Cost-effectiveness Analysis of Alternate Strategies to Redress Iodine Deficiency in Australia

Report developed for the Department of Health and Ageing, Australian Government

Centre for Health Economics Research and Evaluation

September 2007

Final Report

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Acknowledgments

CHERE would like to thank and acknowledge the following individuals who provided expert advice:

- Food Standards Australia New Zealand, in particular John Davies, Christian Thoma and Dr Dorothy Mackerras
- Dr. Lone Banke Rasmussen, Department of Nutrition, Mørkhøj, Bygade, Søborg, Denmark
- Dr Judy Seal, Public Health Nutrition, Population Health, Department of Health and Human Services, Hobart.

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1 Executive Summary

As part of proposal P230-Consideration of Mandatory Fortification with Iodine, Food Standards Australia New Zealand (FSANZ) are currently preparing a proposal for the mandatory fortification of bread-making salt with iodine. The motivation for FSANZ proposal P230, is the re-emergence of iodine deficiency in Australia and New Zealand. In the context of the preparation of this proposal, the Department of Health and Ageing (DOHA) has commissioned the Centre for Health Economic Research and Evaluation (CHERE), University of Technology, Sydney, to assess and compare the cost effectiveness of strategies that are aimed at reducing the prevalence of iodine deficiency in Australia and New Zealand (including but not limited to the mandatory iodine fortification of bread-making salt).

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 an 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.

DOHA are considering the following options for redressing iodine deficiency in Australia:

a) Maintenance of *status quo*;

b) The implementation of an educational program to target either pregnant women and/or the whole population to increase their intake of dietary iodine;

c) The implementation of an iodine supplementation program to target either pregnant women and/or the whole population to increase their intake of dietary iodine;

d) Mandatory fortification:

  - The mandatory replacement of salt with iodised salt to bread, with the salt iodisation range from 35-55mg of iodine per kg of salt;
  - The mandatory replacement of salt with iodised salt to bread, with the salt iodisation range from 35-55mg of iodine per kg of salt, in conjunction with an iodine supplementation program to target pregnant women.

e) Voluntary fortification:

  - The voluntary replacement of salt with iodised salt to bread, with the salt iodisation range from 35-55mg of iodine per kg of salt;

- o The voluntary replacement of salt with iodised salt to bread, with the salt iodisation range from 35-55mg of iodine per kg of salt, in conjunction with an iodine supplementation program to target pregnant women.

The costs of each option are summarised in Table 1. The costs are representative of the bread making industry, salt manufacturers, government, physician and individual. Potential savings through the parallel introduction of mandatory fortification of bread with folic acid and iodised salt may reduce the costs of iodine fortification significantly.

Table 1: Summary of the costs of each strategy to address iodine deficiency

	Net Present Value (10 years)[1]	
	Australia	**New Zealand**
Maintaining the *status quo*	A$0	NZ$0
Mandatory fortification of bread	A$10,563,000	NZ$2,788,000
Mandatory fortification of bread (minus piggybacked costs from folic acid fortification)	A$3,101,000	NZ$959,000
Voluntary fortification of bread	A$8,710,000	NZ$2,424,000
Voluntary fortification of bread (minus piggybacked costs from folic acid fortification)	A$2,639,000	NZ$894,000
High profile national public health campaign	A$12,108,000	NZ$2,422,000
Iodine supplementation program	A$73,320,000	NZ$16,152,000
Iodine supplementation program with physician counselling	A$74,567,000	NZ$16,401,000

[1] Costs rounded to the nearest $1,000

The cost-effectiveness analysis involved two major components. Firstly, we looked at population-level interventions. These were the mandatory and voluntary fortification of bread, and the use of an educational program. The second component focused on pregnant women as they are of particular significance due to their iodine status playing a significant role in the neurological development of their unborn child.

We also estimate the cost per person (mandatory and voluntary) removed from cohorts with levels below 50 μg/l and 100 μg/l over a ten year period. For mandatory fortification, our estimates suggest that there will be approximately 128,000 and 7,320,000 fewer people with average annual iodine levels of <50 μg/l and <100 μg/l respectively in Australia. In New Zealand the corresponding figures are 224,000 and 2,567,000 for the <50 μg/l and <100 μg/l cohorts, respectively. The relatively greater impact in New Zealand reflects the higher severity of iodine deficiency at baseline. Finally, the cost-effectiveness ratios, which estimate the costs of reducing the population below 50 μg/l UIC (100 μg/l) by one for a ten-year period are $24.32 ($0.42) for Australia and $4.28 ($0.37) for New Zealand. These are summarised in Table 2.

For voluntary fortification, our estimates suggest that there will be 102,200 and 5,834,000 fewer person with an annual average UIC of <50 μg/l and <100 μg/l respectively in Australia. In New Zealand the corresponding figures are 179,000 and 1,874,300 for the <50 μg/l and <100 μg/l cohorts, respectively. Finally, the cost-effectiveness ratios, which estimate the costs of reducing the population below 50 μg/l UIC (100 μg/l) for a ten-year period are $25.82 ($0.45) for Australia and $4.99 ($0.48) for New Zealand.

It should be noted that, in comparing voluntary fortification with mandatory fortification, economic evaluation would conventionally exclude voluntary fortification since it is subject to extended dominance. Mandatory fortification has a greater effect in reducing iodine deficiency, and reduces the population at a lower cost per person (despite having a higher overall cost).

Table 2: Summary of cost-effectiveness ratios (Mandatory versus status quo)

			Australia	**New Zealand**
Cost (10 years) (local$000) (assumed lower due to piggy-back)		(A)	$3,101	$959
Cost (10 years) (local$000) (no piggy-back)		(B)	$10,563	$2,788
Outcome	Reduction in people below 50 μg/l	(C)	127,529	224,116
	Total reduction below 100 μg/l	(D)	7,319,647	2,567,469
Piggy-backed costs	Cost per person reduction below 50 μg/l (A/C)		$24.32	$4.28
	Cost per person reduction below 100 μg/l (A/D)		$0.42	$0.37
Non-piggy-backed costs	Cost per person reduction below 50 μg/l (B/C)		$82.83	$12.44
	Cost per person reduction below 100 μg/l (B/D)		$1.44	$1.09

Looking at the targeted strategies for pregnant women, the cost of reducing the at-risk population by one person was, as expected, higher than for the population. This was because the population of pregnant women below 50 and 150 μg/l was small, especially if mandatory fortification of salt in bread in undertaken in parallel. The cost of reducing the Australian (New Zealander) population below 50 μg/l by one unit was $745,700 ($108,600). Regarding the WHO criterion for pregnant women of 150 μg/l, the respective figures for Australia and New Zealand were $6,100 and $8,000. These are summarised in Table 3.

Table 3: Cost-effectiveness ratios for adding supplementation and education for pregnant women to mandatory fortification

		Australia	New Zealand
Cost (10 years) (local$000) (A)		$74,567	$16,401
Outcome	Reduction in people below 50 µg/l (B)	100	151
	Total reduction of those below 150µg/l (C)	12,241	2,042
	Cost per person reduction below 50 µg/l (rounded to nearest $100) (A/B)	$745,700	$108,600
	Cost per person reduction below 150 µg/l(rounded to nearest $100) (A/C)	$6,100	$8,000

Mandatory iodine fortification of bread may lead to an increase in the number of hyperthyroidism cases. We estimate potentially 2,676 extra cases per year in Australia and 507 in New Zealand. Caution is required when interpreting these findings. Firstly, these values may be over estimates, since they are based upon a Copenhagen population that was more iodine deficient than the current Australian population. Secondly, evidence from Switzerland demonstrated a reduction in hyperthyroidism, ten years post iodine fortification. This suggests that the number of cases of hyperthyroidism in Australia and New Zealand may actually fall in the long term.

Due to the uncertainty of the evidence pertaining to hypothyroidism, we have not estimated the impact of iodine fortification on the number of cases of hypothyroidism or goitre in Australia and 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 World Health Organization (WHO). This deficiency is more pronounced in New Zealand. After either mandatory or voluntary iodine fortification of bread, we estimate that Australia and New Zealand will become iodine adequate.

Assessed in terms of cost-effectiveness ratios, the cost of moving individuals from the cohort with median levels of iodine 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 Food Standards Australia New Zealand (FSANZ)/DOHA Australian Government decides to adopt mandatory/voluntary 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 of this report

As part of proposal P230-Consideration of Mandatory Fortification with Iodine, Food Standards Australia New Zealand (FSANZ) are currently preparing a proposal for the mandatory fortification of bread-making salt with iodine. The motivation for FSANZ proposal P230, is the re-emergence of iodine deficiency in Australia and New Zealand.

In the context of the preparation of this proposal, the DOHA is seeking to assess and compare the cost effectiveness of strategies that are aimed at reducing the prevalence of iodine deficiency in Australia and New Zealand (including but not limited to the mandatory iodine fortification of bread-making salt). DOHA has commissioned the Centre for Health Economic Research and Evaluation (CHERE), University of Technology, Sydney, to perform this analysis. The assessment will inform the preparation of advice on the most effective strategy for achieving this aim.

2.2 What is iodine and why is it important?

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 4) (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 4: 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 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

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 (Food Standards Australia New Zealand, 2004). 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 iodine levels in the population

There are two methods of measuring iodine levels in the population. These are; 1) monitoring the iodine intake or 2) assaying the urinary iodine concentrations.

[1] Although processed foods contain salt, to our knowledge this salt tends to be non-iodised.
[2] Iodised salt is also permitted to be added to other foods as long as the food is appropriately labelled.

2.6.1 Recommended dietary iodine intake

Two measures of dietary intake are commonly used; the estimated average requirement (EAR) and the recommended daily intake (RDI). EAR is defined as "a daily nutrient level estimated to meet the requirements of half the healthy individuals in a particular life stage and gender group" and 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). The EAR for iodine for non-pregnant and non-lactating adults has been estimated at 100 µg/day and RDI of iodine in adults is 150 µg/day.

Higher levels, >250 µg/day (RDI), are required during pregnancy and breastfeeding. (International Council for Control of Iodine Deficiency Disorders, 2007) This is due to enhanced maternal requirements, increased renal clearance and diversion of iodine for foetal thyroid hormone production (Boyages, 1993).

The WHO recommends a daily intake of: 90 µg of iodine for infants (0-59 months); 120 µg for schoolchildren (6-12 years) and 150 µg for adolescents and adults (World Health Organization. WHO. UNICEF. ICCIDD, 1996). The ICCIDD recommends 250 µg per day for pregnant and lactating women. (International Council for Control of Iodine Deficiency Disorders, 2007) In Australia the recommended daily 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 5: 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 Daily 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

2.6.2 Recommended urinary iodine levels

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.

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 UIC for iodine sufficiency (See Table 6) (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. (World Health Organization. WHO. UNICEF. ICCIDD, 1994)[3]. 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 6: 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)[4]

Median UIC (µg/l)	Iodine intake	Iodine nutrition
< 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).

[3] Also less than 3% of neonates should have a whole blood TSH concentration greater than 5mIU/l
[4] NB. The WHO median UIC refers to the population iodine concentration, not the iodine concentration of an individual.

2.7 History of iodine fortification in Australia and New Zealand

Historically, Australian and New Zealand populations have had problems maintaining iodine sufficiency.

New Zealand

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[5] (Mann and Aitken, 2003, Thomson, 2004).

Tasmania

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 the soil (Thomson, 2003). A State-wide iodine supplementation program[6] 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.

Australia mainland

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).

2.7.1 Current fortification strategies

As discussed, Australia and New Zealand have implemented several strategies in the past aimed at reducing iodine deficiency. These have had varying degrees of success. 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. There are concerns about the actual effectiveness of this program since only 15% of Australian and 50% New Zealand salt manufactured for households is iodised[7] (Food Standards Australia New Zealand, 2006).

[5] 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.
[6] Children were given 10mg potassium iodine table per week.
[7] Iodised salt is also permitted to be added to other foods as long as the food is appropriately labelled.

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[8] 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).

2.8 Current evidence of 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 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.

2.9 Why 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

[8] The fortification of bread in Tasmania is an interim measure until iodine supplementation is adopted as a national standard.

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.

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).

