Cost-effectiveness Analysis of Iodine Fortification in Australia and New Zealand

Report developed for Food Standards Australia New Zealand

Centre for Health Economics Research and Evaluation

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About CHERE

CHERE is an independent research unit affiliated with the University of Technology, Sydney. It has been established since 1991, and in that time has developed a strong reputation for excellence in research and teaching in health economics and public health and for providing timely and high quality policy advice and support. Its research program is policy-relevant and concerned with issues at the forefront of the sub-discipline.

CHERE has extensive experience in evaluating health services and programs, and in assessing the effectiveness of policy initiatives. The Centre provides policy support to all levels of the health care system, through both formal and informal involvement in working parties, committees, and by undertaking commissioned projects. For further details on our work, see www.chere.uts.edu.au.

Table of Contents

<p style="text-align: center;">**List of Tables**</p>

List of Figures

1 Executive Summary

As part of Proposal P230 - Consideration of Mandatory Fortification with Iodine, Food Standards Australia New Zealand (FSANZ) commissioned the Centre for Health Economics Research and Evaluation (CHERE), University of Technology, Sydney, to investigate the cost-effectiveness of iodine fortification of bread in Australia and New Zealand. The motivation for FSANZ proposal P230 is the re-emergence of iodine deficiency in Australia and New Zealand

Iodine is an essential trace element that must be derived exogenously. Iodine is required for the formation of thyroid hormones, which are essential for normal thyroid function, growth and development. The thyroid gland is able to maintain, synthesise and secrete thyroid hormones even during extended periods of excessively low or high iodine intake. However extended periods of relatively high or low iodine intake can lead to illness. Insufficient dietary iodine results in a range of adverse conditions known collectively as Iodine Deficiency Disorders (IDDs).

The World Health Organisation (WHO) criteria for a iodine adequate population states that the median urinary iodine levels in the target population are at least 100 μg/l, and that no more than 20% of the population should have a urinary iodine level less than 50 μg/l. Based on the evidence collated in this report, both Australian and New Zealand populations had mild iodine deficiency. We estimate that mandatory fortification will result in the Australian and New Zealand populations being iodine sufficient.

We modelled the distribution of average annual urine iodine content (UIC) in both Australia and New Zealand, stratified into children, pregnant women, and other adults. This modelling accounted for both the median level of UIC and the distribution of iodine levels around this median. Using Tasmanian data on voluntary fortification, we estimated the effect on the median UIC after mandatory fortification is introduced. The results suggest a significant decrease both in the proportion of individuals with iodine levels below 50 μg/l, and in those with levels between 50 μg/l and 100 μg/l. These results are relatively robust to changing the effect of fortification on UIC.

Using these data, we then estimated the cost per unit reduction in at-risk populations over a ten year period. Our estimates suggest that there will be 102,509 and 5,912,315 fewer people below 50μg/l and 100μg/l respectively, in Australia. In New Zealand the corresponding figures are 181,709 and 1,901,722 for the <50μg/l and <100μg/l cohorts, respectively. The relatively greater impact in New Zealand reflects the higher severity of iodine deficiency at baseline, and the likelihood of a greater intake of iodised salt bread. Finally, the cost-effectiveness ratios, which estimate the costs of preventing one person from having an iodine level below 50μg/l (100μg/l) are A$104.35 (A$1.81) for Australia and NZ$15.30 (NZ$1.46) for New Zealand.

1.1 Conclusion

Our findings are based on estimates of iodine deficiency obtained from recently published peer-reviewed journal articles pertaining to the Australian and New Zealand population. Consequently our assumptions are based on the fact that these papers are representative of the respective populations. Any deviation from this assumption will bias our results and introduce uncertainty.

Our findings suggest that both the Australian and New Zealand populations are mildly iodine deficient, as defined by the WHO. This deficiency is more pronounced in New Zealand. After iodine fortification of bread, we estimate that both Australia and New Zealand will become iodine sufficient.

Assessed in terms of cost-effectiveness ratios, the cost of moving individuals from the cohort with iodine levels below 50 µg/l (those most at risk of developing IDDs in the future), appears small compared with the potential benefits associated with improved health, reduced health care costs and/or gains in productivity and GDP.

The following points will require further clarification as the published evidence becomes available:

- An accurate estimate of the benefit of the potential increase in population IQ in terms of productivity gains and therefore increases in GDP.

- A more detailed estimate of the costs associated with mandatory fortification. These should reflect a broader societal perspective and include the costs of health care utilisation (both negative and positive), and the costs associated with ongoing monitoring of iodine levels in the population.

- Irrespective of whether FSANZ recommends mandatory fortification of bread with iodine, the evidence pertaining to the re-emergence of iodine deficiency in Australia and New Zealand warrants the development of a strategic ongoing nutrition monitoring and surveillance program.

As stated in the introduction, our aim was to produce a report that builds upon the considerable evidence that has already been assimilated by FSANZ (including a detailed cost-benefit analysis completed by Access Economics). We did not attempt to duplicate any of this work for obvious reasons. This report is therefore to be viewed both as a stand-alone piece of evidence, and in the context of this stream of evidence.

2 Introduction

2.1 Background and purpose for this report

As part of Proposal P230, Food Standards Australia New Zealand (FSANZ) commissioned the Centre for Health Economic Research and Evaluation (CHERE), University of Technology, Sydney, to investigate the cost-effectiveness of iodine fortification of bread in Australia and New Zealand. The motivation for FSANZ proposal P230, is the re-emergence of iodine deficiency in Australia and New Zealand.

2.2 What is iodine?

Iodine is a naturally occurring mineral and an essential trace element that must be derived exogenously. Iodine is required as a component of thyroid hormones, which are an important regulator of energy metabolism and crucial for the development of brain tissue (Visser, 2006). The thyroid gland is able to maintain synthesis and secretion of thyroid hormones even during extended periods of excessively high or low iodine intake. During periods of excessive iodine, the healthy thyroid can maintain normal iodine levels by inhibition of the organification of iodine. This autoregulatory mechanism is termed the acute Wolff-Chaikoff effect, and is an effective means of rejecting large quantities of iodine. The Wolff-Chaikoff effect prevents the thyroid from producing large quantities of thyroid hormones (Markou, et al., 2001). During iodine deficiency, the depletion of iodine availability results in a multi-step response. There is increased secretion of thyroid-stimulation hormone (TSH), thyroid growth is stimulated leading to an enlarged thryroid, iodine trapping is enhanced, and there is a shift from the intrathyroidal formation of thyroxin to the more active metabolite triodothyronin (Markou, et al., 2001).

In spite of the robust nature of the thyroid gland, prolonged periods of iodine insufficiency can result in severe health consequences.

2.3 Iodine deficiency

Insufficient dietary iodine results in a range of adverse conditions known collectively as Iodine Deficiency Disorders (IDDs). Globally, iodine deficiency is a major public health problem and the largest preventable cause of brain damage in children (World Health Organization. WHO. UNICEF. ICCIDD, 2001). Goitre is the most recognised and visible consequence of iodine deficiency however with the exception of severe goitre, it is probably the least important condition. Although in the context of mild and moderate deficiency the development of goitres, especially autonomous nodular goitres, is predisposing to spontaneous or iodine induced hyperthyroidism. Biochemical hypothyroidism, due to iodine deficiency at critical periods during foetal development in pregnancy and early childhood results in impaired development of the brain and consequently in impaired mental function (Boyages, 1993).

Iodine deficiency has harmful effects on individuals, especially on children (See Table 1) (World Health Organization. WHO. UNICEF. ICCIDD, 1994). In early pregnancy the foetus is totally dependant on maternal thyroxin for normal brain development (Becker, et al., 2006). A small decrease in serum thyroxine level during pregnancy, either because of iodine deficiency or thyroid disease, is an

important risk factor for impaired psychomotor development in infants (Boyages, 1993). This deficiency during pregnancy may lead to irreversible foetal brain damage (Becker, et al., 2006).

Children (including newborn and infants) are at an increased risk of experiencing adverse effects in response to iodine deficiency (Angermayr and Clar, 2004). It is now appreciated that there is a general diminution in intelligence quotient (IQ) in communities where iodine deficiency is severe. Intellectual impairment in children of American women who had mild hypothyroidism during pregnancy has demonstrated the need for better detection and treatment of hypothyroidism during early pregnancy, irrespective of its cause (Utiger, 1999). Interestingly, the median urine iodine level during pregnancy in the Australian population is half that of the United States (Burgess, et al., 2007).

Table 1: The spectrum of Iodine deficiency disorders (IDDs) (World Health Organization. WHO. UNICEF. ICCIDD, 1994)

Population	Feature
Foetus	Stillbirth Congenital abnormalities Increased perinatal mortality Increased infant mortality Neurological cretinism: mental deficiency, deaf mutism, spastic diplegia, squint Myxoedematous cretinism: dwarfism. Mental deficiency Psychomotor defects
Neonate	Neonatal goitre Neonatal hypothyroidism
Child and adolescent	Goitre Juvenile hypothyroidism Impaired mental function Retarded physical development
Adult	Goitre with its complications Hypothryroidism Impaired mental function Iodine-induced hyperthyroidism

2.4 Dietary iodine

Iodine must be derived exogenously; therefore dietary intake is important. Some food products contain naturally high levels of iodine; these include dairy products, seafood, kelp and eggs. Kelp and certain seafood can contain very high levels of iodine. Historically milk was a good source of iodine; however, the level of iodine in milk has declined primarily due to the reduced use of iodine-based cleaning products within the dairy industry (Gunton, et al., 1999). Individuals may also obtain iodine from drinking water, but the intake is dependant on the concentration of iodine in the local water supply.

It is possible to increase dietary iodine intake by using iodised salt. However, the amount of iodised salt being consumed has been decreasing. This is due to a greater use of non-iodised salt, more reliance on processed foods[1] and a general reduction in total salt intake. The overall reduction in total salt intake reflects the success of health promotion campaigns, aimed at preventing hypertension in

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[1] Although processed foods contain salt, to our knowledge this salt tends to be non-iodised.

adults due to excess salt consumption in adults (Cappuccio, 2007, Little, et al., 2004). Additionally, some individuals may acquire iodine from food supplements or medicines.

2.5 Australia and New Zealand's responsibility

Globally, iodine deficiency is the largest preventable cause of brain damage and mental impairment in children (World Health Organization, 1999). Additionally, iodine deficient adults are at risk of goitre formation, which can lead to hypothyroidism or hyperthyroidism in the long term. Australia and New Zealand have obligations to prevent iodine deficiency, since both countries are signatories to the 1990 United Nations sponsored *Declaration for the Survival, Protection and Development of Children* which states *'every child has the right to an adequate supply of iodine to ensure its normal development'* (United Nations, 1990).

The specific objective of any program designed to improve the status of iodine sufficiency in a population is to reduce the risk of IDDs for vulnerable sub-populations, such as the developing foetus and young children. In 1993, the World Health Organization (WHO), in collaboration with UNICEF, The International Council for the Control of Iodine Deficiency Disorders (ICCIDD) and other international organisations recommended universal salt iodisation (USI) (Food Standards Australia New Zealand, 2004). USI is defined as fortification of all salt for human and animal consumption and for food industry (World Health Organization. WHO. UNICEF. ICCIDD, 1994). In 1999 of the 130 countries recognised as at risk of IDD 75% had a legislation on salt iodisation (World Health Organization, 1999).

Many developed countries have adopted iodine fortification (predominantly through salt), although countries have differed in whether they have adopted mandatory or voluntary iodisation. Whilst improvements in population iodine levels have been observed, concerns remain about their sustainability in the absence of legislative measures.

The specific objective of FSANZ's Proposal P230 is to reduce the prevalence of iodine deficiency in Australia and New Zealand, especially in children. The current guideline, (Current Standard 2.10.2 – Salt and Salt Products of the Australia New Zealand Standards Code (the Code)) is a voluntary standard that allows the fortification of salt with iodine at a concentration of 25-65 mg iodine/kg salt. There are concerns about the effectiveness of this program since only 15% of Australian and half of New Zealand salt manufactured for households is iodised[2] (Food Standards Australia New Zealand, 2006). There are other disadvantages associated with iodised salt, the main one being that vulnerable groups such as children, and pregnant and lactating women may not have (or be recommended not to have) high salt consumption, (Angermayr and Clar, 2004).

2.6 Recommended dietary iodine intake

The estimated average requirement (EAR) has been defined as "a daily nutrient level estimated to meet the requirements of half the healthy individuals in a particular life stage and gender group" (National Health and Medical Research

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[2] Iodised salt is also permitted to be added to other foods as long as the food is appropriately labelled.

Council and the New Zealand Ministry of Health, 2006). The EAR for iodine for non-pregnant and non-lactating adults has been estimated at 100 µg/day.

The recommended daily intake (RDI) of iodine in adults is 150 µg/day. The RDI represents "the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97–98 per cent) healthy individuals in a particular life stage and gender group" (National Health and Medical Research Council and the New Zealand Ministry of Health, 2006). In Australia the recommended daily dietary intake of iodine is between (90-120) µg for children, 150 µg for adults and 250 µg for pregnant and lactating women (Li, et al., 2006).

Table 2: **Iodine reference values for Australia and New Zealand (National Health and Medical Research Council and the New Zealand Ministry of Health, 2006).**

Age Group	Estimated average requirement (EAR) µg/day	Recommended Dietary Intake (RDI) µg/day
Infants (Breast milk)	-	90
Infants (Breast milk & food)	-	110
Children (1-8 yrs)	65	90
Children (9-13yrs)	75	120
Adolescents (14-18yrs)	95	150
Adults	150	150
Pregnant Women	220	250

Measuring iodine intake is problematic, since it requires an estimate of the quantity and type of food consumed. Most iodine absorbed in the body is eventually excreted in the urine. Therefore, urinary iodine levels represent a good proxy for recent dietary iodine intake. It is worth noting that during the day an individual's urinary iodine excretion can vary. However, over the population these trends even out. Several authors have suggested that measurement of urine iodine excretion provides the single best measurement of the iodine nutritional status of a population (Soldin, 2002, Stanbury, et al., 1998, World Health Organization. WHO. UNICEF. ICCIDD, 1994, World Health Organization. WHO. UNICEF. ICCIDD, 2001). Dietary iodine intake is positively correlated with urinary iodine excretion in an iodine adequate area (Kim, et al., 1998), and correlates well in a mild iodine deficient area (Rasmussen, et al., 1999). Gibson *et al*, (1995) estimated that daily urinary iodine excretion corresponds to 85-90% of the amount of iodine consumed per day.

2.7   Recommended urinary iodine levels

As discussed, the traditional method of assessing iodine intake is daily urinary excretion of iodide. Daily iodine intake may be estimated from 24 hour urine iodide excretion based on the assumption that 90% of iodine intake is excreted in the urine (Thomson, 2004). However, due to the difficulties of collecting 24 hour samples, population studies use casual or fasting urine samples to measure iodine concentration (Thomson, et al., 1997). Since population values are not usually normally distributed, the median rather than the mean is used as a measure of central tendency (Andersson, et al., 2005).

