

# Estimating the iodine supplementation level to recommend for pregnant and breastfeeding women in Australia

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**D**ietary requirements for all nutrients are higher for women during pregnancy and lactation than when not pregnant or breastfeeding. During pregnancy, there is an increase of about 50% in maternal thyroxine production, a high rate of transfer of iodine and thyroxine from mother to fetus and increased maternal renal iodine clearance.<sup>1</sup> Increased iodine requirements during breastfeeding allow for secretion of iodine in breastmilk. In Australia, the recommended iodine intake increases from 150 µg/day for non-pregnant adult women to 220 µg/day during pregnancy and 270 µg/day while breastfeeding<sup>2</sup> (Box 1). The National Iodine Nutrition Survey conducted in 2003 and 2004 found that children living in south-eastern Australia were mildly iodine deficient.<sup>5</sup> The results of several small contemporaneous studies of urinary iodine concentration in pregnant women were consistent with iodine insufficiency in pregnant women in the same states<sup>6–11</sup> (Box 2).

Since October 2009, it has been mandatory to replace salt used in breadmaking with iodised salt, except in bread represented as organic.<sup>19</sup> Food Standards Australia New Zealand (FSANZ) estimated that, in the general population of women aged 19–44 years, this strategy would increase mean iodine intake by 46 µg/day and reduce the proportion of women with inadequate intakes from 59% to 9%.<sup>19</sup> Mean iodine intakes in pregnant and

## Abstract

**Objective:** To identify a level of iodine supplementation to recommend for pregnant and breastfeeding women in Australia.

**Design, setting and participants:** Dietary modelling indicated that mandatory fortification of bread with iodine by replacing salt with iodised salt would still leave a gap in iodine intakes in pregnant and breastfeeding women in Australia. Iodine shortfall was estimated by two separate methods: (i) analysis of data from published studies reporting mean urinary iodine concentrations in populations of Australian women who were pregnant or had given birth in the past 6 months; and (ii) modelling based on the postmandatory fortification iodine intake estimates calculated by Food Standards Australia New Zealand using food consumption reported by women aged 19–44 years who participated in the 1995 National Nutrition Survey.

**Main outcome measure:** Estimated level of daily supplementation required to provide sufficient iodine to result in a low proportion of pregnant and breastfeeding women having inadequate iodine intakes.

**Results:** Estimations from both data sources indicate that a supplement of 100–150 µg/day would increase iodine intakes to a suitable extent in pregnant and breastfeeding women in Australia.

**Conclusions:** The final level of supplementation we recommend should be based on these calculations and other factors. There will be population subgroups for whom our general recommendation is not appropriate.

breastfeeding women were not calculated separately because there are too few of them in the dataset to allow separate estimation. Assuming that food consumption during pregnancy or lactation is the same as for the general population, FSANZ estimated that most of these women would still have inadequate intakes<sup>19</sup> owing to their higher iodine requirements (Box 1).<sup>2</sup>

These concerns led to the National Health and Medical Research Council convening an expert group to consider if, and what level of, iodine supplementation should be recommended to pregnant and breastfeeding Australian women.<sup>20</sup> As there is

no nationally representative survey of iodine status in pregnant and breastfeeding women, the gap between the postfortification intake and the desirable intake was calculated using two different approaches and presented to the expert group. We describe these calculations and include more recent studies to update the information.

## Methods

The two approaches we used to estimate iodine intake involved calculations based on (i) urine iodine concentrations and (ii) estimates of dietary intake. To this end, we

### 1 Iodine intake recommendations for adult women

Source of recommendation and group of women	Estimated average requirement	Recommended dietary intake	Upper level of intake
<b>National Health and Medical Research Council and New Zealand Ministry of Health<sup>2</sup></b>			
Not pregnant or lactating, ≥ 19 years	100 µg/day	150 µg/day	1100 µg/day
Pregnant, ≥ 19 years	160 µg/day	220 µg/day	1100 µg/day
Lactating, ≥ 19 years	190 µg/day	270 µg/day	1100 µg/day
<b>Food and Agriculture Organization/World Health Organization<sup>3,4</sup></b>			
Not pregnant or lactating	Not defined	150 µg/day	40 µg/kg bodyweight/day
Pregnant and lactating	Not defined	250 µg/day	40 µg/kg bodyweight/day

## 2 Estimated iodine intakes calculated from median urinary iodine concentrations reported in studies of pregnant or breastfeeding women and level of daily iodine supplementation needed to achieve an average intake of 250 µg/day