2.10 Potential strategies to redress iodine deficiency

In summary, DOHA would like to consider the following options for redressing iodine deficiency in Australia:

a) Maintenance of *status quo*;

b) The implementation of an educational program to target either pregnant women and/or the whole population to increase their intake of dietary iodine;

c) The implementation of an iodine supplementation program to target either pregnant women and/or the whole population to increase their intake of dietary iodine;

d) Mandatory fortification:

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

   - The mandatory replacement of salt with iodised salt to bread, with the salt iodisation range from 35-55mg of iodine per kg of salt, in conjunction with an iodine supplementation program to target pregnant women.

e) Voluntary fortification:

   - The voluntary replacement of salt with iodised salt to bread, with the salt iodisation range from 35-55mg of iodine per kg of salt;

   - The voluntary replacement of salt with iodised salt to bread, with the salt iodisation range from 35-55mg of iodine per kg of salt, in conjunction with an iodine supplementation program to target pregnant women.

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[9].

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.

[9] 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 Scope of this Assessment

Following an invitation from DOHA, Australian Government, the Centre for Health Economics Research and Evaluation (CHERE) was commissioned to investigate the cost-effectiveness analysis of alternate strategies to redress iodine deficiency in Australia. As outlined above a previous report completed by Access Economics used a cost-benefit analysis approach to address a similar question, although this was restricted to the mandatory fortification of bread with iodine. Our aim in this report is to complement the original evaluation, rather than duplicate it. This investigation aims to address the following issues:

- cost of the intervention;
- effect on the population (at the national level, divided into adults, children and pregnant women);
- cost effectiveness in terms of reduction of people no longer at risk of iodine deficiency;
- reduction in cases of hypothyroidism and potential increase in hyperthyroidism; and
- whether the strategy will result in an iodine ‘replete’ population, as determined by International Council for the Control of Iodine Deficiency Disorders (ICCIDD) criteria.

The purpose of this report is *not* to:

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

This section summarises the currently available published evidence. We begin by presenting the evidence for iodine deficiency in Australia and New Zealand. This is followed by linking current knowledge of iodine deficiency with IDDs. Some of the current iodine fortification/supplementation programs within the developed world are discussed next, along with interventions that are designed to encourage the use of iodised salt or iodine containing supplements. We finished with a brief overview of iodine requirements during pregnancy.

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:

- published 1990 - 2007
- available in English
- specifically focused on IDDs
- preference given to meta-analysis and systematic reviews where available
- articles were selected on relevance to the topic
- hand searching of relevant articles and reports
- relevant Australian and overseas reports/publications known to the researchers

4.1.2 Search terms used

- Iodine deficiency, and
- intelligence quotient, and
- fortification,
- thyroid,
- Iodine deficit disorder$

- dietary supplement$, and/or
- iodine suppl$
- pregnant women,
- intake
- nutrition survey

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 et 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[10] 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).

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

Descriptive characteristics of New Zealand studies are listed in Table 7 and Australian studies in Table 8.

Table 9 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).

Table 7: Summary of studies conducted in New Zealand– study details

Author & Year	Study details	Sample size	Measure of iodine status	Study Results	Iodine deficiency reported by the authors in the sample studied
(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%	Mild Deficiency Severe Deficiency Moderate Deficiency Mild Deficiency Moderate Deficiency Mild Deficiency
(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)	Mild deficiency
(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	30% of the children had iodine concentrations < 50 µg/l Severe Deficiency Moderate Deficiency Mild Deficiency Indicative of mild deficiency
(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	Mild Deficiency ICCIDD recommends that no more than 20% of children should have a urinary iodine level of less than 50 µg/l

Author & Year	Study details	Sample size	Measure of iodine status	Study Results	Iodine deficiency reported by the authors in the sample studied
(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 UIC in breast milk 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 Iodine concentration in breast milk: 22 µg/l (CI 18-26)	Mild Deficiency Severe Deficiency Moderate Deficiency Mild Deficiency Mild Deficiency Moderate Deficiency Moderate Deficiency Moderate Deficiency Expected iodine concentration 100-200 µg/

Table 8: Summary of studies conducted in Australia– study details

Author & Year	Study details	Sample size	Measure of iodine status	Study Results	Iodine deficiency reported by the authors in the sample studied
(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)	Normal Mild Deficiency Mild Deficiency Mild deficiency Moderate Deficiency Mild Deficiency

Author & Year	Study details	Sample size	Measure of iodine status	Study Results	Iodine deficiency reported by the authors in the sample studied
(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)	Mild deficiency Mild deficiency Mild deficiency Mild deficiency Moderate deficiency
(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)	Mild iodine deficiency based on WHO criteria for iodine adequate population <3% of neonates with whole blood TSH concentrations > 5mIU/l

Author & Year	Study details	Sample size	Measure of iodine status	Study Results	Iodine deficiency reported by the authors in the sample studied
(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	Mild deficiency
(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	Mild deficiency
(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)	Mild deficiency Moderate deficiency Mild deficiency Normal
(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	Iodine deficiency reported by the authors in the sample studied
(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%	Mild deficiency Mild deficiency
(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%	Mild deficiency
(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	Normal Mild Mild Normal Normal Normal Mild deficiency

Author & Year	Study details	Sample size	Measure of iodine status	Study Results	Iodine deficiency reported by the authors in the sample studied
(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)	Mild deficiency Normal
(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	Mild deficiency Normal levels

Author & Year	Study details	Sample size	Measure of iodine status	Study Results	Iodine deficiency reported by the authors in the sample studied
(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%	Mild deficiency Mild deficiency Mild deficiency

UIC: Urinary Iodine Concentration
UIE: Urinary Iodine Excretion

Table 9: Summary of results for urinary iodine excretion in New Zealand and Australian adults and children

Population	Year	Number	Urinary iodide (µg/l) Median	Distribution	Study
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 deficiency and IDDs

4.3.1 Iodine deficiency and IQ

The most important consequence of iodine deficiency has been described as mental retardation. (World Health Organization. WHO. UNICEF. ICCIDD, 1994) 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 such 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.

4.3.2 Iodine induced hyperthyroidism (IIH)

Hyperthyroidism is a condition in which the thyroid gland produces excessive amounts of the thyroid hormones; thyroxine and triiodothyronine. 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* 2006, 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)

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

4.3.3 Hypothyroidism and goitre

Hypothyroidism is a condition in which the thyroid gland produces insufficient amounts of thyroid hormone. 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.

4.4 Iodine supplementation/fortification

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

4.4.1 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.

4.4.2 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 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.

4.4.3 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).

4.4.4 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%.

4.4.5 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 10.

Table 10: Summary of fortification studies

Author & Year	Study location	Vehicle	Study details	UIC/Intake Before	UIC/Intake After
Seal et al (2007)*	Australia (Tasmania)	Iodised 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)	Iodised salt 40 mg/kg in bread (Voluntary)	Pregnant women **Before (2000-01)** n=285 in 2000-01 **After (2003-2006)** 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)**: 4649 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. UIC concentration was not reported.
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 8 and Table 9

4.5 Interventions aimed at promoting the use of iodised salt and/or iodine intake

Universal salt iodisation may be a permanent or long-term solution to iodine deficiency (Mannar, 2006). However, within individuals salt intake varies greatly. The WHO recommends at least 15-20 ppm of iodine in salt at the point of consumption (Dunn, 2000). To provide 150-200 µg of iodine per day, an individual needs to eat 10g of iodised salt per day[11]. Interestingly, when salt consumption decreased in Austria and Switzerland, the respective Governments responded by increasing the iodine content in salt (Burgi, et al., 1990, Mostbeck, et al., 1998).

Most of the evidence for the effectiveness of strategies aimed at promoting iodised salt consumption is derived from studies conducted in the developing world (See Table 11).

To date, there have been no public health campaigns, promoting the use of iodised salt in Australia (Li, et al., 2007). On the other hand, reduction in salt intake (sodium chloride) has been widely publicised. One example of this is the "Drop the Salt" campaign launched on the 15th of May 2007 (The George Institute for International Health, 2007). According to WHO a *"comprehensive strategy that effectively encompasses both public health problems must be developed".* This is to diminish the risk of confusion that might emerge with potentially conflicting public health messages (World Health Organization, 2007).

In Australia, Li *et al* conducted a study examining changes in iodised salt sales after a brief period of television and newspaper reports (Li, et al., 2007). The Factiva database was used to search for "iodine" in all Australian newspapers from 1 January 1997 until 30 April 2006. Sales of iodised salt were obtained from Synovate AZTEC grocery data. Interestingly, the study found that iodised salt sales increased significantly (5.2%) after modest news coverage (television or newspaper) regarding the benefits of using iodised salt or negative aspects of IDDs. During the study period the most obvious increase in iodised salt sales came after the NINS project was launched in (Sep/Oct) 2003 and when the results were presented in September 2005. In the period between September 2003 and April 2006 there was a 29% increase in the volume (units) of iodised salt purchased.

[11] Assuming no other source of iodine

Table 11: Summary of studies increasing the use of iodised salt and/or iodine intake

Author & Year	Study details	Intervention	Pre intervention	Post intervention
(Umemoto, et al., 1999)	Study conducted in Guatemala in the hamlet of Vista Hermosa. Two schools were randomly assigned to be control or intervention.	School based approach to community education. Four 1-hour educational sessions conducted once a week in 2nd and 5th grade. Session 1: understanding of iodine deficiency and the importance of iodised salt. Session 2: benefit of iodine for physical development Session 3: iodine for mental development and productivity. Children played memory games Session 4: puppet show focussing on consequences to pregnant women. Each session was followed by a review of the previous one	Use of iodised salt by Households of 2nd and 5th grades. Control (103 children): 39.2% Intervention (94 children): 29.7%	Use of iodised salt by Households of 2nd and 5th grades. Control: 44.4% ($p>0.05$) Intervention: 75% ($p < 0.001$)
(Can, et al., 2001)	Study conducted in Turkey, Trabzon region. Two-stage random sampling targeting married women. 672 women were interviewed before the intervention and 768 were interviewed post intervention.	Media mass campaign to increase consumption of iodised salt. Feb – May 1999 two television programs each running for three hours (late evening and mornings) Key messages reinforced were: "For your health use iodised salt", "Shortage of iodine may cause mental retardation-choose iodised salt for your children" and "Iodised salt is no different from non-iodised salt; same taste and price".	Knowledge about iodised salt: 67% Use of iodised salt: 55%	Knowledge about iodised salt: 73% Use of iodised salt: 62% Unaware of the campaign and iodised salt not used (n=160) 42%
(Rossi and Branca, 2003)	Evaluation conducted in Armenia (area of endemic goitre) Pre intervention (1997): cross sectional study n= 2627 households. Post intervention (2000): Demographic and Health Survey (DHS): n= 5976 households	Multi-channel information dissemination: eight IDD-focused TV programs and six TV spots broadcasted nationally. Information and education campaigns were undertaken in the South and North regions. Endocrinologists and paediatricians visited villages and organised community meetings with local authorities, health providers and the village to disseminate IDD information and promote the use of iodised salt.	66% of households consumed iodised salt.	83% of households consumed iodised salt. 17% increased in iodised salt intake

4.6 Responses to (non-iodine) health education programs

In the absence of evidence regarding the use of health campaigns aimed at increasing iodine consumption. We now demonstrate the effectiveness of comparable public health campaigns targeting other nutritional deficiencies.

The literature suggests that the use of multiple channels to deliver public health messages is more effective than relying on a single source (Schooler, et al., 1998). Campaign effectiveness can vary in terms of impact, reach and specificity (targeting). However behaviour change is a complex process and it does not follow directly from exposure to a message (Schooler, et al., 1998).

Reger *et al* (2000), conducted a study in rural communities in West Virginia (USA) examining the effectiveness of various educational approaches to promote the "1% Or Less" message. The "1% Or Less" campaign promotes the switch between high-fat (whole or 2%) to low fat milk (1% or fat free) for adults and children over the age of 2. The primary outcome measures of the study were: supermarket milk sales and self-reported milk consumption. Three communities took part in the study and they were assigned to campaign or control (Reger, et al., 2000). Study results are summarised in Table 12.