A median urinary iodine concentration (UIC) of 100 micrograms per litre (µg/l) is considered by the World Health Organization (WHO), the United Nation Children's Fund (UNICEF) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) as the minimal median UIC for iodine sufficiency (See Table 3) (World Health Organization. WHO. UNICEF. ICCIDD, 1994). The WHO/ICCIDD criteria for an iodine adequate population states that the median urinary iodine levels in the target population should be at least 100 µg/l and no more than 20% of the population should have a urinary iodine level of less than 50 µg/l. Also less than 3% of neonates should have a whole blood TSH concentration greater than 5mIU/l (World Health Organization. WHO. UNICEF. ICCIDD, 1994). The ICCIDD recommends that the median UIC during pregnancy should range between 150-249 µg/l (International Council for Control of Iodine Deficiency Disorders, 2007).

Table 3: Epidemiological criteria for assessing iodine nutrition based on median iodine urine concentrations (UIC) in school aged children. Adapted from (World Health Organization. WHO. UNICEF. ICCIDD, 2001) [3]

Median UIC (µg/l)	Iodine intake	Severity of Iodine deficiency
< 20	Insufficient	Severe
20-49	Insufficient	Moderate
50-99	Insufficient	Mild
100-199	Adequate	Optimal
200-299	More than* adequate	Risk of Iodine induced hyperthyroidism for those who were iodine deficient.*
≥ 300	Excessive	Risk of adverse health consequences (iodine induced hyperthyroidism, autoimmune thyroid diseases)

* This adverse risk could occur during five to ten years following the introduction of iodised salt. It has been reported that beyond this period of time, in populations with adequately iodised salt, median values up to 300 µg/l have not demostrated side-effects (World Health Organization. WHO. UNICEF. ICCIDD, 1994).

2.8   History of fortification in Australia and New Zealand

Historically, Australian and New Zealand populations have had problems maintaining iodine sufficiency. By the 1920s, the initial response to this population deficiency in both countries was to introduce voluntary fortification of household salt (Food Standards Australia New Zealand, 2004, Thomson, et al., 2001). New Zealand began with an iodine content of 4mg per kg of salt, which was later increased to 40-80mg iodine/kg of salt in 1938. The initial program was also accompanied by a public health promotion campaign. Despite the availability of non-iodised household salt, the incidence of goitre had virtually disappeared by the 1950s[4] (Mann and Aitken, 2003, Thomson, 2004).

The Tasmanian population has always been at a higher risk of iodine deficiency than the Australian mainland, mainly attributable to the lower levels of iodine in

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[3] NB. The WHO median UIC refers to the population iodine concentration, not the iodine concentration of an individual.
[4] It is worth noting that at this time, the amount of dietary salt derived from household salt was higher than now because more food was prepared at home. Also successful health campaigns for hypertension and heart disease have seen the overall dietary salt intake reduce.

the soil (Thomson, 2003). A State-wide iodine supplementation program[5] was introduced in 1950, in response to a 1949 Tasmania Health department initiative that demonstrated a high goitre rate and low urinary iodine excretion in children (Gibson, 1995). The program was discontinued in the 1960s because of limited success. In 1966, potassium iodate was added to bread improvers. This intervention, along with increased iodine availability from iodophor contamination of dairy foods and increased importation of food from mainland Australia, led to an increase in the incidence of iodine-induced hyperthyroidism, (Connolly, et al., 1970) and was subsequently discontinued in 1976.

Endemic goitre was also a significant problem in certain regions of mainland Australia. In response, the Australian government initiated the goitre prevention program, in 1947, which included iodine supplementation. By 1953, iodised salt was being added to bread in the ACT, but this was discontinued in the 1980s (Food Standards Australia New Zealand, 2006).

2.8.1   Current fortification strategies

As we discussed above, Australia and New Zealand have implemented several strategies in the past aimed at reducing iodine deficiency. Our attention now turns to the current practice.

The current guideline, (Current Standard 2.10.2 – Salt and Salt Products of the Australia New Zealand Standards Code (the Code)) is a voluntary code that allows the fortification of salt with iodine at a concentration of 25-65 mg iodine/kg salt and allows for the use of iodised salt in food manufacturing (as long as the food is appropriately labelled). However there are concerns about the actual effectiveness of this program since only 15-20% of Australian and 50% New Zealand salt manufactured for households is iodised (Food Standards Australia New Zealand, 2006).

Tasmania is the only Australian state with a voluntary iodine fortification program in bread. Despite demonstrating iodine sufficiency in the 1980s, a series of investigations in the 1990s concluded that Tasmanians had become mildly iodine deficient. In response, the Tasmanian Government began an interim[6] voluntary fortification program in October 2001 (Seal, et al., 2003). As a consequence, an estimated 80% of bread baked and sold in Tasmania was manufactured with salt containing ~40mg iodine/kg (Seal, et al., 2003).

2.9   Iodine deficiency in Australia and New Zealand

By the late 1980s, the Australian population was considered iodine adequate (Stanbury, et al., 1998). Subsequent evidence has suggested that iodine deficiency has returned in both the Australian and New Zealand populations (Thomson, et al., 2001).

The re-emergence of iodine deficiency, as indicated by urinary iodine levels is inevitably linked with a decrease in dietary iodine intake. One reason for this could be different practices within the dairy industry. Traditionally, milk was the predominant source of iodine in Australia. This was mainly due to accidental

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[5] Children were given 10mg potassium iodine table per week.
[6] The fortification of bread in Tasmania is an interim measure until iodine supplementation is adopted as a national standard.

iodine contamination from iodine-based disinfectants. However, cleaning solutions have gradually been replaced by more effective non-iodised equivalents. Consequently, the levels of iodine in present day milk are lower. (Gunton, et al., 1999). This is compounded by the fact that less iodised salt is being consumed, through a combination of purchasing more non-iodised salt, eating more processed food (i.e. containing mainly non-iodised salt) and a decrease in overall salt consumption.

The current iodine status of Australian and New Zealand populations will be discussed in detail in Chapter 4.

2.10 Mandatory iodine fortification of bread

One of the problems of voluntary fortification of bread is that it relies upon 'good will' or 'setting the correct incentives', to ensure that the bakeries adopt the strategy. In Tasmania, 20% of bread is not fortified with iodised salt, which means that some individuals will not be receiving the potential benefits. The obvious solution to this problem is to implement mandatory fortification.

Box 1. Summarises the factors that must be present when considering the successful implementation of a new public health initiative.

Box 1. Requirements for public health intervention

Any public health initiatives designed to increase the nutrient intake of iodine in a population are required where:
- o There is demonstrated evidence of iodine deficiency and the current low intake may be detrimental to health. This may relate to the whole, or a subgroup of the population,
- o Iodine requirements can not be realistically replenished by normal dietary practices,
- o The intervention does not raise the iodine intake to levels that are judged unsafe, and
- o Any intervention considered can demonstrate relative cost-effectiveness.

Proponents of mandatory iodine fortification suggest several advantages when compared to voluntary fortification. Firstly equity, since the introduction of mandatory codes will enable the benefits to reach the largest proportion of individuals, especially from the lowest socio-economic groups. Secondly sustainability, since this type of code ensures that changes in food industry practices and manufacturing techniques persist over time. Finally, there would be enhanced certainty in food–related iodine levels, which should make monitoring levels and intake in the population more feasible and reliable. Voluntary fortification also has the inherent flaw that the lack of legislative framework can lead to inaction. Therefore ongoing investment and promotion may be required to maintain support for the program.

On the negative side, opponents of mandatory fortification argue against the lack of consumer choice, although organic products will be free of any mandatory

obligations. Ironically, this raises equity issues, since organic foods are generally more expensive than their non-organic equivalent.

There are alternatives to iodine fortification of bread such as the use of supplements and dietary education. Both alternatives have drawbacks. Supplements have the advantage of being able to target a defined population sub-group, such as pregnant women. However, when supplements are required in early pregnancy, the target population can be missed in the event of an unplanned pregnancy[7] or where a woman may not receive medical attention in the early stages of pregnancy. Supplement usage is also more concentrated amongst higher socio-economic groups, therefore raising equity issues. Also supplement use requires significant levels of public health resources for ongoing promotion. Finally, without mandatory or voluntary fortification, over half of the Australian and New Zealand populations would require iodine supplementation, since iodine deficiency is not limited to only pregnant women and children. Therefore, this would make supplementation an unlikely alternative.

Like supplement use, dietary education requires ongoing public health promotion to maintain effectiveness and is likely to be most beneficial in well-educated individuals (Stanley, et al., 2005). It also relies on the assumption that sufficient iodine is available in the general food supply, which may not be the case.

The final option is to maintain the status quo, which is the best option if iodine deficiency is demonstrated not to be a serious public health concern or none of the alternative options demonstrate safety, effectiveness and cost-effectiveness.

2.11 Why should FSANZ choose bread?

The food vehicle under review for iodine fortification is bread. FSANZ initially proposed mandating the use of iodised salt in biscuits and breakfast cereals in addition to bread. However, problems have been highlighted regarding trade restrictions due to the import/export of biscuits and manufacturing technical difficulties with respect to the delivery of a consistent amount of iodine in breakfast cereals (Food Standards Australia New Zealand, 2007).

Bread has several advantages that make it suitable for mandatory fortification of iodine: it is typically produced locally for the domestic market, therefore it does not suffer from import/export concerns; bread has a short shelf-life so avoiding technical difficulties affecting products with longer shelf-lives; and feasibility studies have demonstrated that iodised salt can be successfully added to bread without significantly varying the salt content. In addition bread is a staple part of most individuals' daily diet. FSANZ estimates that 88% of Australians aged 2 years and above, and 87% of New Zealanders aged 15 years and above consume bread (Food Standards Australia New Zealand, 2007).

FSANZ has suggested two exemptions to mandatory fortification of breads. These are for organic breads and yeast-free breads. We were unable to obtain a reliable estimate of organic bread consumption in Australia and New Zealand, although our estimate is that it would be below 5%. We also do not have estimates for the percentage of bread sold that is unleavened.

In summary, at Final Assessment FSANZ are considering the following; (Food Standards Australia New Zealand, 2007)

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[7] A significantly large proportion of pregnancies in Australia and New Zealand are unplanned.

o the mandatory replacement of salt with iodised salt in bread as the preferred approach to address the re-emergence of iodine deficiency in Australia and New Zealand, with a salt iodisation range from 35-55 mg of iodine per kg of salt.

o Retain the voluntary permission for iodine in iodised salt and reduced sodium salt but adjust it from the current range of 25-65 mg/kg to 35-55 mg/kg, to make it consistent with the mandatory requirement.

For a thorough discussion of FSANZ proposal for iodine fortification, see Proposal P230, Consideration of Mandatory Fortification with Iodine – Key issues for consideration at Final Assessment (May 2007) (Food Standards Australia New Zealand, 2007).

3 Previous FSANZ assessments

3.1 Summary of the report produced by Access Economics

Prior to this report, Access Economics were commissioned to model the benefit of mandatory iodine supplementation using a cost-benefit analysis approach (Access Economics, 2006). The authors use a human capital technique to assign money valuation to health outcomes. The money valuation is based on the estimated lost earnings and production due to both disability and premature death. The basis for the modelling is that an increase in average IQ (intelligence quotient) of a proportion of the population is linked to an increase in their average weekly earnings[8].

The size of benefit per person was estimated using a three step approach. Firstly, the size of IQ increase when a person moves from mild deficiency to adequate secondly, the size of productivity increase per IQ point and finally the size of total productivity increase per person. The model was based on a lognormal distribution for increase IQ, with a mean IQ increase of 0.8 points, and a standard deviation of 1 point. The relationship between IQ and earnings was estimated with the impact of a 1 point increase in IQ correlating to a mean increase on productivity of 0.9 percent. The sensitivity testing was based on zero percent and 3.5 percent increase in productivity, representing the minimum and maximum scenarios respectively. The calculated size of the total productivity increase per person was 0.48 percent, with a standard deviation of 1.06 percent. This meant the minimum and maximum productivity increase per person was 0.0005% and 28.25%, respectively.

The estimated benefit, in terms of mean productivity gain, of mandatory iodine fortification using the estimates stated above was A$1.85 billion (95% CI, A$44.9 million, A$7.23 billon) for Australia and NZ$286 million (95% CI, NZ$6.56 million, NZ$1.14 billion) for New Zealand.

Access Economics also estimated the potential cost of mandatory iodine fortification of bread in Australia and New Zealand. These results are reported later in the report and are used for the basis of our cost-effectiveness estimates.

Finally, Access Economics estimated the net benefits of iodine fortification over a 15 year time period. They estimated the mean net benefit of iodine fortification to be A$1,759,772,000 (95% CI, A$-9,835,839 to A$7,329,940,000) in Australia and NZ$265,180,900 (95% CI, NZ$909,793 to NZ$1,044,035,000) in New Zealand. The wide range of the confidence intervals reflects the significant uncertainty underlying the results. Whilst the clarity, transparency and prudence of this economic evaluation should be complimented, the results are based on a series of key assumptions, as they correctly acknowledged.

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[8] A limitation of this approach is that it assumes that the number of individuals benefiting from fortification should not be of sufficient magnitude to substantially influence the overall clearing of the labour market, thus making a net addition to productivity capacity. If the proportion of individuals is large enough, a general rise in IQ may affect the level of earnings at which the market clears, i.e. in the long term, a raise in the average IQ may not affect earnings. The authors correctly acknowledge this limitation.

3.2 The estimated costs of mandatory iodine fortification

The cost of mandatory fortification of bread was estimated in a previous report by Access Economics (Access Economics, 2007). The cost estimates are shown in Table 4. The authors only estimate the costs to industry and to government of administering and enforcing mandatory fortification. Only the additional costs attributed to the FSANZ proposal are included in the cost analysis. The authors do not include: costs attributable to the restriction in consumer choice; potential adverse health problems associated with excess iodine intake; the costs of monitoring nutrient intake and urinary iodine concentration; or complementary policies required alongside fortification that are outside the scope of FSANZ.

Table 4: The cost of mandatory fortification of bread

	Upfront Cost	Ongoing (per annum)
Australia		
Salt Industry	A$161,000	A$314,000
Bakers	A$6,950,000	A$30,000
Government	A$31,000	A$137,000
Total	**A$7.1 million**	**A$482,000**
New Zealand		
Salt Industry	NZ$303,000	NZ$20,000
Bakers	NZ$1.5 million	NZ$30,000
Government	NZ$8,000	NZ$89,000
Total	**NZ$1.8 million**	**NZ$138,000**

Source: (Access Economics, 2007)

These costs refer to a mandatory fortification process. In cost terms, the relative costs of a voluntary fortification process have not been determined. On one hand, it could be assumed that voluntary fortification costs may be higher because of continued advertisement and advocacy required to sustain fortification. On the other hand, enforcement costs may be higher in a mandatory fortification program. The net cost of moving between mandatory and voluntary is therefore, in our opinion, uncertain.

3.3 Scope of this assessment

Following an invitation from Food Standards Australia and New Zealand (FSANZ), the Centre for Health Economics Research and Evaluation (CHERE) was commissioned to investigate the cost-effectiveness of iodine fortification of bread in Australia and New Zealand. As outlined above a previous report completed by Access Economics used a cost-benefit analysis approach to address a similar question. Our aim in this report is to complement the original evaluation, rather than duplicate it.   This investigation aims to address the following issues.

o   Investigate the extent and quality of evidence concerning the link between iodine deficiency, lower IQ and productivity impacts, and whether addressing iodine deficiency would impact materially on the burden of disease; and

o   Undertake a cost-effectiveness analysis of these issues, if there is sufficient evidence, and to draw conclusions that can reasonably be made of the basis of the current evidence.