Source and location of sampled population	Year of data collection	No. and details of women	Status	Median urine iodine concentration (µg/L)	Iodine (µg/day)	
					Estimated median intake*	Supplementation required to raise median intake to 250 µg/day
<b>Before fortification</b>						
Gunton et al, Northern Sydney, NSW <sup>6</sup>	1998–1999	81	Pregnant	104	166	84
Li et al, Western Sydney, NSW <sup>7</sup>	1998–1999	101	Pregnant	88	141	109
Hamrosi et al, Melbourne, VIC <sup>9</sup>	1998–2001	227 white	Pregnant	52	83	167
		263 Vietnamese	Pregnant	58	93	157
		262 Indian/Sri Lankan	Pregnant	61	97	153
Burgess et al, Hobart, TAS <sup>10</sup>	2000–2001	285 hospital antenatal care	Pregnant	76	121	129
Chan et al, Sydney, NSW <sup>12</sup>	2000	49	Breastfeeding 3–9 days postpartum	46	na	na
Travers et al, central coast, NSW <sup>11</sup>	2004	815	Pregnant	85	136	114
Mackerras et al, Darwin region, NT <sup>13</sup>	2006–2007	24 Aboriginal teenagers	Pregnant	49	78	172
		11 Aboriginal teenagers	Breastfeeding <sup>†</sup> < 6 months postpartum	39	na	na
Charlton et al, Wollongong, NSW <sup>14</sup>	2008	110	Pregnant	88	141	109
Nguyen et al, ACT <sup>15</sup>	Early 2009	100	Pregnant	62	99	151
Rahman et al, Gippsland, VIC <sup>16</sup>	2009 before fortification	24	Pregnant	96	153	97
<b>After fortification</b>						
Burgess et al, Hobart, TAS <sup>10</sup>	2006 <sup>‡</sup>	229 hospital antenatal care	Pregnant	86	137	113
	2003–2006 <sup>‡</sup>	288 primary health care	Pregnant	81	129	121
Rahman et al, Gippsland, VIC <sup>16</sup>	2009 after fortification to February 2010	62	Pregnant	95.5	153	97
	2010	27 taking a supplement containing iodine	Breastfeeding 2.6 months postpartum	206	na	na
33, no iodine supplements		Breastfeeding	97	na	na	

ACT = Australian Capital Territory, na = Not applicable, NSW = New South Wales, NT = Northern Territory, TAS = Tasmania, VIC = Victoria.

\*Calculated using the formula daily iodine intake (µg) = urinary iodine concentration (µg/L) × 0.0235 × bodyweight (kg) and using an average bodyweight of 68 kg. The formula is not applied to studies of breastfeeding women because it does not capture secretion of iodine in breastmilk. † Women with infants aged < 6 months were assumed to be breastfeeding as this is the norm in this group.<sup>13</sup> ‡ An agreement with bakeries led to an estimated 80% of bread in Tasmania containing iodised salt from October 2001 onwards.<sup>13</sup> ◆

selected 11 studies conducted before and/or after fortification of bread with iodine, that reported the median urinary iodine concentration (MUI) in Australian women who were pregnant or had given birth in the past 6 months. To estimate iodine intake from diet, we used the datafile compiled by FSANZ using food consumption data from the 1995 National Nutrition Survey (NNS) and subsequent iodine analyses of food.

### Urine iodine concentrations

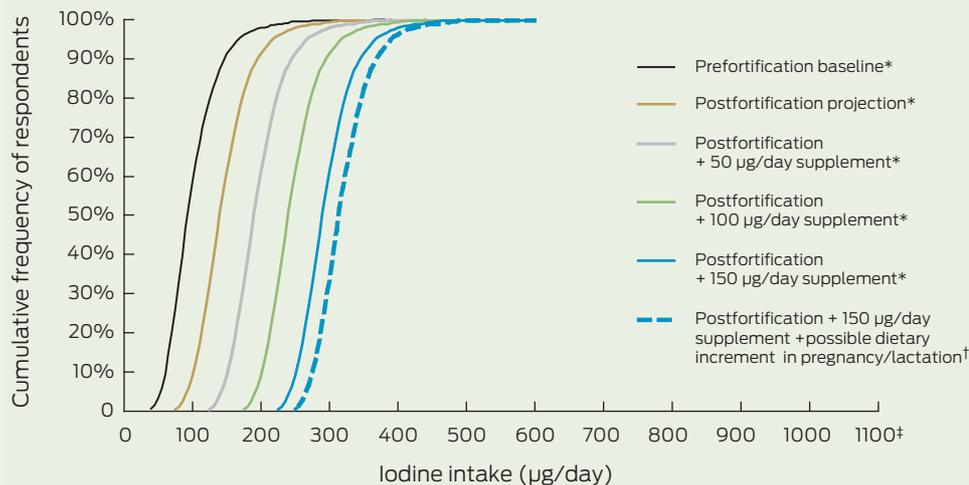
Except in breastfeeding women, urinary iodine excretion (µg/day) accurately reflects recent iodine

