

Original Article

Iodine deficiency in women of childbearing age: not bread alone?

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Background and Objectives: Iodine deficiency remains a public health concern, particularly in pregnant women and those planning pregnancy because of the risk of impaired fetal neurological development. Following implementation of strategies to improve iodine intake in Australia, there has been minimal investigation into current iodine status. We aimed to characterise iodine status in a population of women of childbearing-age in Australia. **Methods and Study Design:** A cross-sectional study was performed in 97 women of childbearing-age attending outpatient clinics at a tertiary hospital in Sydney. Pregnant and postmenopausal women were excluded. Iodine intake was surveyed via questionnaire. Spot urinary iodine (UI) was concurrently measured. The relationships between UI, dietary intake and use of iodine-containing multivitamins/medications were examined. **Results:** Median UI was 117 ug/L. Forty women (41%) were iodine deficient (UI <100 ug/L). The most commonly consumed source of dietary iodine was bread (29/97, 30% daily). Forty-three women took iodine-containing multivitamins but 18/43 (41.2%) remained deficient. There were no significant associations between UI and diet. There was a smaller proportion of deficient people than in our previous study (125/180 non-pregnant subjects, 69%, vs 41% in this study, $p < 0.001$). **Conclusion:** The overall population median is now sufficient, however, a significant proportion of this multicultural group are iodine deficient. There are similar proportions of deficiency in those using iodine supplements versus not. Contributors may include ethnicity-related dietary practices, limited awareness or poor adherence to iodine supplements. Despite public health strategies, a significant proportion of women of child-bearing age remained iodine deficient. Further research involving a larger population and contributors to iodine deficiency is warranted.

Key Words: pregnancy-planning, iodine deficiency, women, public health, urine iodine

INTRODUCTION

Iodine deficiency is recognised as the single most preventable cause of neurological impairment on a global level.^{1,2} Although it was thought that Australia was an iodine replete nation, studies since 1999 have proven that deficiency was a significant problem in this country.³⁻⁵ Public health measures aimed at boosting dietary iodine by mandatory iodine fortification of bread were implemented in 2009.^{2,6}

Iodine is a trace mineral essential for growth. It is of particular importance to foetal neurological development and deficiency is associated with higher rates of congenital anomalies, miscarriage and stillbirth.^{2,7} Pregnant women and women planning pregnancy are therefore a specific group that should be targeted in terms of education and iodine supplementation. Other at risk groups include children and breast feeding mothers.^{2,5}

Iodine deficiency has re-emerged as an issue in Australia secondary to changes in the use of iodophore-containing cleansing agents in the dairy industry.⁴ Since

the introduction of new methods of milk storage, there was a decline in population iodine levels.^{8,9} Furthermore, with increasing consumption of processed foods, often using non-iodised salt, dietary intake is often limited.⁹

The majority of iodine absorbed is excreted in the urine, hence urine levels are a validated method of determining deficiency.² In population-based studies, random urine samples, collected at any time of the day are acceptable for iodine quantification.^{1,2} Using spot urine iodine levels (UI), the degree of deficiency is stratified into mild (50-99 ug/L), moderate (20-49 ug/L) and severe (<20 ug/L).²

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Guidelines suggest that UI <100 ug/L requires intervention.²

Following the confirmation of suboptimal dietary iodine in Australia, public health initiatives have aimed to improve population iodine levels with dietary strategies.⁶ Internationally, iodised salt has been the main food source of additional iodine, in accordance with World Health Organisation recommendations.² In 2001 a voluntary iodine fortification program was implemented in Tasmania through the baking industry, with reported improvement in iodine status.¹⁰ Research assessing the impact on iodine levels, however, focused specifically on schoolchildren.¹⁰ In 2009, the mandatory iodine fortification of bread was implemented in Australia.⁶ With the increasing ethnic diversity of the Australian population, however, such a measure may not reach a large proportion of iodine deficient patients due to cultural differences in food consumption. Furthermore, iodised salt is not widely used in processed and restaurant foods and the majority of salt sold is not iodised.¹¹⁻¹³

There has been little investigation into the current state of iodine deficiency in Australia and thus the efficacy of public health strategies. One study from Tasmania found a significant increase in UI following this intervention, but the levels were still inadequate overall.⁵

Because neurological development commences very early in pregnancy, attaining normal iodine status before pregnancy is desirable. This study investigated the iodine status in women of childbearing age and correlated levels with exogenous iodine intake.