The purpose of this report is *not* to:

o   repeat the work produced in an earlier report by Access Economics, which estimated the net benefit of iodine fortification using a cost-benefit analysis approach (Access Economics, 2006).

o   discuss the relative merits of choosing bread as the most suitable vehicle of fortifying the food supply. This has already been discussed in a previous FSANZ report (Food Standards Australia New Zealand, 2007).

o   model the relative benefits of choosing bread only, versus; bread and breakfast cereal, milk or salt. Or,

o   discuss, or model, any ethical issues, pertaining to '*freedom of choice*', that may arise from mandatory fortification as opposed to voluntary fortification.

4 Review of the Literature

4.1 Literature sources and search strategies

The literature was searched to identify relevant studies and reviews concerning iodine deficiency for the period between 1990 and May 2007. Databases of peer-reviewed literature including Medline, PubMed, CINAHL and Cochrane were searched. The bibliographies of all retrieved publications were hand searched for any relevant references missing in the database search.

Web-based searches, using the internet search engines 'Google' and 'Google scholar', were conducted to identify national and international position statements and reports on iodine fortification. Additional relevant Australian reports were obtained from FSANZ and the researchers' professional contacts. Grey literature such as conference abstracts and reports were also included.

4.1.1 Inclusion/selection criteria

The following criteria were used for the review and selection of the studies:

o published 1990 - 2007

o available in English

o specifically focused on IDDs

o preference given to meta-analysis and systematic reviews where available

o articles were selected on relevance to the topic

o hand searching of relevant articles and reports

o relevant Australian and overseas reports/publications known to the researchers

4.1.2 Search terms used

o Iodine deficiency, and

o intelligence quotient, and

o fortification,

o thyroid,

o Iodine deficit disorder$

4.2 Evidence of iodine deficiency in Australia and New Zealand

Six studies in New Zealand and thirteen studies in Australia assessing iodine status in different populations were identified through the search strategy. As recommended by WHO/UNICEF/ICCIDD (World Health Organization. WHO. UNICEF. ICCIDD, 2001) most surveys were conducted in school aged children, and the number of participants was similar across studies. The exceptions were the National Nutrition Survey in New Zealand and the Australian National Iodine Nutrition study which included a larger number of participants. The Australian survey (Li, et al., 2006, NZ Food NZ Children, 2003) used the Thyromobile model to collect samples for urinary iodine determination. The advantage of this is that the methodology is standardised and allows more reliable comparisons among other populations of children which use the same methodology. Delange el al have described that the Thyromobile has been used across Europe (Delange, et al., 1997). All other studies conducted in children used casual urine samples[9] to measure iodine concentration. Studies in adults in New Zealand used 24 hour urine collection.

Goitre rates and serum thyroid-stimulating hormone (TSH) levels were not commonly assessed in these studies. Three Australian studies were conducted in newborns using TSH concentration to determine iodine deficiency (Chan, et al., 2003, McElduff, et al., 2002, Travers, et al., 2006). However, caution should be exercised when comparing these results as TSH measurements in newborns are influenced by a number of factors including: timing of specimen collection, newborn exposure to iodine containing antiseptics and the TSH assay (Copeland, et al., 2002).

Two studies, one in New Zealand and one in Australia, measured thryroid volumes by ultrasound (Li, et al., 2006, Skeaff, et al., 2002). However it was been reported that inter-observer error, type of transducer, type of instrument, and position of the child may all contribute to variations in the results of thyroid volumes (Anonymous, 2000).

No published studies have assessed the iodine status of pregnant women in New Zealand. An abstract presented at the New Zealand Dietetic Association Conference in 2006 reported that the median UIC of 170 pregnant women was 38 µg/l (IQR 24-56 µg/l) and a goitre rate of 7% (Pettigrew Porter A, et al., 2006)). However the authors have not published these results in a peer-reviewed journal. One study investigated the influence of pregnancy and lactation on selenium metabolism. Pregnant women (n=35) were assigned to control (n=17) or 50 µg selenium supplment (n=18). Results for these two groups were combined and a range of iodide excretion for 2–9 months was reported. The median values were somewhat consistent during pregnancy (Range 0.19 – 0.41 µmol/L or 24 µg/l – 52 µg/l) (Thomson, et al., 2001). This result is has to be reviewed with caution since half of the women were receiving Selenium, this trace element influences the metabolism of iodine (Thomson, et al., 2005).

Descriptive characteristics of New Zealand studies are listed in Table 5 and Australian studies in Table 6.

Table 7 focuses on the median UIC level reported by these studies. This allows comparisons between populations (children, adults), places (Sydney, Melbourne) and time (before/after fortification).

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[9] These may be either spot urine samples or fasting samples

Table 5: Summary of studies conducted in New Zealand– study details

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(Thomson, et al., 1997)	Recruitment from blood transfusion centres in Otago and Waikato	Adults between 18-72 years 183* subjects – Otago 128* subjects – Waikato (*Excluding subjects taking supplements including iodine)	UIC in fasting overnight urine specimen and 24 hour urine* sample (*Positive relationship between total 24-h urinary iodine excretion and iodide concentrations in fasting urine samples).	Median UIC: 60 µg/l (Otago) 76 µg/l (Waikato) < 20 µg/l: 7% (n=23) Otago < 50 µg/l: 30% < 100 µg/l: 79% Waikato < 50 µg/l: 23% < 100 µg/l: 71%
(Thomson, et al., 2001)	Recruitment from blood transfusion centre in Otago	Adults aged 18-49 years	24 hour urine sample	Median UIC: 54 µg/l (CI:55-64)
(Skeaff, et al., 2002)	8 schools randomly selected in Dunedin (South) 22 schools using sampling interval in Wellington (North) (Weighting factor was used to account for difference)	282 children between 8-10 years	UIC in urine samples taken between 8 am -12 pm Thyroid volume assessed by ultrasound	Median UIC = 66 µg/l < 20 µg/l: 3.6% (CI: 1.1-6.2) < 50 µg/l: 31.4% (CI: 24.2 – 38.6) < 100 µg/l: 80% (CI:74.1-85.3) 11.3% had enlarged thyroid glands
(NZ Food NZ Children, 2003)	Cross sectional population survey 172 schools across New Zealand	3275 children between 5-14 years old	UIC in urine samples	Median urinary iodine concentration of 66 µg/l 28 % had a urinary iodine concentration below 50 µg/l

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(Skeaff, et al., 2005)	Three cities: Christchurch, Dunedin and Invercargill. Children were randomly selected in each city as a proportion of the population.	n = 230 children between 6 - 24 month old n = 39 Mothers	UIC in casual urine sample	Median urinary iodine concentration in children: 67 µg/l < 20 µg/l: 11.7% (CI 7.6-15.6) < 50 µg/l: 37.0% (CI: 30.5 – 43.4) < 100 µg/l: 67.4% (CI:60.5-74.3) Median in children by food intake Formula fed (n=51): 99 µg/l Breast fed (n=43): 44 µg/l Both (n=17): 59 µg/l Not breast or formula (n=119) 59 µg/l
			UIC in breast milk sample	Iodine concentration in breast milk: 22 µg/l (CI 18-26)

Table 6: Summary of studies conducted in Australia– study details

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(Gunton, et al., 1999)	Cross sectional study at a tertiary referral hospital in Sydney's North	n = 81 pregnant women and 26 of these postpartum women n = 135 patients with diabetes mellitus n = 19 volunteers	UIC in spot urine samples	Median UIC: Pregnant women: 104 µg/l (CI 89-129) Postpartum women: 79 µg/l (CI 44-229) Patients with diabetes: 65 µg/l (CI 58-89) Volunteers: 64 µg/l (CI 54-75) < 50 µg/l Pregnant women: 19.8%(n=16) Postpartum women: 19.2% (n=5) Patients with diabetes: 34.1% (n=46) Volunteers: 26.3% (n=5) < 100 µg/l Pregnant women: 29.6% (n=24) Postpartum women: 34.6%(n=9) Patients with diabetes: 37.8%(n=51) Volunteers: 47.4% (n=9)
(Li, et al., 2001)	Cross sectional study at an outpatient clinic in a tertiary referral hospital in Sydney's West (Late 1998 early 1999)	School children aged 6-13 years n = 94 schoolchildren n= 63 healthy adults n = 101 pregnant women n = 85 diabetic patients n = 19 volunteers	UIC in spot urine samples	Median UIC: School children: 84 µg/l (Range 28-312) Healthy adults: 88 µg/l (Range 12-200) Pregnant women: 88µg/l (Range 20-448) Diabetic patients: 69 µg/l (Range 20-234) < 50 µg/l School children: 13.8% (n=13) Healthy adults: 20.6%(n=13) Pregnant women: 17.8% (n=18) Diabetic patients: 23.5% (n=20)

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(McElduff, et al., 2002)	Cross sectional survey of infants participating in a neonatal screening program at Royal North Shore Hospital in northern Sydney Anonymous samples of babies born 1) Between August 1998 – April 1999 2) Between 1 March – 31 December 2000 3) Infants whose mother attended the hospital between September 1998 – August 1999 4) Mothers of babies in 3)	1) n = 1316 general neonatal population 2) n = 1457 general neonate population 3) n = 84 identified neonatal group Mothers 4) n = 84 Mothers	TSH concentration in whole blood 3 days after birth (WHO recommendation 72 hours)

UIC in urine samples | Neonatal whole blood TSH values > 5mIU/L Sample 1: 8.1% (CI: 6.6-9.5) Sample 2: 5.4% (CI 4.3-6.6) Median TSH value in Sample 1: 1.77 mIU/L Median TSH value in Sample 3: 1.87 mIU/l

Median UIC in mothers: 109 µg/l (65-168 µg/l) < 50 µg/l: 11.9% (CI 5.0-18.8) |

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(Guttikonda, et al., 2002)	Cross sectional survey of schoolchildren in Tasmania	n=225 school children aged 4-17 years	UIC first morning urine samples Thyroid ultrasound scan	Median UIC: 84 µg/l (IQR: 57-110) < 50 µg/l: 20% No significant differences in the thyroid volumes was found
(Guttikonda, et al., 2003)	Cross sectional survey school children attending a public school on the Central Coast of New South Wales in November 2000	n= 301 school children aged 5-13 years	UIC first morning urine samples Thyroid ultrasound scan	Median UIC: 82 µg/l (IQR: 61-109) < 50 µg/l: 14% (n=42) Goitre prevalence of zero
(McDonnell, et al., 2003)	Cross sectional survey of schoolchildren in urban private schools in Melbourne (August 2001)	Children aged 11-18 years n = 607 thyroid gland palpation n = 577 provided urine sample	UIC in urine samples Thyroid gland palpation Grade 1: palpable but not visible goitre Grade 2: palpable and visible goitre	Median UIC: 70 µg/l (IQR 48-98) < 50 µg/l: 27% (n=156) 50 – 99 µg/l: 49% (n=283) ≥100 µg/l: 24% (n=138) Median grade 1 (n=97): 68 (IQR 50-95) Median grade 2 (n=15): 62 (IQR 54-79)
(Chan, et al., 2003)	Postnatal ward of a tertiary referral hospital in Sydney. March- December 2000	Mothers and their newborns n=50	UIC spot urine sample Breast milk TSH (heel-prick blood sample)	Median UIC:46 µg/l (Range 4-140) < 50 µg/l: 58% (n=29) Median: 84 µg/l (25-234) Median TSH value: 1.15 mIU/l > 5 mIU/l: 6% (n=3)

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(Hynes, et al., 2004)	1998-99 Baseline survey. Two stage stratified sampling Tasmanian schools 2000-01 Follow up survey. No intervention involved	School children aged 4-12 years n= 241 Baseline n= 170 Follow up	UIC spot morning urine samples (first void)	Baseline Median UIC: 75 µg/l (Range 15-240) < 50 µg/l: 13% < 100 µg/l: 77% Follow up Median UIC: 76 µg/l < 50 µg/l: 21% < 100 µg/l: 69%
(Hamrosi, et al., 2005)	Prospective study. Pregnant women participating in a Down Syndrome screening study in Melbourne (1999-2001)	Pregnant women n= 277 Caucasian n = 263 Vietnamese n= 262 Indian/Sri Lankan	UIC in spot urine samples	Median UIC: Caucasian 52 µg/l < 50 µg/l Caucasian 48.4% Vietnamese 38.4% Indian / Sri Lankan 40.8%
(Li, et al., 2006)	Australian National Iodine Nutrition study. Cross sectional survey. One stage random cluster drawn from all Year 4 school classes (July 2003 – December 2004)	n=1709 schoolchildren aged 8-10 years	UIC in first morning urine sample Thyroid ultrasound scan	Median UIC: 104 µg/l* (IQR: 71-147) New South Wales: 89 µg/l (IQR:65-123.5) Victoria: 73.5 µg/l (IQR: 53-104.3) South Australia: 101 µg/l (IQR 74-130) Western Australia: 142.5 µg/l (IQR 103.5-214) Queensland: 136.5 µg/l (IQR 104.3-183.8) < 100 µg/l 72.6% Victoria 58.8% New South Wales 47.5% South Australia Thyroid volumes were marginally increased compared with international normative

* Note that this is unlikely to represent the median UIC for the entire population since this is not weighted for population size. See Section 5.4 for details.

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(Travers, et al., 2006)	Antenatal and community midwife program clinics in public hospitals and community centres in NSW Central Coast (March-May 2004)	n= 796 Pregnant women n= 816 Newborns	Maternal UIC in spot urine samples Newborn whole blood thyroid stimulating hormone (TSH)	Median UIC: 85 µg/l < 50 µg/l: 16.6% (n=132) Median UIC public hospital: 82 µg/l Median UIC in private hospital: 101 µg/l Median TSH value: 1.15 mIU/l > 5 mIU/l: 2.2% (n=18)
(Seal, et al., 2007)	Post intervention (fortification of bread with iodine), cross sectional survey of Tasmanian school children. One stage cluster sampling*. Intervention: voluntary bread fortification	Children between 8 -11 years n= 347 in 2003 n= 430 in 2004 n= 401 in 2005	UIC in spot urine samples*	Median urinary iodine concentration pre intervention: 75 µg/l – 1998 72 µg/l – 2000 Median post intervention (2003-2005) 105 µg/l – 2003 109 µg/l – 2004 105 µg/l – 2005 Pre intervention < 50 µg/l: 16.9% 1998 < 50 µg/l: 18.7% 2000 Post intervention < 50 µg/l: 10.1% 2003 < 50 µg/l: 10.0% 2004 < 50 µg/l: 10.5% 2005

Author & Year	Study details	Sample size	Measure of iodine status	Study Results
(Burgess, et al., 2007)	Cross sectional survey of pregnant women attending 1) An antenatal clinic at the Royal Hobart hospital (RHH). (200-01 & 2006) 2) General practices and family planning clinics around Tasmania (2003-2006) (Post bread fortification)	Pregnant women 1) n=285 in 2000-01 & n= 229 in 2006 2) n=288 in 2003-06	UIC in spot urine samples	Median urinary iodine concentration pre intervention (2000-01): 75 µg/l (IQR: 43-189) Pre intervention < 50 µg/l: 30.9% Median post intervention RHH (2006) 86 µg/l (IQR: 57-160) Post intervention RHH < 50 µg/l: 19.2% Median post intervention (2003-06) 81 µg/l (IQR: 63-115) Post intervention < 50 µg/l: 18.8%

UIC: Urinary Iodine Concentration
UIE: Urinary Iodine Excretion

Table 7: Summary of results for urinary iodine excretion in New Zealand and Australian adults and children

