The prevalence and severity of iodine deficiency in Australia

Prepared for the
Australian Population Health
Development Principal Committee
of the
Australian Health Ministers
Advisory Committee

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This report has been compiled by a working group of representatives of the Australian Population Health Development Principal Committee (APHDPC) coordinated by the Department of Health and Human Services, Tasmania with input from NSW Health, Ministry of Health NZ, Vic Health, Queensland Health and the Department of Health and Ageing. The working group has expertise in public health, nutrition, and epidemiology. The report has also been reviewed by a group of external experts.

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Abbreviations

ADHD	Attention-Deficit Hyperactivity Disorder
AHMAC	Australian Health Ministers Advisory Council
AHMC	Australian Health Ministers Conference
ANZFRMC	Australia and New Zealand Food Regulation Ministerial Council
APHDPC	Australian Population Health Development Principal Committee
CHERE	Centre for Health Economic Research and Evaluation
DoHA	Department of Health and Ageing
FRSC	Food Regulation Standing Committee
FSANZ	Food Standards Australia New Zealand
ICCIDD	International Council for the Control of Iodine Deficiency Disorders
IDD	Iodine deficiency disorders
IIH	Iodine induced hypothyroidism
IQ	Intelligence Quotient
MUIC	Median urinary iodine/iodide concentration (note: iodine and iodide used inter-changeably)
NHANES	National Health and Nutrition Examination Survey
NINS	National Iodine Nutrition Survey
Tg	Thyroglobulin
UIC	Urinary iodine/iodide concentration
UIE	Urinary iodine/iodide Excretion
WHO	World Health Organization

Executive summary

Purpose of this paper

Food Standards Australia New Zealand (FSANZ) released the initial assessment report for *Proposal P230 Consideration of Mandatory Fortification* with Iodine in December 2004.

The Australia and New Zealand Food Regulation Ministerial Council's (ANZFRMC) policy guideline *Fortification of Food with Vitamins and Minerals* stipulates that: *mandatory addition of vitamins and minerals to food should be required only in response to demonstrated significant population health need, taking into account both the severity and the prevalence of the health problem to be addressed.*

The Australian Health Ministers Conference agreed in July 2007 that the prevalence and severity of iodine deficiency in New Zealand is significant enough to warrant mandatory fortification of food with iodine. Australian Health Ministers are awaiting advice on the prevalence and severity of iodine deficiency in Australia in order to make a determination on intervention in Australia.

This report reviews the current prevalence of iodine deficiency in Australia, the health consequences of mild iodine deficiency, and the degree of iodine deficiency that has prompted intervention in other developed countries. A summary of the prevalence and severity of iodine deficiency in New Zealand is attached in Appendix 1.

Prevalence of iodine deficiency in Australia

Evidence from a range of studies of the prevalence of iodine deficiency in Australia indicates that:

- studies of median urinary iodine concentration (MUIC) in school-aged children suggest that according to international criteria, Victoria, New South Wales and Tasmania (prior to implementation of the Tasmanian interim supplementation program) are areas of mild iodine deficiency (1). As south eastern Australia is the most densely populated part of the country this means a large proportion of the Australian population is exposed to the risks of iodine deficiency
- Western Australia and Queensland do not appear to be iodine deficient, while iodine status in South Australia is borderline
- studies of urinary iodine concentration in pregnant women in south eastern Australia consistently suggest iodine intake is inadequate and therefore places unborn babies at risk of iodine deficiency
- there are no studies of iodine status of pregnant women in Western Australia or Queensland. However, in extrapolating the results from school-aged children to pregnant women it could be reasonably inferred that the iodine intake of pregnant women in these states would also be inadequate
- the magnitude of increase in urinary iodine concentration required to correct iodine deficiency in south eastern Australia (around 30μg/L) would not result in other states such as Western Australia and Queensland exceeding the optimal range for iodine status.

Consequences of mild iodine deficiency

The consequence of iodine deficiency depends on the age and duration of exposure, and, the degree of deficiency, with foetal development and early infancy being particularly critical times (2).

The degree of iodine deficiency that results in significant health effects is not easy to define as effects can be subtle at the individual level and are often sub-clinical. In addition, studies are challenged by ethical constraints and the difficulty of controlling for confounding variables.

A review of the evidence of the health consequences of *mild* iodine deficiency reveals:

- there is a limited number of published studies investigating the health consequences of *mild* iodine deficiency
- there is reasonable evidence of an association between *mild* iodine deficiency and sub-optimal neurological development, most notably reduced IQ
- of the studies that have attempted to investigate the effects of *mild* iodine deficiency, many have limitations and some have methodological flaws. Hence, the current literature does not provide unequivocal evidence for significant health effects for populations with urinary iodine in the upper range of *mild* iodine deficiency
- considering the evidence from studies of moderate and severe iodine deficiency and the association with neurological development, there is a suggestion of a dose-response relationship. Specifically, with increasing iodine deficiency there is an increasing impact on neurological development
- there is sufficient evidence to suggest that the known association between neurological outcomes and moderate and severe iodine deficiency is likely to extend to *mild* iodine deficiency
- in constructing a reasonable health-based standard using the precautionary approach, it is clear that urinary iodine levels below 100µg/L, which are in the *mild iodine deficiency* range, warrant intervention.

Interventions to address iodine deficiency in other developed countries

A review of international experience with programs to correct iodine deficiency in developed countries has shown that:

- iodine deficiency has been considered serious enough to warrant intervention (or additional intervention) at levels similar to that currently being experienced in south eastern Australia. Specific examples include Switzerland, Germany and New Zealand
- consistent with World Health Organization recommendations, iodised salt has been used as the predominant source of additional iodine
- where fortification programs have been inadequate, increased legislative measures have been adopted. Examples include increasing the concentration of iodisation of salt or increasing the range of foods to which iodised salt is added
- iodine status can vary over time due to changes in the food environment, independent of food choice. Hence, regular monitoring of iodine status is an essential part of any program to ensure optimal iodine status of a population.

