UNICEF/ICCIDD) this group of mid-life women have been defined as iodine deficient (WHO/UNICEF/ICCIDD, 2008). Mandatory fortification therefore has not benefited the iodine intake of the women in this study, who consume little or no iodine fortified bread, nor will it be able to assist many other low or nil consumers of iodine fortified bread. This has been shown in this small sample of women who actively avoid bread. However, this might not be a concern if regular consumption of iodine rich foods, such as fish and seafood, had occurred in these low bread consumers.

According to the international WHO criteria mild deficiency occurs when the median UIC of a population of school age children falls within the range of 50-99 µg/l and moderate deficiency when the median UIC falls within the range of 20-49 µg/l (WHO/UNICEF/ICCIDD., 2008). The median UIC in this study of 46 participants was 49 (35, 78.0) µg/l which indicates deficiency. This would be on the borderline of moderate deficiency in children, but as the cut off for mild deficiency is most likely lower for adults this would still represent mild deficiency for this population.

Also according to WHO/UNICEF/ICCIDD (2008), the target levels for iodine sufficiency within an adult population are median UIC >100 µg/l in spot urine samples, as long as no more than 20 % of samples are below 50 µg/l. However, the results from this study, found 50 % of the participants to have a UIC <50µg/l.

The UIC found in this study is even lower than a previous study which found the median UIC to be 57 µg/l (39 % < 50 µg/l) amongst a larger group (n=97) of North Island women post fortification. This is to be expected as these women reported consuming an average of 1.8 serves of bread per day whereas mean bread consumption in this study was only 0.3 serves per day. Brough et al,

(2017) posed concern at that time for the effectiveness of fortification among low consumers of bread, calling for further research (Brough et al., 2017).

Another NZ study, based in both Dunedin and Wellington reported the median UIC of 69 (42, 105) µg/l (with 32 % < 50 µg/l) among the 59 mid-life (45-64 years) women included, again indicating deficiency (Edmonds et al., 2016). However, unlike the present study neither of these studies limited participation to include only low or nil bread consumers. The median bread intake in the study by Edmonds et al (2016) was two slices per day. Both studies were conducted post mandatory fortification of bread with iodine.

Zimmerman and Andersson propose that the current recommendations for the UIC cut-off of 100 µg/l in adults is too high, as these are based on the typical urine volume of school aged children of 1 L. They suggest a UIC cut-off of 60-70 µg/l be used to reflect the greater urine volume typical of adults. However, even if these more conservative cut-off values were used for the current population, the median UIC found in this study of 49 µg/l still indicates deficiency (Zimmermann & Andersson, 2012).

New Zealand women who avoid bread are not able to reap the benefits of additional iodine in their diet as intended by the implementation of mandatory fortification and this has resulted in concerning low urine iodine concentrations amongst the women in this study. This situation continues to be due mainly to poor food sources of iodine within New Zealand.

In this study the median iodine intake based on 24-hour urine iodine excretion was 120 (82, 171) µg/day, which is below the RDI of 150 µg/d. Furthermore, 41 % of the participants were found to have intakes (based on UIE) below the EAR of 100 µg/day (Ministry of Health & National Health and Medical Research Council, 2006). Thus, optimal intakes were not shown to be achieved among the majority of participants when assessing iodine intake using this method.

In comparable (gender and age), post fortification studies to this present study, Brough et al (2017) reported median UIE of 124 µg/day and median iodine intake based upon this to be 138 µg/day (with 25% below the EAR) and the Dunedin and Wellington based study reported median UIE of 126 µg/day and median iodine intake of 140 µg/day (Edmonds et al., 2016). However neither of these studies restricted participation to include only low bread consumers such as this study, which found median iodine intake of 120 µg/day, some 18-20µg/day less than these comparable studies and reflecting an inadequate dietary intake.

5.3.2 Iodine intake as estimated from the FFQ

Based on data from the FFQ, the estimated median (25th, 75th percentiles) intake of iodine for all participants was found to be 47 (33, 68) µg/day. Based on the FFQ data the majority (91 %) of participants were estimated to have an iodine intake below the estimated average requirement (EAR) of 100 µg/day. Only a small minority (9 %) achieved the EAR values of between 100 and 149 µg/day when iodine intake was assessed using this method and none achieved the RDI of 150 µg/day (Ministry of Health & National Health and Medical Research Council, 2006).

As it was considered that there was ambiguity in responses to the questions in the FFQ about the use of iodised salt, the addition of 49.3 µg/day to both scores from the FFQ and 3DDD was included only for the 6 participants for whom it was clear that they used iodised salt on a daily basis. If the responses to the use of iodised salt in the FFQ had been less ambiguous then potentially 16, rather than 6 participants may have had the addition of 49.3 µg/day added to their scores and this result would have been higher.

The estimated median intake derived from FFQ data of 47 µg/d found in this study is very different to that found among women in the aforementioned Dunedin/Wellington study of 126 µg/day based on an FFQ including iodised salt (Edmonds et al., 2016). Unlike the present study which found fish/shellfish to be the most significant source of iodine in the diet, Edmonds et al (2016) found bread to be the main contributor to iodine intake, contributing 47 % to the total daily iodine intake, amounting to 35 µg/day, thus suggesting this to be a significant source in the diet. The large variation between the estimated median iodine intake between the two studies could also be due to the use of iodised salt, though difficult to measure with accuracy, 74 % of participants in the Edmonds et al (2016) study reported using iodised salt. Only 13 % clearly reported using iodised salt in the present study.

5.3.3 Iodine as estimated from the 3DDD

The median (25^{th}, 75^{th} percentiles) iodine intake estimated from the 3DDD was 63 (46, 82) µg/d (Table 4.6), which though higher than the 47 µg/d estimated from the FFQ, was still low. A moderate correlation (r = 0.423, p =0.004) was found between dietary iodine intake as estimated from the 3DDD and iodine intake estimated from the FFQ which is not surprising as they were both reporting data for foods rich in iodine. As discussed, ambiguity in responses to questions about iodised salt use may have lowered the score for both the 3DDD and the FFQ.

Though not as low as the findings from this study, the median iodine intake (25^{th}, 75^{th} percentiles) as assessed via 3DDD in the study of post-menopausal women from the North Island of New Zealand, was also found to be low at 79 (55, 97) µg/d, however this study excluded the use of iodised salt, thus iodine intakes in the current study were much lower than this previous study (Brough et al., 2017).

Another explanation for the difference between iodine intake as assessed via the 3DDD in this study and that of Brough et al (2017) could be due to the disparity in amount of bread eaten by the participants. The mean serves of bread per day was 1.8 in the study by Brough et al (2017) whereas this study it was, as expected very low at 0.3 serves per day. Brough et al (2017) did not include the use of iodised salt, so after adjustment in this study to reflect no iodised salt use, the difference between intakes of bread of 1.5 slices per day between the two studies could explain somewhat the difference between the median iodine intakes reported by both studies.

The NZTDS (2009) prior to fortification reported a mean dietary intake, estimated from simulated diets, of iodine of 63 µg/d for females 25 years+ and post fortification 100 µg/d (not including the use of iodised salt) and it is most likely that this is as a result of the mandatory fortification of bread with iodised salt (Ministry of Primary Industries, 2016; Vannoort & Thomson, 2009). The median iodine intake in this study estimated from the 3DDD was 63 µg/d which is the same as that reported for adult women in the NZTDS prior to fortification.

Thus, it was not unexpected that the dietary intake of iodine among the participants of this study was found to be low as NZ has a history of low dietary intake and this was the major reason for the introduction of mandatory fortification of bread with iodised salt. However, this particular vehicle of fortification is unable to improve the intake of low consumers of bread and the findings of this study suggest this also.

There was a marked difference between the median dietary intake estimated using data from the FFQ (47 µg/d) and the 3DDD (63 µg/d) with the median dietary intake from the UIE (120 µg/d). Low iodine intake amongst the women was expected, knowing they were low consumers of bread, however the large variation between the results from both dietary assessment methods (FFQ & 3DDD) with that obtained from UIE was not expected. Reasons for this can only be conjectured, such as inaccurate reporting of iodised salt use and inaccuracy of dietary assessment methods.

Inaccurate reporting of iodised salt use is common and the ambiguity in responses to the questions in the FFQ in this study was no exception. This may have contributed to the low association found between iodine intake as assessed by the three methods, diet diary, FFQ and UIE. It is well recognized that dietary assessment methods are imperfect, prone to recall bias and under-reporting by participants, as well as being subject to quantification errors. Dietary iodine intake is also highly variable. Though biochemical indicators such as UIE may be deemed more accurate for assessing dietary intake of iodine, unlike dietary assessment they are only representative of that particular day's intake whereas dietary records are taken over a longer period of time. Urinary iodine excretion is also subject to day to day variations. Neither assessment method is indicative of actual body stores. Thus both methods have limitations.

5.4 Key contributors to dietary intake of iodine

The estimation of dietary iodine intake from analysis of the FFQ, showed that the fish and shellfish group was the major source (24%) of iodine, contributing 18 % and 6 % respectively despite only 22 % of participants reporting regular consumption of shellfish. Fish and shellfish are both rich sources of iodine, being of marine origin, and even in small quantities are a valuable source of iodine in the diet. Edmonds et al (2016) found the fish and shellfish group, when estimated from the FFQ, only contributed 6 % to total iodine intake and ranked only 4th highest. Bread products were the major contributor to total iodine intake in that study at 47 % (Edmonds et al., 2016). This is in contrast to this study where bread products offered minimal contribution to total iodine intake at 8 %. However, this was expected as mean bread consumption was less than one slice per day.

Eggs were the second major contributor to total iodine intake in this study, with over half of the participants consuming eggs frequently, three or more times per week. Results from this study show that eggs are a valuable source of iodine in the diet of these women. This is unlike the findings of Edmonds et al (2016) who found eggs contributed less to total iodine intake, ranking third highest for overall contribution instead of second, as in this study.

Fruit though consumed most frequently in this study, did not contribute significantly to overall dietary iodine intake and this is not surprising as it is not a rich source of iodine. Similarly, milk alone was not a major contributor to overall intake of iodine either. However, milk together with cheese, yoghurt and ice cream, (as dairy), ranked third after fish/shellfish and eggs, representing 16 % of total iodine intake. Dairy intake in the Edmonds et al (2016) study was higher than in this study at 23 %, behind the large contribution (47 %) made by bread (Edmonds et al., 2016).

Other foods including dark green leafy vegetables, soy milk, tofu, meat, poultry, cake, muffins, fruit, and beer were found to provide negligible amounts of iodine to the overall intake and contribution to total dietary iodine intake by food source is also shown in figure 4.1.

The major contributors to dietary intake of iodine for the participants of this study were, fish/shellfish, eggs, and the dairy group (milk, yoghurt, cheese and ice cream) and these foods are important sources of iodine for these women who avoid bread. This is unlike the findings from the most recent TDS (2016) that showed cereal-grain based foods, i.e. bread now contributes the most iodine in the diet of NZ adults (Ministry of Primary Industries, 2016). Previously, in 2009, prior to the fortification of bread with iodised salt, the NZTDS found dairy products to be the largest contributor of iodine in the NZ diet., followed by “eggs, mussels, fresh fish and oysters” (26 %), takeaways (15 %) and grains (11 %) (Vannoort & Thomson, 2009).