Population	Year	Number	Urinary iodide (µg/l)		Study
			Median	Distribution	
New Zealand					
Otago blood donors[a]	1993-94	183	42	Range: 6-126	(Thomson, et al., 1997)
Waikato blood donors[a]	1993-94	128	53	Range:17-152	(Thomson, et al., 1997)
Otago blood donors[a]	1997-98	233	54	CI: 55-64	(Thomson, et al., 2001)
Breast fed infants and toddlers. South island[b]	1998-99	230	67	IQR: 37-115	(Skeaff, et al., 2005)
Dunedin and Wellington children[2]	1996-97	282	66	IQR: 45-91	(Skeaff, et al., 2002)
New Zealand children[b]	2002	1796	66	Range 1-260	(NZ Food NZ Children, 2003)
Australia					
Sydney North adults	1998-99	19	64	CI: 54-75	(Gunton, et al., 1999)
Western Sydney adults	1998-99	63	88	Range 12-200	(Li, et al., 2001)
Pregnant women in Western Sydney	1998-99	101	88	Range: 20-448	(Li, et al., 2001)
Pregnant women in Sydney North	1998-99	81	104	CI: 89-129	(Gunton, et al., 1999)
Pregnant women in Sydney North	2000	84	109	IQR: 65-168	(McElduff, et al., 2002)
Pregnant women NSW Central Coast	2004	796	85	Range: 19-1510	(Travers, et al., 2006)
Pregnant women in Tasmania	2000-01	285	76	IQR: 43-1289	(Burgess, et al., 2007)
Pregnant women in Tasmania	2006	229	86	IQR: 57-160	(Burgess, et al., 2007)
Pregnant women in Tasmania[4]	2003-06	288	81	IQR: 63-115	(Burgess, et al., 2007)
Postpartum women	1998-99	26	79	CI: 44-229	(Gunton, et al., 1999)
Sydney West children	1998-99	94	84	Range 28-312	(Li, et al., 2001)
Tasmanian children	1998-99	241	75	IQR: 60-96	(Hynes, et al., 2004)
Central Coast New South Wales children	2000	301	82	IQR: 61-109	(Guttikonda, et al., 2003)
Tasmanian children	2000	225	84	IQR: 57-110	(Guttikonda, et al., 2002)
Melbourne children	2001	577	70	IQR: 48-98	(McDonnell, et al., 2003)
Tasmanian children	2000-01	170	76	IQR: 54-105	(Hynes, et al., 2004)
Australian children	2003-04	1709	104	IQR: 71-147	(Li, et al., 2006)
Tasmanian children[c]	2003	347	105	IQR:72-147	(Seal, et al., 2007)
Tasmanian children[c]	2004	430	109	IQR:74-159	(Seal, et al., 2007)
Tasmanian children[c]	2005	401	105	IQR: 72-155	(Seal, et al., 2007)

[a]24 h urine collection; [b]Casual urine samples; [c]After voluntary food fortification; CI: Confidence interval ; IQR: Inter-quartile range

4.3 Iodine supplementation/fortification

This section reviews the success of particular iodine fortification (or supplementation) programs.

4.3.1 Supplementation

In severely affected areas iodine supplementation has been addressed by the administration of a slow-release preparation such as iodised oil. This form of supplementation has been restricted to populations living in areas of severe deficiency and for specific groups such as pregnant women and young children where iodised salt coverage is not sufficient (World Health Organization, 2007).

A Cochrane systematic review, measuring the effects of maternal iodine supplementation in areas of iodine deficiency is currently under revision (Mahomed and Gulmezoglu, 2000). This review will be relevant for populations with high level of endemic goitre.

One systematic review has been conducted on the role of iodised supplementation for preventing IDDs (Angermayr and Clar, 2004). Angermayr *et al* found twenty six prospective controlled trials: twenty of them were classified as low quality and six of moderate quality (Angermayr and Clar, 2004). The main conclusion of the review was that methodological differences between studies and poor quality of the studies did not allow for a meta-analysis to be conducted. However the authors concluded that despite this, the results suggested that iodine supplementation is an effective means of decreasing goitre rates and improving iodine status in children. Also there were indications of positive effects on physical and mental development (although not always significant) (Angermayr and Clar, 2004).

This review does not consider supplementation by intake of iodine-containing dietary supplements.

4.3.2 Fortification

The WHO states that the most appropriate method for increasing dietary iodine is via the fortification of salt (World Health Organization. WHO. UNICEF. ICCIDD, 1994, World Health Organization. WHO. UNICEF. ICCIDD, 2001). Currently more than 98 countries report some form of fortification program using salt. (World Health Organization. WHO. UNICEF. ICCIDD, 2001). However some developing countries such as India have reported difficulties with fortification of animal feeds and good enforcement of USI (International Council for Control of Iodine Deficiency Disorders, 2005). Additionally, some salt forms used in food processing cannot be iodised, rendering universal fortification impossible (Personal correspondence with FSANZ).

Due to the re-emergence of iodine deficiency some salt iodisation programs have undergone changes. What follows is a brief description of three fortification programs which have been evaluated following changes in the legislation.

4.3.3 Denmark

Voluntary fortification of salt (sodium chloride) with iodine was introduced in Denmark in 1998 (Rasmussen, et al., 1996). Due to poor compliance, mandatory fortification of household salt and bread was introduced during the period July 2000-April 2001. The fortified level of iodine also increased from 8 to 13 ppm (Rasmussen, et al., 2002). Median urinary iodine concentration of participants not taking iodine supplements before mandatory fortification was 45 µg/l (moderate)

in Aalborg and 61 µg/l (mild) in Copenhagen (Laurberg, et al., 2006). The main problem with this study was that UIC levels post-fortification were not measured. However, Lauberg *et al* calculated that iodine intake increased by 62 µg iodine per day (Laurberg, et al., 2006).

In another Danish study iodine intake was determined by estimating the content of iodine in bread and household salt after the mandatory fortification program was introduced (Rasmussen, et al., 2007). Rasmussen *et al*, used data from a nationwide dietary survey, completed by 4,124 randomly selected Danish individuals. The study results demonstrated that the median iodine intake from bread increased by 25 µg/day (Range 13-43) and total (salt and bread) intake increased by 63 µg/day (Range 36-104) (Rasmussen, et al., 2007).

4.3.4 Switzerland

In Switzerland iodised salt has been available nationwide since 1952. However, in 1980 due to persisting mild iodine deficiency Swiss authorities decided to increase the iodine content in salt from 7.5 to 15 mg/kg (Burgi, et al., 1990). In the early 1990s mild iodine deficiency was reported in school children (96 µg/l) and pregnant women (83-100 µg/l) (Zimmermann, et al., 2005). As a consequence, in 1998 the minimum content of iodine in salt was increased to 20 mg/kg. Zimmerman *et al* (2005) evaluated the impact of these iodine increases in salt iodine concentration in newborn children, school aged children and pregnant women. In 1999 median UIC in children was 115 µg/l (5-143 µg/l) and 138 µg/l (5-1881 µg/l) in pregnant women. In 2004 UIC was 141 µg/l (0-516 µg/) and 249 µg/l (8-995 µg/), respectively (P<0.01). In addition to this, newborn thyrotropin concentrations > 5 mU/l decreased from 2.9% in 1992-1998 to 1.7% in 1999-2004 (P<0.0001) (Zimmermann, et al., 2005).

In this same study the proportion of children with UIC > 100 µg/l increased from 60 to 86%. The proportion of children above UIC 300 µg/l (iodine excess) increased from 2 to 4%.

4.3.5 Australia

The only paper which reports both UIC before and after an iodine fortification program is that by Seal *et al.* (2007). Between 2000 and 2003, the median UIC increased from 72 µg/l (95%CI:67-84) to 105 µg/l (95%CI:98-111). This increase in median UIC (33 µg/l) was not spread equally across the distribution. The lower quartile median UIC rose from 54 µg/l to 72 µg/l (18 µg/l), and the upper quartile rose from 103 µg/l to 147 µg/l (44 µg/l). This suggests that after iodine fortification, not only is there the expected increase in median UIC, but also a spread in the UIC range.

Recent evidence has suggested that the effect of voluntary fortification on pregnant women may be below this level. Using individuals exposed to the same Tasmanian fortification program, Burgess and colleagues measured the median UIC in individuals attending the Royal Hobart Hospital (RHH) prior to fortification (2001), and compared this with the median UIC after fortification (2006). In addition to this the authors also investigated a population of pregnant women in primary health care centres between 2003 and 2006. Looking only at the comparable RHH populations, the increase in median UIC was 10 µg/l (Burgess, et al., 2007) .

These results of the changes in UIC following a fortification program are summarised in Table 8.

Table 8: Summary of fortification studies

Author & Year	Study location	Vehicle	Study details	UIC/Intake Before	UIC/Intake After
Seal et al (2007)*	Australia (Tasmania)	Iodized salt 40 mg/kg in bread (Voluntary)	Children between 8 -11 y **Before (1998 – 2000)** n= 124 in 1998 n= 91 in 2000 **After (2003 - 2005)** n= 347 in 2003 n= 430 in 2004 n= 401 in 2005	75 µg/l – 1998 (CI 72-80) 72 µg/l – 2000 (CI 67-84)	105 µg/l – 2003 (CI 98-111) 109 µg/l – 2004 (CI 103-115) 105 µg/l – 2005 (CI 98-118)
Burgess et al (2007)*	Australia (Tasmania)	Iodized salt 40 mg/kg in bread (Voluntary)	Pregnant women **Before (2000-01)** **After (2003-2006)** n=285 in 2000-01 n=288 in 2003-06 n=229 in 2006	76 µg/l (IQR: 43-189)	81 µg/l (IQR: 63-115) – 2003 & 2006 86 µg/l (IQR: 57-160) - 2006
Lauberg et al (2006)	Denmark	Bread and salt 13 ppm (Mandatory)	**Before (1997-1998)**: 4616 subjects living in either Aalborg or Copenhagen before iodine fortification was started **After (2004-2005):** 3500 subjects from the same cities about 5 years after iodine fortification was started	45 µg/l Aalborg 61 µg/l Copenhagen	Iodine intake was calculated to increase by 62 µg iodine per day. 101 µg/l (57-151) Copenhagen, (n=3553 subjects who did not take dietary supplements)**
Rasmussen et al (2007)	Denmark	Bread and salt 13 ppm (Mandatory)	**After (2000-2002):** 4,124 randomly selected Danish subjects who completed a nationwide dietary survey. A total of 312 bread samples and 18 table salts were analysed for iodine content.		Median intake Bread: 25 µg/day (13-43) Total: 63 µg/day (36-104)
Zimmermann et al (2005)	Switzerland	Salt 20mg/kg Mandatory	**After 1999 (1 year after iodine increase)** n= 610 school children n= 511 pregnant women **After 2004 (5 years after iodine increase)** n=386 school children n=279 pregnant women	96 µg/l school children (Zurich & Engadine valley) (Zimmermann, et al., 1998) 115 µg/l school children Range (5-413) 138 µg/l pregnant women. Range (5-1881)	115 µg/l school children Range (5-413) 138 µg/l pregnant women. Range (5-1881) 141 µg/l school children Range (0-516) 249 µg/l pregnant women. Range (8-995)

* Study details are provided in Table 6 and Table 7 ** Personal communication from Dr. Lone Banke Rasmussen

4.4 Iodine deficiency and IQ

The most important consequence of iodine deficiency has been described as mental retardation. (World Health Organization. WHO. UNICEF. ICCIDD, 1994) Haddow *et al* have shown that sub clinical hypothyroidism has subtle effects on foetal neurodevelopment (Haddow, et al., 1999). This study explored the association between thyroid deficiency during pregnancy and lower IQ scores of their children in the absence of neonatal hypothyroidism. Women with thyroid deficiency were four times more likely to have children with an IQ significantly below the average. IQ scores on average were seven points lower (Haddow, et al., 1999). A meta-analysis of 18 studies on mental development in iodine deficient areas (17 severe and 1 mild) demonstrated that there is a loss of 13.5 IQ points compared to controls from iodine sufficient areas (Bleichrodt and Born, 1994). There are some limitations to Bleichrodt's study: firstly, the mixture of outcomes of IQ and non-IQ tests and secondly, limiting the selection of studies to those reported in English language journals.

The evidence linking populations with mild or moderate iodine deficiency to cognitive development is not as well-established or widely studied as the link with severe iodine deficiency. Mild maternal iodine deficiency can result in a decrease in cognitive capacity and subtle psychomotor defects in the population (Boyages, 1993). Mild iodine deficiency is associated with neurological deficits and hearing impairments (Azizi, et al., 1995, Azizi, et al., 1993, Bleichrodt and Born, 1994, Boyages, 1994). A number of papers clearly identify that a society with a lower level of iodine is likely to have a higher level of intellectual impairment (Azizi, et al., 1995, Azizi, et al., 1993, Bleichrodt and Born, 1994, Boyages, 1994). Evidence suggests that this is particularly relevant in iodine deficiency in the early stages of pregnancy (Delange, 2005).

Most publications have aimed to ascertain the effect of iodine supplementation on cognitive and motor performance in moderately to severely iodine deficient children (van den Briel, et al., 2000, Zimmermann, et al., 2006) However these results may not be generalisable to areas with a different degree of iodine deficiency. As previously discussed children in Australia and New Zealand are mildly iodine deficient. Most studies have been also conducted in developing countries. Therefore the group of children in these studies are also less likely to compare to the Australian/New Zealand, characteristics like as health, socioeconomic status and the accessibility and quality of the education are likely to differ. There are also differences in terms of methodology and transferability of the instruments used in different studies.

A recently published article by Santiago-Fernandez *et al.* measured the relationship between urinary iodine concentration and intellectual capacity in schoolchildren in Spain (Santiago-Fernandez, et al., 2004). The median UIC for the iodine deficient cohort was 90 µg/l (i.e. mild deficiency). This study identified a significant difference in IQ between those with a UIC below 100 µg/l (96.40 IQ points), and those above 100 µg/l (99.03 IQ points), p-value of 0.01 (Santiago-Fernandez, et al., 2004). This study is relevant to Australia/New Zealand as it was conducted in an area of mild deficiency and in a developed country.

4.5 Iodine induced hyperthyroidism (IIH)

Iodine induced hyperthyroidism (IIH) has been reported in iodine supplementation programs. (Bulow Pedersen, et al., 2006). IIH seems to occur primarily in older

populations (Laurberg, et al., 2006) with autonomous thyroid nodules caused by longstanding low iodine intake (Bulow Pedersen, et al., 2006) .

Connolly *et al* reported an increase in the incidence of thyrotoxicosis after bread was iodised with potassium iodate in 1966 in Tasmania. Toxic nodular goitre was more common than Grave's disease and the incidence was higher in older people (Connolly, et al., 1970).

In China, salt has been iodised since 1996. Since then the median UIC has increased from 165 µg/l in 1995 to 330 µg/l in 1997 (Teng, et al., 2006). Teng *et al* investigated the iodine induced thyroid disease after 1999 (4 years after fortification). This study demonstrated that an area with adequate iodine intake (median 243 µg/l) had a higher prevalence of subclinical hypothyroidism and of autoimmune thyroiditis compared to a mild iodine deficient area (median 84 µg/l) (Teng, et al., 2006). The authors concluded that more than adequate or excessive iodine intake may lead to hypothyroidism and autoimmune thyroiditis.