PARTICIPANTS AND METHODS

A cross sectional study was performed. Women of childbearing age (16-45 years) were recruited during the period August 2014-October 2015 from outpatient clinics; pregnancy planning, young-adult diabetes and a fertility clinic at a tertiary referral centre in Sydney, New South Wales, Australia. Participation was voluntary. Patient lists were reviewed at the start of clinics to identify eligible women, and subjects were approached at the end of their consultations. Eligible women were identified based on childbearing age (18-45). Pregnant and post-menopausal women were excluded based on history obtained at the time of recruitment.

A questionnaire surveying dietary iodine intake, iodine-containing medications and recent intravenous (IV) radiological contrast exposure was completed. (Appendix 1) Demographic information collected included age and ethnicity. Women were asked to indicate, via Likert Scale, the frequency of consumption of iodine containing foods, from 'Daily' through to 'Never'. Surveyed food groups included sliced bread, seaweed, marine seafood and iodised salt. The iodine content of these surveyed food groups is presented in Table 1.¹⁴ Medication use was surveyed as yes/ no and included iodine-containing multivitamins, thyroxine, amiodarone and any exposure to radiological contrast in the preceding six months. The iodine containing multivitamins commonly used in Australia include Elevit®, Blackmores Pregnancy and Breast-feeding Formula® and Blackmores I-Folic®. These formulations contain 250 ug, 150 ug and 150 ug of iodine respectively. The women were then asked to provide a

Table 1. Iodine content of surveyed foods¹⁴

Iodine source	Iodine content ug/100 g
Sliced bread	46
Seaweed (in sushi)	92
Iodised salt	2000 (0.002% to 0.004% iodine)
Seafood	
Tinned tuna	10
Tinned salmon	60
Snapper (steamed)	40

Relative iodine content of surveyed foods [ug/100g].

single spot urine for concurrent UI measurement. This was the key outcome. Ethnicity was self-assigned by the women.

All UI samples were analysed at the same accredited laboratory: The Institute of Clinical Pathology and Medical Research, Westmead Hospital, NSW. Samples were delivered to the laboratory on the same day as collection and stored at -80 degrees Celsius for batch analysis. UI was determined using a method based on colorimetry of Sandell-Kolthoff reaction after the samples are digested at 95°C using ammonium persulfate to remove interfering substances.¹⁵ This method is used based on efficiency, its ability to adapt to different analysers and cost. The average coefficient of variation (CV) for the test is 15%. The laboratory is enrolled in both the Royal College of Pathologists External Assurance Program in Australia and the Quality Assurance Program (EQUIP) of the National Centre for Environmental Health, USA. The CV of the method in use is in line with other laboratories using the same method as shown from the External Quality Assurance Program data.

Ethics

Ethics approval was obtained through the Westmead Ethics Committee (HREC Ref LNR/14/WMEAD/240). The procedures followed were in accordance with this committee.

Statistical analysis

Statistical analysis was performed using SPSS IBM software Version 22.0. Simple descriptive statistics were used to analyse cohort characteristics. Spearman Rank Correlation Coefficients were used to assess the relationship between UI and exogenous iodine intake from both diet and medications. Mann Whitney U tests were used to compare median UI in different groups of women e.g. using iodine-containing multivitamins versus no use. Fisher's exact test was used to compare proportions of deficiency in women of Caucasian vs. non-Caucasian background.