Introduction

Globally, iodine deficiency is considered the single most important cause of preventable brain damage and mental retardation (3). Iodine deficiency has profound effects on intellectual development with the most extreme being cretinism occurring in the context of severe deficiency (1).

Iodine deficiency is not a new phenomenon in Australia or New Zealand. Efforts to address iodine deficiency in both countries were implemented during the early and mid 1900s (4). During the later part of the twentieth century, additional though unplanned, protection from iodine deficiency was provided from residues in milk resulting from the widespread use of iodine-containing sanitising agents in the dairy industry in Australia and New Zealand.

The Australian Health Ministers Conference agreed in July 2007 that *if prevalence and severity [of iodine deficiency] were considered sufficient to warrant intervention then mandatory fortification is the most effective strategy to address iodine deficiencies.*

It was also noted at the Ministers meeting that *the prevalence and severity of iodine deficiency in New Zealand is significant and mandatory fortification with iodine is considered the most effective strategy to address it.*

This paper has been compiled to provide information to the members of the Australian Population Health Development Principal Committee (APHDPC) to assist them in providing advice to the Australian Health Ministers Advisory Council (AHMAC) and the Australian Health Ministers Conference (AHMC) on the prevalence and severity of iodine deficiency in Australia.

Specifically, the purpose of this paper is to:

- describe the prevalence of iodine deficiency in the Australian population, including a focus on pregnant women
- review the evidence of the consequences of mild iodine deficiency on human health
- determine the levels of iodine deficiency that have prompted intervention in other developed countries.

A brief summary of the prevalence and severity of iodine deficiency in New Zealand is included in Appendix 1.

Further background information on iodine nutrition is outlined in Appendix 2 including a description of the role and function of iodine; iodine requirements in Australia and New Zealand; food sources of iodine; iodine deficiency disorders; and, methods of assessment of iodine status.

The purpose of this paper is *NOT* to describe the relative effectiveness or safety of intervention options to address iodine deficiency in Australia. These issues are being dealt with through the consideration of mandatory fortification of food with iodine *Proposal 230* through the food standards setting process and through a review being conducted by the Centre for Health Economics Research and Evaluation (CHERE) on the cost effectiveness of alternative strategies to redress iodine deficiency in Australia.

Background

At the August 2007 meeting of the APHDPC it was agreed that Tasmania, New Zealand and other interested jurisdictions would work together to review all available data and research on the prevalence of iodine deficiency in Australia and provide supplementary advice relating to the clinical consequences of *mild* iodine deficiency for the consideration of the APHDPC.

This review aims to assist APHDPC in providing advice to AHMAC and AHMC to enable Health Ministers to determine if there is a significant population health need associated with iodine status, as required by the ANZFRMC's policy guideline. The progress to date associated with the consideration of mandatory fortification with iodine is summarised in Figure 1.

Figure 1: Progress towards consideration of mandatory fortification with iodine.

July 2000	Tasmania raises concern with ANZFA (now FSANZ) following evidence of iodine deficiency re-emerging in Tasmania & preliminary reports of iodine deficiency re-emerging in Vic, NSW & NZ
↓	
May 2004	ANZFRMC adopts Policy Guideline on the Fortification of Food with Vitamins and Minerals & Requests FSANZ give mandatory fortification with iodine priority consideration
↓	
Dec 2004	FSANZ releases Initial Assessment Report: *Proposal P230 Iodine Fortification* for public consultation
↓	
Feb 2005	FRSC requests advice from AHMAC regarding the effectiveness of mandatory fortification of food with iodine as a strategy to reduce iodine deficiency.
↓	
July 2005	AHMAC & AHMC endorse mandatory fortification as an effective public health strategy, subject to clinical safety and cost effectiveness
↓	
June 2007	AHMAC agree to finalise advice to AHMC on effectiveness of mandatory fortification of food with iodine, requesting APHDPC provide technical advice for the July 2007 AHMC meeting
↓	
June 2007	APHDPC Executive agreed for DoHA to commission a cost effectiveness analysis of mandatory fortification and voluntary fortification to assist AHMAC & AHMC in their consideration. CHERE contracted to undertake work by DoHA
↓	
July 2007	APHDPC Executive considered preliminary information on cost effectiveness of a range of public health strategies for decreasing the incidence of iodine deficiency and agreed to forward this information to AHMAC & AHMC
↓	
July 2007	AHMAC & AHMC request APHDPC provide advice on prevalence and severity of iodine deficiency. AHMC agree that if prevalence and severity are sufficient to warrant intervention then mandatory fortification is the most effective strategy

Prevalence of Iodine Deficiency in Australia

Iodine status is considered optimal if population median urinary iodine concentration (MUIC) falls between 100 and 200μg/L and not considered excessive until MUIC exceeds 300μg/L. Mild iodine deficiency is defined as MUIC between 50 and 100μg/L (1). Further information on criteria for assessing iodine status is included in Appendix 2.

Iodine status of Australians

In 2004 a National Iodine Nutrition Survey (NINS) was conducted across five of the eight states and territories in Australia (New South Wales, South Australia, Victoria, Queensland and Western Australia (5). Urinary iodine concentration was determined from 1709 children with samples sizes from each state ranging from 294-427. In Queensland and Western Australia the MUIC levels fell within the optimal range of 100-199ug/L; South Australia was found to have borderline optimal iodine status with a MUIC of 101ug/L and New South Wales and Victoria were both in the mild deficiency range with MUICs below 100ug/L (Table 1).

Whilst the MUIC for the total sample was 104μg/L, suggesting borderline-optimal iodine status, the total sample was not nationally representative. Specifically, samples were not collected from all states and territories (Tasmania, ACT and NT were not included) and more importantly, the data were not population weighted. If the data are weighted according to population, the sample MUIC falls within the mild deficiency range, albeit borderline (personal communication Eastman, 2007).