In Austria, the level of salt iodisation doubled in 1990. Mostbeck *et al* conducted a study to assess the annual incidence of hyperthyroidism before and after the intervention (Mostbeck, et al., 1998). According to the study results hyperthyroidism could be divided into two phases after salt iodisation; first the incidence of hyperthyroidism increases and peaks after 1-4 years, this is then followed by a decrease. Sub clinical Graves disease did not follow this pattern (Mostbeck, et al., 1998).

In Denmark, Bulow Pedersen *et al* identified that, while the incidence of hyperthyroidism was consistently higher in older cohorts, the increased incidence of hyperthyroidism under a fortification scheme was greater in younger populations. The Danish approach had two main stages. (Bulow Pedersen, et al., 2006)

- o In June 1998, they introduced a voluntary scheme, adding 8 parts per million (ppm) iodine to all salt

- o In June 2000 the program became mandatory. In addition, the level of iodine increased to 13 ppm in household salt and iodised salt in commercial bread production was also included

The Copenhagen cohort used in this paper is largely representative of the Australian population, since, at baseline, the population was mildly iodine deficient (rather than moderate as seen in Aalborg). However, Denmark has a long history of iodine deficiency having only included voluntary iodised salt in the 1990s (Rasmussen, et al., 1996). The Copenhagen experience was an increase in hyperthyroidism from a baseline figure of approximately 80 cases per 100,000 per year to approximately 100/100,000.

The Danish results differ from those in Switzerland (Baltisberger, et al., 1995). In 1980, Switzerland raised the iodine content of salt from 7.5 mg/kg to 15 mg/kg. This raised the iodine level of the population from mild deficiency to iodine sufficiency. In the first year, there was a 27% rise in hyperthyroidism. However, this declined year on year until, at the end of a ten year period, the number of cases of hyperthyroidism had reduced to 44% of the level seen before fortification. This was predominantly caused by a decrease in the number of toxic nodular goitre. Thus, the number of cases of hyperthyroidism began at 62.3 per 100,000 per year, increased in year one to approximately 79 per 100,000, and then declined to approximately 27 per 100,000 at year ten.

These contrasting results may be explained by the fact that the incidence of hyperthyroidism depends on the severity of iodine deficiency and the magnitude of the increase in iodine intake (Stanbury, et al., 1998). These experiences illustrate the importance of population monitoring during iodine fortification programs.

4.6 Hypothyroidism and goitre

Laurberg *et al* used the same Danish data to contrast the rates of hypothyroidism and goitre between Copenhagen and Aalborg. The standardised incidence rates of hypothyroidism in the two areas were 38.9 and 29.2 cases per 100,000 per year, respectively. As expected, the area with a greater deficiency had an elevated level of hypothyroidism. (Laurberg, et al., 2006) Unfortunately, in the absence of time series data, it is not possible to estimate accurately the number of cases averted through the fortification program.

Similarly, the prevalence of palpable goitre was higher in the Aalborg cohort across four age ranges considered (women aged 18-22, 25-30, 40-45 and 60-65, and men 60-65). Unfortunately, time series data was not presented. The excess prevalence of goitre in the moderate relative to the mildly deficient population, ranged from approximately one percentage point in the youngest cohort of women to almost ten percentage points for the cohort of men aged 60-65.

5 Economic Modelling of Mandatory Fortification of Bread with Iodine

Economic evaluation of new health care initiatives is important where the new initiative offers health benefits at additional costs. When a constraint is applied to the additional cost that would be paid for a given health gain, economic evaluation can determine whether such incremental costs represent value for money.

The usual process for an economic evaluation is first to determine the incremental effectiveness, which is the additional benefits associated with the new initiative relative to current practice. Secondly, to determine the incremental costs, this is the difference in costs between the new initiative and current practice. Finally the incremental cost-effectiveness ratio (ICER) can be calculated using the following ratio:

$$ICER = \frac{Cost_{New} - Cost_{Comparator}}{Effectiveness_{New} - Effectiveness_{Comparator}}$$

The fortification options assessed during the evaluation are:

o Current approach – maintenance of *status quo*, which would see the continuation of the existing code which allows for the voluntary addition of iodine to household discretionary salt.

o The mandatory replacement of salt with iodised salt in bread, with the salt iodisation range from 35-55mg of iodine per kg of salt.

5.1 Assumptions

This modelling is based on a series of assumptions, necessitated by a lack of suitable information. These are listed now, and discussed in more depth in this section and the discussion.

o We do not include the costs of treating conditions which are caused or prevented by changing levels of iodine.

o Due to uncertainty regarding the market share of organic bread (which would be exempt from mandatory fortification), we have excluded it from the analysis.

o The cost of regulation (of a mandatory approach) or promotion (of a voluntary approach) are excluded since there is no appropriate data available

o We have limited our investigation to hyperthyroidism, hypothyroidism, goitre and intellectual impairment.

o In the base case, we have not investigated children aged 0-2 years, as their source of iodine is uncertain, and the effect of fortification on their UIC is uncertain. In the sensitivity analysis, we consider the effect of including this age group as children.

o We have assumed that both national populations can each be summarised by one distribution, although there are areas of iodine deficiency and iodine sufficiency (such as 8-10 year olds in Queensland and Western Australia). However, since targeting fortification by region is unrealistic, we have not considered this in the analysis.

5.2 Introduction

During the economic evaluation of mandatory iodine fortification in bread, we adopted an iterative approach, asking three sequential questions. The answer to each was based on a combination of the previous result and a number of additional assumptions (predominantly drawn from the existing literature).

The three steps are laid out below. For each, we identify the main question contained within the step, sub-questions that provide parameters for the calculations, and the outcome we expect to produce.

Step 1: Identification of the number of individuals who would receive iodine-fortified bread who would not have otherwise done so

1. Australian / New Zealand population size

2. Proportion of population who eat bread

3. Proportion of bread that is currently subject to voluntary fortification

The result from this question will be an estimate of the population over which the intervention would be applied.

Step 2: Identification of the number of individuals with averted iodine deficiency under the intervention (mandatory fortification) relative to the control

1. Details of the pre-intervention Australian and New Zealand population in terms of urine iodine content (UIC). This is stratified into children, pregnant women, and other adults.

2. The likely effect of fortification on this measure

The result from this will be the estimated reduction in individuals with an average annual UIC below 50 µg/l, and between 50 µg/l and 100 µg/l (and also an increase in individuals with a UIC greater than 300 µg/l).

Step 3: Identification of the number of cases of condition linked to iodine deficiency that have been averted (or possibly caused)

o Probabilities of different conditions (such as hypothyroidism, intellectual impairment, goitre and hyperthyroidism) given mild, moderate or severe IDD, or an excessive UIC.

The result from this will be an estimate of the number of cases of each of these conditions that have been averted. It is worth noting that the level of uncertainty surrounding the results increases as we move from step1 through to step 3.

5.3 Estimation of the impact of iodine-fortified bread

Step 1: Identification of the number of individuals who would receive iodine-fortified bread who would not have otherwise done so

5.3.1 Australian / New Zealand population size

The populations of the two countries were identified through the Australian Bureau of Statistics website[10] and the Statistics New Zealand website[11]. The populations are shown in Table 9. The number of women with unborn children was estimated by multiplying the number of children born in one year by (nine months / 12).

Table 9: Population Sizes in Australia and New Zealand

	Australia	New Zealand
Pregnant Women	194,850	42,600
Children (2-18 years old)	4,589,076	1,000,422
Adults (18 and over)	15,496,635	2,916,207

5.3.2 Proportion of population who eat bread

The proportion of the population who eat bread was identified in a previous FSANZ report at 87% in New Zealand and 88% in Australia (Food Standards Australia New Zealand, 2006). These values were used to estimate the numbers of individuals receiving iodine via bread in each country.

5.3.3 Proportion of bread that is currently subject to fortification

At present, there is limited fortification of bread in Australia and New Zealand. The main example of such an approach is in Tasmania, which has a voluntary fortification scheme covering approximately 80% of the bread consumed. Of the entire bread-eating population of Australia, that amounts to approximately 1.88% of the Australian population (based on ABS population figures for Tasmania and Australia). The modelling assumed that there was currently no fortification of bread in New Zealand[12].

Using these assumptions, and allowing for the number of Tasmanians currently receiving fortified bread, the numbers of people exposed to iodine-fortified bread in Australia and New Zealand who would not have otherwise been, is presented in Table 10.

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[10] http://www.abs.gov.au/
[11] http://www.stats.govt.nz/default.htm
[12] It is worth noting that a proportion of salt is iodised in Australia and New Zealand. However since this proportion is unlikely to change we ignored this from the analysis.

Table 10: The exposed population

	Australia	New Zealand
Pregnant Women	168,244	37,062
Children (2-18 years old)	3,962,433	870,367
Adults (18 and over)	13,380,550	2,537,100

To illustrate how these figures are derived, consider pregnant women in Australia. The total population is 194,850. 88% of these eat bread (which is equal to 171,468) and, of those 98.12% are not currently receiving fortified bread (171,468 x 0.9812 = 168,244)

5.4   Estimation of deficiency averted

Step 2: Identification of the number of individuals with an averted iodine deficiency disorder (IDD), both under the intervention (mandatory fortification) and the control (status quo)

- o   Details of the pre-intervention Australian and New Zealand population in terms of urine iodine content (UIC). This is stratified into children, pregnant women, and other adults.

Due to the limited nature of the evidence, it was necessary to estimate distributional shapes for the present annual average UIC. A normal distribution was considered, but rejected on the grounds that most papers identify the UIC distribution to be skewed, which cannot be captured under an assumption of normality. Since we are considering the average iodine level over a year, it could be argued that the Central Limit Theorem applies. However, the gamma distribution modelled the data successfully so we retained it[13].

The important feature of the gamma distribution is that it is very flexible, and, by setting alpha and beta correctly, a wide variety of distributions are able to be modelled. The six sub-populations we are considering here (pregnant women, other adults and children in Australia and NZ) have different data on which we fitted the gamma distribution for a pre-intervention distribution. We identified articles which provide details on the current distribution of UIC. The most common measure of this was single UIC levels. However, this is not an appropriate measure for the estimation of deficiency in an individual since it varies significantly in non-deficient individuals over time. (Andersen, et al., 2001) (Busnardo, et al., 2006) (Rasmussen, et al., 1999) Data from Denmark (Andersen, et al., 2001) suggested that the variation around the mean was 2.4 times larger for individual samples than for annual average values. Therefore, we transformed the distributions, identified in the literature in this way (e.g. an inter-quartile range (IQR) of 24 in individual observations is transformed into an IQR of 10 for annual average values).

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[13] The probability density function for the gamma distribution is defined as:

$$g(x; \alpha, \beta) = x^{\alpha-1} \frac{\beta^{\alpha} e^{-\beta x}}{\Gamma(\alpha)} \ \text{ for } x > 0$$

To estimate gamma distributions for the six sub-populations (after adjusting as described previously), we used a systematic approach to varying alpha and beta and identified the distribution which best estimated our desired median and IQR. We generated 1,000 observations under each gamma distribution with an even mean between 40 and 180, and an even standard deviation between 2 and 100 (thus 3,550 distributions providing 3,550,000 observations). Knowing that a particular sub-population had an identified median and IQR (or percentage below a particular threshold), we then identified those combinations of alpha and beta which matched these desired figures (allowing divergence of three in the median, lower and upper quartiles for random variation). If more than one combination of alpha and beta matched our desired properties of the distribution, we averaged the parameters. This information for the six sub-populations is summarised in the appendix. It should be noted that, when a study refers to a proportion of the population below a particular level, this refers to a survey of spot samples. Therefore, in generalising to an annual average Iodine level, we used the 2.4 factor adjustment described previously to adjust for this. For example, if we identify a study with a spot sample median of 74, and 20% of the population below 50 µg/l, we assert that, on annual average Iodine levels, this 20% below 50 µg/l on the spot sample are below 64 µg/l (i.e. reducing the spread between the median and lowest 20% by a factor of 2.4) on the annual average figures.

One important caveat to this concerns the Australian child population. The National Iodine Nutrition Survey did not produce a weighted median for UIC levels (Li, et al., 2006). As noted in Table 6, the raw median was 104 µg/l. However, this is likely to overestimate the true population median since the relatively highly populated states (New South Wales and Victoria) reported a low median (89 µg/l and 73.5 µg/l respectively) and are underrepresented in the raw median. In correspondence with FSANZ, we estimated that the figure in this population was likely to be approximately 94 µg/l.

5.4.1 The possible effect of fortification

One paper which reports both before and after a fortification program is that by Seal *et al* (2007). Between 2000 and 2003, the median UIC increased from 72 µg/l (95%CI:67-84) to 105 µg/l (95%CI:98-111). This increase (of 33 µg/l) was not spread equally across the distribution with the lower quartile rising from 54 µg/l to 72 µg/l (18µg/l), and the upper quartile rose from 103 µg/l to 147 µg/l (44 µg/l). Since this paper was based on a voluntary fortification scheme, covering 80% of the population, we assumed that the effect of mandatory fortification would be scaled up to the entire population (i.e. by dividing the increase in UIC by 0.8), as shown in Table 11.

Table 11: The effect of fortification on UIC

	Lower Quartile		Median		Upper Quartile	
	Tasmanian	Mandatory	Tasmanian	Mandatory	Tasmanian	Mandatory
Increase in UIC (µg/l)	18	22.5	33	41.25	44	55

We assumed a linear relationship between pre-existing iodine level and effect of fortification (thus giving us expected effect of fortification across the entire range).

There are two caveats to the assumption presented in Table 11. The first is that recent evidence (Burgess, et al., 2007) has suggested that the effect of voluntary fortification on pregnant women may be below this level. Using the same Tasmanian program, Burgess and colleagues examined the median UIC of women attending the Royal Hobart Hospital (RHH) prior to fortification (2001), and contrasted this with the median UIC for women attending the hospital in 2006, and in a population of pregnant women attending primary health care centres between 2003 and 2006. If only the comparable RHH populations are considered, the increase in median UIC was 10 µg/l. If this is scaled up to estimate the effect of a mandatory fortification scheme (as in Table 11), the increase in median UIC is 12.5 µg/l. However, the overall results are counter-intuitive in that while the lower quartile figure increases by 14 µg/l, the upper quartile decreases by 29 µg/l. Another reason for ignoring these data, is that the pre-fortification distribution was much more dispersed than any of the other population studies identified; thus it is our opinion that this sample was not representative of the true Tasmanian population. Finally, international evidence suggests that pregnant women are likely to see a considerably higher increase in urinary iodine levels than 10 µg/l (Zimmermann, et al., 2005). For these reasons, we decided to use the figures reported in Seal *et al* (2007) Although it should be noted that if there is any reason to assume that pregnant women will benefit less by fortification, the reduction in iodine deficiency will be less than that stated here.

The second caveat is that evidence suggests that the effect of fortification (either mandatory or voluntary) will be amplified in New Zealand as they tend to eat relatively more bread and have a slightly elevated level of salt in their bread (Personal correspondence with FSANZ). The two factors combined mean that, on average, the effect of fortification will be 1.559 times greater in New Zealand children relative to their Australian contemporaries, 1.569 times greater for pregnant women in New Zealand, and 1.551 times higher for other New Zealand adults.

To investigate the effect of fortification on the proportion of people with an iodine deficiency, the next step was to calculate the proportion of the population under mandatory fortification and the status quo who were expected to have an annual average UIC of below 50 µg/l and 100 µg/l, and multiply this by the populations exposed to bread. In this way, we identify the number of people who would have been below these thresholds, but are now not. The proportions of the population are shown in Table 12 and Table 13, and the numbers are shown in Table 14 and Table 15.