RESULTS

A convenience sample of 131 women was assessed for eligibility, with 13 excluded due to postmenopausal status or pregnancy. Participation was declined by 18 women and 3 patients failed to provide urine samples, resulting in a total of 97 subjects who completed surveys and provided matched urine samples for iodine measurement (Figure 1). Population characteristics are presented in Table 2. The most common ethnic group was Caucasian (47%) with Asian and Indian Subcontinental ethnicities equally

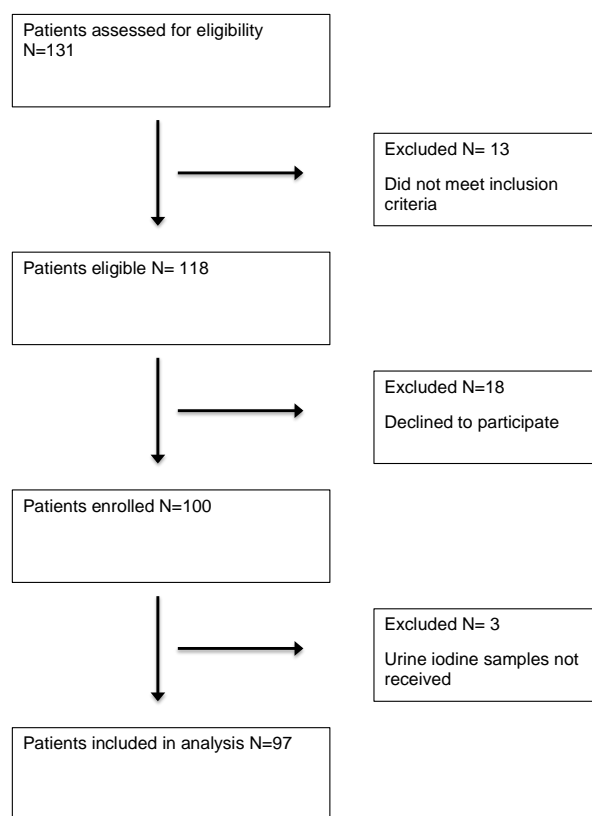


Figure 1. Participant flow chart outlining numbers of eligible patients, excluded patients and those included in final analysis.

Table 2. Population characteristics

Descriptor	Result
N	97
Med age, yrs (IQR)	33.0 (27.0-37.0)
Ethnicity,	
Caucasian	47 (47)
Indian Subcontinental	16 (16.5)
Chinese/ SE Asian	16 (16.5)
Middle Eastern	12 (12.4)
Eastern European	2 (2)
Pacific Islander	3 (3.1)
African	1 (1.0)
Women planning pregnancy, n (%)	70 (72.2)

represented (16.5% in each).

The median UI concentration for the group was 117 ug/L (IQR 60.5-264.0), which is classified as iodine sufficient by the World Health Organisation (≥ 100 ug/L). However, among the group, 40 women were iodine deficient (40/97, 41.2%) (Figure 2). The most commonly consumed source of dietary iodine was bread (30% consumed every day). Almost half the population (41/97, 42.3%) reported never using iodised salt (Table 3). There was no statistically significant association between UI and reported dietary iodine consumption (all Spearman rank correlations $r < 0.10$ in absolute value).

Iodine containing multivitamins were used by 43 (44.3%) women, and of these subjects 18/43, (41.9%) were deficient. The majority of women in the group (70 of 97) (72.2%) were planning pregnancy in the short term, though only 41 of these 70 (58.5%) were using an iodine-containing multivitamin. Of those women not using an

iodine-containing supplement, 22/54 (40.8%) were iodine deficient. These proportions did not differ between women who reported taking an iodine-containing supplement and those who did not. There was no difference in the median urine iodine between the two groups (medians 117 (supplements) vs 113 ug/L, (no supplements), $p=0.385$ by Mann Whitney). There was a significantly higher UI in women who reported taking I-folic (medians 307 vs 113 ug/L, $p=0.047$ by Mann Whitney). Unexpectedly, there was no significant association between UI and use of iodine-containing multivitamins or medications. (Figure 3)

A total of 5 women reported using more than one iodine-containing multivitamin. Of these patients, 4 were taking two of the supplements and 1 was taking all three supplements. Looking at these cases individually, 2/5 (40%) patients had low UI and 3/5 (60%) had replete levels. Analyses were also performed excluding these cases ($n=92$). The median UI was 115 ug/L (IQR 60.3-261.0) and the proportion of deficient women was 41.3% (38/92), there was no statistically significant difference with respect to these findings between these groups before and after exclusion of cases ($p > 0.05$). After exclusion of these cases, there was no difference in UI levels between women taking iodine-containing multivitamins vs not, nor any significant difference between women taking specific brands of multivitamins vs not.