However, in the most recent NZTDS (2016), dairy products ranked only 3rd for contribution to total iodine intake after bread, “the main source”, then the “meat, chicken, fish, and eggs” group (Ministry of Primary Industries, 2016). As some of these groups within the NZTDS contain multiple foods, i.e. “eggs, mussels, fresh fish and oysters” in the 2009 study, it is difficult to make direct comparisons between all of the food groups in this study and those of the TDS of different years (Vannoort & Thomson, 2009).

The NZTDS does not include the use of iodised salt within their simulated diets, unlike this study which made an allowance of 1 g of salt (49.3 µg/day) for each person who clearly indicated they used iodised salt on a daily basis.

5.5 Factors contributing to low iodine intake and urinary iodine excretion

NZ soils contain low amounts of iodine. This means that the food supply also contains low concentrations and iodine deficiency has been found amongst the population both in the past and as reported (Brough et al., 2017; Edmonds et al., 2016; Mann & Aitken, 2003; Thomson et al., 2008; Thomson et al., 1997; Thomson, Woodruffe, et al., 2001). This decline is also consistent with the decline and removal of iodine based cleansers as sanitizers by the dairy industry (Skeaff et al., 2003; Sutcliffe, 1990).

Changes in eating habits have also contributed to low dietary intake and status of the NZ population (Sutcliffe, 1990; Thomson, 2004). Convenience foods, takeaways and restaurant meals though likely to contain considerable salt, often use uniodised salt and the consumption of these foods has increased (Thomson et al., 2008). Lack of public awareness of the importance of iodised salt and its inherent lack in convenience foods is a significant problem (Charlton et al., 2010).

Conflict about public health recommendations for reducing salt intake throughout the world, including NZ, is also a factor contributing to low iodine intake. The potential for increased risk of cardiovascular disease from salt intake conflicts with policies that enforce the use of salt as a vehicle for iodine in the diet (Charlton et al., 2010; Tayie & Jourdan, 2010). Thus public health messages for salt reduction have reduced exposure to iodine in the diet from this source. The use of non-iodised salts is another contributing factor for low iodine intake (Charlton et al., 2010; Yeatman et al., 2010).

However, from the results of this study, it can be assumed that avoiding bread that has been fortified with iodine is also contributing to low iodine intake as the participants are unable to benefit from fortification if it is contained in the very food they avoid. Iodine intakes in the current study are similar to that found in women prior to fortification (Vannoort & Thomson, 2009).

5.6 Limitations of the study

5.6.1 Urinary iodine excretion (UIE)

The collection of a 24-hour urine sample is somewhat burdensome for the participant which can result in non-compliance, however the participants of this study were compliant in completion of this task. This study could not determine the individual iodine status of participants as this would have required the collection of ten 24 hour urine samples from each individual to assess with precision of 20 % recommended by Konig et al (König et al., 2011). Though this would have allowed a better estimate of typical iodine intake, both budget resource constraints and participant burden prohibited this. However, a strength of this study is that 24 hour urine collections are considered to be better than spot sample testing as it can reduce the issue of diurnal variation and hydration that has been shown to occur with spot sample collections of urine (Vejbjerg et al., 2009).

Iodine concentration as found in urinary excretion is influenced by both hydration and dietary intake of iodine therefore variability inevitably results, also iodine concentration measured this way does not represent thyroid function nor is it a measure of iodine stores within the thyroid (Vejbjerg et al., 2009).

5.6.2 Food Frequency Questionnaire (FFQ)

Assessment of iodine intake could not be deemed completely accurate but rather representative of dietary iodine intake. There is the potential for misreporting or inaccuracy with any method of dietary assessment due to respondent error and/or burden and this study would also be subject to this potential error when surveying free living individuals (Thompson & Subar, 2008).

The FFQ in this study did not include all possible foods within the NZ diet, nor did it include a survey of the participants' entire diet. However the FFQ was intended only to survey foods determined to be the most concentrated sources of iodine within the NZ diet (Hine et al., 2018). Inclusion of other foods known to be less concentrated sources of iodine would have increased respondent burden and only added noise to the data analysis and result.

Any dietary assessment method relies upon values determined within food composition databases which may not provide reliable estimation of iodine values, particularly if these are not updated regularly, or use values from other countries such as the United Kingdom or America which are not applicable or appropriate to NZ. Iodine content is naturally highly variable between different foods, which is another difficulty with accurate estimation of iodine content. There is some degree of uncertainty with processed foods also as to whether they contain iodised or uniodised salt so this represents further potential for inaccuracy (Rohner et al., 2014).

Ice cream and yoghurt were grouped together as one food as part of the FFQ which could be perceived to be limiting if the aim of the study was assessing other than iodine intake. For the purposes of this study it was not of significance to identify these two foods separately for assessing their contribution to iodine intake.

Upon analysis of the participants' responses to the FFQ, it appeared that some participants may not have fully comprehended the difference between iodised salt and rock salt when answering questions. This highlighted a limitation of the study but further demonstrates the difficulty of assessing salt intake, both amount and frequency as often discussed amongst other studies quantifying iodine intake among populations (Rohner et al., 2014).

More participants responded in the FFQ that they used iodised salt than that recorded in the 3DDD and there was some ambiguity regarding answers to questions about iodised salt use. Some participants indicated that they used iodised salt but not on a daily basis therefore this was not included. Therefore, the results from this study should not be relied upon to make meaningful conclusions about iodised salt usage.

5.6.3 Dietary assessment

Results from this study cannot be generalized to the NZ population as a whole as the characteristics of the sample group were somewhat homogenous. This was an opportunistic sample recruited from the local area. It was not the aim of this study to assess iodine status or intake of other age groups and gender as these groups had been studied elsewhere (Ministry of Primary Industries, 2016).

Also, the recruitment advertisements may have attracted women who were more likely to respond to messages about health or diet, and/or be of a higher educational or socio-economic status. These factors may have affected the food choices of these women and as a result their food sources of iodine, i.e. fish/shellfish may be eaten more frequently by these women than those from a different background. In consideration therefore, it would be ideal for future research to include a larger sample size from a more diverse background and wider geographic area of New Zealand.

Another limitation of assessment of dietary intake of iodine from the 3DDD in this study was due to the ambiguity in responses to questions about iodised salt use in the FFQ therefore, as previously discussed, this could have lowered both scores from the 3DDD and the FFQ. It was not possible therefore to determine the accuracy of iodised salt use for 10 of the 46 participants.

5.6.4 Further biomarkers

To be able to have other biomarkers of thyroid function as they relate to iodine, such as T3, T4, TSH, thyroid antibodies, thyroglobulin and thyroglobulin antibodies to support findings was the intention of this study, and blood draws were taken, however funding constraints unfortunately prohibited both their analysis and inclusion.

Despite these limitations, the results of this study show similar patterns to comparable studies which assessed iodine intake within the New Zealand population.

6 Conclusion and Recommendations

6.1 Conclusion

Edmonds et al (2016) found bread fortified with iodine to be the major contributor to iodine intake amongst its study population of 301 adults living in NZ and that iodine adequacy was likely being achieved at that time, some 3 years after the introduction of mandatory fortification. However, the current study found suboptimal levels of iodine intake among the participants with a median iodine intake of 120 (82, 171) µg/day, well below the RDI of 150 µg/d, and one third of the participants had intakes below the EAR of 100 µg/day (Ministry of Health & National Health and Medical Research Council, 2006).

The finding of low iodine intake in this study was not surprising and was somewhat expected due to the majority of women not consuming iodine fortified bread on a regular basis (less than once per day) thus unable to reap the benefit from this source of mandatory fortification of iodine in their diet. This low level of iodine intake is the same as that found amongst adult women in the TDS prior to fortification with iodised salt (Vannoort & Thomson, 2009). As expected, the median UIC was lower than that shown in previous studies of midlife women who were consuming more bread.

The main foods contributing to iodine intake in this study were fish/shellfish group, followed by eggs, and the dairy group (milk, yoghurt & ice cream, cheese) and it was concerning that only six participants recorded using iodised salt on a daily basis. Persons avoiding iodine fortified bread therefore would be recommended to improve their knowledge of iodine rich food sources and correspondingly increase their intake of iodine rich foods, such as eggs, seafood and fish and consume all more regularly. In addition, they should include the use of iodised salt instead of other non-iodised salts. Despite not having an in-depth qualitative assessment of the participants' knowledge and perception of the different types of salt, it became apparent in discussion that there was poor understanding of the iodine levels in different types of salt and this could be a potential area for increasing iodine intake and awareness.

Overall, the findings from this study emphasize the need for continued monitoring of the iodine status of the NZ population. It also highlights the need for continued evaluation of the iodine fortification programme as it affects the whole population including at-risk groups such as those who choose to avoid the very vehicle that is fortified, in this case bread, and subgroups such as older women who are also at increased risk of iodine deficiency and iodine deficiency related thyroid disease.

6.2 Recommendations

The median total iodine intake of participants in this study using estimations from both UIE, 3DDD and FFQ has been found inadequate. This is in contrast to findings from the latest total diet study which estimated an improvement in the median iodine intake of the NZ population (Ministry of Primary Industries, 2016). However, as previously discussed the NZTDS uses a simulated diet for analysis of nutrient content which is not based upon the diet of mid-life women or an older person of either gender, nor does it base its nutrient analysis upon the diet of sub groups of the NZ population who exclude bread fortified with iodine.

It is well recognized that the NZ population is aging and that this group will soon comprise a larger proportion of the population and correspondingly place a greater burden upon health resources. For this reason, public awareness of the issue of iodine intake as it relates specifically to the older person living in New Zealand and those with diets that exclude major food groups such as bread subject to fortification urgently needs attention, emphasis and addressing.

Another concern regarding iodine deficiency and thyroid dysfunction is due to its association with other disease that is known to disproportionately affect the ageing person, such as cardiovascular disease and osteoporosis. The progression of both diseases may be accelerated in persons at mid-life and beyond if thyroid function is compromised due to inadequate iodine intake. Women, in particular, with advanced age and change in hormonal status, are also more likely to experience thyroid dysfunction than men, reinforcing the timely importance of this target group for further research (del Ghianda et al., 2014).

It is highly recommended therefore that further studies involving larger groups of mid-life and older women to assess other biomarkers of thyroid function, cardiovascular and bone health and iodine status is undertaken. In addition, further research relating to public perception and knowledge about iodine and the available sources of iodine and the importance within the NZ diet is recommended.

Overall, this study shows that the iodine fortification programme must be continually monitored and evaluated for its effectiveness in achieving its primary aim of improving the iodine status of the whole population. At-risk groups must also be considered within this paradigm. It cannot be assumed that all people will eat bread or in sufficient quantity to effectively raise their iodine status.