Table 12: Bread eating population percentages below thresholds under mandatory fortification in Australia

	Adults		Children		Pregnant Women^	
UIC(µg/l)	Status Quo	Mandatory Fortification	Status Quo	Mandatory Fortification	Status Quo	Mandatory Fortification
<50	1.5%	0.7%	1.0%	0.5%	0.7%	0.3%
<100	71.3%	27.2%	55.4%	22.5%	79.7%	27.6%
<300	>99.9%	>99.9%	>99.9%	>99.9%	>99.9%	>99.9%

Table 13: Bread eating population percentages below thresholds under mandatory fortification in New Zealand

UIC(µg/l)	Adults*^		Children	
	Status Quo	Mandatory Fortification	Status Quo	Mandatory Fortification
<50	7.5%	1.6%	10.9%	2.6%
<100	97.2%	28.6%	96.1%	29.5%
<300	>99.9%	>99.9%	>99.9%	>99.9%

* This includes pregnant women due to a lack of baseline evidence in New Zealand in this group. ^ The WHO recommendation for pregnant women is 150 µg/l. We have used 100 µg/l to investigate the relevant deficiency in pregnant women relative to the rest of the population. However, it is important to look at the proportion of pregnant women below 150 µg/l with and without fortification. This is discussed following Table 15.

Table 14: Expected levels of iodine deficiency (defined by average annual UIC) in the Australian bread-eating population

UIC(µg/l)	Adults		Children		Pregnant women	
	Status quo	Mandatory	Status quo	Mandatory	Status quo	Mandatory
<50	200,700	93,700	39,600	19,800	1,200	500
<100	9,540,300	3,639,500	2,195,200	891,500	134,100	46,400

*All figures rounded to the nearest 100

Table 15: Expected levels of iodine deficiency (defined by average annual UIC) in the New Zealand bread-eating population

UIC(µg/l)	Adults		Children		Pregnant women	
	Status quo	Mandatory	Status quo	Mandatory	Status quo	Mandatory
<50	190,300	40,600	94,900	22,600	2,800	600
<100	2,466,100	725,600	836,400	256,800	36,000	10,600

*All figures rounded to the nearest 100

As noted previously, the WHO has suggested pregnant women should have an iodine intake of 250 µg/day. Using the median UIC as an indicator of iodine status, pregnant women should have an UIC of 150 µg/l to be categorised as an adequate iodine intake. It is important to consider the effect of using this different threshold (150 µg/l) on the results presented above. Without fortification, our modelling estimates that, in the bread-eating population, 168,200 Australian pregnant women and 37,000 New Zealand pregnant women are below 150 µg/l. In both cases, this represents almost the entire population. Under fortification, the figures drop to 122,500 in Australia and 23,700 in New Zealand. This suggests that, even under mandatory fortification, 72.8% of Australian pregnant women and 64.0% of the New Zealand pregnant women fail to reach the WHO guidelines. Arguably, this suggests a role for further supplementation in

this high-risk group, especially since a proportion of women are not affected by fortification of salt in bread due to their consumption patterns.

5.5 Estimated number of IDD linked conditions averted

Step 3: Identification of the number of cases of condition linked to an IDD that would be averted (or caused in the case of hyperthyroidism)

- o Probabilities of different conditions (such as hypothyroidism, intellectual impairment, goitre and hyperthyroidism) given mild, moderate or severe IDD, or an excessive UIC.

We could not identify any good quality studies which either demonstrated or refuted a quantifiable link between particular levels of iodine deficiency and particular conditions in individuals (e.g. showing that a particular level of Iodine deficiency corresponds to a particular level of risk for a person). However, there is a significant literature identifying a relationship between iodine levels and hypothyroidism, intellectual impairment, goitre and hyperthyroidism at a population level (showing that a changing level of Iodine will prevent a proportion of cases of various conditions). We believe that identifying the proportion of individuals with an annual average UIC of below a particular level (50 µg/l or 100 µg/l) before and after fortifications provides valuable information regarding the size of the at-risk population.

5.5.1 Intellectual Impairment

Pregnant Women: As we have already identified, unborn babies are at particular risk from iodine deficiency. Consequently pregnant women are an important cohort as their iodine levels affect those of their unborn infants, with subsequent effects on the intellectual development of these children. If we assume intellectual impairment is most likely to occur in the unborn children of pregnant women with a very low iodine level (i.e. an average annual UIC less than 50 µg/l), the modelling we have undertaken here suggests that fortification will result in a reduction in the at-risk population of 673 in Australia, and 2,187 in New Zealand. This represents a reduction in the at-risk population of 57.1% in Australia and 78.7% in New Zealand.

Children: A study conducted in Spain by Santiago-Fernandez and colleagues (2004) identified a significant difference in IQ between those with a UIC below 100 µg/l (96.40 IQ), and those above 100 µg/l (99.03 IQ), p-value = 0.01. In our estimation of the parameters, we estimated that fortification would enable an increase in iodine (above 100ug/l) for 32.9% of children in Australia and 67.5% of children in New Zealand. As noted by Access Economics (2006), the importance of this conclusion rests partially on this issue of reversibility of intellectual impairment. However, since mandatory fortification applies to an individual throughout their lives, and hence to the factors which caused the raised IQ level in the iodine-sufficient population, it is reasonable to assume this increase in IQ would apply. Applying this 2.63 IQ point increase to this group, and assuming that no other IQ benefit was elicited (for example, through severely deficient individuals becoming only mildly or moderately deficient), the effect on average IQ in the entire childhood cohort considered in Table 10 would be to increase it by 0.598 IQ points in Australia, and by 1.235 IQ points in New Zealand.

5.5.2 Hyperthyroidism

Hyperthyroidism is usually observed in older populations (Laurberg, et al., 2006). Evidence from Switzerland indicates the possibility effect of fortification on hyperthyroidism. (Baltisberger, et al., 1995) In 1980, Switzerland raised the iodine content of salt from 7.5 mg/kg to 15 mg/kg. This raised the iodine level of the population from that of mild deficiency to that of iodine sufficiency (which is similar to the expectation of the effect of fortification in Australia). In the first year, there was a 27% rise in hyperthyroidism. However, this declined year on year until, at the end of a ten year period, the number of cases of hyperthyroidism had reduced to 44% of the level seen before fortification. This was predominantly caused by a decrease in the number of cases of toxic nodular goitre. Thus, the number of cases of hyperthyroidism began at 62.3 per 100,000 per year, increased in year one to approximately 79 per 100,000, and then declined to approximately 27 per 100,000 in year ten.

Evidence from Denmark relies on observations of a fortification scheme with two distinct stages, as previously discussed in section 4.3.3. Of the Danish cohorts considered, the Copenhagen cohort used in this paper (Bulow Pedersen, et al., 2006) is more representative of the Australian population since, at baseline, it has a mild iodine deficiency (rather than the moderate observed in Aalborg). One noteworthy difference between Denmark and Australia is that Denmark has a long history of iodine deficiency: Thus, the cases of hyperthyroidism observed in the immediate post-fortification period might over-estimate those occurring following mandatory fortification in Australia. The respective median UICs for Copenhagen and Aalborg were 61 µg/l and 44 µg/l, both lower levels than those measured in the Australian population. The effect on hyperthyroidism of the program in Copenhagen was to increase it from a baseline figure of approximately 80 cases per 100,000 per year to approximately 100 per 100,000. If these results were applied to the adult population of 13 million identified in Table 10, it would suggest an increase in hyperthyroidism cases of 2,676 per year in Australia.

5.5.3 Hypothyroidism and Goitre

Laurberg *et al* use the same Danish data to contrast the rates of hypothyroidism and goitre between Copenhagen and Aalborg (Laurberg, et al., 2006). The standardised incidence rates of hypothyroidism in the two areas were 29.2 and 38.9 cases per 100,000 per year respectively. The area with a milder iodine deficiency had an elevated level of hypothyroidism. However, in the absence of time series data, it is not possible to estimate accurately the number of cases averted through the fortification program.

Similarly, the prevalence of palpable goitre was higher in the Aalborg cohort across four age ranges considered (women aged 18-22, 25-30, 40-45 and 60-65, and men 60-65). However, time series data were not presented. The excess prevalence in the moderately deficient population, relative to the mildly deficient one, ranged from approximately one percentage point for the youngest cohort of women to almost ten percentage points for the cohort of men aged 60-65.Due to the uncertainty of these data, we have not estimated the impact of fortification on the cases of hypothyroidism or goitre in Australia and New Zealand.

One German study investigates the cost of thyroid disorder-related morbidity. (Kahaly and Dietlein, 2002) They identified endemic iodine-deficiency goitre as the most significant condition in this area. They do not deal with the effect of fortification on these costs but do claim that the costs of thyroid disorder-related morbidity are approximately one billion Euros (A$1.58 billion). If this is scaled to Australian and New Zealand populations, it is approximately A$450 million. While it is uncertain whether this cost would be significantly reduced through fortification, any argument that it would should be considered in addition to the cost-effectiveness evidence provided in this report.

5.6 The cost of mandatory fortification

The cost of mandatory fortification was estimated in a previous report by Access Economics (2006). They estimated the costs as shown in Table 16. FSANZ recommended that we use the same cost for this report.

Table 16: The cost of mandatory fortification of bread

	Upfront Cost	Ongoing (per annum)
Australia		
Salt Industry	A$161,000	A$314,000
Bakers	A$6,950,000	A$30,000
Government	A$31,000	A$137,000
Total	**A$7.1 million**	**A$482,000**
New Zealand		
Salt Industry	NZ$303,000	NZ$20,000
Bakers	NZ$1.5 million	NZ$30,000
Government	NZ$8,000	NZ$89,000
Total	**NZ$1.8 million**	**NZ$138,000**

These costs refer to a mandatory fortification process. The relative cost of a voluntary fortification process would be uncertain. On the one hand, voluntary fortification is likely to require continued advertisement and advocacy to sustain fortification. On the other hand, enforcement costs would be higher in a mandatory fortification program compared to voluntary. The net cost of moving between mandatory and voluntary is therefore, in our opinion, uncertain.

5.6.1 Cost associated with productivity

One substantial additional cost issue which needs to be considered is the benefit on productivity of raised IQ levels across the population. In principle, if an increase in IQ across a population leads to an improvement in productivity, the extra production could partially or wholly pay for the costs of implementing the fortification program.

We previously estimated that IQ would increase in Australian children by approximately 0.598 points, and in New Zealand by 1.219 points. The question of how to quantify the benefits of this to society is methodologically challenging. Access Economics approached this using a Human Capital Approach (Access

Economics, 2006). This approach attempts to value the growth in expected income caused by an elevated IQ.

The relationship between IQ and earnings is complex. It is difficult to control for other unobserved factors which influence both variables (such as wealth). Zax and Rees (2002) attempt to control for a variety of possible confounding factors at the individual level, and identify that an increase in IQ of one point results in a 0.363% increase in earnings at age 35, and a 0.898% increase at age 53. However, linking this with aggregate data (i.e. saying that if there is an increase in the population mean IQ of one point, GDP will increase by a certain percentage) is a further step which is not justified for three reasons. Firstly, as noted by Access Economics, the market clearing rate may adjust to allow for the increased productivity of the workforce. Secondly, while the population IQ may increase by a certain percentage, the distribution (and therefore the cause) of such an increase is limited to a small group of people who improve dramatically. Therefore, in aggregating to a societal benefit from this percentage improvement, we have to assume that the Zax and Rees figures can be applied in a linear way (i.e. a 50 point increase will cause income to increase by 50 x 0.363% at age 35 etc). Thirdly, societal productivity depends on more than just the intellectual capacity of the population. Issues such as low capital investment can obstruct growth in productivity. Therefore, we prefer to present the increase in IQ as a result in itself, as synergising the various outcomes into one measure of outcome (such as in a cost-benefit analysis) is likely to introduce more uncertainty than it resolves.

5.7 Producing cost-effectiveness ratios

Conventionally, cost-effectiveness analysis results are presented in terms of cost-effectiveness ratios. These are obtained by dividing the additional costs associated with the intervention by the additional benefit gained as a result of its use. In this case, the reduction in the number of individuals with UIC levels <50 µg/l, and <100 µg/l, are the key outcome measures. The relevant numbers are presented in Table 14 and Table 15.

We decided also that a suitable time horizon was ten years. This period is long enough to allow the amortisation of upfront costs. Thus, we extended the costs identified by Access Economics (2006) over ten years, discounting future costs at five percent per annum[14]. People with low iodine UIC averted were also spread over ten years, and discounted at five percent per annum.

> **In these tables, note that the declining numbers over time do not reflect a diminishing effect of fortification, but the effect of discounting the future**

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[14] Discounting is an economic tool to account for the empirical finding that individuals consider future events to be less significant than immediate ones. (Gravelle, et al., 2007)

Table 17: Generating cost-effectiveness ratios for Australia

Year	Cost (A$000)	Reduction in people with average annual UIC below 50 µg/l			Reduction in people with average annual UIC below 100 µg/l		
		Pregnant Women	Other Adults	Children	Pregnant Women	Other Adults	Children
1	7,100.0	673	107,044	19,812	87,656	5,900,822	1,303,641
2	482.0	639	101,692	18,869	83,480	5,619,830	1,241,563
3	459.0	607	96,607	17,970	79,504	5,352,220	1,182,441
4	437.2	577	91,777	17,114	75,716	5,097,352	1,126,134
5	416.4	548	87,188	16,299	72,109	4,854,621	1,072,509
6	396.5	521	82,829	15,523	68,674	4,623,448	1,021,437
7	377.7	495	78,687	14,784	65,403	4,403,284	972,797
8	359.7	470	74,753	14,080	62,287	4,193,604	926,473
9	342.5	446	71,015	13,410	59,320	3,993,909	882,356
10	326.2	424	67,464	12,771	56,494	3,803,722	840,339
Total	10,697	5,401	859,056	160,632	710,644	47,842,813	10,569,689
	Total	**1,025,089**			Total	**59,123,146**	

Table 18: Generating cost-effectiveness ratios for New Zealand

Year	Cost (A$000)	Reduction in people with average annual UIC below 50 µg/l			Reduction in people with average annual UIC below 100 µg/l		
		Pregnant Women	Other Adults	Children	Pregnant Women	Other Adults	Children
1	1800.0	2,187	149,689	72,240	25,424	1,740,451	579,665
2	131.4	2,083	142,561	68,800	24,213	1,657,572	552,062
3	125.1	1,984	135,772	65,524	23,060	1,578,640	525,773
4	119.2	1,889	129,307	62,404	21,962	1,503,467	500,736
5	113.5	1,799	123,150	59,432	20,916	1,431,873	476,892
6	108.1	1,714	117,285	56,602	19,920	1,363,689	454,183
7	103.0	1,632	111,700	53,907	18,972	1,298,751	432,555
8	98.1	1,554	106,381	51,340	18,068	1,236,906	411,957
9	93.4	1,480	101,315	48,895	17,208	1,178,006	392,340
10	89.0	1,410	96,491	46,567	16,389	1,121,910	373,657
Total	**2,780.8**	**17,732**	**1,213,652**	**585,709**	**206,133**	**14,111,266**	**4,699,820**
	Total	**1,817,093**			Total	**19,017,219**	

Table 19: Cost-effectiveness ratios (base case)

			Australia	New Zealand
Cost (10 years) (local$000)		(A)	10,697.2	2,780.8
Outcome	Reduction in people below 50 µg/l	(B)	102,509	181,709
	Total reduction below 100 µg/l	(C)	5,912,315	1,901,722
Ratio	Cost per person reduction below 50 µg/l (A/B)		$104.35	$15.30
	Cost per person reduction below 100 µg/l (A/C)		$1.81	$1.46

These results should be interpreted as the reduction of people below 50 µg/l for a period of ten years. For example, 102,509 Australians are no longer below 50 µg/l due to fortification over a ten-year period. The cost-effectiveness ratios should be interpreted as the cost of preventing one person from being below this level (be it 50 or 100 µg/l) for ten years. We were unable to identify studies with similar outcome measures to benchmark these figures. However, the costs seem to be relatively low compared with the outcomes.