Table 1: Iodine status from the National Iodine Nutrition Survey 2004 (5):

State	*Sample size*	*MUIC (μg/L)*	*Population iodine status*
New South Wales	427	89.0	mild deficiency
Victoria	348	73.5	mild deficiency
South Australia	317	101.0	borderline optimal
Western Australia	323	142.5	optimal
Queensland	294	136.5	optimal
Total sample (un-weighted)	***1709***	***104.0***	***borderline optimal***
Total sample (weighted)	***1709***	***98.0****	***borderline deficiency***

**Personal communication, Eastman, 2007; mild deficiency = MUIC 50-100μg/L; optimal = MUIC 100-200μg/L;*

Other recent studies in Victoria, New South Wales and Tasmania (prior to the Tasmanian interim iodine supplementation program) have shown levels of deficiency consistent with those found in the NINS. These are detailed in Table 2.

Table 2: Studies of iodine status of Australians 1998-2007

Year	Location	Study design	Sample size	MUIC		Population iodine status	Reference
				(μg/L)	%<50μg/L		
2001	Melbourne	Cross sectional survey of School children aged 5-12	607	70	27	mild deficiency	(6)
2000	New South Wales	Cross sectional survey School children aged 5-13	301	82	14	mild deficiency	(7)
1998-2000	Tasmania*	Repeated cross sectional survey School children aged 4-14	241 (1998)	75	13	mild deficiency	(8)
			170 (2000)	76	21	mild deficiency	
1998-1999	New South Wales	Cross sectional survey School children aged 6-13	94	84	14	mild deficiency	(9)
2003-2005	Tasmania**	Cross sectional survey with one-stage cluster sampling of school children age 8-11	347 (2003)	105	10	borderline optimal	(10)
			430 (2004)	109	10	borderline optimal	
			401(2005)	105	10	borderline optimal	

** pre-implementation of the 2001 Tasmanian (interim) iodine supplementation program*
***post-implementation of the 2001 Tasmanian (interim) iodine supplementation program*

To increase the iodine status of south eastern Australia to an optimal level would require an increase in MUIC of about 30μg/L. Such an increase would not result in Western Australia or Queensland exceeding the optimal range.

Iodine status of pregnant women in Australia

Iodine requirements increase substantially during pregnancy and lactation making pregnant and lactating women and their babies high risk groups for iodine deficiency. In 2005 a World Health Organization (WHO) Technical Consultant group made recommendations for the interpretation of MUIC in pregnancy with levels considered to be inadequate <150μg/L; adequate 150 -249μg/L; more than adequate 250-499μg/L; and, excessive >500μg/L. These recommendations have now been accepted by the Public Health Committee of the American Thyroid Association and the International Council for the Control of Iodine Deficiency Disorders (11, 12)

Published studies of the iodine status of pregnant women in Australia over the last 10 years are limited to south eastern Australia. All the studies of iodine status of pregnant women in Australia consistently suggest iodine intake is inadequate. Median urinary iodine concentration levels in studies of pregnant women in Australia range from 47-104μg/L. These levels are well below the MUIC level of 150-249μg/L which is considered adequate for pregnant women. In addition, between 19 and 58 percent of these women had urinary iodine concentration levels below 50ug/L (Table 3).

Table 3: Iodine Status of pregnant women in Australia 1998-2007

Year	Location	Study design	Sample size	MUIC		Iodine status	Reference
				(μg/L)	%<50 μg/L		
2003	Sydney	Cross sectional survey	50 (postpartum women)	47	58	*inadequate*	(13)
2004	NSW	Cross sectional survey	815	85	17	*inadequate*	(14)
1998-1999	Sydney	Cross sectional survey	101	88	21	*inadequate*	(9)
1998-1999	Sydney	Cross sectional survey	81	104	20	*inadequate*	(15)
1998-2002	Melbourne	Cross sectional survey	227 (Caucasian)	52	48	*inadequate*	(16)
			263 (Vietnamese)	58	38	*inadequate*	
			262 Indian/Sri Lankan	61	41	*inadequate*	
2000-2006	Tasmania	Cross sectional survey	285 (antenatal clinic – pre-intervention, 2000)*	76	31	*inadequate*	(17)
			288 (primary health care setting-post intervention 2003-6)*	81	19	*inadequate*	
			229 (antenatal setting post – intervention, 2006)*	86	19	*inadequate*	

** intervention = voluntary fortification using iodised salt in bread.*

It is noteworthy that the MUIC in pregnant women is similar, if not lower, than the corresponding MUIC measured in school-age children in the same state. There is currently no published data on the urinary iodine concentration of pregnant women from Western Australia and Queensland, where iodine status of the general population is considered optimal. However, it can be inferred that pregnant women in Western Australia and Queensland would have MUIC either similar to, or lower than that of the general population (MUIC of 142.5 and 136.5ug/L respectively). These levels fall below the level considered adequate for pregnancy.

Changing iodine status in Australia

In the early 1990s sporadic surveys of iodine status indicated parts of Australia were iodine replete with population MUIC levels above 200ug/L (18). Whilst the reason for the current decline in iodine status is not fully understood, the most plausible explanations relate to changes in the food supply including:

- reduced use of iodine containing sanitising agents by the dairy industry, leading to lower concentrations of iodine in milk
- decreased consumption of iodised discretionary (household) salt, with a shift towards increased consumption of foods processed outside the home. Processed foods use commercial salt which is generally not iodised. Research shows that only 0.5 percent of commercial salt is iodised (19)

- cessation of past food fortification or supplementation initiatives to correct iodine deficiency.

Consequences of mild iodine deficiency

To inform this paper an epidemiological review of the evidence for health effects of *mild* iodine deficiency was undertaken. The review is restricted to published papers that are concerned with subjects whose urinary iodine concentration falls into the range 50-99μg/L.