There was no significant difference in UI between specific ethnicities. However, when considered as Caucasian versus non-Caucasian, there was a significant difference. A higher proportion of Caucasian women had UI above the group median value than non-Caucasian patients (27/47 vs 16/50) ($p=0.012$). The proportion of patients within ethnic subgroups with deficient and replete iodine status is presented in Table 4.

We compared the results with our previous report.³ It is noteworthy that although many women are deficient, levels have improved since 1999 when 125 of 180 non-pregnant subjects were deficient (69% vs 41% in this cohort $p < 0.001$).³

DISCUSSION

The median UI concentration for this group of women was in the iodine replete range as defined by WHO epidemiological criteria for iodine status. Notwithstanding this result, a significant proportion of women of potential child-bearing age were iodine deficient, despite the introduction of mandatory fortification of bread in 2009. The mandatory fortification of bread with iodine therefore does not provide sufficient iodine to a large proportion of this patient group; women planning pregnancy.

The recommended daily intake of iodine for pregnant and lactating women is 250 ug.² Accordingly, this group have been advised to use an iodine containing multivitamin at a dose of 150 ug of iodine per day in addition to dietary sources.¹⁶ This should also be used preconception in those women planning pregnancy as prenatal iodine levels are also correlated with the child's neurological development.^{11,17} This message, delivered in Australia by the National Health and Medical Research Council, is not widely appreciated by women planning pregnancy and there is no formal program targeting this issue. Inter-

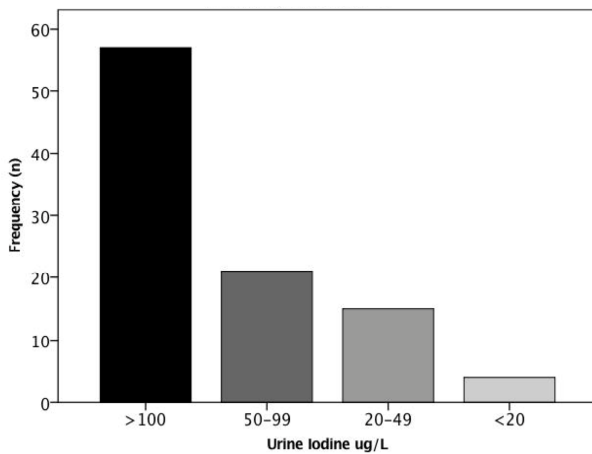


Figure 2. Population Iodine Levels indicating number of women in each category of iodine deficiency. Category 1 iodine replete (UI ≥ 100 ug/L), Category 2 mildly deficient (UI 50-99 ug/L), Category 3 moderately deficient (UI 20-49 ug/L), Category 4 severely deficient (UI < 20 ug/L).

national research has shown that use of these supplements remains generally low with one audit finding only 20% of pregnant women in the US were found to be taking an iodine containing multivitamin during pregnancy based on NHANES data.¹⁸

In the Australian setting, it has been demonstrated that iodine deficiency is an under-recognised issue.^{13,19} Furthermore, it has been noted that provision of information to women regarding this issue is often ad hoc and dependent on the healthcare provider.²⁰ The majority of the cohort surveyed was actively planning pregnancy and almost a half of those women were not using an iodine-containing multivitamin. Previous research has confirmed that there is poor understanding of the consequences of iodine deficiency, and that many women do not recognise its importance during pregnancy.^{13,19,21,22} This concept is supported by one study that reported only 35% of pregnant women used an iodine-containing supplement.⁷ It has been shown that supplement use correlates with socioeconomic status, specifically household income and level of education.^{19,21,23} Though these parameters were not

specifically addressed in this study, the local health district population is recognised to be of low-middle income; hence these issues may be implicated in this cohort. These findings may therefore not translate to all women of Australia due to variation in socioeconomic status.