5.8   Sensitivity analysis

This sensitivity analysis considers one major area of uncertainty, specifically that the effect of fortification on UIC may differ from that presented in Table 11.

The key driver of the results presented here is the effect of fortification on the median IUC. Therefore, we undertook a simple univariate analysis, investigating the effect of changing this model parameter. In the base case, we assumed that median UIC increased by 41.25 µg/l, representing the data from Seal *et al* (2007) scaled up from an 80% voluntary fortification scheme to a 100% mandatory fortification scheme. The purpose of this sensitivity analysis is to investigate what would happen if this figure were 25% higher or lower. This means an increase of 30.9375 for the lower pessimistic range, and of 51.5625 for the upper optimistic range.

Figure 1: The reduction in the population of Australia with low average annual UIC under mandatory fortification
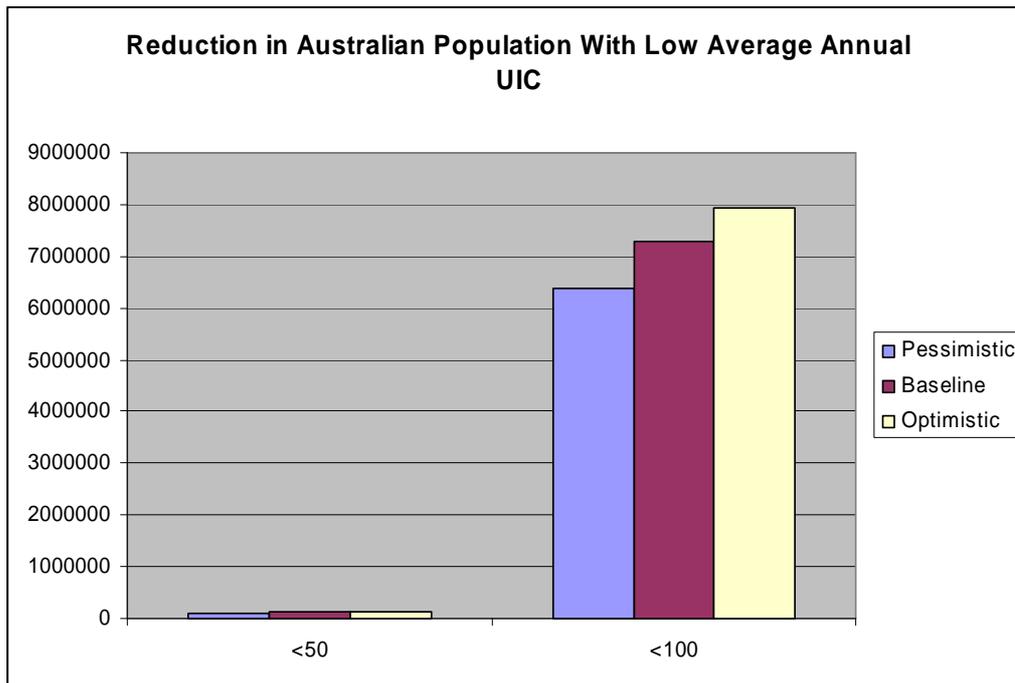
Figure 2: The reduction in the low iodine population of New Zealand with low average annual UIC under mandatory fortification
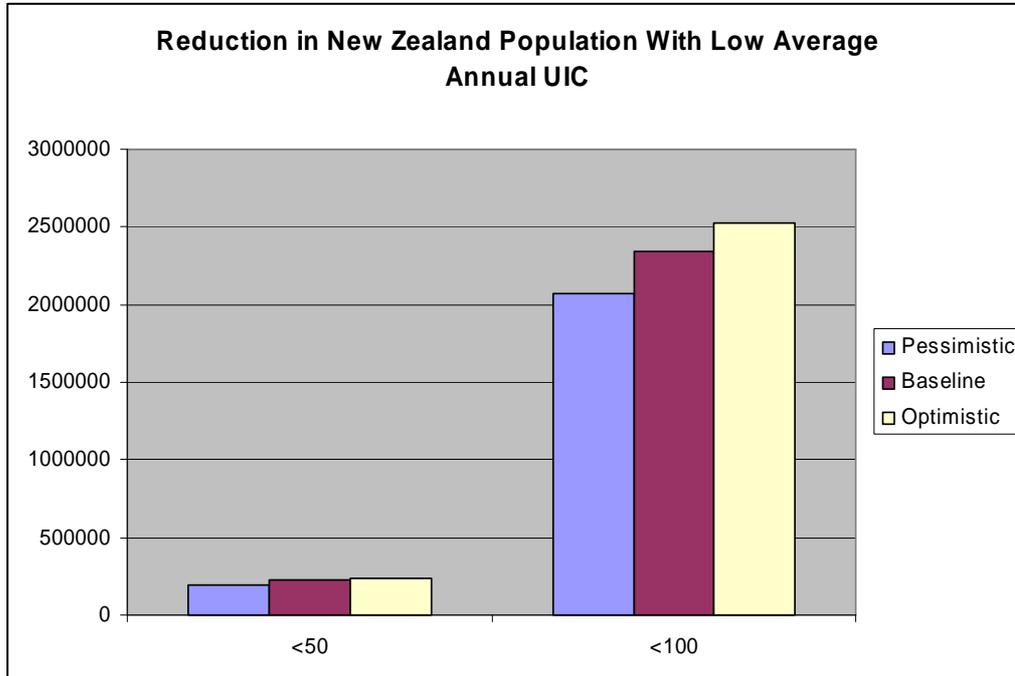
The sensitivity analysis suggests that the effect is responsive to a changing assumption around the increase in urine iodine content due to fortification. However, fortification still has a large effect on the total number of iodine deficient individuals in both countries under the pessimistic assumption.

The second issue is the population of children aged 0-<2. This population was excluded from the base case analysis, not because iodine intake is not of

importance in this group, but because estimating the effect of fortification would involve large assumptions relating to the way they receive iodine, and to their consumption of bread. They were also excluded from the National Nutrition Survey so we have no suitable dietary intake information. However, it may be of interest to consider the effect on this group, assuming they will respond to fortification in a comparable way to older children. Using the Australian and New Zealand National Statistics websites, estimates for the number of infants younger than two years were 111,306 in New Zealand and 519,777 in Australia (2006 data). If these figures are added to those in Table 9, the number of children in New Zealand is 1,111,728 (an increase of 11.13%) and in Australia 5,108,853 (an increase of 11.33%). If an assumption is made that the pattern of iodine levels is the same across the childhood group, and the effect of fortification is the same, iodine fortification reduces the number of children aged 0- <2 with an average annual UIC of below 50 µg/l by 2,245 in Australia and by 8,040 in New Zealand. The reduction in those below 100 µg/l is 147,703 in Australia and 64,517 in New Zealand.

6   Discussion

As part of proposal P230, Food Standards Australia New Zealand (FSANZ) commissioned the Centre for Health Economics Research and Evaluation (CHERE), University of Technology, Sydney, to investigate the cost-effectiveness of iodine fortification of bread in Australia and New Zealand. The motivation for FSANZ proposal P230 is the re-emergence of iodine deficiency in Australia and New Zealand.

We initially attempted to calculate the current burden of disease associated with iodine deficiency in Australia and New Zealand. Even though mild iodine deficiency is re-emerging in both countries, it has "apparently" not yet reached the level to cause hypothyroidism (Eastman, 1999). Unlike severe deficient subjects those with moderate iodine deficiency do not show clear signs (Kibirige, et al., 2004). Therefore, while it is likely that a relationship exists between mild / moderate deficiency and morbidity, there is limited evidence concerning the magnitude of the relationships between iodine levels and specific IDDs in either Australia or New Zealand. It should be noted that this is partially because the link between mild iodine deficiency and specific conditions is not as widely studied as the link with severe iodine deficiency. There is a wealth of evidence describing IDDs in severely deficient areas most of this evidence derives from studies conducted in developing countries.   However, the comparability of these populations to those in Australia and New Zealand is limited.   Therefore this report mainly draws on data from Denmark, Spain and Switzerland, which are developed countries where evidence is available linking mild iodine deficiency with IDDs (Laurberg, et al., 2006, Santiago-Fernandez, et al., 2004, Zimmermann, et al., 2005).   The most significant impact of IDD is on the developing brain (Boyages, 1994). This is why we focussed primarily on the relationship between mild iodine deficiency and diminution of IQ.

Results of cost-effectiveness analysis

We modelled the distribution of UIC in both Australia and New Zealand, stratified into children, pregnant women, and other adults. This modelling accounted for both the median level of UIC and the distribution of levels around this median. We found that a gamma distribution provided the best fit for the published evidence as this distribution has sufficient flexibility to reflect any underlying skewness in the distribution. Using Tasmanian data on voluntary fortification, we estimated the effect on the median and standard deviation of the distributions, and then plotted how the various population groups would lie in relation to previous UIC after mandatory fortification. The results suggest a significant decrease in individuals with median iodine levels below 50 µg/l and 100 µg/l. This result is relative robust to changing the effect of fortification by 25% (See Figure 1and Figure 2).

Using these data, we then estimated the cost per unit reduction in at-risk populations over a ten year period. Our estimates suggest that in Australia there will be 102,509 and 5,912,315 fewer people below 50µg/l and 100µg/l respectively. In New Zealand the corresponding figures are 181,709 and 1,901,722 for the <50µg/l and <100µg/l cohorts, respectively. The relatively greater impact in New Zealand reflects the higher severity of iodine deficiency at baseline, and the likelihood of a higher intake of iodised salt. Finally, the cost-effectiveness ratios, which estimate the costs of preventing one person from

having an iodine level below 50µg/l (100µg/l) are $104.35 ($1.81) for Australia and $15.30 ($1.46) for New Zealand.

The WHO criteria

As discussed, the WHO/ICCIDD criteria for a iodine adequate population are that the median urinary iodine levels in the target population should be at least 100 µg/l, and no more than 20% of the population should have a urinary iodine level of less than 50 µg/l (World Health Organization. WHO. UNICEF. ICCIDD, 1994). In should be noted that these values are based on urine spot tests. Based on the evidence collated in this report, both Australian and New Zealand populations demonstrated mild deficiency, since the median IUC in both countries is less than 100 µg/l. After mandatory fortification we estimate that both the Australian and New Zealand population will be iodine sufficient, since the median UIC will be greater than 100 µg/l and less than 20% of the population will have an UIC below 50 µg/l.

Table 20: Iodine status as defined by the WHO criteria [15]

WHO criteria	Australia	New Zealand
No Fortification (current practice)		
Median urinary iodine level >100 µg/l	X	X
<20% of population with UIC below 50 µg/l	✔	X
Mandatory Fortification of Bread		
Median urinary iodine level >100 µg/l	✔	✔
<20% of population with UIC below 50 µg/l	✔	✔

Our evidence suggests that the median UIC for pregnant and lactating women in Australia and New Zealand will be significantly below the WHO recommended 150 µg/l. Therefore in this cohort, addition supplementation may be required.

Limitation of using urinary iodine levels

The motivation for using UIC as a measure of the iodine deficiency in the Australian and New Zealand populations was driven by the availability of published data. Virtually all international studies and studies conducted in Australia and New Zealand report UIC rather than dietary intake. The main reason for its use is that UIC has been demonstrated to be a good proxy for recent iodine intake (Soldin, 2002, Stanbury, et al., 1998, World Health Organization. WHO. UNICEF. ICCIDD, 1994, World Health Organization. WHO. UNICEF. ICCIDD, 2001), and it is estimated that 85-90% of iodine intake is directly measurable in urine (Gibson, 1995). UIC is easy to collect and measure compared to self-reported measures of iodine intake which are usually estimated

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[15] The results presented in the table relate to iodine spot tests (as recommended by the WHO), therefore we have not adjusted the distributions.

using food diaries, which may suffer from memory bias. One limitation of using UIC is that during the day an individual's level of iodine will fluctuate. Therefore we cannot automatically infer that an individual with a low UIC will develop an IDD. Consequently when using UIC it is important to remember that the data refer to the population level rather than the individual level.

Costs

As advised by FSANZ, the costs used in this reports are based on the estimates derived by Access Economics (2007). These costs relate to the direct costs to the salt industry, bread making industry and Government for administrating and enforcing mandatory fortification. Only the additional costs attributed to the FSANZ are included in the cost analysis. It is our view that a broader societal perspective should be adopted. Other associated costs that have not been included are; the costs of monitoring nutrient intake and urinary iodine concentration within the population after fortification, and complementary health information programs. There is also uncertainty regarding the costs to the health service, since it can be argued that alleviation of IDDs will be associated with a negative cost, but the potential adverse health problems linked with excess iodine intake may have a positive health cost component. It could also be argued that there are costs attributable to the restriction in consumer choice which would follow mandatory fortification; however modelling such a cost would be problematic if not futile.

We did not attempt to compare voluntary and mandatory fortification programs. In cost terms, the relative cost of a voluntary fortification process would be uncertain. On the one hand, voluntary fortification is likely to require continued advertisement and advocacy to sustain fortification. On the other hand, enforcement costs may be higher in a mandatory fortification program. The net cost of moving between mandatory and voluntary is therefore, in our opinion, uncertain.

Also related to costs is the possibility of combining iodine fortification with the proposed folic acid fortification, which as recently been approved FSANZ. If folic acid and iodine were both included in a mandatory permission, there would be significant synergies and cost savings between programs.

Iodine and IDD

One substantial additional cost issue which needs to be considered is the benefit on productivity of raised IQ levels across the population. In principle, an increase in IQ across the population should lead to an improvement in productivity. We estimated that IQ would increase in Australian children by approximately 0.598 points, and in New Zealand by 1.235 points. The question of how to quantify the benefits of this to society is methodologically challenging. The Access Economics report used a Human Capital Approach and estimated a significant net benefit of fortification (Access Economics, 2006). The uncertainty around this estimate of net benefit is substantial. Consequently, we chose not to duplicate this method which would run the risk of coming to the same or very similar conclusions. Instead, if the reader is prepared to accept the basic tenet that increased IQ leads to increased productivity without market clearing, then the additional production which would occur as a result of mandatory fortification would partially or wholly pay for the costs of implementing the fortification program. In reality

most nominal benefits added to the economic model would probably dwarf the costs of implementing mandatory fortification.