7 References

Aggarwal, A., Keluskar, V., Goyal, R., & Dahiya, P. (2013). Salivary thiocyanate: a biochemical indicator of cigarette smoking in adolescents. *Oral Health Prev Dent, 11*(3), 221-227. doi:10.3290/j.ohpd.a30169

Andersson, M., de Benoist, B., & Rogers, L. (2010). Epidemiology of iodine deficiency: Salt iodisation and iodine status. *Best Practice & Research Clinical Endocrinology & Metabolism, 24*(1), 1-11. http://dx.doi.org/10.1016/j.beem.2009.08.005

Andersson, M., Karumbunathan, V., & Zimmermann, M. B. (2012). Global Iodine Status in 2011 and Trends over the Past Decade. *The Journal of Nutrition, 142*(4), 744-750. doi:10.3945/jn.111.149393

Aoki, Y., Belin, R. M., Clickner, R., Jeffries, R., Phillips, L., & Mahaffey, K. R. (2008). Subclinical Hypothyroidism and the Risk of Coronary Heart Disease and Mortality. *Thyroid, 17*(12), 1211-1223. doi:10.1089/thy.2006.0235

Arab, L., Tseng, C. H., Ang, A., & Jardack, P. (2011). Validity of a multipass, web-based, 24-hour self-administered recall for assessment of total energy intake in blacks and whites. *Am J Epidemiol, 174*(11), 1256-1265. doi:10.1093/aje/kwr224

Bath, S. C., Steer, C. D., Golding, J., Emmett, P., & Rayman, M. P. (2013). Effect of inadequate iodine status in UK pregnant women on outcomes on cognitive outcomes in their children: results from the Avon longitudinal Study of Parents and Children (ALSPAC). *Lancet, 382*, 331-337.

Biondi, B., & Cooper, D. S. (2008). The Clinical Significance of Subclinical Thyroid Dysfunction. *Endocrine Reviews, 29*(1), 76-131. doi:10.1210/er.2006-0043

Bours, S. P. G., van Geel, T. A. C. M., Geusens, P. P. M. M., Janssen, M. J. W., Janzing, H. M. J., Hoffland, G. A., . . . van den Bergh, J. P. W. (2011). Contributors to Secondary Osteoporosis and Metabolic Bone Diseases in Patients Presenting with a Clinical Fracture. *The Journal of Clinical Endocrinology & Metabolism, 96*(5), 1360-1367. doi:10.1210/jc.2010-2135

Braganza, M. Z., Potischman, N., Park, Y., Thompson, F. E., Hollenbeck, A. R., & Kitahara, C. M. (2015). Adolescent and mid-life diet and subsequent risk of thyroid cancer in the NIH-AARP diet and health study. *International Journal of Cancer, 137*(10), 2413-2423. doi:10.1002/ijc.29600

Brauer, V. F. H., Below, H., Kramer, A., Fuhrer, D., & Paschke, R. (2006). The role of thiocyanate in the etiology of goiter in an industrial metropolitan area. *European Journal of Endocrinology, 154*(2), 229-235. doi:10.1530/eje.1.02076

Brent, G. A. (2012). Mechanisms of thyroid hormone action. *The Journal of Clinical Investigation, 122*(9), 3035-3043. doi:10.1172/JCI60047

Brody, T. (1999). *Nutritional Biochemistry* (2nd ed.). Berkeley, CA: Academic Press.

Brough, L., Gunn, C. A., Weber, J. L., Coad, J., Jin, Y., Thomson, J. S., . . . Kruger, M. C. (2017). Iodine and Selenium Intakes of Postmenopausal Women in New Zealand. *Nutrients, 9*(3). doi:10.3390/nu9030254

Butler, E. C. V., Grose, M., Burrett, C., Pook, M., & Doyle, R. (2007). The iodine cycle: iodine cycling in the ecosphere, and its relevance to Tasmania-consortium environmental iodine research (pp. 10-66). Launceston, Australia: Myola Publishing.

Canaris, G. J., Manowitz, N. R., Mayor, G., & Ridgway, E. (2000). The colorado thyroid disease prevalence study. *Archives of Internal Medicine, 160*(4), 526-534. doi:10.1001/archinte.160.4.526

Carriquiry, A. L., Spungen, J. H., Murphy, S. P., Pehrsson, P. R., Dwyer, J. T., Juan, W., & Wirtz, M. S. (2016). Variation in the iodine concentrations of foods: considerations for dietary assessment. *The American Journal of Clinical Nutrition, 104*(Supplement 3), 877S-887S. doi:10.3945/ajcn.115.110353

Charlton, K. E., Yeatman, H. R., & Houweling, F. (2010). Poor iodine status and knowledge related to iodine on the eve of mandatory iodine fortification in Australia. *Asia Pacific Journal of Clinical Nutrition, 19*(2), 250-255.

del Ghianda, S., Tonacchera, M., & Vitti, P. (2014). Thyroid and menopause. *Climacteric, 17*(3), 225-234. doi:10.3109/13697137.2013.838554

Delange, F. (2001). Iodine deficiency as a cause of brain damage. *Postgraduate Medical Journal, 77*(906), 217-220. doi:10.1136/pmj.77.906.217

Delange, F., de Benoist, B., Pretell, E., & Dunn, J. T. (2001). Iodine deficiency in the world: Where do we stand at the turn of the century? *Thyroid, 11*(5), 437-447. doi:10.1089/105072501300176390

Demers, L. M., & Spencer, C. A. (2003). Laboratory medicine practice guidelines: laboratory support for the diagnosis and monitoring of thyroid disease. *Clinical Endocrinology, 58*(2), 138-140. doi:10.1046/j.1365-2265.2003.01681.x

Dillmann, W. H. (2002). Cellular action of thyroid hormone on the heart. *Thyroid, 12*(6), 447-452. doi:10.1089/105072502760143809

Edmonds, J. C., McLean, R. M., Williams, S. M., & Skeaff, S. A. (2016). Urinary iodine concentration of New Zealand adults improves with mandatory fortification of bread with iodised salt but not to predicted levels. *Eur J Nutr, 55*(3), 1201-1212. doi:10.1007/s00394-015-0933-y

Fardet, A. (2015). Wheat-based foods and non celiac gluten/wheat sensitivity: Is drastic processing the main key issue? *Med Hypotheses, 85*(6), 934-939. doi:10.1016/j.mehy.2015.09.007

Food Standards Australia and New Zealand. (2009). *Australia New Zealand Food Standards Code, Standard 2.1.1, Cereals and Cereal Products*. Retrieved from https://www.legislation.gov.au/Details/F2014C01190.

Food Standards Australia and New Zealand. (2016). *Australia New Zealand Food Standards Code – Standard 2.10.2 – Salt and salt products*. Retrieved from https://www.legislation.gov.au/Details/F2016C00184

Gaitan, E. (1990). Goitrogens in Food and Water. *Annu Rev Nutr, 10*, 21-39.

Giugliano, D., Maiorino, M. I., Bellastella, G., & Esposito, K. (2018). More sugar? No, thank you! The elusive nature of low carbohydrate diets. *Endocrine*, *61*(3), 383-387. doi:10.1007/s12020-018-1580-x

Gordon, R. C., Rose, M. C., Skeaff, S. A., Gray, A. R., Morgan, K. M., & Ruffman, T. (2009). Iodine supplementation improves cognition in mildly iodine-deficient children. *Am J Clin Nutr, 90*(5), 1264-1271. doi:10.3945/ajcn.2009.28145

Hak, A. E., & Pols, H. A. P. (2000). Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial. *Ann Intern Med, 132*(4), 270-278.

Hak, A. E., Pols, H. A. P., van Hemert, A. M., Hofman, A., & Witteman, J. C. M. (2000). Progression of Aortic Calcification Is Associated With Metacarpal Bone Loss During Menopause: A Population-Based Longitudinal Study. *Arteriosclerosis, Thrombosis, and Vascular Biology, 20*(8), 1926-1931. doi:10.1161/01.atv.20.8.1926

Haldimann, M., Alt, A., Blanc, A., & Blondeau, K. (2005). Iodine content of food groups. *Journal of Food Composition and Analysis, 18*(6), 461-471. https://doi.org/10.1016/j.jfca.2004.06.003

Herter-Aeberli, I., Cherkaoui, M., El Ansari, N., Rohner, R., Stinca, S., Chabaa, L., . . . Zimmermann, M. B. (2015). Iodine Supplementation Decreases Hypercholesterolemia in Iodine-Deficient, Overweight Women: A Randomized Controlled Trial. *The Journal of Nutrition, 145*(9), 2067-2075. doi:10.3945/jn.115.213439

Hetzel, B. S. (1983). Iodine Deficiency Disorders (IDD) and their Eradication. *Lancet, 2*, 1126-1129.

Hine, T., Zhao, Y., Begley, A., Skeaff, S., & Sherriff, J. (2018). Iodine-containing supplement use by pregnant women attending antenatal clinics in Western Australia. *Aust N Z J Obstet Gynaecol*, 636-642. doi:10.1111/ajo.12785

Hollowell, J. G., Staehling, N. W., Flanders, W. D., Hannon, W. H., Gunter, E. W., Spencer, C. A., & Braverman, L. E. (2002). Serum TSH, T4, and Thyroid Antibodies in the United States Population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *The Journal of Clinical Endocrinology & Metabolism, 87*(2), 489-499.

IBM Corp. (2016). *IBM SPSS Statistics for Windows Version 24.0.* Armonk, NY: IBM Corporation.

Janssen, M., Busch, C., Rodiger, M., & Hamm, U. (2016). Motives of consumers following a vegan diet and their attitudes towards animal agriculture. *Appetite, 105*, 643-651. doi:10.1016/j.appet.2016.06.039

Jones, E., McLean, R., Davies, B., Hawkins, R., Meiklejohn, E., Ma, Z., & Skeaff, S. (2016). Adequate Iodine Status in New Zealand School Children Post-Fortification of Bread with Iodised Salt. *Nutrients, 8*(5), 298.

Jooste, P. L., & Strydom, E. (2010). Methods for determination of iodine in urine and salt. *Best Practice & Research Clinical Endocrinology & Metabolism, 24*(1), 77-88. https://doi.org/10.1016/j.beem.2009.08.006

Jooste, P. L., Upson, N., & Charlton, K. E. (2005). Knowledge of iodine nutrition in the south african adult population. *Public Health Nutr, 8*(4), 382-386. http://dx.doi.org/10.1079/PHN2004696

Jorgensen, A., O'Leary, P., James, I., Skeaff, S., & Sherriff, J. (2016). Assessment of Breast Milk Iodine Concentrations in Lactating Women in Western Australia. *Nutrients, 8*(11). doi:10.3390/nu8110699

Kahaly, G. J., & Dillmann, W. H. (2005). Thyroid hormone action in the heart. *Endocr Rev, 26*(5), 704-728. doi:10.1210/er.2003-0033

Knudsen, N., Bülow, I., Jørgensen, T., Laurberg, P., Ovesen, L., & Perrild, H. (2000). Goitre prevalence and thyroid abnormalities at ultrasonography: a comparative epidemiological study in two regions with slightly different iodine status. *Clinical Endocrinology, 53*(4), 479-485. doi:10.1046/j.1365-2265.2000.01121.x

König, F., Andersson, M., Hotz, K., Aeberli, I., & Zimmermann, M. B. (2011). Ten repeat collections for urinary iodine from spot samples or 24-Hour samples are needed to reliably estimate individual iodine status in women. *The Journal of Nutrition, 141*(11), 2049-2054. doi:10.3945/jn.111.144071

Langer, P. (1980). Eastern and Southeastern Europe. *Endemic Goiter and Endemic Cretinism* (pp. 141-154). New York, NY: John Wiley.