Table 12: Example of a public health campaign in the USA

	% of Low-Fat Milk sales			Self reported switching to low-fat milk
Strategy used	**Pre campaign**	**Post campaign**	**6-month follow up**	
Public relations, community based educational activities	23	28	29	19.6*
Paid advertising	28	34	27	12.8**
None	23	22	21	6.8

Milk sales are reported as a percent of all milk sold for the month before, the month after, and 6 months after the "1% Or Less" campaign was introduced in West Virginia (1997). * $p < 0.001$, ** $p < 0.01$

Public relations plus a community based educational campaign was the most effective strategy to promote the switch from high-fat to low fat milk. Nearly 20% of individuals responded to these strategies. However, the study design (non random) and the setting (rural USA) might limit the generalisability of these results.

In 1998, New South Wales (NSW) introduced a health campaign aimed at promoting moderate intensity activity. The strategies used included; paid and unpaid television, media advertising (printed), physician mail-outs and community level support programs. To evaluate the effectiveness of this campaign a study was conducted using a quasi-experimental and cohort study design. Cross sectional surveys were conducted before and after the campaign and other states were used as controls. The target group of this campaign was adults aged 25 to 60 years and the primary outcome measures were: physical activity, media message awareness, physical activity knowledge and reported behaviour (Bauman, et al., 2001).

Individuals in the target group (25-60 years) were 2.08 (95% CI 1.51-2.86) times more likely to increase their activity by at least half an hour per week. Recall (unprompted) of the activity messages before/after increased from 2.1 to 20.9%

(p< 0.01). Prompted awareness of the campaign theme increased from 14.2% to 59.0% (p< 0.001). These results show that the short-term physical activity message recall was positively influenced by this integrated campaign.

4.7 Iodine requirements during pregnancy and lactation

During pregnancy thyroid physiology is altered by several factors that increase thyroid hormone requirements. If hypothyroidism develops early in pregnancy the neurological damage may be more severe. This can be prevented by correcting maternal iodine deficiency before or during the first three months of pregnancy (Picciano, 2003). Therefore it is important to establish iodine sufficiency during pregnancy (Dunn and Delange, 2001).

A WHO Technical Consultation produced recent guidelines on iodine requirements in pregnancy and infancy. Early recommendations have recently been summarised (International Council for Control of Iodine Deficiency Disorders, 2007). Iodine intake during pregnancy and lactation should be 250 µg/day and not exceed 500 µg/day (International Council for Control of Iodine Deficiency Disorders, 2007).

The RDI for pregnant women in Australia and New Zealand is 220 µg/day and 270 µg/day during lactation (National Health and Medical Research Council and the New Zealand Ministry of Health, 2006).

4.7.1 Iodine status of pregnant women in Australia and New Zealand

The WHO Technical Consultation proposed that the median UIC was the best indicator to use in population (national) surveys to assess the iodine nutrition of pregnant and lactating women (International Council for Control of Iodine Deficiency Disorders, 2007). The median UIC for iodine categorisation of pregnant and lactating women are summarised in Table 13.

Table 13: Median UIC in pregnant and lactating women

Population Group	Median UIC (µg//L)	Category of iodine intake
Pregnant women	< 150 150 – 249 250 – 499 ≥ 500	Insufficient Adequate More than adequate Excessive‡
Lactating women§	< 100 ≥ 100	Insufficient Adequate

‡ Means excess of the amount required to prevent and control iodine deficiency
§Figures are lower than iodine requirements because of the iodine excreted in breast milk.

Source: (International Council for Control of Iodine Deficiency Disorders, 2007)

As previously discussed recent studies have reported low urinary iodine concentrations (UIC) in pregnant women in Australia (Burgess, et al., 2007, Hamrosi, et al., 2005, Travers, et al., 2006). UIC below 50ug/l was found in almost half of the Caucasian pregnant women who participated in a Down syndrome study in Melbourne. This study also found that 40% of the Vietnamese and Indian/Sri Lankan women surveyed had UIC below 50ug/l (Hamrosi, et al., 2005).

No published studies have reported the iodine status of pregnant women in New Zealand. A paper entitled: "The Thyromobile and iodine in pregnancy (TRIP) survey: Assessing the iodine status of New Zealand pregnant women" was presented at the New Zealand Dietetic Association Conference in 2006. However, this abstract is unavailable and the authors have not published these results.

4.7.2 Effectiveness of iodine supplementation during pregnancy and lactation

The strategy recommended by the WHO to eliminate IDD is salt iodisation. Iodine supplementation using a slow-release preparation such as iodised oil administered orally once a year (1 dose of iodised oil given once a year) 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. Therefore, this study will not be relevant to the Australian and New Zealand populations.

One review has been conducted on iodine supplementation of pregnant women in Europe (Zimmermann and Delange, 2004). The authors found six randomised controlled trials involving 450 women from mild-moderate deficient populations. The main conclusion of the review was that iodine containing supplements have beneficial impact on the iodine and thyroid status of both the mother and newborn (Zimmermann and Delange, 2004). The trials were reviewed to determine the concentration and mode of iodine supplementation, as well as the relevance to the Australian/New Zealand population. See Table 14.

Supplementation ranged from 50 to 230 ug/day and consistently resulted in increased maternal UIC. However, there was no clear dose response relationship between UIC and supplementation. The relationship between iodine supplementation during lactation and the iodine content in human milk needs further exploration (Chierici, et al., 1999). A study conducted in New Zealand found that iodine concentration in breast milk was 22 µg/l (CI 18-26) (Skeaff, et al., 2005). However the UIC of the 39 mothers that participated in the study was not reported.

A study conducted in Switzerland, reported that seventy percent of pregnant women received a prenatal supplement, of which 13% contained iodine (Hess, et al., 2001). This study demonstrated a statistically significant difference between those women taking iodine-containing supplement and those not (median 194 µg/l (range 31-990) and 130 µg/l (5-1881)) (Hess, et al., 2001).

Most pregnant women in Denmark take prenatal supplements, with one third containing iodine (Nohr and Laurberg, 2000). Women who took iodine-containing supplements had a higher UIC than those who did not (median 57 µg/g cr (IQR 39.8-91.8) and 39.7 µg/g cr (IQR27.1-59.8)) (Nohr, et al., 1993).

Table 14: Summary of studies of iodine supplementation in pregnancy

Author & Year	Study details	Intervention	Pre treatment	Post treatment
(Romano, et al., 1991)	Study conducted in Italy in an area of moderate iodine deficiency. Thirty five first trimester pregnant women randomly selected from Obstetrics and Gynaecology Department of the University of L'Aquila. UIC was determined by 24 hour urine collection. Thyroid volume was determined by ultrasound	Iodised salt 20 mg of iodine/kg. Daily Iodine intake: 120-180 ug Group A (intervention) = 17 Group B (control) = 18	First Trimester (mean ± SD) Group A Iodine excretion (µg/l) = 37.0 ± 36.0 Thyroid volume: 9.8 ml ± 1.9 Group B Iodine excretion (µg/l= 30.5 ± 42.0 Thyroid volume:10.1 ml ± 2.3	Last Trimester (mean ± SD) Group A Iodine excretion (µg/l) = 100.0 ± 39.0 Thyroid volume: no significant change Group B Iodine excretion (µg/l) = 50.0 ± 37.0 Thyroid volume: mean increase 1.6 ml ± 0.6
(Pedersen, et al., 1993)	Study conducted in Denmark in an area of moderate iodine deficiency. Fifty four pregnant women were randomised to receive placebo or iodine supplement from 17-18 weeks of pregnancy until 12 months after delivery. UIC was determined from morning spot urine samples Thyroid volume was determined by ultrasound	10 drops of potassium iodide. Daily iodine intake: 200 µg Group A (control) = 26 Group B (intervention) = 28	Median UIC (95% CI) Group A: 51 µg/l (32-58). Group B: 55 µg/l (30-73).	Median UIC (95% CI) Group A: Not reported Thyroid volume: increased 30% Group B: 90-110 µg//l. Thyroid volume: increased 16% One woman in the treatment group had persistent biochemical signs of hyperthyroidism

Author & Year	Study details	Intervention	Pre treatment	Post treatment
(Glinoer, et al., 1995)	Double-blind placebo controlled trial conducted in Belgium in an area of mild deficiency. One hundred and twenty pregnant women at the end of the first trimester with biochemical criteria of excessive thyroid stimulation were randomised into three arms. Thyroid volume was determined by ultrasound	Group A: Placebo Group B: 100 µg/day of iodine Group C: 100 µg/day of iodine plus 100 µg $_{L}$-T_4/day.	Before treatment % of women with UIC ≥ 100 µg/l Group A: 9 Group B: 13 Group C: 12 Overall mean thyroid volume: 14.3 ml ± 0.5	Third trimester % of women with UIC ≥100 µg/l Group A: 9 Group B: 50 Group C: 54 Thyroid volume (mean increase) Group A: 30%.Gestational goitre: 16% Group B: 15%.Gestational goitre: 10% Group C: 8%. Gestational goitre: 3%
(Nohr, et al., 2000)	Double-blind placebo controlled trial conducted in Denmark. Sixty two pregnant women were randomised according to their thyroid peroxidise antibody (TPO-Ab) level in three groups. UIC was determine by 24h urine collection Development of post partum thyroid dysfunction (PPTD) defined as abnormal TSH in the postpartum period.	Vitamin tablets (LivolSuper®) Daily iodine intake 150 µg Group A (n=22) pregnancy/postpartum Group B (n=20) only pregnancy Group C (n=24) no supplementation	Baseline median UIC µg//L Group A: 50 (35-101) µg//L Group B: 52 (36-81) µg//L Group C: 51 (30-80) µg//L	35 weeks median UIC µg//l Group A and B: 105 µg//l Group C: 53 µg//l Development of PPTD 60% treatment group 46% of control
(Antonangeli, et al., 2002)	Randomised open label trial conducted in a marginal iodine deficient area in Italy. Sixty seven pregnant women completed the study. UIC on casual urinary samples. Thyroid volume was determined by ultrasound	Iodid® Group A (n=32): 200 µg/day Group B (n=35): 50 µg/day.	Baseline median UIC µg/ g cr Group A: 91 µg/ g cr ± 14 Group B: 65.5 µg/ g cr ± 12 Mean ± SE Thyroid volume (ml) Group A: 11.3 ± 0.8 Group B: 11.2 ± 0.5	Pre partum median UIC µg/ g cr Group A: 230 µg/ g cr. Group B: 128 µg/ g cr Mean ± SE Thyroid volume (ml) Group A: 12.3 ± 0.7 Group B: 10.7 ± 0.9
(Liesenkotter, et al., 1996)	Quasi randomised controlled trial conducted in Germany. One hundred and eight pregnant women in a moderate iodine deficient area. UIC in random urine samples Thyroid volume using ultrasound	300 µg of Potassium iodide Daily iodine intake 230 µg/day Group A (n=38): treatment Group B (n=70): no supplementation	Baseline median UIC: 53 µg/ g cr Group A: 49.2 µg/ g cr Group B: 54.9 µg/ g cr Thyroid volume (ml) Group A: 16.2 Group B: 16.8	Baseline median UIC: 64 µg//L Group A: 104.5 µg/ g cr $p < 0.001$ Group B: not reported Thyroid volume: iodine supplementation did not prevent an increase on thyroid volume

4.7.3 Availability of iodine-containing supplements

In Australia, pregnancy supplements can be purchased at pharmacies and health food stores. Of the pregnancy supplements currently available only six contain iodine (as Potassium Iodide – KI). The iodine content of these supplements varies (76.6 to 250 µg/day) and the costs range from A$16 to A$25.95 for a month supply.

We did not identify any surveys of Australian or New Zealand women reporting use of iodine-containing supplements during pregnancy and/or lactation. There are no formal policies for iodine supplement usage in pregnant and lactation women in Australia or New Zealand. Furthermore increased iodine intake (i.e. via supplement use) is not currently advised in the fact sheets for pregnant women produced by the Australian Government DOHA[12] or the Victorian Government[13].

We did not identify any public health interventions in Australia or New Zealand aimed at increasing the intake of iodine-containing supplements during pregnancy or lactation. A call for iodine supplementation in pregnant and lactating women, in Australia and New Zealand, was made in a newsletter from the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (Eastman, 2005).