Whilst there are a plethora of papers describing the health consequences of severe iodine deficiency (MUIC<20 μg/L), and some addressing moderate iodine deficiency (MUIC 20-49μg/L), there is a limited number of peer-reviewed papers assessing the health consequences of mild iodine deficiency defined as MUIC of between 50 and 99μg/L.

The literature linking severe (and to a lesser extent) moderate iodine deficiency with a range of adverse health outcomes is well established. The most concerning health consequence is the effect on intellectual development. Two significant meta-analyses have summarised the international literature pointing to the clear association between cognitive development and iodine deficiency (20, 21). The first of these is a review published in 2005 of all the Chinese studies of iodine and children. This meta-analysis demonstrates that the intelligence damage to children exposed to severe iodine deficiency is profound with a reduction in IQ of 12.45 IQ points. This meta-analysis also demonstrates that iodine supplementation can prevent the degree of damage. The second meta-analysis by Bleichrodt and Born published in 1994 found that the mean scores for the iodine deficient populations were 13.5 IQ points below that of non-iodine deficient populations. It should be stressed that the papers included in these meta-analyses all described populations with moderate to severe iodine deficiency.

This review involved identifying relevant studies by:

- a literature search of:
  i. PubMed, including the keywords iodine, deficiency, mild, moderate, human
  ii. mBase
  iii. the Cochrane database
- identifying relevant articles:
  i. exploring related articles,
  ii. reviewing references of identified papers
  iii. contacting peers for relevant articles

Table 4 summarises the studies considered relevant to the question of the health consequences of *mild* iodine deficiency. The main findings from this review include:

- there is a limited number of published studies investigating the health consequences of *mild* iodine deficiency
- there is reasonable evidence of an association between *mild* iodine deficiency and sub-optimal neurological development, most notably reduced IQ
- of those studies that have attempted to investigate the effects of *mild* iodine deficiency, many have limitations and some have methodological flaws. Hence, the current literature does not provide unequivocal evidence for significant health effects for populations with urinary iodine in the upper range of *mild* iodine deficiency
- considering the evidence from studies of moderate and severe iodine deficiency and the association with neurological development, there is a suggestion of a dose-response relationship. Specifically, with increasing urinary iodine deficiency there is an increasing impact on neurological development

- there is sufficient evidence to suggest that the known association between neurological outcomes and moderate and severe iodine deficiency is likely to extend to *mild* iodine deficiency.

There are two risk assessment and management approaches that should be applied in this situation.

First, as there is some scientific uncertainty, risk assessment and risk management of mild iodine deficiency should include the use of the *precautionary principle*. The precautionary principle is a risk management tool to be used where there is:

- scientific uncertainty
- need for action in the case of a potentially serious risk without awaiting the results of scientific research (22).

In this case, there is a substantial body of scientific research, albeit with some methodological limitations, concerning moderate and severe iodine deficiency. Both moderate and severe iodine deficiency are associated with significant public health risks including sub-optimal neurological development. However, for mild iodine deficiency there is more uncertainty as to the risks from a public health perspective.

Second, a No Observed Adverse Effect Level (NOAEL) can be derived, and a health-based standard set, which would include a margin of safety (23). The margin of safety is arbitrary although levels from 33-to 50 percent of the value of an observable effect have been used in practice. As observable effects are unequivocal for moderate iodine deficiency, and the evidence from the papers in Table 4 suggests an observable effect somewhere in the mild iodine deficiency range, a reasonable approach would be to set that point at the mid-mild iodine deficiency range. Therefore, a health-based standard for urinary iodine, including a safety factor would be somewhere in the range of 100 to 115 µg/L – ie 33-50 percent above 75 µg/L. This would represent the minimum urinary iodine concentration to achieve to ensure adequate iodine status at the population level.

On the basis of constructing a reasonable health-based standard using the precautionary approach, the conclusion is clear that urinary iodine levels below 100µg/L in the *mild iodine deficiency* range warrant intervention, providing there are no significant adverse health consequences from intervention.

Table 4. Studies investigating the association between iodine deficiency and health impacts

Subject of investigation (sample)	Key findings	Comments	Ref
Intelligence quotient (IQ) and iodine intake. (1221 school children in SE Spain)	IQ of children in a developed country can be influenced by iodine intake. IQ significantly higher in those with urinary iodine >100μg/L.	**Assesses mild iodine deficiency (UIC 50-99μg/L).** Prevalence study. Sampling design appears to be reasonable, limited consideration of potential confounders.	(24)
Auditory threshold is related to iodine intake and thyroid function. (150 children in Malaga, Spain)	In children with palpable goitre, there was an inverse association between auditory threshold and urinary iodine level.	**Assesses mild (UIC 50-99μg/L) to moderate (UIC 20-49μg/L) iodine deficiency.** Association influenced predominantly by those with urinary iodine levels <50μg/L – ie moderate deficiency. No clear association for mild iodine deficiency.	(25)
Mild iodine deficiency during foetal/neonatal life and neuropsychological impairment. (1132 school children across three areas of Tuscany, Italy)	Mild iodine deficiency may impair rate of motor response to perceptive stimuli.	**Assesses mild iodine deficiency (UIC 50-99μg/L).** Cross sectional study comparing subjects in different regions. No measurement of or adjustment for potential confounders.	(26) .
Attention deficit and hyperactivity disorders (ADHD) in the offspring of mothers exposed to mild-moderate iodine deficiency. (16 children born to women from an iodine deficient area compared to 11 from an iodine sufficient area)	ADHD associated with being born to mothers living in iodine deficient areas.	**Assesses mild (UIC 50-99μg/L) to moderate (UIC 20-49μg/L) iodine deficiency.** Ecological study. Small sample size. Not statistically significant.	(27)
Sub-clinical prenatal iodine deficiency negatively affects infant development. (284 infants from endemic region of Northern China)	Sub-clinical prenatal iodine deficiency is associated with delayed mental development (information processing skills and cognitive development).	**Assesses moderate (TSH>10mu/L) iodine deficiency.** Historical cohort design, no data on current iodine intake. Adjusted for maternal education and place of residence. Subject to potential confounding and response bias (participation rate not reported).	(28)
Randomised controlled trial of iodine supplementation and cognition. (310 children from rural SE Albania)	Information processing, fine motor skills and visual problem solving are improved by iodine repletion in moderately iodine-deficient children.	**Assesses moderate iodine deficiency (UIC 20-49μg/L).** Double blind placebo-controlled RCT, but details of randomisation process not clear (was randomisation done by individual or by school?). Randomisation questionable.	(29)

Table 4. Studies investigating the association between iodine deficiency and health impacts (cont).