Laurberg, P., Cerqueira, C., Ovesen, L., Rasmussen, L. B., Perrild, H., Andersen, S., . . . Carle, A. (2010). Iodine intake as a determinant of thyroid disorders in populations. *Best Practice & Research Clinical Endocrinology & Metabolism, 24*(1), 13-27.

Laurberg, P., Cerqueira, C., Ovesen, L., Rasmussen, L. B., Perrild, H., Andersen, S., . . . Carlé, A. (2010). Iodine intake as a determinant of thyroid disorders in populations. *Best Practice & Research Clinical Endocrinology & Metabolism, 24*(1), 13-27. http://dx.doi.org/10.1016/j.beem.2009.08.013

Laurberg, P., Jørgensen, T., Perrild, H., Ovesen, L., Knudsen, N., Pedersen, I. B., . . . Vejbjerg, P. (2006). The Danish investigation on iodine intake and thyroid disease, DanThyr: status and perspectives. *European Journal of Endocrinology, 155*(2), 219-228. doi:10.1530/eje.1.02210

Leung, A., & Braverman, L. E. (2010). Role of iodine in thyroid physiology. *Expert Review of Endocrinology & Metabolism; London, 5*(4), 593-602. http://dx.doi.org/10.1586/eem.10.40

Li, M., & Eastman, C. J. (2012). The changing epidemiology of iodine deficiency. *Nat Rev Endocrinol, 8*(7), 434-440.

Ma, Z. F., & Skeaff, S. A. (2014). Thyroglobulin as a Biomarker of Iodine Deficiency: A Review. *Thyroid, 24*(8), 1195-1209. doi:10.1089/thy.2014.0052

Ma, Z. F., Venn, B. J., Manning, P. J., Cameron, C. M., & Skeaff, S. A. (2016). Iodine Supplementation of Mildly Iodine-Deficient Adults Lowers Thyroglobulin: A Randomized Controlled Trial. *J Clin Endocrinol Metab, 101*(4), 1737-1744. doi:10.1210/jc.2015-3591

Mann, J., & Aitken, E. (2003). The re-emergence of iodine deficiency in New Zealand. *New Zealand Medical Journal, 116*(351), 1161-1170.

Ministry of Health & National Health and Medical Research Council, New Zealand Ministry of Health. (2006). *Nutrient Reference Values for Australia and New Zealand including Recommended Dietary Intakes* Canberra: Australia: National Health and Medical Research Council. Retrieved from https://www.nhmrc.gov.au/guidelines-publications/n35-n36-n37.

Ministry of Primary Industries. (2014). *Update report on the dietary iodine intake of New Zealand children following fortification of bread with iodine*. MPI Technical Paper No: 2014/21. Retrieved from https://www.mpi.govt.nz/dmsdocument/4596-update-report-on-the-dietary-iodine-intake-of-new-zealand-children-following-fortification-of-bread-with-iodine/loggedin.

Ministry of Primary Industries. (2016). *The New Zealand 2016 Total Diet Study* Wellington, NZ. Retrieved from https://www.mpi.govt.nz/dmsdocument/28976/loggedIn.

Murphy, S. P., Barr, S. I., & Poos, M. I. (2002). Using the New Dietary Reference Intakes to Assess Diets: A Map to the Maze. *Nutrition Reviews, 60*(9), 267-275. doi:10.1301/002966402320387189

National Health and Medical Research Council & New Zealand Ministry of Health. (2006). *Nutrient Reference Values for Australia and New Zealand including Recommended Dietary Intakes.* Retrieved from https://www.nrv.gov.au/nutrients/iodine

Nazeri, P., Mirmiran, P., Asghari, G., Shiva, N., Mehrabi, Y., & Azizi, F (2015). Mothers' behaviour contributes to suboptimal iodine status of family members: Findings from an iodine-sufficient area. *Public Health Nutr, 18*(4), 686-694. https://dx.doi.org/10.1017/S1368980014000743

North, K. A., & Fraser, S. (1966). Iodine intake as revealed by urinary iodide excretion. *The New Zealand medical journal, 65*(408), 512-513.

O'Kane, S. M., Pourshahidi, L. K., Farren, K. M., Mulhern, M. S., Strain, J. J., & Yeates, A. J. (2016). Iodine knowledge is positively associated with dietary iodine intake among women of childbearing age in the UK and Ireland. *British Journal of Nutrition, 116*(10), 1728-1735. doi:10.1017/S0007114516003925

Patel, K. V., Brennan, K. L., Brennan, M. L., Jupiter, D. C., Shar, A., & Davis, M. L. (2014). Association of a Modified Frailty Index With Mortality After Femoral Neck Fracture in Patients Aged 60 Years and Older. *Clinical Orthopaedics and Related Research®, 472*(3), 1010-1017. doi:10.1007/s11999-013-3334-7

Pearce, E. N., Andersson, M., & Zimmermann, M. B. (2013). Global iodine nutrition: Where do we stand in 2013? *Thyroid: Official Journal Of The American Thyroid Association, 23*(5), 523-528. doi:10.1089/thy.2013.0128

Pearce, E. N., & Caldwell, K. L. (2016). Urinary iodine, thyroid function, and thyroglobulin as biomarkers of iodine status. *The American Journal of Clinical Nutrition, 104*(Supplement 3), 898S-901S. doi:10.3945/ajcn.115.110395

Pearce, E. N., Pino, S., He, X., Bazrafshan, H. R., Lee, S. L., & Braverman, L. E. (2004). Sources of Dietary Iodine: Bread, Cows' Milk, and Infant Formula in the Boston Area. *The Journal of Clinical Endocrinology & Metabolism, 89*(7), 3421-3424. doi:10.1210/jc.2003-032002

Razvi, S., Weaver, J. U., Vanderpump, M. P., & Pearce, S. H. S. (2010). The Incidence of Ischemic Heart Disease and Mortality in People with Subclinical Hypothyroidism: Reanalysis of the Whickham Survey Cohort. *The Journal of Clinical Endocrinology & Metabolism, 95*(4), 1734-1740. doi:10.1210/jc.2009-1749

Ristic-Medic, D., Piskackova, Z., Hooper, L., Ruprich, J., Casgrain, A., Ashton, K., . . . Glibetic, M. (2009). Methods of assessment of iodine status in humans: a systematic review. *The American Journal of Clinical Nutrition, 89*(6), 2052S-2069S. doi:10.3945/ajcn.2009.27230H

Rodondi, N., & Bauer, D. C. (2013). Subclinical Hypothyroidism and Cardiovascular Risk: How to End the Controversy. *The Journal of Clinical Endocrinology & Metabolism, 98*(6), 2267-2269. doi:10.1210/jc.2013-1875

Rodondi, N., den Elzen, W. J., & Bauer, D. C. (2010). Subclinical hypothyroidism and the risk of coronary heart disease and mortality. *JAMA, 304*(12), 1365-1374. doi:10.1001/jama.2010.1361

Rohner, F., Zimmermann, M., Jooste, P., Pandav, C., Caldwell, K., Raghavan, R., & Raiten, D. J. (2014). Biomarkers of nutrition for development-Iodine review. *The Journal of Nutrition, 144*(8), 1322S-1342S. doi:10.3945/jn.113.181974

Simpson, F. O., Thaler, B. I., Paulin, J. M., Phelan, E. L., & Cooper, G. J. S. (1984). Iodide Excretion in a Salt-restriction Trial. *New Zealand Medical Journal, 97*(770), 890-893.

Skeaff, S. A., & Lonsdale-Cooper, E. (2013). Mandatory fortification of bread with iodised salt modestly improves iodine status in schoolchildren. *British Journal of Nutrition, 109*(06), 1109-1113. doi:10.1017/S0007114512003236

Skeaff, S. A., McLean, R., Mann, J., & Williams, S. (2013). *The Impact of Mandatory Fortification of Bread with Iodine*. Wellington: Ministry of Primary Industries Technical Paper No: 2013/025. Retrieved from https://www.mpi.govt.nz/dmsdocument/4097-the-impact-of-mandatory-fortification-of-bread-with-iodine

Skeaff, S. A., Thomson, C. D., & Eastman, C. (2009). Iodine deficiency does exist but is difficult to assess in individuals. *New Zealand Medical Journal, 122*, 101-102.

Skeaff, S. A., Thomson, C. D., & Gibson, R. S. (2003). Iodine Deficiency Disorders (IDD) in the New Zealand population: another example of an outmoded IDD control programme. *Asia Pacific Journal of Clinical Nutrition, 12*.

Spencer, C. A., & Wang, C. C. (1995). Thyroglobulin measurement. Techniques, clinical benefits, and pitfalls. *Endocrinol Metab Clin North Am, 24*(4), 841-863.

Stanbury, J. B., Brownell, G. L., & Riggs, D. S. (1954). *Endemic Goitre: The Adaptation of Man to Iodine Deficiency*: Harvard University Press.

Subar, A. F., Kirkpatrick, S. I., Mittl, B., Zimmerman, T. P., Thompson, F. E., Bingley, C., . . . Potischman, N. (2012). The Automated Self-Administered 24-hour dietary recall (ASA24): a resource for researchers, clinicians, and educators from the National Cancer Institute. *J Acad Nutr Diet, 112*(8), 1134-1137. doi:10.1016/j.jand.2012.04.016

Sutcliffe, E. (1990). Iodine in New Zealand milk. *Food Technology in New Zealand*(July), 32-38.

Tayie, F. A. K., & Jourdan, K. (2010). Hypertension, Dietary Salt Restriction, and Iodine Deficiency Among Adults. *American Journal of Hypertension, 23*(10), 1095-1102. doi:10.1038/ajh.2010.120

The Iodine Global Network. (2016). Global Iodine Nutrition Scorecard 2015 (Internet). Retrieved from http://www.ign.org/cm_data/IGN_Global_Scorecard_AllPop_and_PW_May2017.pdf

The New Zealand Institute for Plant and Food Research. (2014). *The NZ Foodfiles*. Retrieved from https://www.foodcomposition.co.nz/foodfiles

Thompson, F. E., & Subar, A. F. (2008). *Dietary Assessment Methodology: Nutrition in the Prevention of Disease.* Retrieved from https://www.elsevier.com/books/nutrition-in-the-prevention-and-treatment-of-disease/coulston/978-0-12-374118-9#

Thomson, B. M. (2009). *Levels of Iodine in NZ Retail Salt*. Retrieved from https://www.mpi.govt.nz/dmsdocument/22690/loggedIn

Thomson, B. M., Vannoort, R. W., & Haslemore, R. M. (2008). Dietary exposure and trends of exposure to nutrient elements iodine, iron, selenium and sodium from the 2003–4 New Zealand Total Diet Survey. *British Journal of Nutrition, 99*(3), 614-625. doi:10.1017/S0007114507812001

Thomson, C. D. (2003). *Australia and New Zealand Nutrient Reference Values for Iodine*. Retrieved from http://www.moh.govt.nz/notebook/nbbooks.nsf/0/BAE179A5C4AF58A8CC257DB500728597/$file/iodine.pdf.