intake, with about 90% of dietary iodine appearing in the urine.<sup>1</sup> The median urinary iodine concentration (MUI) in a population, calculated from a single sample in each participant, is well accepted as a surrogate marker for population iodine intake because variations in hydration, although influential for individual iodine concentration measurements, generally even out when calculating the population median. The formula daily iodine intake (µg) = urinary iodine concentration (µg/L) × 0.0235 × bodyweight (kg) is used for adults to estimate iodine intake from the iodine concen-

tration in a spot urine sample.<sup>1</sup> For example, an MUI of 100 µg/L corresponds to an intake of 160 µg/day for a bodyweight of 68 kg. Conversely, an average population intake of 250 µg/day would give an MUI of about 156 µg/L. This formula cannot be used to estimate iodine intake in breastfeeding women because it does not include the iodine content of breastmilk.

In addition to studies reporting MUI data in pregnant Australian women<sup>6–11</sup> described in earlier reviews,<sup>7,19,20</sup> we identified four more recent studies<sup>13–16</sup> and three reports on breastfeeding women (Box 2).<sup>13,12,17</sup> One study (McElduff

### 3 Projected iodine intake of Australian women aged 19–44 years under different fortification and iodine supplement scenarios



The upper level of intake recommended for adult Australian women is 1100 µg/day.<sup>2</sup>

\* Food consumption data from the 1995 National Nutrition Survey with Food Standards Australia New Zealand analytical iodine concentrations and estimated postfortification iodine concentration in bread.<sup>19</sup>

† Food-frequency data of key iodine-containing foods from a cohort study<sup>22</sup> added to the 150 µg/day level of iodine supplementation.

et al<sup>8</sup>) was excluded owing to the overlap of women with those of another study (Gunton et al<sup>6</sup>). Most studies took opportunistic samples from hospital clinics and did not describe whether women were using iodine supplements.

Pregnant women were recruited at stages of gestation ranging from early pregnancy to full term. Owing to lack of information about women's weight in the studies, we applied a weight of 68 kg to all studies of pregnant women to back-calculate iodine intake from the MUIC. This allows for some of the weight gain during pregnancy compared with the reference bodyweight of 61 kg used to derive nutrient reference values for non-pregnant Australian women (Box 1).<sup>2</sup> For simplicity, we used a target dietary intake of 250 µg (midway between the recommended daily intakes [RDIs] for pregnant and breastfeeding women) to calculate the gap in iodine intake in each study. The gap between calculated intake and the RDI of iodine for pregnant women (220 µg) or breastfeeding women (270 µg) can be determined by subtracting 30 µg from, or adding 20 µg to, respectively, the values shown in Box 2.

#### Dietary estimates

We used data on Australian women aged 19–44 years as a surrogate for food consumption of pregnant and

breastfeeding women because the 1995 NNS data do not permit the iodine intakes of pregnant and breastfeeding women to be estimated directly.

We performed dietary calculations using the datafile of iodine intake estimates (excluding supplements and corrected for within-person variation) generated by FSANZ during their work on iodine fortification.<sup>19</sup> The prefortification estimate was calculated by applying the iodine content of Australian food analysed between 2001 and 2005 to the reported food consumption in the NNS. The amount of iodine in bread after mandatory replacement of salt with iodised salt (using an average of 45 mg iodine/kg salt), allowing for 10% loss of iodine with baking, was calculated for each woman based on her reported bread consumption.<sup>19</sup>

Box 3 shows the prefortification and postfortification cumulative distribution of iodine intakes for the 2960 women aged 19–44 years in the NNS estimated by FSANZ, and allows the proportion of the population with intakes greater than and less than any iodine level to be read. For example, before fortification, about 60% of women had estimated iodine intakes below 100 µg/day (therefore, about 40% had an intake greater than 100 µg/day). Box 3 shows the progressive shift in the

postfortification distribution of iodine intakes in Australian women with increasing increments of 50 µg/day of iodine.