It was interesting that overall the women who reported taking a supplement did not have higher UI, suggesting suboptimal adherence. Cost may play an important role in the use of pregnancy multi-vitamins. Previous studies have demonstrated that adequate use of iodine supplementation during pregnancy does lead to higher UI concentrations, thus supporting the efficacy of supplements when taken regularly.²⁴⁻²⁶ One study performed in a private obstetric clinic in NSW, Australia, showed a statistically significant association with the use of iodine containing multivitamins and UI concentration (72 ug/L in those not using a supplement vs 115 ug/L in those using a supplement, $p=0.001$).²⁶ The private practice setting of this study implies a higher socioeconomic status of patients than the cohort examined in our study, sourced from public hospital clinics. This difference again supports the potential implication of supplement cost in adherence and therefore efficacy. Details regarding adherence and possible associated barriers were not specifically investigated and this may represent a limitation of this study. Five of 97 women reported taking more than one iodine-containing multivitamin, though whether they were using these concurrently was not questioned and remains unclear. Statistical analysis found no difference in UI nor proportion of deficient women if these cases were excluded, though with respect to small sample sizes within each brand of multivitamin surveyed this may account for large variance. Socioeconomic status, English language comprehension and level of education may have provided further insight into potential demographic factors associated with limited iodine intake. Other potential limitations acknowledged in this study include the relatively small sample size of women surveyed in a particular location, Western Sydney. This may have implications for less generalisability to the rest of the population of women of childbearing age in Australia. Basic demo-

Table 3. Dietary and exogenous iodine exposure

	Every day, n (%)	Never, n (%)
Dietary iodine source	29 (29.9)	4 (4.1)
Bread		
Iodised salt	27 (27.8)	41 (42.3)
Marine seafood	3 (3.1)	13 (13.4)
Seaweed	2 (2.1)	45 (46.4)
Exogenous iodine source (note some women reported >1)	Yes, n (%)	No, n (%)
Iodine-containing multivitamin [†]	43 (44.3)	54 (55.7)
Thyroxine	14 (14.4)	83 (85.6)
Amiodarone	0 (0.0)	97 (100)
Contrast exposure (within 6 months)	12 (12.4)	84 (86.6)

Subjects were asked to rate their intake of dietary iodine sources according to Likert Scale 1 (Every Day) through to 5 (Never). For the sake of brevity only responses 1 and 5 have been listed to highlight differences.

Exogenous iodine intake, including iodine containing multivitamins and medications were surveyed with Yes/No questions.

[†]Iodine containing multivitamins included:

- Elevit® (250 ug iodine) multivitamin, n=26 (26.8%)
- Blackmores® Pregnancy Multivitamin (150 ug iodine), n=15 (15.5%)
- I-Folic® (150 ug iodine), n=8 (8.2%)
- Note: some women used >1 Multivitamin.