Subject of investigation	Key findings	Comments	Ref
Improved iodine status associated with improved mental and psychomotor performance. (196 school children from the North of the Republic of Benin in Western Africa).	An improvement in iodine status, rather than iodine status itself, determined mental and psychomotor performance in children.	**Assesses moderate (UIC 20-49μg/L) to severe (<20 μg/L) iodine deficiency.** Originally RCT, but not analysed by intention to treat, only by change in urinary iodine status. Questionable methodologically.	(30)
Iodine deficiency and hearing threshold. (197 school children from the North of the Republic of Benin in Western Africa).	Children with higher serum thyroglobulin concentrations had significantly higher hearing thresholds in high frequency range than children with lower serum thyroglobulin concentrations.	**Assesses moderate (UIC 20-49μg/L) to severe (UIC <20 μg/L) iodine deficiency.** Contaminated RCT. Baseline hearing tests not conducted so no change analysis possible. Association only with serum thyroglobulin concentration. Negative non-significant association with urinary iodine concentration. No adjustment for multiple comparisons.	(31)
Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. (25 216 pregnant women from Maine, USA)	IQ scores of children of women who are hypothyroid during pregnancy are 7 points lower than the children of matched control women.	**Assesses moderate to severe iodine deficiency: women with thyrotropin above 99.7th percentile during pregnancy.** Historical cohort study. No measurement of potential confounders.	(32)
Effect of iodine intake on thyroid diseases. (3018 residents of 3 areas of NE China).	More than adequate or excessive iodine intake may lead to hypothyroidism and autoimmune thyroiditis.	**Assesses mild iodine deficiency (UIC 50-99μg/L), more than adequate (UIC~240μg/L) and excessive (UIC~650μg/L) iodine intake.** Ecological study. Assesses both prevalence and incidence, does not measure potential confounders.	(33)
Review of Iodine supplementation to prevent IDD in children. (includes 22 papers - those considering mild iodine deficiency are included in this table.)	Indications of positive effects on physical and mental development were seen, although results were not always significant.	**Assesses moderate (20-49μg/L) to severe (<20 μg/L) iodine deficiency.**	(34)

Interventions to address iodine deficiency in other developed countries

Nutrient deficiencies are often associated with developing countries. However, iodine deficiency has been described as *unique among nutritional deficiencies as it can occur in populations whose food supply is adequate in all other respects* (35). Internationally, the importance of increasing iodine status of populations that are iodine deficiency is well recognised (1). A number of developed countries including the USA, Canada, Germany, Switzerland, Denmark and The Netherlands have introduced measures to address iodine deficiency at a population level. In the past both Australia and New Zealand have also adopted population measures to correct iodine deficiency. A summary of interventions implemented in these countries is included in Table 5.

Previous interventions to correct iodine deficiency in Australia

Iodine deficiency is not new in Australia or New Zealand. Endemic goitre due to iodine deficiency has been recorded in certain regions of Australia since the early 1900's. Areas affected include the Atherton Tablelands in Queensland, scattered areas throughout NSW and Victoria as well as Tasmania (36). In South Australia the only area with reported increased rates of goitre was the Adelaide Hills, whilst increased rates of goitre were not reported in Western Australia or the Northern Territory (37).

Interventions to address iodine deficiency in Australia have been instigated in the past with varying degrees of success. Efforts have been predominantly localised population-based strategies of iodine supplementation and food fortification. Key interventions in Australia have been:

- in the 1920s iodised household salt was introduced in Australia
- in 1947 the Australian government provided funding for iodine tablets as part of a goitre prevention program (38)
- in 1953 fortification of food with iodine was adopted in the ACT, and in 1966 in Tasmania, via the introduction of potassium iodate into bread improvers (4).

Fortification of bread with iodine was discontinued in Tasmania in 1976 due to unacceptably high rates of iodine-induced hyperthyroidism (IIH), particularly in those with longstanding iodine deficiency (4). Based on the experience in Tasmania, the ACT also discontinued fortification of bread with iodine in the 1980s.

The unexpected rates of IIH were caused by unplanned increases in the iodine content of milk from the residues of iodine containing sanitizing agents used by the dairy industry. From the 1960s a major source of iodine in the Australian food supply was unintentionally derived from milk (4, 39). In more recent times reliance on iodine containing sanitising agents has been reduced with some replaced by more effective non-iodine containing disinfectants and best practice standards have improved to minimise contamination irrespective of the type of sanitising agents used. These changes are likely to have resulted in reduced availability of iodine in the Australian food supply.

Interventions to correct iodine deficiency in other developed countries

Internationally a range of countries have implemented programs to correct iodine deficiency. These countries include the USA, Canada, Germany, Switzerland, Denmark and the Netherlands. Experience in these countries and past experience from Australia and New Zealand is summarised in Table 5.

These studies demonstrated:

- consistent with WHO recommendations, iodised salt has been used as the predominant source of additional iodine
- fortification programs shown to be ineffective or inadequate have resulted in increased legislative measures. These measures either increased the concentration of iodisation of salt or increased the range of foods to which iodised salt is added
- iodine status can vary over time due to changes in the food environment, independent of food choice. Hence, regular monitoring of iodine status is an essential part of any program to ensure optimal iodine status of a population.