Thomson, C. D. (2004). Selenium and iodine intakes and status in New Zealand and Australia. *British Journal of Nutrition, 91*(05), 661-672. doi:10.1079/BJN20041110
Thomson, C. D., Campbell, J. M., Miller, J., Skeaff, S. A., & Livingstone, V. (2009). Selenium and iodine supplementation: effect on thyroid function of older New Zealanders. *The American Journal of Clinical Nutrition, 90*(4), 1038-1046. doi:10.3945/ajcn.2009.28190
Thomson, C. D., Colls, A. J., Conaglen, J. V., Macormack, M., Stiles, M., & Mann, J. (1997). Iodine status of New Zealand residents as assessed by urinary iodide excretion and thyroid hormones. *British Journal of Nutrition, 78*(06), 901-912. doi:10.1079/BJN19970208
Thomson, C. D., Packer, M. A., Butler, J. A., Duffield, A. J., O'Donaghue, K. L., & Whanger, P. D. (2001). Urinary selenium and iodine during pregnancy and lactation. *J Trace Elem Med Biol, 14*(4), 210-217. doi:10.1016/s0946-672x(01)80004-3
Thomson, C. D., Woodruffe, S., Colls, A. J., Joseph, J., & Doyle, T. C. (2001). Urinary iodine and thyroid status of New Zealand residents. *European Journal of Clinical Nutrition, 55*(5), 387-392.
Tseng, F.Y., Lin, W.Y., Lin, C.C., Lee, L.T., Li, T.C., Sung, P.K., & Huang, K.C. (2012). Subclinical Hypothyroidism Is Associated With Increased Risk for All-Cause and Cardiovascular Mortality in Adults. *Journal of the American College of Cardiology, 60*(8), 730-737. http://dx.doi.org/10.1016/j.jacc.2012.03.047
Vanderpas, J. (2006). Nutritional epidemiology and thyroid hormone metabolism. *Annu Rev Nutr, 26*, 293-322. doi:10.1146/annurev.nutr.26.010506.103810
Vanderpump, M. P., Tunbridge, W. M., French, J. M., Appleton, D., Bates, D., Clark, F., . . . et al. (1995). The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol (Oxf), 43*(1), 55-68.
Vannoort, R. W., & Thomson, B. M. (2005). *New Zealand 2003/04 Total Diet Study*. Retrieved from https://www.mpi.govt.nz/dmsdocument/22189/direct
Vannoort, R. W., & Thomson, B. M. (2009). *New Zealand 2007/08 Total-diet-study*. Retrieved from http://www.foodsafety.govt.nz/elibrary/industry/total-diet-study.pdf.
Vejbjerg, P., Knudsen, N., Perrild, H., Laurberg, P., Andersen, S., Rasmussen, L. B., . . . Jørgensen, T. (2009). Estimation of Iodine Intake from Various Urinary Iodine Measurements in Population Studies. *Thyroid, 19*(11), 1281-1286. doi:10.1089/thy.2009.0094
WHO/FAO. (2004). *Vitamin and Mineral Requirements in Human Nutrition; Iodine*. Retrieved from http://www.who.int/nutrition/publications/micronutrients/9241546123/en/
WHO/UNICEF/ICCIDD. (2008). *Assessment of the iodine deficiency disorders and monitoring their elimination. A Guide for program managers.* Retrieved from http://www.who.int/nutrition/publications/micronutrients/iodine_deficiency/9789241595827/en/ :
Williams, G. R., & Bassett, J. H. D. (2018). Thyroid diseases and bone health. *Journal of Endocrinological Investigation, 41*(1), 99-109. doi:10.1007/s40618-017-0753-4
Wirth, C. D., Blum, M. R., Da Costa, B. R., Baumgartner, C., Collet, T. H., Medici, M., . . . Rodondi, N. (2014). Subclinical thyroid dysfunction and the risk for fractures: A systematic review and meta-analysis. *Ann Intern Med, 161*(3), 189-199. doi:10.7326/M14-0125
Xyris software (Australia) Pty Ltd. (2015). *Foodworks 8 Professional edition Version: 8.0.3553*. Retrieved from https://xyris.com.au/
Yeatman, H., Player, C., & Charlton, K. (2010). Women's perceptions relating to the introduction of mandatory iodine fortification in Australia. *Nutrition & Dietetics, 67*(1), 13-17. doi:10.1111/j.1747-0080.2010.01390.x
Zimmermann, M. B. (2004). Assessing Iodine Status and Monitoring Progress of Iodized Salt Programs. *The Journal of Nutrition, 134*(7), 1673-1677.

Zimmermann, M. B. (2008). Methods to assess iron and iodine status. *British Journal of Nutrition, 99*(SupplementS3), S2-S9. doi:10.1017/S000711450800679X
Zimmermann, M. B. (2009). Iodine Deficiency. *Endocrine Reviews, 30*(4), 376-408. doi:10.1210/er.2009-0011
Zimmermann, M. B. (2010). Iodine deficiency in industrialised countries. *Proceedings of the Nutrition Society, 69*(1), 133-143. doi:10.1017/s0029665109991819
Zimmermann, M. B. (2011). Iodine deficiency in industrialized countries. *Clin Endocrinol (Oxf), 75*(3), 287-288. doi:10.1111/j.1365-2265.2011.04168.x
Zimmermann, M. B. (2014). Iodine Deficiency Disorders and Their Correction Using Iodized Salt and/or Iodine Supplements. *Iodine Chemistry and Applications*. Hoboken, NJ: Wiley.
Zimmermann, M. B., Aeberli, I., Andersson, M., Assey, V., Yorg, J. A. J., Jooste, P., . . . Timmer, A. (2013). Thyroglobulin Is a Sensitive Measure of Both Deficient and Excess Iodine Intakes in Children and Indicates No Adverse Effects on Thyroid Function in the UIC Range of 100–299 μg/L: A UNICEF/ICCIDD Study Group Report. *The Journal of Clinical Endocrinology & Metabolism, 98*(3), 1271-1280. doi:10.1210/jc.2012-3952
Zimmermann, M. B., & Andersson, M. (2012). Assessment of iodine nutrition in populations: past, present, and future. *Nutr Rev, 70*(10), 553-570. doi:10.1111/j.1753-4887.2012.00528.x
Zimmermann, M. B., Jooste, P. L., & Pandav, C. S. (2008). Iodine-deficiency disorders. *The Lancet, 372*(9645), 1251-1262. http://dx.doi.org/10.1016/S0140-6736(08)61005-3

APPENDICES

1-13

Appendix 1: Calling Mid-life Women

Calling Midlife Women! Do you avoid bread? Then we need your help!"

New Zealand has low levels of iodine and we want to find out if avoiding bread (which is fortified with iodine) results in low iodine status. We are seeking women, 40-65yrs to take part in the "**Women, Bread and Iodine (WOMBI) study".**

You would need to:

- Visit the research unit at the Institute of Food, Nutrition & Human Health, Albany
- Complete an online questionnaire & food diary
- Have body measurements taken, & provide a urine & blood sample

Your involvement will enable valuable information to be gathered about the iodine status of women of your age. Low iodine affects many aspects of health, most notably the thyroid gland and its function. You will also gain valuable information about your diet and body composition.

Interested? Register at www.massey.ac.nz/wombistudy

This study has been approved by the Massey Human Ethics committee no: Ref 16/52

Appendix 2: Email to Albany All

"Calling Midlife Women! Do you avoid bread? Then we need your help!"

New Zealand has low levels of iodine and we want to find out if avoiding bread (which is fortified with iodine) results in low iodine status. We are seeking women, 40-65yrs to take part in the "**Women, Bread and Iodine (WOMBI) study".**

You would need to:

- Visit the research unit at the Institute of Food, Nutrition & Human Health, Albany
- Complete an online questionnaire & food diary
- Have body measurements taken, & provide a urine & blood sample

Your involvement will enable valuable information to be gathered about the iodine status of women of your age. Low iodine affects many aspects of health, most notably the thyroid gland and its function. You will also gain valuable information about your diet and body composition.

Interested? Register at www.massey.ac.nz/wombistudy

Appendix 3: Facebook Poster for WOMBI study

Appendix 4: Media Release

Getting enough Iodine? Not eating bread?

Worldwide iodine deficiency remains one of the most common nutrient deficiencies and New Zealand naturally has low levels of iodine in the soil which results in low levels of iodine in the food supply. Iodine is a mineral required by the thyroid gland to make thyroid hormones essential for growth and development, especially of the brain and central nervous system. In adulthood, iodine is still essential for the synthesis of thyroid hormones for metabolism and brain function as well as other minor bodily functions. Inadequate iodine in mid-life to older women could play a role in thyroid dysfunction.

Earlier last century the rate of goitre (a response to iodine deficiency) in New Zealand was sufficient enough for the iodisation of salt to be introduced and by the 1950s this had almost all but disappeared. However, since the 1990s iodine deficiency had re-emerged. To address the New Zealand situation, in 2009 the NZ government introduced the mandatory addition of iodised salt to all bread (except organic bread). However, if bread is not a habitual part of the diet then the effect of this fortification does not reach all groups of the population.

Massey University's School of Food and Nutrition Master's student Jacqui Finlayson's interest in iodine and specifically the New Zealand situation ignited the idea for research investigating the iodine levels of women living in New Zealand who choose to avoid bread. As mid-life women are more vulnerable to thyroid dysfunction this was the target group chosen and the Women, Bread and Iodine Study, nicknamed the WOMBI study commenced www.massey.ac.nz/wombistudy

To date no other study investigating iodine levels of mid-life women who avoid bread has been undertaken in New Zealand. Effects of low iodine levels are not always obvious and are not routinely tested for. In her work, Jacqui has noticed that even knowledge about dietary sources of iodine is lacking and wishes to raise this awareness through the research undertaken. Recruitment is well under-way but more participants are needed.

By taking part in this study you will be contributing to the health, wellbeing and knowledge for women of New Zealand and also learn valuable information about your own dietary sources and intake of iodine.

If you wish to take part in this study please register your interest at www.massey.ac.nz/wombistudy

Appendix 5: Participant Information Sheet

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

The WOMBI (Women bread and iodine) Study

Does the exclusion of iodine fortified bread in the diet of mid-life women result in low iodine status?

<u>Information for Participants</u>

You are invited to take part in a post graduate research study investigating the effect of avoiding iodine fortified bread products on iodine status of mid-life women living in the northern suburbs of Auckland. The principal investigators are as follows:

Principal Investigator:	Supervisor:	Supervisor:
Jacqui Finlayson – Postgraduate student School of Food and Nutrition Massey University, Albany Tel: [redacted] Mob: [redacted] Email: jacqui.finlayson.1@uni.massey.ac.nz	**Dr Pamela von Hurst** School of Food and Nutrition Massey University, Albany Tel: 414 0800 ext. 43657 Email: **P.R.vonHurst@massey.ac.nz**	**Dr Louise Brough,** School of Food and Nutrition Massey University, Palmerston North Tel: (06) 356 9099 ext. 84575 Email: **L.Brough@massey.ac.nz**

We are looking for 50 mid-life women to participate in this study.