[12] http://www.healthyactive.gov.au/internet/healthyactive/publishing.nsf/content/pregnant-women
[13] http://www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/Pregnancy_and_diet?open

5 Cost Considerations

The estimated costs associated with each strategy are presented in this section. The cost of mandatory and voluntary fortification of bread with iodised salt has been adapted from the report prepared by Access Economics[14]. Titled: "Costs of fortifying bread and bread products with iodine" (Access Economics, 2007). We were unable to identify any studies that estimated the costs of implementing an educational program and/or supplementation program specific to iodine, within Australia or New Zealand. Therefore we have based the costs estimates on the costs associated with comparable strategies for addressing folate deficiency. This report was prepared for FSANZ, titled: "Informing a strategy for increasing folate levels to prevent neural tube defects: A cost effectiveness analysis of options". (Segal, et al., 2007)

5.1 Costs estimated by Access Economics

The costs of mandatory fortification of bread as estimated by Access Economics are shown in Table 15. The authors estimated the costs to the salt and bread making industries, and to Government. Government costs are restricted to the administration and enforcement of 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; complementary policies required alongside fortification that are outside the scope of FSANZ; or health care costs.

Table 15: The cost of mandatory fortification of bread (Access Economics)

	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

[14] The Access Economic report addresses the cost estimates in much more detail than present in this report. We aim to provide an overview of their cost estimates and any systematic deviations that we have made. For a thorough review please see the Access Economic report.

program. The net cost of moving between mandatory and voluntary, therefore, introduces a degree of uncertainty. We will deal with this below.

5.2 Discount rate

Discounting in economic evaluations has long been a subject of some debate. Access Economics estimated the discount rate by subtracting the long run inflation rate from the positive time preference (i.e. long term nominal bond rate). This gave discount rates of 5.8 – 2.5 = 3.3% for Australia and 6.0 – 2.2 = 3.8% for New Zealand.

The discount rate we have chosen reflects the societal rate of time preferences in Australia. This is consistent with the discount rate used by the Pharmaceutical Benefits Advisory Committee (PBAC) and Medical Services Advisory Committee (MSAC). MSAC and PBAC both use a discount rate of 5%. For consistency, costs and benefits have been discounted at the same rate.

In addition, we have also based the Net Present Value (NPV) over a 10 year period, rather than a 15 year period. Again this is to be more consistent with other economic evaluations.

5.3 Cost of mandatory fortification of bread with iodised salt

The cost of mandatory fortification of bread with iodised salt has been adapted from the costs estimated above, by Access Economics (Access Economics, 2007). We have used the raw data presented in the report and altered some of the assumptions, which we feel are more consistent with other health economic evaluations. Therefore, our total cost estimates are slightly different to those presented earlier. In addition, because of the recent approval of mandatory fortification of bread with folic acid, we have also reduced the costs to reflect the potential 'piggyback' savings. These are reported separately. The following assumptions have been used when modelling the costs:

- Raw data taken from Access Economic estimates
- Costs discounted at 5%, same as outcomes
- Time horizons 10 years
- A$ for Australia and NZ$ for New Zealand.
- Include/exclude piggyback savings of mandatory fortification of bread with folate.
- Costs which have been excluded:
    - Costs associated with loss of consumer choice
    - Costs of awareness raising amongst GPs
    - Costs of monitoring the effectiveness of the regulation.

The costs of mandatory fortification are present in Table 16. The costs represented are reflective of those borne by the salt manufacturers, bread manufacturers and Government.

5.3.1 Costs to the salt manufacturers

The upfront costs borne by the salt manufacturers are; those of plant upgrades (machinery and instruments). For example, dry mixing systems to enable increased production of iodised salt, and re-labelling of products. These costs are estimated to be A$143,000 and A$18,050, respectively in Australia and NZ$300,000 and NZ$3,000, respectively in New Zealand. This means the total upfront cost to the salt industry are A$161050 in Australia and NZ$303000 in New Zealand.

Ongoing costs relate to the maintenance, transport, process labour, iodine, analytic testing and storage. In Australia, the estimated costs of: maintenance = A$5,000; iodine = A$47,736; analytic testing = A$14,333; transport = A$233,333; and storage = A$13,867. This gives a total of A$314,269 ongoing costs in Australia. In New Zealand, the estimated costs of: maintenance = NZ$2,000; process labour = NZ$3,016; analytic testing = NZ$4,000; iodine = NZ$8,726; transport = NZ$0; and storage = NZ$ 1,933. This gives a total of NZ$19,675 ongoing costs in New Zealand.

The NPV, calculated over a 10 year period discounted at 5%, are A$2,587,752 in Australia and NZ$454,925 in New Zealand.

5.3.2 Costs to the bread manufacturers

To avoid double counting, iodine costs have been excluded from the bread manufacturers estimates. The upfront costs refer to revising and relabelling the packaging and writing off old packaging. In Australia, these are estimated to be A$6,950,000 and in New Zealand NZ$1,495,040

Ongoing costs are associated with analytical testing. In Australia these are A$30,000 and in New Zealand NZ$30,000. The NPV, over 10 years, to the bread making industry are $7,181,652 in Australia and NZ$ 1,726,692 in New Zealand.

5.3.3 Cost to the Government

The upfront cost to Government refers to the set-up costs, auditing, and training and awareness of the bread making industry. In Australia, the set-up costs are A$31,000. In New Zealand the set-up costs are NZ$2,520, the costs of training and awareness are NZ$4,800, and the costs of auditing are NZ$600 (total = NZ$7,920).

Ongoing costs are associated with; training and awareness of the bread making industry, administration, auditing and enforcement. In Australia these are estimate to be A$137,000 per year. In New Zealand the estimated costs are; training NZ$2,400, administration NZ$1,320, auditing NZ$80,000 and enforcement NZ$4,780 (total NZ$88,500 per year). The NPV, over 10 years, to the Government are A$1,088,878 in Australia and NZ$691,294 in New Zealand.

5.3.4 Summary of the costs of mandatory fortification of bread

The cost estimates are summarised in Table 16. Total costs are the sum of those borne by the salt and bread manufacturing industries and the Government.

- In Australia, the total upfront costs are A$7,142,050, the total ongoing costs are A$481,269 and NPV = A$10,858,282.
- In New Zealand, the total upfront costs are NZ$1,805,960, the total ongoing costs are NZ$138,175 and NPV = NZ$2,872,911.

Table 16: The cost of mandatory fortification of bread

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia			
Salt Industry	A$2,394,818	A$161,050	A$314,269
Bakers	A$7,163,235	A$6,950,000	A$30,000
Government	A$1,004,772	A$31,000	A$137,000
Total	A$**10,562,824**	A$**7,142,050**	A$**481,269**
New Zealand			
Salt Industry	NZ$442,846	NZ$303,000	NZ$19,675
Bakers	NZ$1,708,275	NZ$1,495,040	NZ$30,000
Government	NZ$636,962	NZ$7,920	NZ$88,500
Total	NZ$**2,788,083**	NZ$**1,805,960**	NZ$**138,175**

5.3.5 Mandatory fortification minus piggyback costs

Potential savings through the parallel introduction of mandatory fortification of bread with folic acid and iodised salt may reduce the costs of iodine fortification significantly. Folic acid is not involved in the salt making process; therefore we do not envisage that the salt manufacturing industry would be able to reduce their costs. Consequently, the costs to the salt manufacturers are the same as above.

We estimate that the upfront costs to the bread manufacturers in Australia and New Zealand will be zero. This is because the labels and packaging will need to be changed to accommodate the folic acid permissions. However, ongoing analytic testing will still need to be carried out. Therefore, these costs remain the same.

We estimate that the upfront cost to Government will be reduced to 20% of the original estimate. This is because the costs of administration and training will be zero and we estimate the costs of set-up and auditing will be 50%. Therefore, the upfront costs to government under this option will be A$6,200 in Australia and NZ$1,560 in New Zealand. Ongoing costs of auditing and enforcement are also estimated to be 50%.

The cost estimates of mandatory fortification minus piggyback costs are summarised in Table 17. Total costs are those borne by the salt and bread manufacturing industries and the Government.

- In Australia, the total upfront costs are A$167,250, the total ongoing costs are A$412,769 and NPV = A$3,354,543.

- In New Zealand, the total upfront costs are NZ$304,560, the total ongoing costs are NZ$92,065 and NPV = NZ$1,015,462.

Table 17: The cost of mandatory fortification of bread (minus piggyback costs of mandatory folic acid fortification of bread)

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia			
Salt Industry	A$2,394,818	A$161,050	A$314,269
Bakers	A$213,235	A$0	A$30,000
Government	A$493,086	A$6,200	A$68,500
Total	A$**3,101,138**	A$**167,250**	A$**412,769**
New Zealand			
Salt Industry	NZ$442,846	NZ$303,000	NZ$19,675
Bakers	NZ$213,235	NZ$0	NZ$30,000
Government	NZ$302,861	NZ$1,560	NZ$42,390
Total	NZ$**958,942**	NZ$**304,560**	NZ$**92,065**

5.4 Cost of voluntary fortification of bread with iodised salt

The costs of voluntary fortification of bread with iodised salt have been adapted from the section above. We have based our calculations on the experiences of voluntary fortification in Tasmania, where 80% of bread became fortified under the voluntary permission. Like before, because of the recent approval of mandatory fortification of bread with folic acid, we have also reduced the costs to reflect the potential 'piggyback' savings. These are reported separately. The following assumptions have been used when modelling the costs:

- Raw data taken from Access Economic estimates
- 80% of bread will be fortified under a voluntary fortification scheme
- Costs discounted at 5%, same as outcomes
- Time horizons 10 years
- A$ for Australia and NZ$ for New Zealand.
- Include/exclude savings through piggyback costs of mandatory fortification of bread with folic acid.
- Costs which have been excluded:
  - Costs associated with loss of consumer choice
  - Costs of awareness raising amongst GPs
  - Costs of monitoring the effectiveness of the regulation.

The costs of voluntary fortification are present in Table 18. The costs represented are reflective of those borne by the salt manufacturers, bread manufacturers and Government.

5.4.1 Costs to the salt manufacturers

The upfront costs borne by the salt manufacturers remain unchanged. This is because salt is produced by a small number of manufacturers. Therefore plant upgrades would still be required. The only potential saving would be if a manufacturer decides not to supply iodised salt, but this is unlikely since 80% of bread manufacturers would demand iodised salt.

We estimate that some ongoing costs can be reduced by 80%. These include the costs of iodine, labour, analytical testing and transport. The costs of maintenance and storage will potentially remain the same as under the mandatory fortification option.

5.4.2 Costs to the bread manufacturers

The upfront costs of revising and relabelling the packaging, and writing off old packaging will be 80%. This is because if 20% of bakers decide not to fortify their bread, they will incur no costs. Using the same rationale, ongoing costs will also be 80% of the mandatory costs.

5.4.3 Cost to the Government

We estimate that the ongoing and upfront costs to Government will be the same under voluntary and mandatory fortification options. Since the Government will target all bread manufacturers in the first instance. Potentially there may be savings from auditing 80% of manufacturers instead of 100%. However, there may be increased costs of continued promotion, to maintain compliance, without legislative support. However, there is a large amount of uncertainty regarding this issue, so we have not included them in this report.

5.4.4 Summary of costs of voluntary fortification of bread

The cost estimates for voluntary fortification are summarised in Table 18. Total costs are those borne by the salt and bread manufacturing industries and the Government.

- In Australia, the total upfront costs are A$5,752,050, the total ongoing costs are A$416,189 and NPV = A$8,965,748.
- In New Zealand, the total upfront costs are NZ$1,506,952, the total ongoing costs are NZ$129,027 and NPV = NZ$2,503,261.