Of particular interest is the level at which some countries have considered iodine deficiency serious enough to warrant intervention (or additional intervention). For example:

- the iodine status in New Zealand is only marginally worse than in south eastern Australia and there is agreement that this level of deficiency is serious enough to warrant mandatory fortification
- In 1997 Switzerland decided to increase the concentration of iodised salt from 15mg/kg to 20mg/kg when the population MUIC was 96μg/L (borderline deficiency) which is comparable with the population weighted results from the NINS in Australia
- In 1993 Germany removed the requirement for iodised salt used in manufacturing to be labelled separately in order to encourage more manufacturers to use iodised salt. This was in response to a MUIC of 95μg/L.

Table 5: Iodine interventions in developed countries

Country	*Year*	*Intervention*	*Iodine status*	*Comments*	*References*
USA	1924	Voluntary salt iodisation (50-60% of salt is iodised).	1924: High prevalence of goitre in certain areas of the US 1971-74 (NHANES 1) MUIC=320μg/L 1988-91(NHANES III) MUIC=145μg/L 2001-02 (NHANES) MUIC=168μg/L	Concern remains about iodine status of pregnant women	(40)
Canada	1949	Universal mandatory salt iodisation.	No monitoring results identified		
Germany	1981	Level of iodine added to table salt enforced.	1986 MUIC= 68μg/L		(41-43)
	1989	Legislation permitting iodised salt addition to processed foods and canteen meals.			
	1991	Legislation permitting addition of iodised salt to pickled meats and sausages	1992 MUIC= 67μg/L		
	1993	Removal of requirement for iodised salt use in manufacturing to be separately labelled.	1997 MUIC=95μg/L 1999 MUIC (n=3065)=148μg/L; 7%<50μg/L 2001 MUIC (n=591) =183μg/L: 4.3%<50μg/L		
Switzerland	1952	Iodised table salt available			(44, 45)
	1962	Concentration of iodised table salt increase			
	1980	Concentration of iodised table salt increase again to 15mg/kg.	1980s – adequate 1994 MUIC (pregnant women) = 83-100mg/g creatinine 1997 MUIC (school children in Zurich and Engadine) = 96μg/L mild deficiency 1997 MUIC (school children, Bernese area) = 94μg/L	Around 95% of household salt is iodised and around 70% used in commercial food preparation.	
	1998	Concentration of iodised table salt increase again to 20mg/kg	1999 MUIC (school children)=115μg/L (pregnant women)=138μg/L 2004 MUIC (school children)=141μg/L (pregnant women) 249μg/L		
The Netherlands	1942	Introduction of iodised salt for use in bread	Endemic goitre prompted intervention	Use of iodised salt by baking industry is voluntary but widely practiced.	(46-48)
	1960	Iodised salt in bread use made mandatory	1976 Goitre prevalence still high		
	1982	Level of iodine increased in bread and table salt	1995/96 MUIC (school children) =154μg/L ; 4-5 slices bread/day 1997 MUIC (adult men & women)=mild deficiency; related to bread intake		

Table 5: Iodine interventions in developed countries

Country	*Year*	*Intervention*	*Iodine status*	*Comments*	*References*
Denmark	1998	Iodised household salt at 8mg/kg made available - voluntary	1997-98 MUIC (n=4649 in two areas) =45μg/L & 61μg/L (excluding those taking iodine supps) or 53μg/L & 68μg/L (including those taking supps.).	Prior to 1998 iodised salt was prohibited. After 18months only 50% of household salt was iodised and none for industry use.	(49, 50)
	2000	Mandatory iodisation of household salt and that used for bread and cake production at 13mg/kg.	2004-05 MUIC (n=3570 in two areas) =86μg/L & 99μg/L (excluding those taking supplements) or 93μg/L & 108μg/L (including those taking supps.).	Differences in regions of Denmark due to varying levels of iodine in water. Denmark considers their approach to be cautious and have a good monitoring program to complement.	
New Zealand	1924	Iodisation of table and cooking salt	Endemic goitre 1920: 61% of children with enlarged thyroids		(51) (52, 53)
	1938	Increased concentration of iodisation of cooking salt	1953: 1.1% of children with enlarged thyroids 1960-1980 iodine status adequate or more than adequate 2002 MUIC school children (n=1796) = 68 males; 62 females 2005 MUIC pregnant women (n=170) = 38		
Australia	1920	Introduction of iodised table salt	Endemic goitre		(8, 17, 54, 55)
	1947	Iodine tablets provided to school children and pregnant and lactating women (ACT and Tasmania)			
	1953	Iodine containing bread improvers (ACT only)			
	1966	Iodine containing bread improvers (Tasmania)			
	1976	Discontinued use of iodine containing bread improvers due to high rates of Iodine induced hyperthyroidism			
	2001	Voluntary use of iodised salt by the bread industry (Tasmania only)	1998 MUIC: school children = 75μg/L 2000 MUIC: school children = 72μg/L pregnant women 76μg/L 2003 MUIC: school children = 105μg/L pregnant women 88μg/L 2004 MUIC: school children = 109μg/L pregnant women 86μg/L 2005 MUIC: school children = 105μg/L pregnant women 78μg/L	Concern about sustainability, reach and cost to government with a voluntary program. Improvements in iodine status seen in children but not in pregnant women	

Conclusion

This review has demonstrated that *mild* iodine deficiency is prevalent in south eastern Australia. South eastern Australia is the most densely populated area of Australia meaning that a high proportion of the population are at risk of iodine deficiency.

The iodine intake of pregnant women in south eastern Australia is particularly inadequate. In Western Australia and Queensland, where iodine status of the general population is not iodine deficient, it can be inferred that the iodine intake of pregnant women is likely to be inadequate given the level of iodine status in the general population in these two states.

The term *mild iodine deficiency* is potentially misleading as it does not convey the seriousness of the associated health effects. Studies on the health effects of mild iodine deficiency are not unequivocal, due to limitations, methodological flaws and ethical constraints in the research. However, there is a suggestion of a dose response relationship with increasing effects on neurological development with increasing iodine deficiency. Neurological effects associated with *mild* iodine deficiency include reduced IQ, increased auditory threshold and increased rates of ADHD.