To be eligible for our study you should:

- Be female, between 40 and 65 years of age
- Live in the northern suburbs of Auckland
- Have no have thyroid, kidney, or heart disease.
- Not be taking thyroid medication, supplements containing more than 10 mcg of iodine, lithium medication, or hormone replacement therapy

- Not smoke more than 5 cigarettes per day
- Not consume more than one slice of bread daily

Following your expression of interest for this study, you will be contacted by the Research team from Massey University to assess your eligibility. Once accepted into the study you will be required to visit the Human Nutrition Research Unit at Massey University on one occasion. At this visit you will be asked to provide personal and medical details. Your height, weight and percentage of body fat will be measured and you will be asked to provide a 16ml blood sample (approximately one tablespoon of blood). A container and instructions for collecting a 24hour urine sample will be given to take home and complete. Lastly you will be asked to complete a food frequency questionnaire and a 3-day food diary.

<u>About the Study</u>

We will make an appointment for you to visit Massey University, Albany campus.

Involvement in this study will include:

<u>A visit to the research unit:</u>

You will be requested to complete a food frequency questionnaire and provide your date of birth. The questionnaire may be completed while you are at the research unit. You will spend approximately one hour with the researcher who will also measure your height, weight and body fat percentage. All measurements will be made in a private area by female researchers over light clothing so you do not need to get undressed.

At this visit you will also be provided with containers to take home to collect a sample of urine collected over 24 hours. You are requested to collect all your urine over a consecutive 24-hour period and keep it in the cool bags provided until collected by the one of the research team. The urine will be subsequently analysed for iodine concentration.

Also, you will be asked to complete a 3-day food diary which can be taken home and returned using the stamped, addressed envelope provided and sent to the Nutrition Research Unit at Massey University.

Lastly you will be asked to provide a blood sample of 16ml. The blood sample will be analysed for thyroglobulin, thyroglobulin antibodies and thyroid hormones (TSH, fT3, fT4).

Risks and Benefits

There will be no charges for any of the tests that you undertake. The main benefit of taking part in this study is that you contribute to a greater understanding if avoiding bread that is fortified with iodine results in a lower iodine status. New Zealand (NZ) has low soil levels of iodine which adversely affects the amount of iodine in the food that is grown and produced here. As a result, the NZ people are vulnerable to iodine deficiency. To improve the iodine status of the population in 2009 the NZ government introduced the mandatory fortification of all non-organic and commercially produced bread with iodised salt. However, as some people choose not to eat bread or choose to eat only organic bread the contribution to dietary iodine intake from bread sources is limited.

You will also receive information about your dietary intake and body composition.

There are no personal risks to your health, but the blood tests could potentially identify thyroglobulin, thyroglobulin antibody and/or thyroid hormone levels outside the normal range. If we identify any possible abnormalities, we will advise you to consult your General Practitioner for further investigation.

Participation

You are under no obligation to accept this invitation to take part in this study. If you do decide to participate, you have the right to:

- Decline to answer any question;
- Withdraw from this study (at any time without having to give a reason);
- Ask any questions about this study at any time during participation;
- Provide information on the understanding that your name will not be used unless you give permission to the researcher;
- Be given access to a summary of the project findings when it is concluded.

General

If you want to discuss any aspect of this study you should contact the Principal investigator, Jacqui Finlayson ([redacted]; email; jacqui.finlayson.1@uni.massey.ac.nz)

If you have any queries or concerns regarding your rights as a participant in this study you may wish to contact the Health and Disability Advocacy; telephone 0800 555 050.

At the conclusion of the study we will provide a report of the outcome to those involved in this study and we will send the results by mail.

Confidentiality

No material which could personally identify you would be used in any reports on this study. Information collected from you in this study will be stored securely in the Department of Nutrition and will only be available to study personnel. When this study is completed, all material will be destroyed.

Compensation for Injury

If physical injury results from your participation in this study, you should visit a treatment provider to make a claim to ACC as soon as possible. ACC cover and entitlements are not automatic and your claim will be assessed by ACC in accordance with the Accident Compensation Act 2001. If your claim is accepted, ACC must inform you of your entitlements, and must help you access those entitlements. Entitlements may include, but not be limited to, treatment costs, travel costs for rehabilitation, loss of earnings, and/or lump sum for permanent impairment. Compensation for mental trauma may also be included, but only if this is incurred as a result of physical injury.

If your ACC claim is not accepted, you should immediately contact the researcher. The researcher will initiate processes to ensure you receive compensation equivalent to that to which you would have been entitled had ACC accepted your claim.

Please feel free to contact the researcher if you have any questions about this study.

This project has been reviewed and approved by Massey University Human Ethics Committee: Southern A, application no 16/52. If you have any concerns about the conduct of this research, please contact Mr Jeremy Hubbard, Chair, Massey University Human Ethics committee: Southern A, telephone 04 801 5799 x 63487, email humanethicssoutha@massey.ac.nz

Appendix 6: Screening Questionnaire

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

SCHOOL OF FOOD and NUTRITION
MASSEY UNIVERSITY

Iodine fortified bread exclusion study

Name:

Contact Address:

Contact Phone Number(s):

Subject identifier:

This page to be detached from remainder of questionnaire at the end of interview. Confidential information - to be stored separately.

Subject identifier: _________

Interview

Thank you volunteering to take part in this study.

I just want to ask you a few questions to check that you are a suitable subject and give you an opportunity to ask any questions that you may have about the study.

We want to recruit mid-life women to ask them about their diet, medical history and record body measurements. We would also like to collect some urine and blood, if possible.

What is your age?

Are you currently excluding iodine fortified bread from your diet?

If not completely avoiding iodine fortified bread, would you eat less than one slice per day?

Do you smoke?

Do you currently have any medical conditions?

Do you have any health concerns at the moment?

Do you have any contagious blood borne disease?

Have you ever been diagnosed with medical conditions such as thyroid, heart of kidney disease?

<u>If yes</u>, are you currently receiving any treatment or consuming medication containing iodine? Or, are you fully recovered?

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

Would you be willing to provide a urine sample collected over 24 hours?

Would you be willing to provide a blood sample (16mls)?

Would you be willing to complete a food frequency questionnaire and 3-day food diary?

Would you be willing to visit the Albany campus of Massey University and have your height, weight and percentage of body fat measured?

Best method of contact:

Appendix 7: Consent Form

School of Food and Nutrition
Massey University
Private Bag 102-904
North Shore Mail Centre
Albany, Auckland
New Zealand

T 09 414 0800

The Women, Bread and Iodine Study (WOMBI) Study

Does the exclusion of iodine fortified bread in the diet of mid-life women result in low iodine status?

PARTICIPANT CONSENT FORM

This consent form will be held for a period of five (5) years

I have read the Information Sheet and have had the details of the study explained to me. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time. I agree to participate in this study under the conditions set out in the Information Sheet. I am aware that I can:

- ☐ Decline to answer any particular question;
- ☐ Withdraw from this study (at any time without having to give a reason);
- ☐ Ask any questions about this study at any time during participation;
- ☐ Provide information on the understanding that your name will not be used unless you give permission to the researcher;
- ☐ Be given access to a summary of the project findings when it is concluded.

Signature: .... **Date:** ....

Full Name - printed

Appendix 8: Food Frequency Questionnaire

Instructions

Think about the foods you ate in the last 2 months and answer each question accordingly.

1. Please enter your study ID no. Your study team member will advise this.

ID no:

2. When were you born? Please answer in the box below in the following format: dd/mm/yy

3. Are you between 40 and 65 years of age?

- ○ No
- ○ Yes

4. Are you currently pregnant, planning a pregnancy or breastfeeding?

- ○ No
- ○ Yes

5. Are you a smoker?

○ No

○ Yes

How many cigarettes do you smoke per day?

6. Have you ever been told by a Doctor that you have thyroid disease?

○ No

○ Yes

7. Please list any medicine(s) that you are currently taking and as much information as you know about them.

8. Have you consumed any dietary supplements in the last 12 months?

- ○ Yes; regularly (more than once per week)
- ○ Yes, ocassionally (less than once per week)
- ○ No

9. Please list any supplements you have taken in the last 2 months, include as much information as you can remember. Example: Multivitamin, Blackmores, once daily

10. How often in the last 2 months have you had cow's milk?

- ○ 2 or more times a day
- ○ Once aday
- ○ 5-6 times per day
- ○ 2-4 times per week
- ○ Once a week
- ○ 1-3 times a month
- ○ Less than once a month
- ○ Never

11. If you have cow's milk what is your usual serving size?

- ○ Small (1/2 cup)
- ○ Medium (1 cup)
- ○ Large (1 1/2 cups)

12. How often in the last 2 months have you had soy milk?

- ○ 2 or more times a day
- ○ Once a day
- ○ 5-6 times per day
- ○ 2-4 times per week
- ○ Once a week
- ○ 1-3 times a month
- ○ Less than once a month
- ○ Never

13. If you drink soy milk, what is your usual serving size?

- ○ Small (1/2 cup)
- ○

Medium (1 cup)

Large (1 1/2 cups)

14. How often in the last 2 months have you had cheese?

2-4 times a day

Once a day

5-6 times per week

2-4 times per week

Once a week

1-3 times a month

Less than once a month

Never

15. If you eat cheese, what is your usual serving size?

1 slice off the end of a block of cheese

2 slices off the end of a block of cheese

3 slices off the end of a block of cheese

16. How often in the last 2 months have you had ice cream or yoghurt?

- ○ 2 or more times a day
- ○ Once a day
- ○ 5-6 times per week
- ○ 2-4 times per week
- ○ Once a week
- ○ 1-3 times a month
- ○ Less than once a month
- ○ Never

17. If you eat ice cream or yoghurt, what is your usual serving size?

- ○ 1 scoop of ice cream or 1/2 a pottle of yoghurt
- ○ 2 scoops of ice cream or a pottle of yoghurt
- ○ 3 scoops of ice cream or 1 1/2 pottles of yoghurt

18. How often in the last 2 months have you eaten sausages, saveloys or frankfurters?

- ◯ 2 or more times a day
- ◯ Once a day
- ◯ 5-6 times per week
- ◯ 2-4 times per week
- ◯ Once a week
- ◯ 1-3 times a month
- ◯ Less than once a month
- ◯ Never

19. If you eat sausages, saveloys or frankfurters, what is your usual serving size?

- ◯ 1/2 sausage
- ◯ 1 sausage
- ◯ 2 sausages

20. How often in the last 2 months have you eaten poultry (i.e.chicken, turkey or duck)?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

21. If you eat poultry, what is your usual serving size?

- 1/2 breast or 1 drumstick
- 1 breast or 2 drumsticks
- 1 and 1/2 breasts or 3 drumsticks

22. How often in the last 2 months, have you eaten other meat (beef, lamb or pork)?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a week
- Less than once a month
- Never

23. If you eat other meat, what is your usual serving size?

- 1/2 the size of the palm of your hand
- the same size as the palm of your hand
- 1 and 1/2 times the size of the palm of your hand

24. How often in the last 2 months have you eaten tofu?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

25. If you eat tofu, what is your usual serving size?

- 1/2 the size of the palm of your hand
- the same size as the palm of your hand
- 1 and 1/2 times the size of the palm of your hand

26. How often in the last 2 months have you had eggs (including in cooked foods like quiche) ?

- 2 or more times per day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

27. If you eat eggs, what is your usual serving size?

- 1 small egg
- 1 medium egg
- 1 large egg

28. How often in the last 2 months have you eaten fish?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than one a month
- Never