Table 18: The cost of voluntary fortification of bread

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia			
Salt Industry	A$1,974,885	A$161,050	A$255,189
Bakers	A$5,730,588	A$5,560,000	A$24,000
Government	A$1,004,772	A$31,000	A$137,000
Total	A$**8,710,244**	A$**5,752,050**	A$**416,189**
New Zealand			
Salt Industry	NZ$420,468	NZ$303,000	NZ$16,527
Bakers	NZ$1,366,620	NZ$1,196,032	NZ$24,000
Government	NZ$636,962	NZ$7,920	NZ$88,500
Total	NZ$**2,424,050**	NZ$**1,506,952**	NZ$**129,027**

5.4.5 Voluntary fortification minus piggyback costs

As before, there are potential savings through the parallel introduction of voluntary fortification of bread with iodised salt and the mandatory fortification of bread with folic acid. As previously discussed we do not envisage any synergies between the salt manufacturers.

We estimate that the upfront costs to the bread manufacturers in Australia and New Zealand will be zero. However, ongoing analytic testing will still need to be carried out. Therefore, these costs remain the same.

We estimate that the upfront cost to Government will be 20% of the original estimate and the set-up costs and auditing will be reduced by 50%. (See before for reasoning)

The cost estimates of voluntary fortification minus piggyback costs are summarised in Table 19. Total costs are those borne by the salt and bread manufacturing industries and the Government.

- In Australia, the total upfront costs are A$167,250, the total ongoing costs are A$347,689 and NPV = A$2,852,009.
- In New Zealand, the total upfront costs are NZ$304,560, the total ongoing costs are NZ$82,917 and NPV = NZ$944,820.

Table 19: The cost of voluntary fortification of bread (minus piggyback costs of mandatory folic acid fortification of bread)

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia			
Salt Industry	A$1,974,885	A$161,050	A$255,189
Bakers	A$170,588	A$0	A$24,000
Government	A$493,086	A$6,200	A$68,500
Total	**A$2,638,559**	A$**167,250**	A$**347,689**
New Zealand			
Salt Industry	NZ$420,468	NZ$303,000	NZ$16,527
Bakers	NZ$170,588	NZ$0	NZ$24,000
Government	NZ$302,861	NZ$1,560	NZ$42,390
Total	NZ$**893,916**	NZ$**304,560**	NZ$**82,917**

Table 20 demonstrates the reduction in overall cost of voluntary fortification compared to mandatory fortification. Despite 80% of bread becoming iodised under a voluntary option, this does not translate into an 80% reduction in costs.

Table 20: The total costs of mandatory versus voluntary fortification (minus piggyback costs)

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Not including piggyback savings			
Australia			
Mandatory	A$1,0562,824	A$7,142,050	A$481,269
Voluntary	A$8,710,244	A$5,752,050	A$416,189
Proportion of costs	**82.5%**	**80.5%**	**86.5%**
New Zealand			
Mandatory	NZ$2,788,083	NZ$1,805,960	NZ$138,175
Voluntary	NZ$2,424,050	NZ$1,506,952	NZ$129,027
Proportion of costs	**86.9%**	**83.4%**	**93.4%**
Including piggyback savings			
Australia			
Mandatory	A$3,101,138	A$167,250	A$412,769
Voluntary	A$2,698,559	A$167,250	A$347,689
Proportion of costs	**85.1%**	**100.0%**	**84.2%**
New Zealand			
Mandatory	NZ$958,942	NZ$304,560	NZ$92,065
Voluntary	NZ$893,916	NZ$304,560	NZ$82,917
Proportion of costs	**93.2%**	**100.0%**	**90.1%**

5.5 Cost of implementing an educational health campaign targeting the whole population

The costs of implementing an educational health campaign targeting the whole population have been adapted from the costs estimated for a comparable strategy to address folic acid deficiency (Segal, et al., 2007). We have used the raw data presented in the report and altered some of the assumptions. The following assumptions have been used when modelling the costs:

- Raw data taken from FSANZ report for folic acid
- Costs discounted at 5%, same as outcomes
- Time horizons 10 years
- A$ for Australia and NZ$ for New Zealand.
- Costs are the direct costs of media and community based elements

The costs of comparable high profile national public health campaigns are summarised in Table 21.

Table 21: Summary of costs of selected high profile national public health campaigns

Campaign	**Cost** (current dollars)
National Tobacco Campaign 1997	A$9 million
National Go for 2 & 5 Campaign 2005	A$4.76 million
Skin Cancer Awareness 2006-7	A$5.5 million
TAC Road safety advertising 1990-1992	A$4.95-6.83 million per year

Source: (Segal, et al., 2007)

The authors of the ‘Cost-effectiveness of folate supplementation’ report (Segal, et al., 2007), estimated that the reasonable cost estimates, based on the above examples, for a national folate education program is A$5 million up front, plus an ongoing annual investment of A$1 million for Australia. This would fund a high profile campaign with a combination of media and community-based elements. The values for New Zealand are scaled down by one fifth, using a simple population pro-rota basis. We believe that these values represent a good estimate of the costs of undertaking a similar campaign to encourage the use of iodised salt as an alternative to non-iodised salt. These are summarised in Table 22.

Table 22: Summary of costs of a high profile national public health campaign

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia	A$12,107,822	A$5 million	A$1 million
New Zealand	NZ$242,1564	NZ$1 million	NZ$200,000

5.6 Costs of targeting pregnant women

The costs of targeting pregnant and lactating women are explained in this section. No evidence is available for the costs of this intervention using iodine supplements. Therefore we have adapted the costs estimated for a comparable strategy to address folate deficiency (Segal, et al., 2007). The following assumptions have been made:

- Raw data taken from FSANZ report for folate
- Costs discounted at 5%, same as outcomes
- Time horizons 10 years
- A$ for Australia and NZ$ for New Zealand.
- Costs are restricted to the cost of physician advice and the costs of iodine supplements

The costs are divided into two types; the costs of physician counselling and the costs to the patient of the iodine supplements.

5.6.1 Costs of physician counselling

Encouraging pregnant women to take additional supplementation is best achieved when the advice is given by a clinician. The costs associated with this intervention are those of training and informing, via information packs, clinicians regarding the importance of iodine supplementation. We assume that the physician counselling, concerning the use of iodine supplements forms part of the standard physician role during a gynaecological consultation. Therefore incurring no additional cost in terms of physician time.

The costs are broken down as follows: 1) Personnel to conduct education campaign to target obstetricians and gynaecologists. We estimate that during the first year between 0.5 to 1 educators per state/territory (total = 4.8 FTE[15]) and for ongoing education 1.5 educators per year in Australian. This would give 4.8 x A$78,000 (average salary) = A$376,000 set-up costs and 1.5 x A$78,000 = A$117,000 ongoing costs. 2) Education campaign material. We estimate that all obstetricians and gynaecologists (1200[16]) would receive a information pack ($10), therefore the set-up cost would be A$12,000. Ongoing education material costs are estimate to be A$4000. The values for New Zealand are scale down by one

[15] FTE = Full time equivalent
[16] The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

fifth, using a simple population pro-rota basis. These data are summarised in Table 23.

Table 23: Costs for a physician counselling intervention

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia	A$1,246,446	A$386,400	A$121,000
New Zealand	NZ$249,289	NZ$77,280	NZ$24,200

5.6.2 Costs of iodine supplements to pregnant women

The costs of iodine supplementation are the direct costs faced by the pregnant or lactating women. The estimates are based on pregnant women (168,244 in Australia and 37,062 in New Zealand) taking the supplements for 18 months (three months before pregnancy, nine months during pregnancy and 6 months during breast feeding). We also estimate, based on the evidence presented earlier, that 15% of women will take iodine supplements that would otherwise not have. Finally, the costs of the supplements (A$19.91 per month) are based on an average of iodine supplements available in Australia, MIMS online. (2007) These data are summarised in Table 24. Total costs of iodine supplementation including physician costs are presented in Table 25.

Table 24: Costs of iodine supplements for pregnant women

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia	A$73,320,305	A$0	A$9,043,157
New Zealand	NZ$16,151,525	NZ$0	NZ$1,992,092

Table 25: Total costs of an iodine supplementation program in pregnant women

	Net Present Value (10 years)	Upfront Cost	Ongoing (per annum)
Australia			
Physician cost	A$1,246,446	A$386,400	A$121,000
Supplement cost	A$73,320,305	A$0	A$9,043,157
Total	**A$74,566,751**	**A$386,400**	**A$9,164,157**
New Zealand			
Physician cost	NZ$249,289	NZ$77,280	NZ$24,200
Supplement cost	NZ$16,151,525	NZ$0	NZ$1,992,092
Total	**NZ$16,400,814**	**NZ$77,280**	**NZ$2,016,292**

6 Population level economic modelling of mandatory and voluntary 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 economic modelling contained in this report is divided into two sections. In this section, we look at population-level options for improving Iodine status of the Australia and New Zealand populations. The fortification options assessed during the evaluation are:

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

Following this, we focus on pregnant women as the reduction of deficiency in this group is of particular importance due to the issues surrounding neurological development of the unborn child, reflected in the WHO recommended level for UIC being 150 μg/l in this group.

6.1 Assumptions for population level modelling

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.

- We do not formally include the costs of treating conditions which may be caused/ prevented by changing levels of Iodine.
- 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 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.

- o We have assumed that the Australian population can be summarised by one distribution, although there are areas of iodine deficiency and iodine sufficiency. The median IUC for Australia relates to the most representative value of the whole population.

- o Similarly, we have assumed that voluntary fortification will lead to a reduced penetration of iodised salt, and that this reduced penetration is uncorrelated with individual's current iodine status (that is, a certain proportion of people will not receive iodised salt who would have done under a mandatory scheme, and these people do not differ systematically from the rest of the population).

6.2 Introduction

During the economic evaluation of mandatory and voluntary 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

4. (Voluntary bread only) Proportion of bread manufacturers who are likely to choose to use fortified salt under a voluntary scheme

The result from this question will be an estimate of the populations over which the two interventions (mandatory and voluntary fortification) would be applied.

Step 2: Identification of the number of individuals with an annual average iodine level of below 50 and 100 µg/l, under both interventions (mandatory and voluntary fortification) and status quo

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 both fortification schemes on this measure

The result from this will be the estimated reduction in individuals with an average 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 an IDD that have been averted

- 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 step 1 through to step 3.

6.3 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

6.3.1 Australian / New Zealand population size

The populations of the two countries were identified through the Australian Bureau of Statistics website[17] and the Statistics New Zealand website[18]. The populations are shown in Table 26. The number of women with unborn children was estimated by multiplying the number of children born in one year by (nine months / 12).

Table 26: 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**

6.3.2 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.

[17] http://www.abs.gov.au/
[18] http://www.stats.govt.nz/default.htm

6.3.3 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[19].

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 27.

Table 27: The exposed population under mandatory fortification

	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)

For voluntary fortification, it was assumed that, as in Tasmania, 80% of bakers would choose to fortify under a voluntary scheme. Thus, to estimate the exposed population under voluntary fortification, the figures in Table 27 are multiplied through by 0.8. This is shown in Table 28.

Table 28: The exposed population under voluntary fortification

	Australia	New Zealand
Pregnant Women	134,595	29,650
Children (2-18 years old)	3,169,946	696,294
Adults (18 and over)	10,704,440	2,029,680

6.4 Estimation of deficiency averted

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

[19] 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.

- 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 urine iodine contents (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[20].

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 inappropriate 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).

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, in Figure 3 through to Figure 7.

6.4.1 The likely 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

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

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

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 29.

Table 29: The effect of fortification in Australia on UIC

	Lower Quartile		Median		Upper Quartile	
	Voluntary	Mandatory	Voluntary	Mandatory	Voluntary	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 29. 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 29), 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. 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 anecdotal 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, voluntary 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. These populations are shown in Table 32 and Table 33.

It should be noted that the World Health Organisation recommended level of UIC for pregnant women is 150 µg/l. Therefore, it might be appropriate to set different thresholds for this group. However, in the absence of an identified consensus on this issue, we have omitted it from the base case findings.

Table 30: 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 31: Bread eating population percentages below thresholds under mandatory fortification in New Zealand

	Adults*		Children	
UIC(µg/l)	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.