Other developed countries that have considered it necessary to intervene (or increase the level of intervention) at similar levels of iodine deficiency include Switzerland, Germany and New Zealand.

In constructing a reasonable health-based standard using the precautionary principle, intervention is warranted where median urinary iodine concentration falls below 100μg/L. On this basis intervention to reduce iodine deficiency would be considered warranted in Australia.

The magnitude of intervention required to correct *mild* iodine deficiency in the general population of south eastern Australia would be very unlikely to result in areas of Australia, that are currently not iodine deficient (Western Australia and Queensland), exceeding optimal levels of iodine status.

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Appendix 1: Summary of current iodine status in New Zealand, Oct 2007

"Ministers noted that the prevalence and severity of iodine deficiency in New Zealand is significant and mandatory fortification with iodine is considered the most effective strategy to address it"

Minutes of the Australian Health Ministers Conference, 24 July 2007

Brief history of iodine status in New Zealand until the early 1990s

New Zealand has a very low iodine environment. In the early 1900s, goitre was endemic in New Zealand. In order to decrease the incidence of goitre, table salt was iodised at a low level from 1924. However, this had little effect and the level was increased to 40-80mg of iodine per kilogram of salt in 1938 (56).

Following the increase in iodisation of salt, the proportion of children with enlarged thyroid glands fell from around 60 percent in 1920 to 1percent in 1953. When iodised table salt was introduced there was a major public education campaign to ensure people understood the benefits of using iodised salt in the home. However non-iodised salt has always continued to be available in New Zealand.

Studies of iodine status from the mid 1960s to the mid 1980s indicated that iodine intake throughout this period was adequate or more than adequate due to iodised table salt use and use of iodine containing sanitising agents by the dairy industry (57, 58).

Iodine Status in New Zealand from the early 1990s until 2007

The Ministry of Health identified in the 1987/88 and 1990/91 Total Diet Surveys that iodine available in the food supply, excluding discretionary salt, was at or below the Australian Recommended Dietary Intakes and was a possible public health issue. This information is summarised in Table 1.

Adults

Mild iodine deficiency was reported in urine samples of adult volunteers in the 1990s (59, 60). In the 1993-94 study thyroid hormone concentrations were within normal ranges but in the later study, 1997-98, lower iodine status was reflected in enlarged thyroid glands and elevated serum thyroglobulin levels. Urinary iodide excretion is likely to be measured in the 2008 New Zealand National Adult Nutrition Survey. It is anticipated that these data will be available in the latter part of 2009.

Children, including infants and toddlers

A proportionate to population size school-based cluster survey was used to randomly select children aged eight to ten years living in Wellington and Dunedin in the mid-to-late 1990s. Mild iodine deficiency was found in this sample and around 11 percent of those children had goitre (61). This raised concern as

a prevalence of goitre greater than five percent is considered endemic. These findings were confirmed in a larger, nationally representative sample of children, aged five to fourteen years, as part of the 2002 National Children's Nutrition Survey (52). In 2004, the remaining blood samples (n=1154) from the CNS were analysed for thyroid hormone status. This confirmed that New Zealand children were at risk of mild iodine deficiency and those children with particularly low levels of urinary iodide concentration might be at greater risk of suboptimal cognitive and psychomotor development (62).

Infants and toddlers have also been found to have mild iodine deficiency (63). In this latter study breastfed infants had less than half the urinary iodide excretion of bottle fed infants. This reflects low breast milk iodine content due to suboptimal maternal intakes which was consistent with earlier findings.

Pregnant women

Thomson et al found mild deficiency in a group of pregnant women in Dunedin in the early 1990s (64). During 2005 a nationwide survey of the iodine status of 170 pregnant women was undertaken by the University of Otago (53).The results showed moderate iodine deficiency in these subjects with 7 percent of the women having goitre. No differences were found across the regions or between the stages of pregnancy.

Table 1: Summary of iodine status in New Zealand from the 1990s

Year	*Location*	*Sample size*	*UIE (median µg/day)*	*Goitre (%)*	*Thyro-globulin hormone*	*Reference*
1993-1994	Waikato & Otago	333	70 (males) 59 (females)	NR	NM	(59)
1991-1992	Otago (pregnant women)	52	46-60*	NR	NM	(64)
1997-1998	Otago	233	81 (males) 69 (females)	↑ thyroid volume = ↓ iodine intake	Indicative of mild iodine deficiency (IMID)	(60)
			MUIC (µg/L)			
1996-1997	Wellington & Dunedin (children, 8-10 years)	300	67 (males) 65 (females)**	11	NM	(61)
1998-1999	South Isl. (6-24 month olds)	230	67 (44 breastfed vs 99 formula-fed)	NR	NR	(63)
2002	NZ (children 5-14 years, national sample)	1796	68 (males) 62 (females)	NM	Indicative of mild iodine deficiency (IMID) n=1154	(52);(62)
2005	NZ (Thyromobile survey, iodine status of pregnant women (TRIP))	170	38 (70% <50µg/L)	7	Measured but not yet reported	(65)

*NR = not reported; NM = not measured; * based on the reported range for pregnant women of 0.36-0.47µmol/day; **based on the averaged median for both boys and girls aged 8, 9 and 10 years.*

Appendix 2: Background information on iodine nutrition

What is iodine?

Iodine is a trace element that is essential for the healthy function of the thyroid gland. The thyroid gland stores and uses iodine to produce thyroid hormones. Thyroid hormones play a key role in regulating cellular metabolism and metabolic rate including the regulation of body temperature. They are also required for maturation of the central nervous system. The majority of the body's iodine is found in the thyroid gland and the rest in the blood. Excess iodine is excreted in the urine.