29. If you eat fish, what is your usual serving size?

- 1/2 fillet
- 1 fillet
- 1 and half fillet

30. How often in the last 2 months have you had shellfish (mussels, oysters, etc)?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

31. If you eat shellfish, what is your usual serving size?

- 3 oysters or mussels
- 6 (i.e. half a dozen) oysters or mussels
- 12 (i.e.dozen) oysters or mussels

32. How often in the last 2 months have you had sushi?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

33. If you eat sushi, what is your usual serving size?

- 4 pieces
- 6 pieces
- 8 pieces

34. How often in the last 2 months have you had bread and bread products (e.g. rolls, pita breads, pizza bases, bagels, English muffins, sticky buns etc)?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

35. If you do eat bread is it less than one slice per day?

- Yes
- No

36. If you do eat more than one slice per day of bread, is the bread mostly

- Shop bought-organic
- Shop bought-gluten free
- Shop bought-not organic or gluten free
- Home made - with **iodised** salt added
- Home made - with **non-iodised** salt added

37. How often in the last 2 months, have you had dark green leafy vegetables (e.g. spinach, silverbeet, bok choy, etc)?

- 2 or more time a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month

Never

38. If you eat vegetables, what is your usual serving size?

1/4 cup cooked

1/2 cup cooked

1 cup cooked

39. How often in the last 2 months have you had fruit (fresh, canned or dried)?

2 or more times per day

Once a day

5-6 times per week

2-4 times per week

Once a week

1-3 times a month

Less than once a month

Never

40. If you eat fruit what is your usual serving size?

- ◯ 1/2 fresh piece, or 1/4 cup of dried or canned fruit
- ◯ 1 fresh piece, or 1/2 cup dried or canned fruit
- ◯ 1 and 1/2 fresh pieces, or 1 cup of dried or canned fruit

41. How often in the last 2 months have you had cake?

- ◯ 2 or more times a day
- ◯ Once a day
- ◯ 5-6 times per week
- ◯ 2-4 times per week
- ◯ Once a week
- ◯ 1-3 times a month
- ◯ Less than once a month
- ◯ Never

42. If you eat cake, what is your usual serving size?

- ◯ 1 small slice
- ◯ 1 medium slice
- ◯ 1 large slice

43. How often in the last 2 months have you had muffins?

- ◯ 2 or more times a day
- ◯ Once a day
- ◯ 5-6 times per week
- ◯ 2-4 times per week
- ◯ Once a week
- ◯ 1-3 times a month
- ◯ Less than once a month
- ◯ Never

44. If you eat muffins, what is your usual serving size?

- ○ 1 small muffin
- ○ 1 medium muffin
- ○ 1 large muffin

45. How often in the last 2 months have you had a snack bar (e.g.fruit or muesli)?

- ○ 2 or more times a day
- ○ Once a day
- ○ 5-6 times per week
- ○ 2-4 times per week
- ○ Once a week
- ○ 1-3 times a month
- ○ Less than once a month
- ○ Never

46. How often in the last 2 months have you had nuts or seeds (e.g. sunflowers, almonds, peanuts etc)

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

47. If you eat nuts and seeds, what is your usual serving size?

- 1/8 cup
- 1/4 cup
- 1/2 cup

48. How often in the last 2 months have you had chocolate?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less than once a month
- Never

49. If you eat chocolate, what is your usual serving size (i.e. compared to a Moro bar)?

- 1/2 bar
- 1 bar
- 2 bars

50. How often in the last 2 months have you had beer?

- ○ 2 or more times a day
- ○ Once a day
- ○ 5-6 times per week
- ○ 2-4 times per week
- ○ Once a week
- ○ 1-3 times a month
- ○ Less than once a month
- ○ Never

51. If you drink beer, what is your usual serving size?

- ○ Half a can or bottle
- ○ 1 can or bottle
- ○ 2 cans or bottles

52. What type of salt do you mostly use at home?

- ○ Iodised salt
- ○ Non-iodised salt
- ○ Flakey salt
- ○ Rock salt
- ○ I do not use any salt

53. How often do you add iodised salt during cooking?

- ○ 2 or more times a day
- ○ Once a day
- ○ 5-6 times per week
- ○ 2-4 times per week
- ○ Once a week
- ○ 1-3 times a month
- ○ Less than once a month
- ○ Never

54. If you use iodised salt, what is your usual serving size?

- 1/4 teaspoon
- 1/2 teaspoon
- 1 teaspoon

55. How often do you add iodised salt to your food at the table?

- 2 or more times a day
- Once a day
- 5-6 times per week
- 2-4 times per week
- Once a week
- 1-3 times a month
- Less then once a month
- Never

56. If you use iodised salt at the table, what is your usual serving size?

- ◯ Just a sprinkle
- ◯ 1/8 teaspoon
- ◯ 1/4 teaspoon

Appendix 9: Three Day Diet Diary Instructions

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

ID Code:

3-day Food Dietary Diary

The WOMBI Study – The Women, Bread & Iodine Study

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 you eat and drink over **3 DAYS**, including food consumed at home and outside the home. It is very important that you continue to eat and drink what you normally eat and drink during the period of recording. Please describe all the food you eat in as much detail as possible. Be as specific as you can.

When to fill in the diary

Please record the food you eat as you go, **do 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 you 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 number of people the recipe serves, and the cooking method; record how much of the whole recipe you personally have eaten.

Take-away and eating out

Please record as much detail about the amount and ingredients as you can, e.g. Vegetable curry containing chickpeas, eggplant, onion and tomato.

Brand name

Please note the brand name (if known). Most packed foods will list a brand name, e.g. Bird's eye, Watties, or Supermarket own brands

Portion Size

Examples for how to describe the quantity or portion size you had of a particular food or drink are shown on pages 17-21 of this diary.

For foods, quantity can be described using:

- household measures, e.g. two thick slices of bread, 4 tablespoons (tbsp.) of peas.
- weights from labels, e.g. 500g steak, 420g tin of baked beans, 125g pot of yoghurt
- number of items, e.g. 4 fish fingers, 2 pieces of chicken nuggets,

For drinks, quantity can be described using (see page 21 for a real size glass):

- the size of glass, cup or the volume (e.g. 300ml).
- volumes from labels (e.g. 330ml can of fizzy drink).

We would like to know the amount that was actually eaten which means taking any leftovers into account. You can do this in two ways:

- Record what was served and make notes of what was not eaten e.g. 3 tbsp of peas, 1 tbsp not eaten; 1 large sausage roll, ½ not eaten
- Only record the amount actually eaten e.g. 2 tbsp of peas, ½ a large sausage roll

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 whether this was a typical day or whether there were any reasons why you ate or drank 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 you took. Brand name, full name of supplement, strength and the amount taken should be recorded.

Overleaf (page 4-8) you can see an example day that has been filled in to show you how we would like you to record your food and drink.

EXAMPLE

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

Code: _____

DAY 1		Date: __________Day ____________Month________Year		
Time	**Where**	**Food/drink description & preparation**	**Brand name**	**Portion size or quantity eaten**
<u>6am to 9am</u>				
6.30am	Kitchen	Filter coffee, decaffeinated Milk (fresh, blue top) Sugar white Toast, multigrain bread Marmalade	Robert Harris Anchor Pams Pams Pams	Mug A dash 1 level teaspoon 1 slice 1 heaped teaspoon
<u>9am to 12noon</u>				
		Did not eat or drink anything		

Time	**Where**	**Food/drink description & preparation**	**Brand name**	**Portion size or quantity eaten**
<u>12noon to 2pm</u>				
12.30pm	**Work tea room**	**Ham salad sandwich from home:** **Bread wholemeal thick sliced** **Margarine light** **Smoked ham thin sliced** **Lettuce, iceberg** **Cucumber with skin**	 **Pams** **Sunlight** **Supermarket**	 **2 slices** **1 tablespoon** **2 slices** **1 leaf** **4 thin slices**
<u>2pm to 5pm</u>				
3pm	**Meeting room**	**Herbal tea** **Louise slice**	**Healtheries** **bakery**	**1 cup** **1 regular slice**
Time	**Where**	**Food/drink description & preparation**	**Brand name**	**Portion size or quantity eaten**

<u>5pm to 8pm</u>				
6.30pm	**At table with husband and children**	**Spaghetti, wholemeal** **Bolognese sauce (see recipe)** **Courgettes** **Orange juice**	**Pams** **Homemade** **Fresh** **Just Juice**	**100g** **1 serve** **50g** **200mls**
<u>8pm to 10pm</u>				
9pm	**Sitting room alone**	**Milk Chocolates**	**Canterbury**	**25g**
<u>10pm to 6am</u>				
10pm	**bedroom**	**water**	**tap**	**200mls**

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: Bolognese sauce		Serves: 4	
Ingredients	Amount	Ingredients	Amount
Low fat beef mince	500g		
garlic	3 cloves		
Brown onion	100g		
Sweet red pepper (capsicum)	50g		
Watties chopped tomatoes	400g		
Tesco tomato puree	1 tablespoon		
Pams canola oil	2 tablespoon		
Greggs mixed herbs	2 tablespoon		
Pams Worcester sauce	1 teaspoon		
Brief description of cooking method: Fry onion and garlic in oil, add mince and fry till brown. Add pepper, tomatoes, puree, Worcester sauce and herbs. Simmer for 30 minutes.			

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

Code: _____

Use the pictures to help you indicate the size of the portion you have eaten.

Write on the food record the picture number and size A, B or C nearest to your own helping.

Remember that the pictures are much smaller than life size.

The actual size of the dinner plate is 10 inches (25cm), the side plate, 7 inches (18cm), and the bowl, 6.3 inches (16cm).

The tables on pages 16-21 also give examples of foods that you might eat and how much information is required about them.