Table 32: Expected levels of iodine deficiency (defined by average annual UIC) in the Australian bread-eating population

	Adults			Children			Pregnant women		
UIC(µg/l)	Status Quo	Voluntary	Mandatory	Status Quo	Voluntary	Mandatory	Status Quo	Voluntary	Mandatory
<50	200,708	115,073	93,664	39,624	23,774	19,812	1,178	640	505
50-100	9,540,332	4,819,674	3,639,510	2,195,188	1,152,275	891,547	134,090	63,966	46,435

Table 33: Expected levels of iodine deficiency (defined by average annual UIC) in the New Zealand bread-eating population

	Adults			Children			Pregnant women		
UIC(µg/l)	Status Quo	Voluntary	Mandatory	Status Quo	Voluntary	Mandatory	Status Quo	Voluntary	Mandatory
<50	190,283	70,532	40,594	94,870	37,078	22,630	2,780	1,030	593
50-100	2,466,061	1,073,701	725,611	836,423	372,691	256,758	33,245	14,655	10,007

6.4.2 The likely effect of a population-level education campaign

As a potential alternative to fortification of salt in bread, we now consider the likely effect of a population-level education campaign to encourage people to use iodised salt. In section 7, we will consider the use of education alongside supplementation in pregnant women. There is significant uncertainty in estimating the effect of a population-level education campaign. For example, we have assumed that evidence from education campaigns in other areas can be generalised to iodine. The structure of our argument is as follows:

1) Identify the proportion of the population who are likely to change their diet as a result of a population-level education campaign.
2) Estimate the likely cost of such a campaign, using the experiences of similar health-related population-level education campaigns.
3) Consider the effect of changing behaviour on UIC levels that would be necessary to make education an option comparable to mandatory fortification in cost-effectiveness terms.

We identified no evidence for the proportion of a population likely to respond to a population level education campaign. It is difficult to ascribe a take-up rate from public health campaigns in general since they, as a group, are likely to be hugely heterogeneous. Segal reported the Western Australia results of a folate promotion campaign (Segal, et al., 2007). In the general population, the increase in folate over the course of the intervention was 10.1%. While there are reasons why this figure might be different for iodine, we decided that, in the absence of more appropriate data, to use it for the base case analysis.

At this point, it is instructive to consider the costs of such an intervention. Previously, we have outlined the major costs associated with a population-level education campaign. The Net Present Value of the costs over ten years were estimated to be $12,107,822 in Australia, and $2,421,564 in New Zealand. This contrasts with $3,101,000 for mandatory fortification in Australia and $959,000 in New Zealand. Therefore, the public health campaign would cost 3.9 times more in Australia and 2.5 times more in New Zealand than mandatory fortification. We can therefore assert that, to achieve reductions at a similar cost per unit, the reduction in the Australian (New Zealand) population of low iodine individuals would have to be 3.9 (2.5) times larger than that cause by mandatory fortification of bread with iodised salt. Even allowing for the fact that a public health campaign would act over a larger population (since a proportion of the population do not eat bread), it would require more than 100% of those currently below either 50 µg/l or 100 µg/l to be increased above those thresholds to allow a comparable cost-effectiveness ratio for education relative to status quo and mandatory fortification relative to status quo. Therefore, a public health campaign affecting the behaviour of 10.1% of the population seems to be more expensive than mandatory fortification, and has less effect. Therefore, it is said to be dominated. While there may be other concerns, such as equity or freedom of choice, the use of a public health campaign is unlikely to be justifiable from a cost-effectiveness perspective on the basis of reducing iodine deficiency compared with mandatory fortification. However, this conclusion does not mean that education should not play a role in sub-groups (such as pregnant women), more that, under our assumptions, it is unlikely to be a better option than mandatory fortification for the entire population.

6.5 Estimated number of IDD linked conditions averted

It should be noted that this section refers to the effect of mandatory fortification. To calculate the effect of voluntary fortification, multiply the effect by 0.8. Since the evidence presented suggests that the public education campaign is dominated by mandatory fortification, we have not presented the data for this intervention in this section.

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 demonstrated a quantifiable link between particular levels of iodine deficiency and particular conditions in individuals. However, there is a significant literature identifying a relationship between iodine levels and hypothyroidism, intellectual impairment, goitre and hyperthyroidism at a population level. Additionally, 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.

6.5.1 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 low iodine level (i.e. a annual average UIC less than 50 µg/l), the modelling we have undertaken here suggests that mandatory 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 Spanish study 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 levels to more than the threshold of 100ug/l for 32.9% of children in Australia and 66.6% of children in New Zealand (meaning 1,042,912 children in Australia and 463,732 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 27 would be to increase it by 0.598 IQ points in Australia, and by 1.219 IQ points in New Zealand.

6.5.2 Hyperthyroidism

Hyperthyroidism is usually observed in older populations (Laurberg, et al., 2006). While the distributions we generated for the post-fortification population see a large increase in annual average UIC, we do not identify a population with a level greater than 300 µg/l. Bulow Pedersen *et al* (2006) identified that, while the incidence of hyperthyroidism was consistently higher in older cohorts, the increasing incidence of hyperthyroidism under a fortification scheme was greater in younger populations. The Danish approach had two main stages, as previously discussed in section 4.3.3.

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 seen in Aalborg). However, it is likely 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 27**,** it would suggest an increase in hyperthyroidism cases of 2,676 per year in Australia. However, this might be an overestimate since the Copenhagen population was more iodine deficient than the current Australian population. If the same approach was taken in New Zealand (again assuming that the Copenhagen population was more representative of the Australian and New Zealand populations), the introduction of mandatory fortification would lead to 507 extra cases per year.

The counter view comes from the Swiss experience of fortification (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.

6.5.3 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 38.9 and 29.2 cases per 100,000 per year respectively. As expected, the area with a greater 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.

6.6 The cost of fortification

The cost of mandatory fortification was estimated in a previous report by Access Economics (2006). They estimated the costs as shown in Table 34. We use the same cost for our economic modelling of mandatory fortification, but have adjusted these costs to reflect voluntary fortification as illustrated previously.

Table 34: 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**

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.

6.7 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, we decided that reduction in the number of individuals with annual average UIC levels <50 µg/l, and <100 µg/l, were the key outcome measures.

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[21]. People with low iodine UIC averted were also spread over ten years, and discounted at five percent per annum.

The first important result is that voluntary fortification is shown to be subject to extended domination. That is, relative to the status quo, mandatory fortification leads to a greater reduction in people below either the 50 µg/l or 100 µg/l thresholds, and at a lower cost per person. This result can be explained intuitively in that the reduction in the deficient population is proportional to the proportion of bread that is fortified, while we have estimated that the cost of voluntary fortification is liable to be reduced relative to mandatory, but to a lesser degree than the benefits. Following standard economic evaluation methodology, it is therefore excluded from the incremental analysis.

The education program is excluded for similar reasons. Relative to both voluntary and mandatory fortification, it leads to a smaller population level improvement in Iodine levels, and at a higher cost. Therefore, it is dominated and excluded.

[21] 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 35: Cost-effectiveness ratios (Mandatory versus status quo)

			Australia	New Zealand
Cost (10 years) (local$000) (assumed lower due to piggy-back)		(A)	3,101	959
Cost (10 years) (local$000) (no piggy-back)		(B)	10,563	2,788
Outcome	Reduction in people below 50 µg/l	(C)	127,529	224,116
	Total reduction below 100 µg/l	(D)	7,319,647	2,567,469
Piggy-backed costs	Cost per person reduction below 50 µg/l (A/C)		$24.32	$4.28
	Cost per person reduction below 100 µg/l (A/D)		$0.42	$0.37
Non-piggy-backed costs	Cost per person reduction below 50 µg/l (B/C)		$82.83	$12.44
	Cost per person reduction below 100 µg/l (B/D)		$1.44	$1.09

These results should be interpreted as the cost per one person reduction in the deficient group (be it below 50 µg/l or below 100 µg/l) for 10-years. Thus, if we want to reduce the number of people in Australia with an annual average UIC below 50 by 1 for a 10-year period, the cost through mandatory fortification of bread is $24.32 if we make the assumptions regarding piggy-backing of costs outlined previously (and $82.83 if we do not make that assumption). We did not identify any benchmark values for these ratios. However, the cost to reduce the population of those at-risk from IDDs seems to be low, especially if we allow costs to be piggy-backed.

6.8 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 29.

The key driver of the results presented here is the effect of fortification on the median iodine urine content. 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, below 100 µg/l, under mandatory fortification

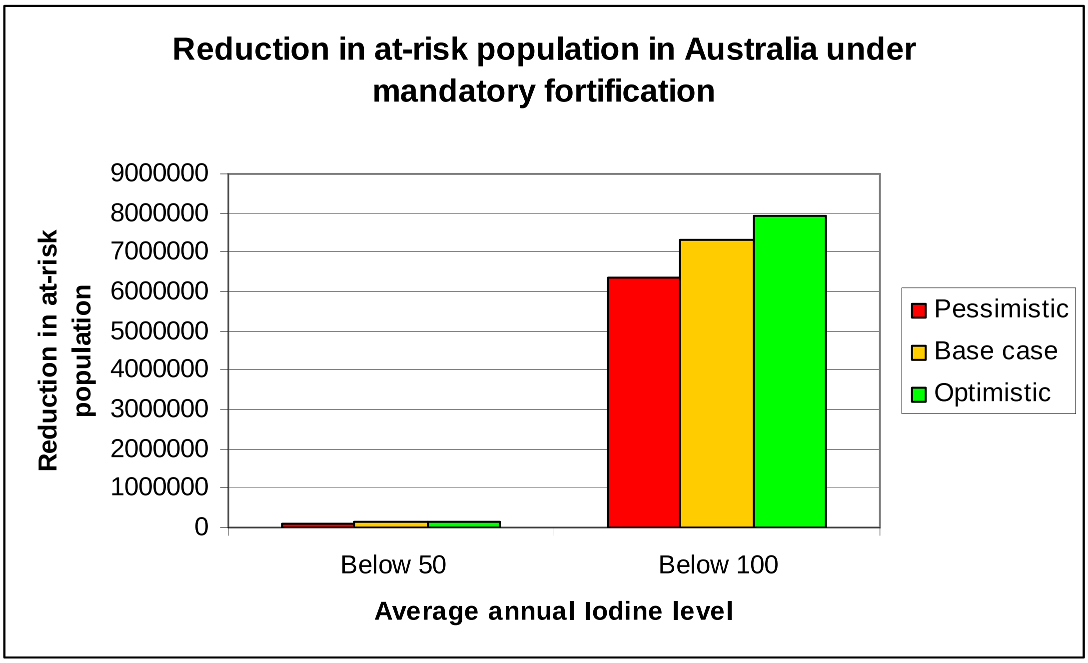
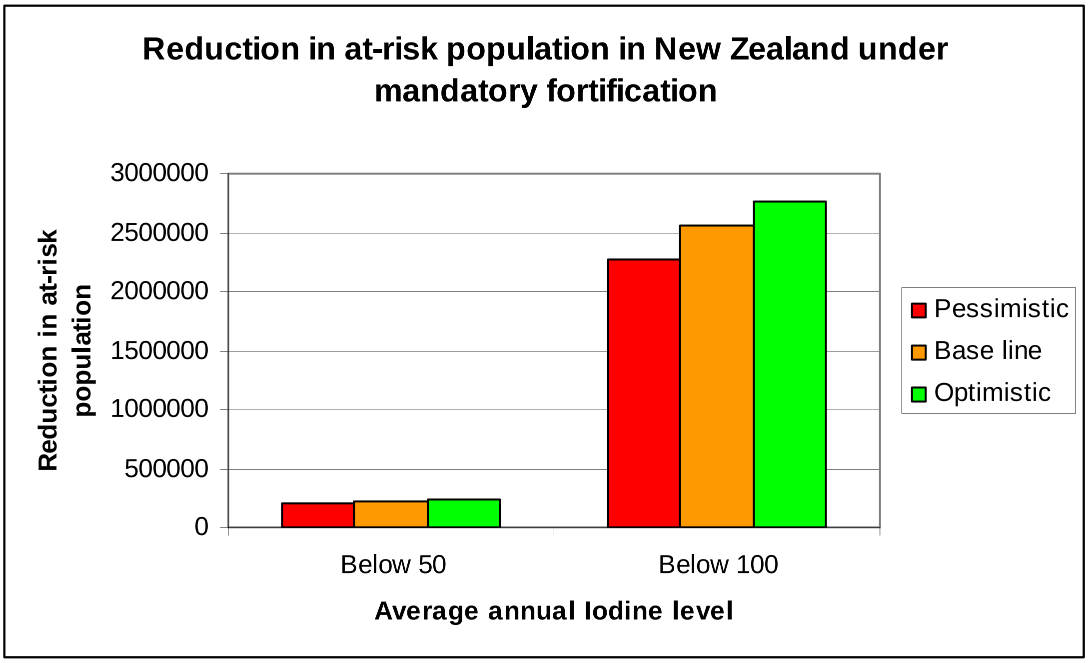


Figure 2: The reduction in the population of New Zealand, below 100 µg/l, under mandatory fortification



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. In Australia, this amounts to a reduction in individuals with an annual average UIC of below 50 of 127,000 (compared to 148,000 in the base case) and in New Zealand of 199,000 (compared to 224,000)

7 Economic modelling of options relevant to pregnant women

The results in the previous section suggested that mandatory fortification will make both the Australian and New Zealand populations iodine sufficient (see Table 41 in the Discussion for details). However, there may be a further role for supplementation and education in targeting those with the greatest capacity to benefit from increased iodine intake. As noted previously, reducing the numbers of individuals with low iodine levels is of particular importance in pregnant women. We have identified that, relative to mandatory fortification, population-level education has a lesser effect per dollar on iodine deficiency. This section is concerned with whether education and supplementation has a role to play in pregnant women as an addition to mandatory fortification of bread with iodised salt. This additional intervention applies both to the bread-eating population, and others, so has the capacity to reach populations not affected by mandatory fortification.