Because the data shown in the first five plots in Box 3 are not specifically for pregnant or breastfeeding women, the food-frequency data of key iodine-containing foods from a cohort study<sup>22</sup> were also considered.

## Results

### Urine iodine concentrations

Before fortification of bread with iodine, the estimated gap between iodine intake and the target ranged from 84–172 µg/day (Box 2). Two studies were repeated after fortification. In Tasmania, after the implementation of a program that resulted in an estimated 80% of bread being made with iodised salt,<sup>18</sup> the average gap was 113–121 µg/day compared with an average gap of 129 µg/day before the program was implemented.<sup>10</sup> In Gippsland, there was no difference before and after the enforcement date for national mandatory fortification.<sup>16</sup> The three small studies in breastfeeding women<sup>12,13,17</sup> had MUICs at the lower end of the MUIC range for pregnant women.

### Dietary estimates

We used the proportion with intakes less than the estimated average requirement (EAR; Box 1) to estimate the proportion of the population with inadequate iodine intakes.<sup>21</sup> Supplementation with 100 µg of iodine per day would result in the proportion of women with intakes below the EAR for pregnant women (160 µg/day) being essentially zero, and fewer than 10% of women having intakes below the EAR for lactating women (190 µg/day). Both of these values would be zero with supplementation with 150 µg of iodine per day. Median iodine intakes would be 240 µg/day with supplementation of 100 µg/day and 290 µg/day with supplementation of 150 µg/day (Box 3). The highest iodine intake resulting from bread fortification plus supplementation with 150 µg of iodine per day would be about 580 µg/day (Box 3), which is well below the upper level of intake of

1100 µg/day for adults in Australia and New Zealand<sup>2</sup> (Box 1).

Food-frequency data of key iodine-containing foods from a cohort study show that the intake of bread and dairy products is higher in pregnant and postpartum women, and this might increase iodine intake by about 20 µg/day compared with that of non-pregnant women.<sup>22</sup> We added this to the 150 µg/day supplementation level in Box 3 (sixth plot) as an approximation for iodine intakes in pregnant and lactating women.

## Discussion

Results from analyses using urinary iodine concentration data or dietary modelling support a conclusion that iodine intake was inadequate in the locations studied before and after bread fortification. Despite using different data sources and assumptions, both methods identify a gap in iodine intake in the range of 100–150 µg/day. We believe that this is the first time that these types of complementary data have been used to derive an estimate of the level of iodine supplementation that should be recommended.

There are no urinary iodine concentration studies of pregnant or breastfeeding women in Western Australia and Queensland where the MUIC is between 100 and 150 µg/L in children.<sup>5</sup> Studies such as those from Tasmania<sup>10,23</sup> indicate that the MUIC in children provides an estimate of the MUIC in adults. MUIC in the range of 100–149 µg/L, while sufficient in children, indicates insufficiency in pregnant women.<sup>4</sup> It is therefore possible that pregnant women in Western Australia and Queensland have insufficient iodine intake.

Most of the urinary concentration studies were in opportunistic samples of women. The large variation in MUIC among them may relate to differences in dietary intake, geographic influences such as the iodide content of local water, time of day when the samples were collected owing to diurnal variation in hydration, different stages of pregnancy of the women in the samples, or may have come about because some studies were conducted in tertiary hospitals while others were community-based.

The urinary concentration data provide the basis for an estimation of the average iodine intake target for the population only. The dietary estimate allows the population iodine intake distribution to be compared with criteria for both adequacy and excessive intakes. Although advice about iodine supplementation is directed at individuals, the amount of iodine in the supplement does not need to equal the RDI. The purpose of this type of recommendation is to improve population nutrient status so that only a low proportion of the population would have inadequate intakes.<sup>24</sup> As shown in Box 3, the median iodine intake of the population is higher than the RDI and a small proportion will have intakes below the EAR with supplementation of 100–150 µg per day.