Breakfast Cereal

Spaghetti Noodles

Rice

Chips

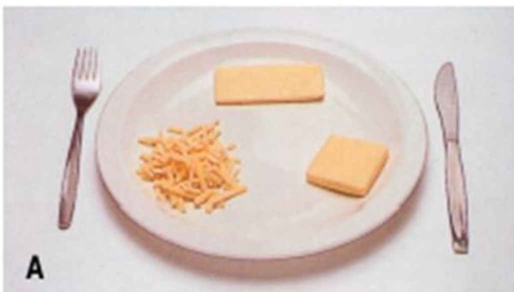
Broccoli or Cauliflower

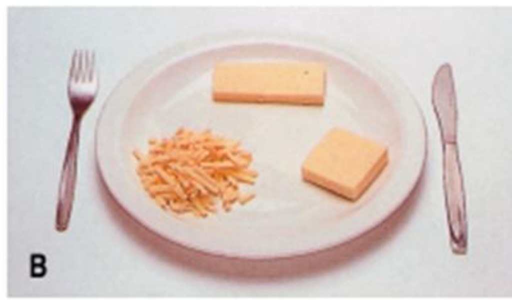
Stew or Curry

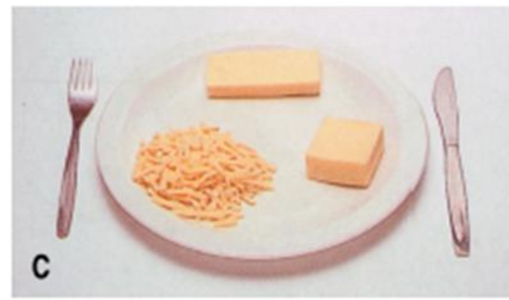
Battered Fish

Quiche or Pie

Cheese

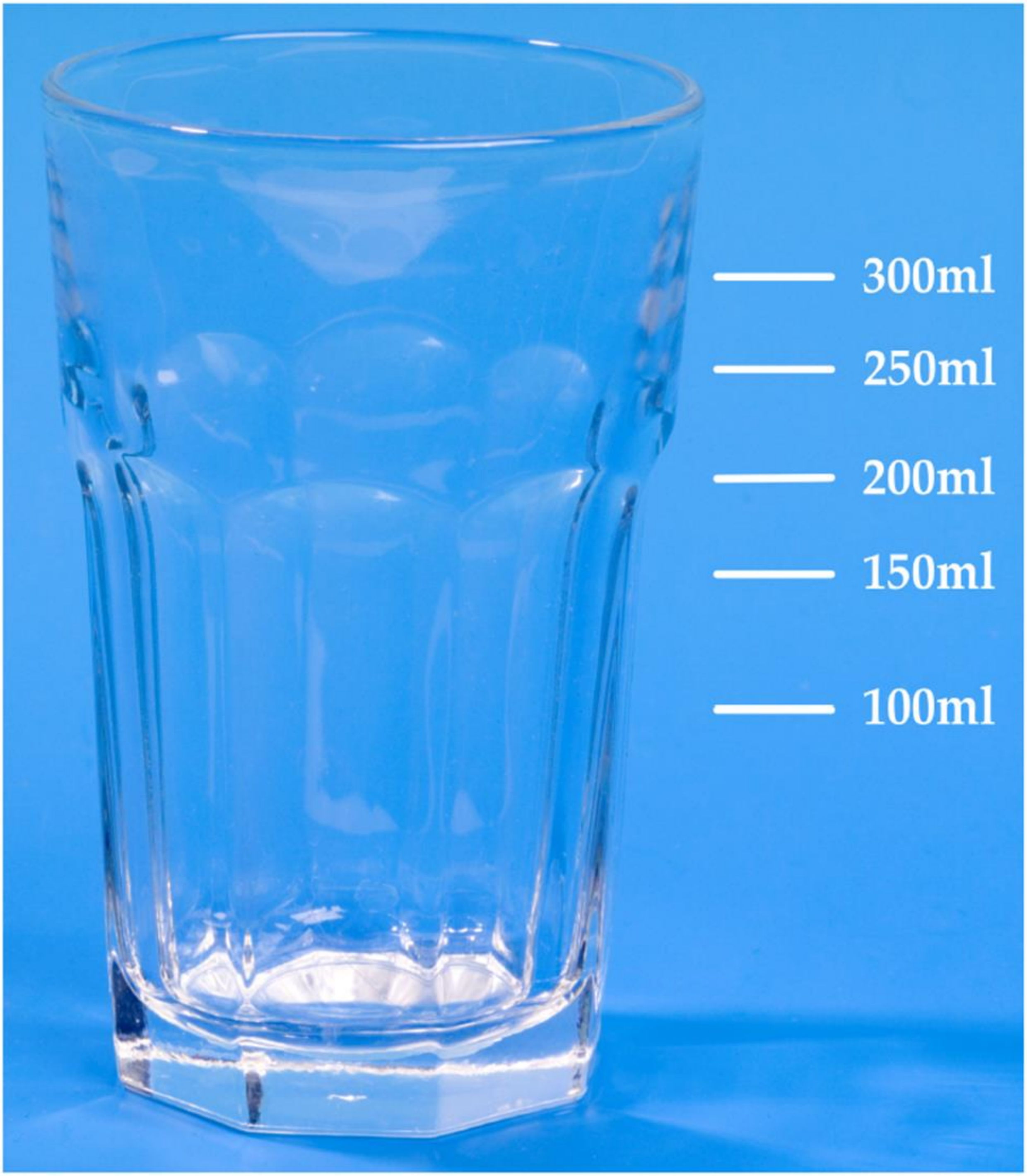






Spongy Cake

Life Size Glass



Appendix 10: Three Day Diet Diary Forms

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

Code: __________WOMBI

Day

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

Code: __________WOMBI

DAY		**Date: __________Day ____________Month________Year**		
Time	**Where**	**Food/drink description & preparation**	**Brand name**	**Portion size or quantity eaten**
6am to 9am				

9am to 12noon				
Time	**Where**	**Food/drink description & preparation**	**Brand name**	**Portion size or quantity eaten**
12noon to 2pm				

2pm to 5pm				
Time	**Where**	**Food/drink description & preparation**	**Brand name**	**Portion size or quantity eaten**
5pm to 8pm				
8pm to 10pm				

10pm to 6am				

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

Code: __________WOMBI

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

☐ Yes, usual

☐ No, **less** than usual.

☐ No, **more** than usual

Please tell us why you had less than usual
Please tell us why you had less than usual

Please tell us why you had more than usual
Please tell us why you had more than usual

2. Was the amount you had to **drink** today, including water, tea, coffee and soft drinks (and alcohol), about what you usually have, less than usual, or more than usual?

☐ Yes, usual

☐ No, **less** than usual

☐ No, **more** than usual

Please tell us why you had less than usual
Please tell us why you had less than usual

Please tell us why you had more than usual
Please tell us why you had more than usual

3. Did you 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 you take any **vitamins, minerals or other food supplements** today?

☐ Yes ☐ No

If yes, **please describe the supplements you took below**

Brand	Name (in full) including strength	Number of pills, capsules, teaspoons
Example Thomson's	Calcium (1000mg) with vitamin D	1 tablet

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:			

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:			

Appendix 11: 24 Hour Urine Collection Instructions

School of Food and Nutrition

Massey University

Albany

Study ID:____________________

Date of collection:_____________

COLLECTION OF URINE

HUMAN NUTRITION RESEARCH UNIT LABORATORY PROCEDURE

You have been provided with:

- Four urine collection bottles
- Cooler bag containing one frozen ice pack
- Funnel for pouring urine into the bottles

Collection

Start collection first thing in the morning & store bottle in the refrigerator or cool bag between collecting.

1. Pass urine into the toilet. This urine is **not wanted,** but this is the "time Commenced", enter this here: Time: am/pm (please circle)
2. From now on collect **all** urine you pass during the rest of the day and night. Use measuring jug for collection and pour carefully into sample bottle. ***When you empty your bowels,*** please collect urine so that you do not lose the urine.
3. **Collect the last** specimen the next morning (i.e. 24 hours after starting). This is the time finished. Note even if you do not feel the need to pass this urine, you must empty your bladder completely. Time finished:- am/pm (circle one)

Store urine bottles in cooler bags containing frozen ice packs and contact:-

Jacqui Finlayson: ph. [redacted] (call/text) to arrange collection of sample.

OR if dropping off to the Research unit;

Owen Mugridge: ph. [redacted] O.Mugridge@massey.ac.nz

Appendix 12: Iodine Content of Iodine Rich Foods In NZ

FOOD	Iodine content (mcg/100g)
Egg	47
Fish (white)	56
Soymilk	2
Sausage (beef)	1.75
Chicken	0.5
Other meat	0.93
Dark green leafy vegetable	4.7
Fruit (citrus/apple)	0.21
Cake	4.94
Snack bar (muesli fruit/nut bar)	2.5
Nuts (mixed)	12
Milk (whole)	4.9
Milk (trim)	6.3
Yoghurt	7.39
Ice cream (standard vanilla)	6.8
Muffin	8.66
Chocolate	10.9
Beer	1.29
Cheese	4.98
Tofu	2.9
Sushi	11
Shellfish (mussels)	144.11
Bread (with iodised salt)	38.8

Source: New Zealand Foodfiles™, 2014 version 01 (The NZ Institute for Food and Plant Research Limited and the Ministry of Health, 2014). (The New Zealand Institute for Plant and Food Research, 2014)

Appendix 13: Certificate of Analysis

ora
TRIED, TESTED AND TRUSTED

R J Hill Laboratories Limited
28 Duke Street Frankton 3204
Private Bag 3205
Hamilton 3240 New Zealand

T 0508 HILL LAB (44 555 22)
T +64 7 858 2000
E mail@hill-labs.co.nz
W www.hill-laboratories.com

Certificate of Analysis

Client:	Massey University	**Lab No:**	1944965 SPv1
Contact:	Louise Brough	**Date Received:**	16-Mar-2018
	C/- Massey University	**Date Reported:**	28-Mar-2018
	Private Bag 11222	**Quote No:**	91083
	Palmerston North 4442	**Order No:**	PN390105
		Client Reference:	Urine testing
		Submitted By:	Louise Brough

Sample Type: Biological Specimens (liquid)

	Sample Name:	520073U1 Dec 17	520025U2 Dec 17	520072U2 Dec 17	520056 Dec 17	520026U2 Dec 17
	Lab Number:	1944965.1	1944965.2	1944965.3	1944965.4	1944965.5
Iodine	mg/kg as rcvd	0.036	0.080	0.139	0.043	0.058

	Sample Name:	Urine CRM				
	Lab Number:	1944965.6				
Iodine	mg/kg as rcvd	0.28	-	-	-	-

Summary of Methods

The following table(s) gives a brief description of the methods used to conduct the analyses for this job. The detection limits given below are those attainable in a relatively clean matrix. Detection limits may be higher for individual samples should insufficient sample be available, or if the matrix requires that dilutions be performed during analysis.

Sample Type: Biological Specimens (liquid)

Test	Method Description	Default Detection Limit	Sample No
TMAH Digestion	Tetramethylammonium hydroxide micro digestion, filtration. P.A.Fecher, I.Goldman and A.Nagengast. Journal of Analytical Atomic Spectrometry, 1998, **13**, 977-982.	-	1-6
Iodine	TMAH digestion. Analysis by ICP-MS. J. Anal. At. Spectrom., 1998, 13, 977 - 982.	0.0010 mg/kg as rcvd	1-6

These samples were collected by yourselves (or your agent) and analysed as received at the laboratory.

Samples are held at the laboratory after reporting for a length of time depending on the preservation used and the stability of the analytes being tested. Once the storage period is completed the samples are discarded unless otherwise advised by the client.

Mark Bryant, NZCS (Chemistry)
Senior Technologist - Food & Bioanalytical

Appendix 14: Ethics Approval

MASSEY UNIVERSITY
TE KUNENGA KI PŪREHUROA
UNIVERSITY OF NEW ZEALAND

Date: 26 October 2016

Dear Jacqui Finlayson

Re: Ethics Notification - **SOA 16/52** - **Iodine Fortifed Bread Exclusion Study (IFBE) 2016**

Thank you for the above application that was considered by the Massey University Human Ethics Committee: **Human Ethics Southern A Committee** at their meeting held on **Wednesday, 26 October, 2016**.

Approval is for three years. If this project has not been completed within three years from the date of this letter, reapproval must be requested.

If the nature, content, location, procedures or personnel of your approved application change, please advise the Secretary of the Committee.

Yours sincerely

Dr Brian Finch
Chair, Human Ethics Chairs' Committee and Director (Research Ethics)