We now summarise the results for mandatory and voluntary fortification with regards to pregnant women.

Table 36: The pregnant women below 50 μg/l and 150 μg/l under voluntary and mandatory fortification

	Australia			New Zealand		
UIC(μg/l)	Status Quo	Voluntary	Mandatory	Status Quo	Voluntary	Mandatory
<50	1,178	640	505	2,780	1,030	593
50-150	167,066	130,995	121,977	34,245	25,351	23,127

The question this section investigates is the extent to which iodine deficiency can be reduced further in this population through targeted education and supplementation for pregnant women, and at what cost to society.

The structure of this section is as follows:

- Identify any evidence linking supplementation, supported by education, with increased nutrient intake (due to lack of evidence, this includes areas beyond iodine)
- Estimate the effect of supplementation of individual UIC levels
- Estimate the cost of providing this supplementation and education program
- Generate cost-effectiveness ratios based on these estimates

A previous FSANZ report identifies studies showing the effect on take-up of supplements (in this case, folate) (Segal, et al., 2007). A key finding of this investigation was that increase in take-up across settings and organisational structure was notably constant at approximately 15%. This settings included

Western Australia (Marsack, et al., 1995) (Bower, et al., 1997), South Australia (Chan, et al., 2001), and a range of American settings. (Chacko, et al., 2003, Robbins, et al., 2005) Therefore, this figure was used in the analysis.

Of the 15% of pregnant women who can be expected to take up supplementation, the next step is to identify the effect on UIC of this increased uptake. As noted in section 4, the published evidence is also relatively stable. Of those reporting UIC, Pedersen identifies an increase of 45 µg/l (Pre-Intervention: 55 µg/l, Post-Intervention 100 µg/l) and Nohr identifies an increase of between 53 and 55 µg/l, depending on the supplementation used (Pedersen, et al., 1993) (Nohr, et al., 2000). Therefore, we assumed that the 15% who take up supplementation increase in UIC by 50 µg/l. The effect in the bread-eating population of using this in parallel with mandatory fortification is shown in Table 37, in those who do not eat bread in Table 38, and summed in Table 39.

Table 37: The effect of using supplementation in parallel with mandatory fortification on the at-risk population of pregnant women (bread eating)

	Australia			New Zealand		
UIC(µg/l)	Status Quo	Mandatory	Mandatory & Supplement	Status Quo	Mandatory	Mandatory& Supplement
<50	1,178	505	429	2,780	593	504
50-150	167,066	121,977	110,646	34,245	23,127	21,159

Table 38: The effect of using supplementation in parallel with mandatory fortification on the at-risk population of pregnant women (not bread eating)

	Australia			New Zealand		
UIC(µg/l)	Status Quo	Mandatory	Mandatory & Supplement	Status Quo	Mandatory	Mandatory& Supplement
<50	161	161	137	415	415	353
50-150	22,782	22,782	21,972	5,117	5,117	5,094

Table 39: The effect of using supplementation in parallel with mandatory fortification on the at-risk population of pregnant women (total)

	Australia			New Zealand		
UIC(µg/l)	Status Quo	Mandatory	Mandatory & Supplement	Status Quo	Mandatory	Mandatory& Supplement
<50	1,339	666	566	3,195	1,008	857
50-150	189,848	144,759	132,618	39,362	28,244	26,253

This table should be interpreted as showing (for example) that, in New Zealand, the number of pregnant women with an annual average UIC of below 50 µg/l is 3,195 at present, would fall to 1,008 if mandatory fortification of salt in bread was introduced, and would fall to 857 if pregnant women were targeted with education and supplementation.

Our methods for estimating the cost of this program are described in detail in Section 5. We assumed that only 15% of pregnant women use supplements and they received them for an average of 18 months. This gave a total cost over ten years of supplementation and education of $74,566,751 in Australia and $16,400,814 in New Zealand (both local currencies). Relative to mandatory fortification alone, this reduced the population of women with a UIC below 50 (150) µg/l by 100 (12,241) in Australia, and by 151 (2,042) in New Zealand. The cost-effectiveness ratios are presented in Table 40.

Table 40: Cost-effectiveness ratios for adding supplementation and education for pregnant women to mandatory fortification

		Australia	New Zealand
	Cost (10 years) (local$000) (A)	74,567	16,401
Outcome	Reduction in people below 50 µg/l (B)	100	151
	Total reduction of those below 150µg/l (C)	12,241	2,042
	Cost per person reduction below 50 µg/l (rounded to nearest $100) (A/B)	745,700	108,600
	Cost per person reduction below 150 µg/l(rounded to nearest $100) (A/C)	6,100	8,000

The first issue to note with these ratios is that they are not comparable to those identified in Table 35, since the outcome is different. In the general population table, we are considering the cost of reducing the population level of low iodine by one unit. Here, we are considering the cost of reducing the number of pregnant women with low iodine by one. This is likely to be a more important outcome due to the importance of iodine in the neurological development of the infant. However, having noted this, the cost-effectiveness ratios seem high. This may be a consequence of uncertainty surrounding the cost of a mass supplementation program. However, it is also largely driven by the fact that mandatory fortification prevents a significant proportion of the expected deficiency under status quo, so the population likely to benefit from further supplementation is small.

8 Discussion

As part of proposal P230, Food Standards Australia New Zealand (FSANZ) are currently preparing a proposal for the mandatory fortification of bread-making salt with iodine. The motivation for FSANZ proposal P230, is the re-emergence of iodine deficiency in Australia and New Zealand. In the context of the preparation of this proposal, DOHA commissioned CHERE, University of Technology, Sydney, to perform a cost effectiveness analysis of strategies that are aimed at reducing the prevalence of iodine deficiency in Australia and New Zealand (including but not limited to the mandatory iodine fortification of bread-making salt).

We initially attempted to calculate the current burden of disease associated with iodine deficiency in Australia and New Zealand. However, there is limited evidence of specific IDDs in either country, and whether these are attributable to iodine insufficiency is debatable. On the other hand the link between iodine deficiency and specific conditions is tenuous, especially in populations which are only mildly iodine deficient. Far more evidence is available in developing countries, which often have populations with severe iodine deficiency. However, the comparability of these populations to those in Australia and New Zealand is limited. 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

The cost-effectiveness analysis involved two major components. Firstly, we looked at population-level interventions. These were the mandatory and voluntary fortification of bread, and the use of an educational program. The second component focused on pregnant women as they are of particular significance due to their iodine status playing a significant role in the neurological development of their unborn child.

We modelled the distribution of urine iodine concentration (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 mean, 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 decrease in individuals with annual average iodine levels below 50 µg/l, alongside a large reduction in the number of people with a level below 100 µg/l. For estimates of the reduction in the iodine deficient population, see Table 32 and Table 33. This result is relatively robust to changing the effect of fortification by 25% (Figure 1).

We also estimate the cost per person (mandatory and voluntary) removed from cohorts with levels below 50 µg/l and 100 µg/l over a ten year period. For mandatory fortification, our estimates suggest that there will be approximately

128,000 and 7,320,000 fewer people with average annual iodine levels of <50 µg/l and <100 µg/l respectively in Australia. In New Zealand the corresponding figures are 224,000 and 2,567,000 for the <50 µg/l and <100 µg/l cohorts, respectively. The relatively greater impact in New Zealand reflects the higher severity of iodine deficiency at baseline. Finally, the cost-effectiveness ratios, which estimate the costs of reducing the population below 50 µg/l UIC (100 µg/l) by one for a ten-year period are $24.32 ($0.42) for Australia and $4.28 ($0.37) for New Zealand.

For voluntary fortification, our estimates suggest that there will be 102,200 and 5,834,000 fewer person with an annual average UIC of <50 µg/l and <100 µg/l respectively in Australia. In New Zealand the corresponding figures are 179,000 and 1,874,300 for the <50 µg/l and <100 µg/l cohorts, respectively. Finally, the cost-effectiveness ratios, which estimate the costs of reducing the population below 50 µg/l UIC (100 µg/l) for a ten-year period are $25.82 ($0.45) for Australia and $4.99 ($0.48) for New Zealand.

It should be noted that, in comparing voluntary fortification with mandatory fortification, economic evaluation would conventionally exclude voluntary fortification since it is subject to extended dominance. Mandatory fortification has a greater effect in reducing iodine deficiency, and reduces the population at a lower cost per person (despite having a higher overall cost).

Looking at the targeted strategies for pregnant women, the cost of reducing the at-risk population by one person was, as expected, higher than for the population. This was because the population of pregnant women below 50 and 150 µg/l was small, especially if mandatory fortification of salt in bread in undertaken in parallel. The cost of reducing the Australian (New Zealander) population below 50 µg/l by one unit was $745,700 ($108,600). Regarding the WHO criterion for pregnant women of 150 µg/l, the respective figures for Australia and New Zealand were $6,100 and $8,000.

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). Based on the evidence collated in this report, both Australian and New Zealand populations demonstrated mild deficiency, since the median UIC 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.

Similarly, after voluntary fortification, we estimate that both the Australian and the New Zealand population will be iodine sufficient. The difference between voluntary and mandatory fortification is that, under mandatory fortification, the WHO criteria are exceeded by a larger margin.

Table 41: Iodine status as defined by the WHO criteria

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	✓	✓
Voluntary 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, additional supplementation may be required.

Limitation of using urinary iodine concentration

The motivation for using UIC as a measure of 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 very 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 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. The median urinary iodine concentration is the best indicator, at the population level, to assess the iodine nutrition of pregnant and lactating women, and of young children less than 2 years.

For the purpose of this investigation, we assumed that the variability around single urinary iodine concentration observations across individuals was 2.4 times larger than that of average annual levels (Andersson, et al., 2005).

Costs

The costs used in this report 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. A broader societal perspective may be preferred. 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.

By comparing voluntary and mandatory fortification programs, we demonstrated that the reduction in bread fortified under a voluntary scheme does not automatically translate into a proportional reduction in costs. This is intuitive, since some costs will be variable and some will be fixed under either option. In cost terms, the relative cost of a voluntary fortification process adds additional uncertainty. 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 recent approved mandatory fortification of bread with folic acid, (piggyback saving). We have highlighted significant synergies and cost savings between programs. Therefore, the cost of both voluntary and mandatory options may be much less than originally estimated.

We could only estimate the cost of a public health campaign from the costs provided from other, similar programs. This was because no public health campaign has been undertaken for iodine deficiency. However, given the convergence of costs between different public health campaigns we feel our estimate is likely to be realistic.