There are few data about the dietary intakes of pregnant and breastfeeding women in Australia. Food frequency data in the 2003 Australian Longitudinal Study on Women's Health showed similar consumption of key iodine-containing foods for both pregnant women and women after giving birth and these were slightly higher than consumption by non-pregnant women in the same cohort.<sup>22</sup> Therefore, we believe that, in the absence of better data, the information from urinary concentration studies of pregnant women can be reasonably extrapolated to breastfeeding women to estimate their iodine intakes, and that the dietary data from the general adult female population do not substantially underestimate iodine intake in the groups of interest. Data on iodine intakes, urinary concentrations and supplement use are being collected in the 2011–2013 Australian Health Survey.<sup>25</sup> The new data will show whether population iodine intake has changed substantially since 1995. This will allow some of the strategies aimed at improving iodine intake in the population to be assessed. Pregnant and breastfeeding women are not being oversampled which limits evaluation in these groups. A minimal effect on MUIC among pregnant women was reported after fortification.<sup>10,16</sup> MUIC excludes additional iodine transferred to the fetus which may partly explain these results. The Tasmanian iodine fortification program achieved a

smaller proportion of fortified bread than national regulation.<sup>10</sup> The result from Gippsland<sup>16</sup> is difficult to interpret without knowing when the samples were obtained and when bread fortification actually started during the year-long transition before the enforcement date in October 2009. Further information about current iodine status of pregnant and lactating women would be desirable.

Our calculations do not yield a single "correct" answer, but show the range of the gap in iodine intake. In addition to these numerical results (Box 2), other factors affect the supplement dose that should be recommended. A committee or organisation needs to consider what weighting should be given to each of the various non-representative studies, extrapolation of results in pregnant women to breastfeeding women and what prevalence of inadequate intake would be tolerable in the population. Other factors include whether a single recommendation to cover both groups could be made, whether the dose should be inflated to allow for missed days in supplement consumption, safety over the period of intended use for those with the highest dietary intakes, and whether it is possible to recommend a dosage that is currently available in the marketplace. A further consideration is how to factor in the uncertainty in the reference values (eg, the Food and Agriculture Organization/World Health Organization has the same recommendation for both groups [Box 1]) and the consequences of making or not making a recommendation.

In summary, two approaches using different types of data to estimate iodine intakes indicate that, after mandatory fortification of bread, supplementation in the range 100–150 µg of iodine per day would increase population iodine intakes in pregnant and breastfeeding Australian women to the levels recommended. The final recommendation depends on a range of other factors as well as these calculations. As with any population-level recommendation, there are subgroups for whom the general recommendation is not appropriate; in this case, women with established thyroid disorders.

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for the prefortification and postfortification iodine estimates that formed the basis for the current analysis.

**Competing Interests:** The work for this study was done while we were both members of the National Health and Medical Research Council Expert Panel on Iodine Supplementation for Pregnant and Lactating women.

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## Stamps of greatness

### Jan Ingenhousz (1730-1799)

INGENHOUSZ was born on 8 December 1730 in Breda, Holland, and studied medicine at the University of Leuven, where he received his degree in 1752.

Although a physician, he was primarily interested in the natural sciences.

He discovered photosynthesis and cellular respiration in plants and published his findings in 1779.

For a time he practised medicine in Holland and in England before joining the Court of Austria to inoculate the royal family against smallpox, as two of the empress's children had died of the disease.

Robert and Daniel Sutton in England in 1760 and Gatti in France in 1769 had been successfully using variolation — the deliberate inoculation with the smallpox virus that was widely practised before the era of vaccination as prophylaxis.

At the urging of Voltaire in 1768, Empress Catherine and Archduke Paul of Russia had been inoculated by Dimsdale. That same year Ingenhousz inoculated three children in the royal household in Austria after preliminary experiments on 200 children in Vienna. Subsequently, the success of Jenner's experiments swept variolation from the field.

In later years Ingenhousz returned to England and was elected to the Fellowship of the Royal Society.



He died in Bowood, near London, on 7 September 1799, and was postally honoured by the Netherlands in 1941 as a great physician.

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### Jacobus Ludovicus Schroeder van der Kolk (1797-1862)

VAN DER KOLK was born in Leeuwarden, the Netherlands, on 14 March 1797 and studied medicine at the University of Groningen. He was an honours student, earning two gold medals and graduating about 1817. After practising in the country for a short time at Hoorn, he became physician to a hospital in Amsterdam. Appointed as Professor of Anatomy and Physiology at the University of Utrecht in 1827, he introduced microscopic and experimental techniques in the study of histologic anatomy. Particularly interested in the contemporary treatment of the mentally ill, he introduced better nursing and medical care in the insane asylums, developed the psychiatric approach and studied the anatomy of the brain of the mentally deficient.

He died in Utrecht, the Netherlands, on 1 May 1862. He was postally honoured by the Netherlands in 1960 on a stamp to commemorate Mental Health year.

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Pfizer Viagra