Linking reduced iodine deficiency with averted cases of various conditions was difficult due to limitations in the scope and consistency of the evidence reported in the literature. Firstly, linking specific UIC levels to labels referring to deficiency is difficult as an individual's UIC fluctuates over time. Any benefit in terms of IQ has to be balanced against the possibility that fortification will result in increased numbers of cases of hyperthyroidism (a maximum of 3,200 extra cases of hyperthyroidism in Australia and New Zealand per year) although this figure is likely to decline in subsequent years, with some evidence suggesting that nine years after fortification, the number of cases would be below the pre-fortification level. (Baltisberger, et al., 1995)

Bread as the fortification vehicle

As was discussed, bread is the preferred vehicle for fortification, because it is locally produced, has a short self-life and is a staple part of most individual's daily diet. However, 12% of Australians and 13% of New Zealanders do not consume bread (Food Standards Australia New Zealand, 2007) and will not benefit from fortification of bread. In addition, organic bread and non-yeast containing bread will be exempt from mandatory requirements. We did not model the effect of organic bread because it is believed to constitute a very small proportion of the whole bread consumed in Australia and New Zealand.

Fortifying bread with iodine does not target one of the most vulnerable groups of individuals, 0-2 year olds. As discussed, iodine is important for normal cognitive development in very young children. This group is unlikely to consume bread; however, we may assume that some of the benefit bestowed by the lactating mother will be passed onto the baby (presuming the baby receives breast milk).

Voluntary versus mandatory fortification

Potential problems with voluntary rather than mandatory fortification of bread are as follows: (Stanley, et al., 2005)

o Voluntary fortification of bread is susceptible to changes in the cost of iodised salt and/or changes in baking practices, for example, reliance on premixed dough.

o There is a potential lack of coverage in some rural areas, where residents may rely on one bakery. If this bakery chose not to fortify their bread with iodine, the whole population in that area would be at risk of iodine deficiency. Even a thorough monitoring program would not be able to identify all isolated pockets of iodine deficiency.

o Initial savings to the industry of not implementing a mandatory fortification program may be lost by having to monitor and maintain an ongoing promotion of the voluntary program to the industry, as well as the cost of encouraging consumers to buy fortified bread which potentially may be more expensive than non-fortified bread. Therefore, a voluntary program has the potential to be more expensive than a mandatory program.

7 Conclusion

Our findings are based on estimates of iodine deficiency obtained from recently published peer-reviewed journal articles pertaining to the Australian and New Zealand population. Consequently our assumptions are based on the fact that these papers are representative of the respective populations. Any deviation from this assumption will bias our results and introduce uncertainty.

Our findings suggest that both the Australian and New Zealand populations are mildly iodine deficient, as defined by the WHO. This deficiency is more pronounced in New Zealand. After iodine fortification of bread, we estimate that Australia will become iodine adequate and to a lesser extent New Zealand will be generally iodine sufficient.

Assessed in terms of cost-effectiveness ratios, the cost of moving individuals from the cohort with iodine levels below 50 μg/l (those most at risk of developing IDDs in the future), appears small compared with the potential benefits associated with improved health, reduced health care costs and/or gains in productivity and GDP.

The following points will require further clarification as the published evidence becomes available:

- o   An accurate estimate of the benefit of the potential increase in population IQ in terms of productivity gains and therefore increases in GDP.

- o   A more detailed estimate of the costs associated with mandatory fortification. These should reflect a broader societal perspective and include the costs of health care utilisation (both negative and positive), and the costs associated with ongoing monitoring of iodine levels in the population.

- o   Irrespective of whether FSANZ decides to adopt mandatory fortification of bread with iodine, the evidence pertaining to the re-emergence of iodine deficiency in Australia and New Zealand warrants the development of a strategic ongoing nutrition monitoring and surveillance program.

As stated in the introduction, our aim was to produce a report that builds upon the considerable evidence that has already been assimilated by FSANZ (including a detailed cost-benefit analysis completed by Access Economics). We did not attempt to duplicate any of this work for obvious reasons. This report is therefore to be viewed both as a stand-alone piece of evidence, and in the context of this stream of evidence.

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9 Appendix

Table 21: Generating Gamma Distributions (see 5.4)

	Children, NZ	**Children, Aus**	**Adults, NZ**	**Adults, Aus**	**Pregnant women, Aus**
Paper	(NZ Food NZ Children, 2003)	(Li, et al., 2006)	(Thomson, et al., 2001)	(Li, et al., 2001)	(Travers, et al., 2006)
SD	16.2	24.73	14.5	21	17
Desired mean	69.2	98.73	69.75	89.5	86.333
Desired median	**66**	**94**	**68**	**88**	**85**
Other Info	28% should be below 59.33333	IQR of 84.42-116.08	26.5% should be below 60.5	20.6% should be below 72.1666	16.6% should be below 70.41666
Alpha	18.24661	15.9386	23.13942	18.16383	25
Beta	3.792486	6.194398	3.014337	4.927374	3.4

Figure 3: UIC Distribution In Australian Children

Effect of Iodine Fortification on Australian Children
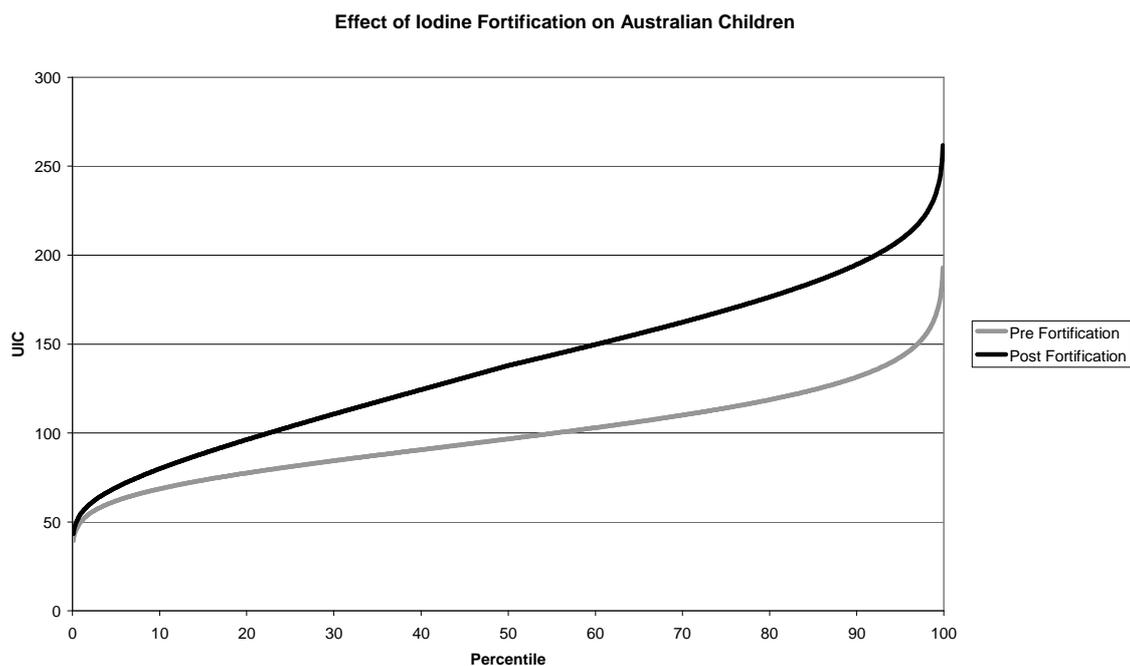
Figure 4: UIC Distribution in New Zealand Children

Effect of Iodine Fortification on New Zealand Children
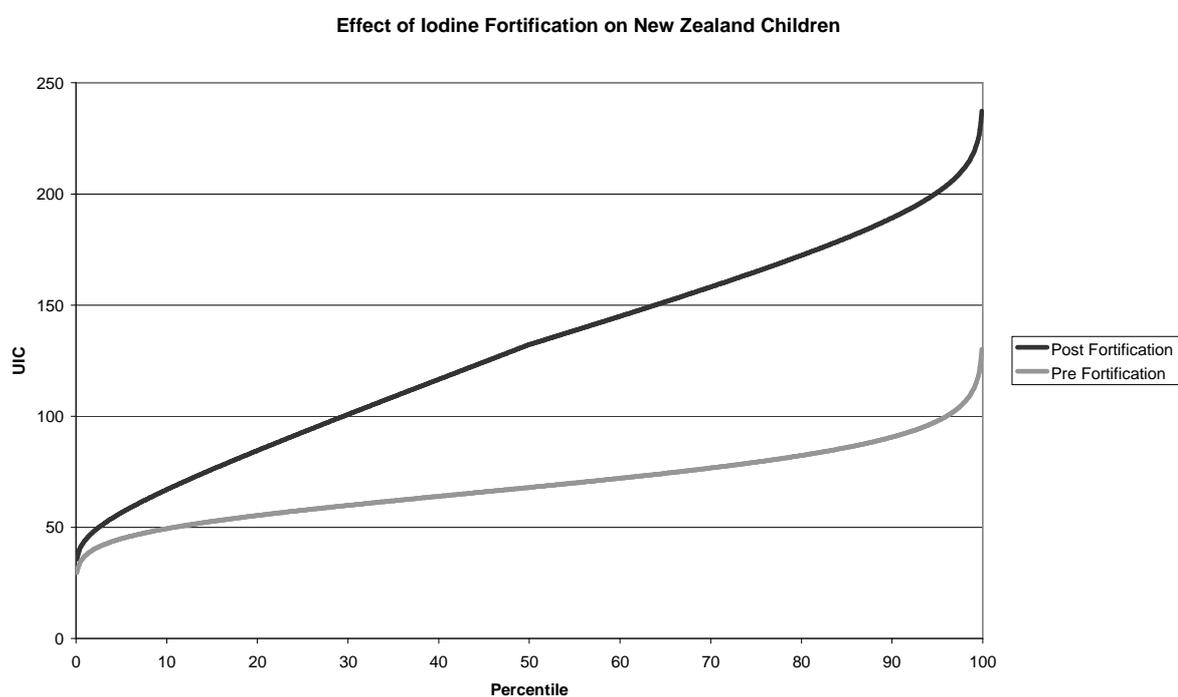
Figure 5: UIC Distribution in Australian Adults

The Effect of Fortification on Australian Adults
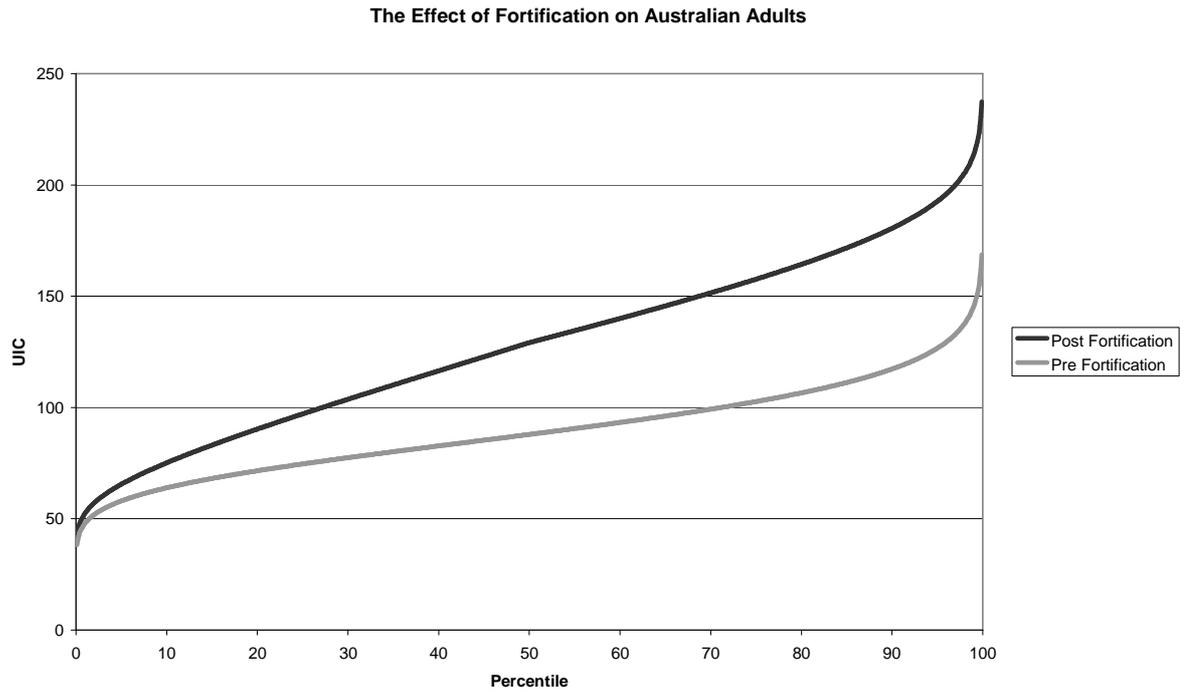
Figure 6: UIC Distribution in New Zealand Adults

Effect of Iodine Fortification on New Zealand Adults
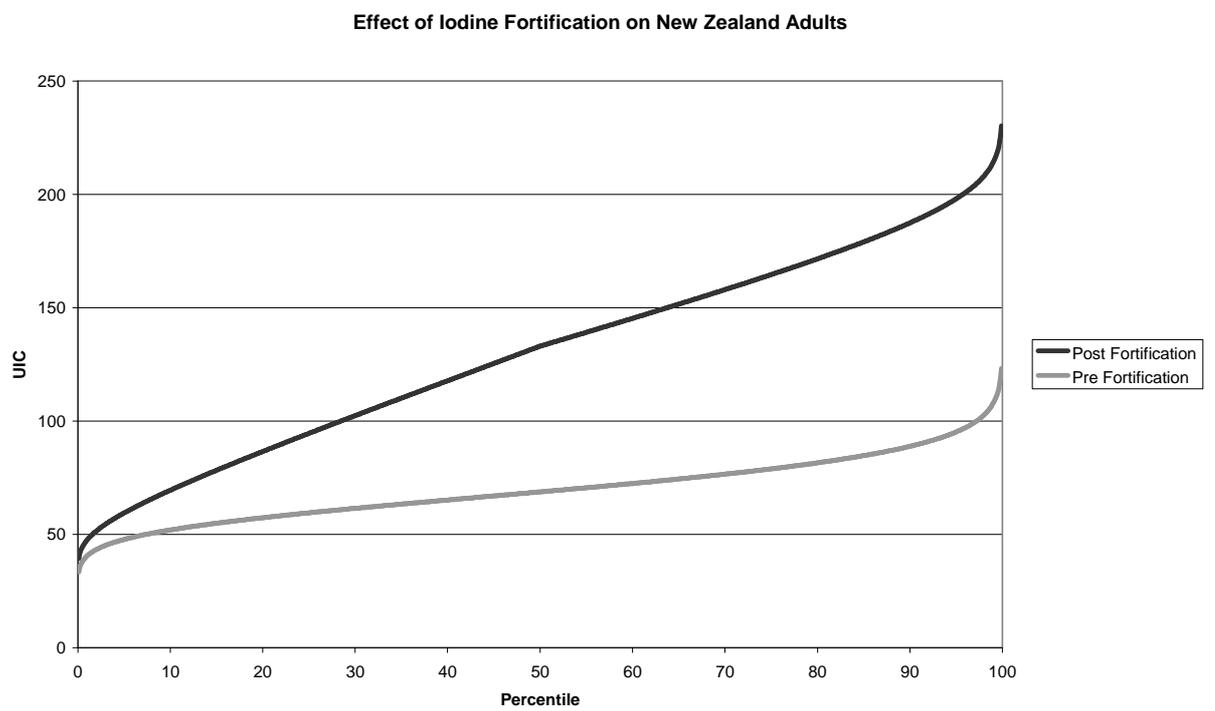
Figure 7: UIC Distribution in Australian Pregnant Women

Effect of Fortification on Australian Pregant Women