Costs of iodine supplementation appear high. This is primarily because of the cost of iodine-containing tablets (approximately A$20 per month). It is worth noting that if iodine supplementation became recommended, such as with folic acid, the cost of iodine supplements would likely fall.

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 1.219 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.

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. It could also be postulated that the cohort most likely to purchase organic bread is the group least likely to be iodine deficient.

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, it can be assumed reasonably that some of the benefit bestowed by the lactating mother will be passed onto the baby (presuming the baby receives breast milk).

8.1 Mandatory versus voluntary fortification of bread with iodine

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:
>
> - 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,
> - Iodine requirements can not be realistically replenished by normal dietary practices,
> - The intervention does not raise the iodine intake to levels that are judged unsafe, and
> - 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.

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

- 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.

- 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.

- 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.

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, if supplements are required in early pregnancy, the target population can be missed in the event of an unplanned pregnancy[22], but these women will still benefit during late 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. 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. We also demonstrated from a cost-effectiveness perspective, that a public health campaign would not be as effective as mandatory fortification.

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.

9 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 either mandatory or voluntary iodine fortification of bread, we estimate that Australia and New Zealand will become iodine adequate.

Assessed in terms of cost-effectiveness ratios, the cost of moving individuals from the cohort with median levels of iodine 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/DOHA decides to adopt mandatory/voluntary fortification of bread with iodine, the evidence

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

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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11 Appendix

Table 42: Generating Gamma Distributions

	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

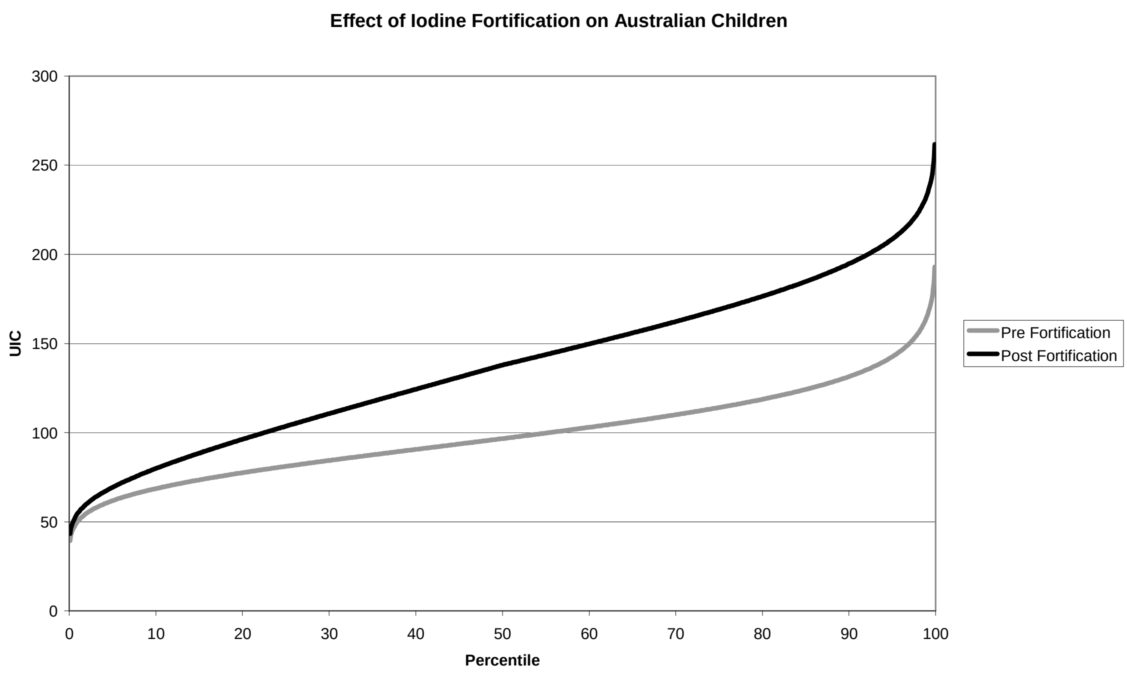

Figure 4: UIC Distribution in New Zealand Children

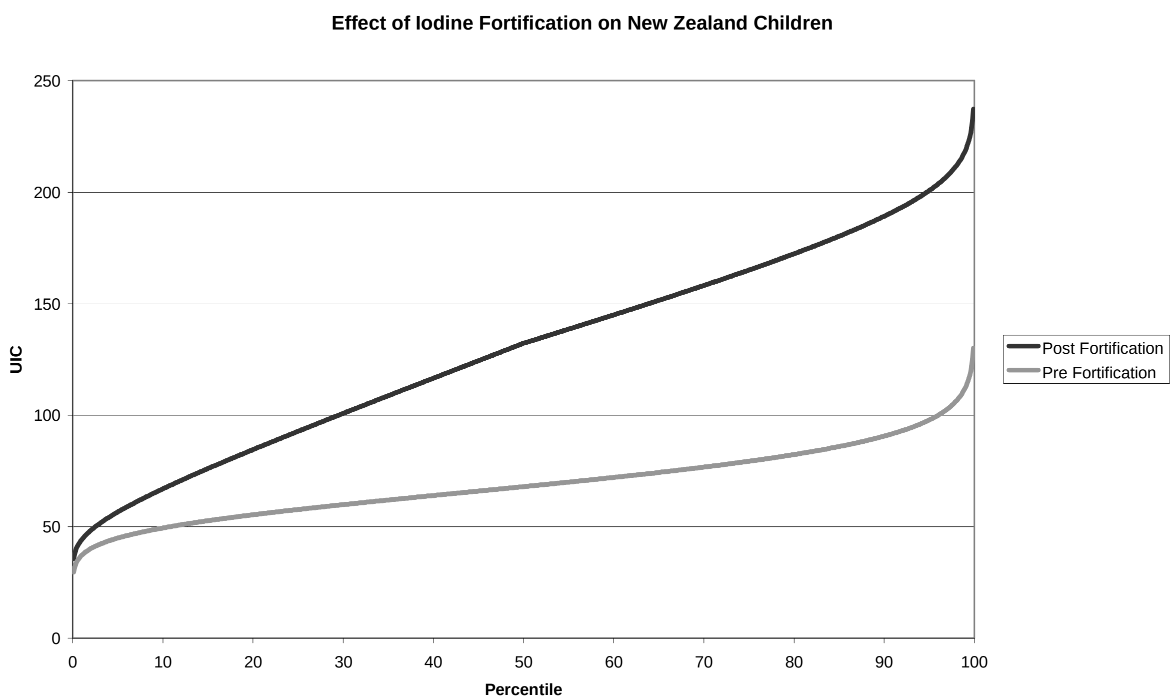

Figure 5: UIC Distribution in Australian Adults

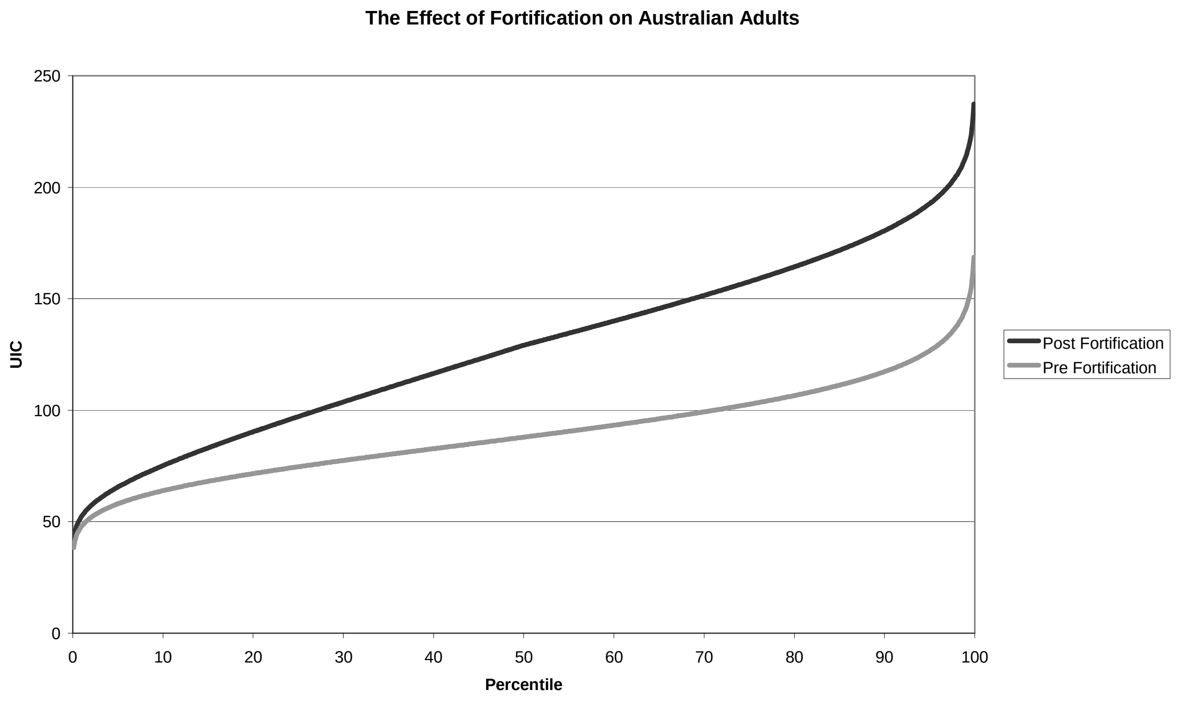

Figure 6: UIC Distribution in New Zealand Adults

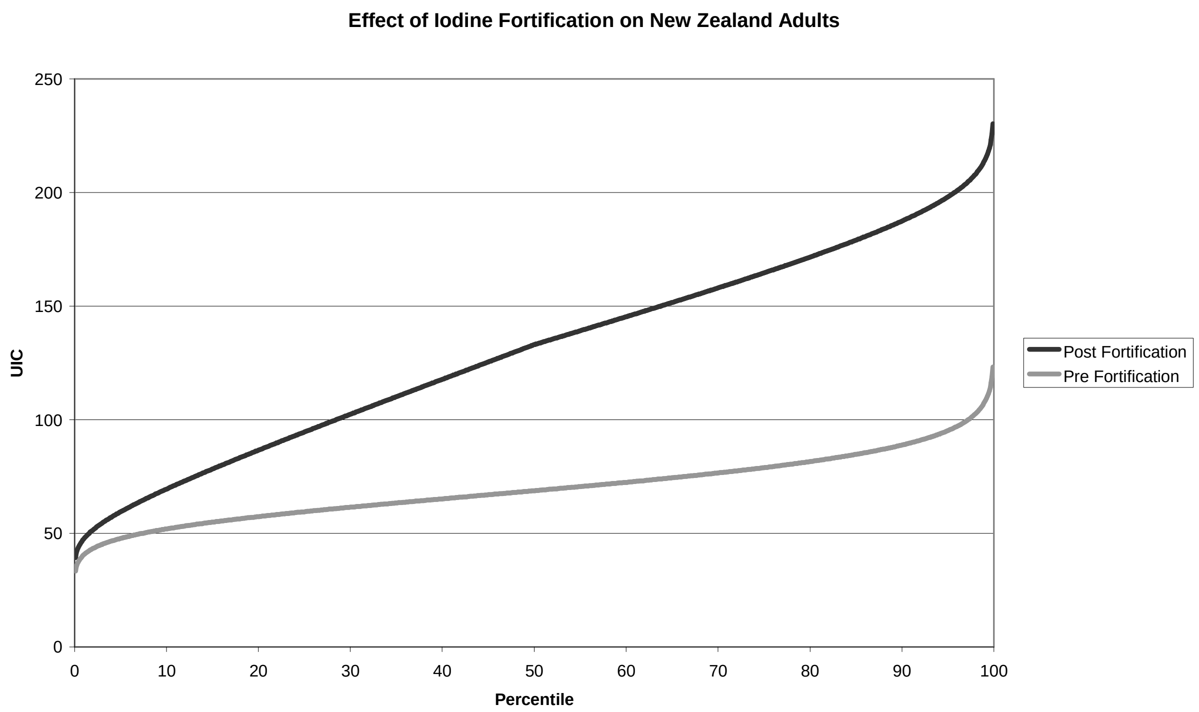

Figure 7: UIC Distribution in Australian Pregnant Women