Iodine requirements in Australia and New Zealand

Dietary iodine requirements recommended by the National Health and Medical Research Council, are described in Table 1 (66). The term *Upper Levels of Intake* refers to the *highest average daily nutrient intake level likely to pose no adverse health effects to almost all individuals in the general population.*

Table 1: Nutrient reference values for iodine for Australia and New Zealand

	Estimated average requirement (µg/day)	Recommended dietary intake (µg/day)	Upper level of intake (µg/day)
Children & adolescents			
1-3	65	90	200
4-8	65	90	300
9-13	75	120	600
14-18	95	150	900
Adults 19+	100	150	1100
Pregnancy			
14-18 yr	160	220	900
19-50 yr	160	220	1100
Lactation			
14-18 yr	190	270	900
19-50 yr	190	270	1100

Food sources of iodine

The amount of iodine in the environment is influenced by a complex interaction of geography, climate, soil structure and soil acidity (67). The major sources of iodine in the Australian diet include seafood and dairy products. Whilst foods from marine sources (various seafood and seaweed) provide a relatively consistent amount of iodine, the iodine content of other foods varies greatly depending on the iodine content of the land on which crops are grown and cattle are raised (68). Additional iodine is obtained from iodised table salt. In Australia approximately 0.5 percent of commercial salt and 15-20

percent of household salt is iodised (19). Relying on current dietary sources of iodine to meet iodine requirements is unlikely to be sufficient for the majority of Australians.

Protection from iodine deficiency in Australia and New Zealand in the later half of the 1900s occurred more as a result of good luck rather than good management. Milk has been an adventitious source of iodine due to residues from iodine containing sanitising agents used in the dairy industry. In more recent times reliance on iodine containing sanitising agents has been reduced with some replaced by more effective non-iodine containing disinfectants and best practice standards have improved to minimise contamination irrespective of the type of sanitising agents used.

Iodine deficiency disorders

Internationally iodine deficiency is considered the leading cause of preventable mental impairment in children (69). Iodine deficiency leads to a wide range of problems collectively known as iodine deficiency disorders (IDD) (70). The nature and severity of these disorders are closely related to the severity and duration of the deficiency (71). As the iodine status of a population deteriorates, the health impact across the population worsens. Further, the lower the iodine status of the group, the greater the risk of there being individuals with very low iodine status.

The spectrum of IDD is wide and varies according to the severity and duration of the deficiency and the life stage of the populations affected. Cretinism and widespread goitre are the most serious and overt consequences of iodine deficiency which occur in the context of severe deficiency (1).

The term IDD was first coined to provide a collective term to expand on goitre (enlargement of the thyroid) and cretinism (severe mental retardation) and to encompass all presentations of the deficiency disease including the most important effect of iodine deficiency on neuropsychological development (70). Table 2 describes the spectrum of effects of IDD focusing on the more obvious and severe forms throughout the life cycle.

Table 2: Iodine Deficiency Disorders throughout the Life Cycle (1)

Foetus	Abortions
	Still births
	Congenital abnormalities
	Increased perinatal mortality
	Increased infant mortality
	Neurological cretinism: mental deficiency, deaf mutism, spastic diplegia, squint
	Myoedematous 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
	Hypothyroidism
	Impaired mental function
	Iodine induced hyperthyroidism

Assessment of iodine status

Urinary iodine concentration is the internationally recommended, and most widely used, marker of population iodine deficiency. Whilst it is not considered an accurate method of assessing an individual's iodine status, due to high intra-individual variability, median urinary iodine concentration (MUIC) is widely used to assess iodine status of populations (1).

To determine population iodine status the WHO and ICCIDD recommend the following (1):

1. school-aged children be used because of ease of access for testing at a population level
2. iodine concentration be determined from casual urine specimens in a sample of at least 200 school aged-children (WHO, 2001)
3. iodine status is optimal if the MUIC is between 100 and 200μg/L and fewer than 20 percent of the samples are below 50μg/L
4. MUIC is used to classify the degree of deficiency or excess according to Table 3.

Table 3: Epidemiological criteria for assessing population iodine status using median urinary iodine concentrations in school-aged children (1)

Median urinary iodine concentration (μg/L)	Iodine intake	Iodine status
< 20	Insufficient	Severe iodine deficiency
20 – 49	Insufficient	Moderate iodine deficiency
50 – 99	Insufficient	Mild iodine deficiency
100 – 199	Adequate	Optimal
200 – 299	More than adequate	Risk of iodine-induced hyperthyroidism in susceptible groups
>300	Excessive	Risk of adverse health consequences

In 2005 a World Health Organization Technical Consultant group made recommendations for the interpretation of median urinary iodine in pregnancy as follows:

- 150 -249μg/L = adequate
- 250-499μg/L = more than adequate
- 500μg/L+ = excessive.

These recommendations have now been accepted by the Public Health Committee of the American Thyroid Association and the ICCIDD (11, 12).

In recognition that IDD is a spectrum of disorders, assessment is not limited to measurement of UIC. Additional measures used for assessing iodine status include thyroid volume (presence of goitre), serum thyroid hormone levels (68), and thyroglobulin (Tg) (1).

Thyroid volume is an index of longstanding significant iodine deficiency and therefore is not sensitive for evaluating recent changes in iodine nutrition (1). Serum levels of the thyroid hormones T3, T4 and thyroid stimulating hormone (TSH) are good indicators of iodine status in individuals with moderate to severe iodine deficiency. Thyroglobulin is the most plentiful protein of the thyroid gland and when the thyroid gland is hyperplasic, as in the case of iodine deficiency, increased amounts of Tg are released into the serum. There is growing evidence to suggest that Tg is the most sensitive indicator of mild iodine deficiency (72, 73). However, use of the tests to measure population iodine status is limited by cost and technical difficulties in obtaining venous blood samples.

Assessment of dietary iodine intake from dietary surveys is complicated by several factors including large variation in iodine content in foods in different regions, incomplete iodine data in food composition databases and the difficulty in assessing discretionary iodised salt use at the individual level. Hence dietary assessment is not widely used to assess iodine status.