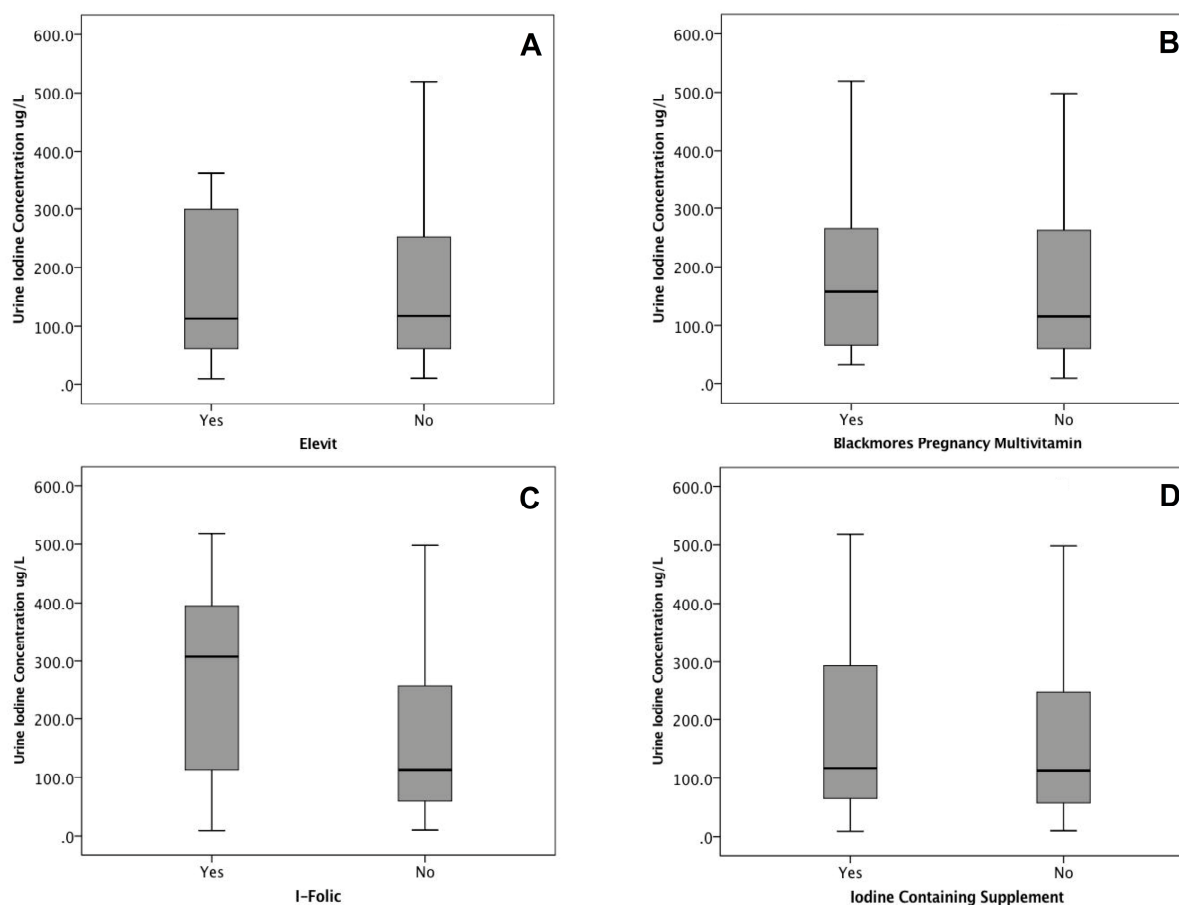


Figure 3. Urine iodine levels in women taking iodine-containing multivitamins versus not. A: Elevit® contains 250 ug iodine per recommended dose, B: Blackmores Pregnancy and Breastfeeding® and C: Blackmores I-Folic® contain 150 ug iodine per recommended dose. Women taking i-folic had higher UI than those not taking it ($p < 0.05$ by Mann-Whitney test).

Table 4. Proportion of iodine-deficient and replete subjects within specific ethnic groups

Ethnic group	Number, n (%)	Deficient, n (%)	Replete, n (%)
Caucasian	47 (47)	18 (38.3)	29 (61.7)
Indian Subcontinental	16 (16.5)	6 (37.5)	10 (62.5)
Chinese/ SE Asian	16 (16.5)	9 (56.3)	7 (43.7)
Middle Eastern	12 (12.4)	3 (25.0)	9 (75.0)
Eastern European	2 (2)	1 (50.0)	1 (50.0)
Pacific Islander	3 (3.1)	2 (66.7)	1 (33.3)
African	1 (1.0)	1 (100.0)	0 (0.0)
Total	97 (100)	40 (41.2)	57 (58.8)

Ethnic breakdown of participating subjects and the relative proportions of women who were iodine deficient (UI <100 ug/L) versus replete (UI ≥100 ug/L) within each ethnic subgroup.

graphic data comparing the population of Western Sydney, specifically the area served by the hospital, to data reflecting NSW and Australia is presented in Table 5.²⁷⁻²⁹

The population recruited for this study was multicultural, reflecting the general population of Australia. Previous research has shown an association between ethnic background and iodine deficiency.³⁰ This research did not find any significant difference in UI between specific ethnic groups, although we did confirm Caucasian patients had higher UI than non-Caucasian patients. Western Sydney is an area of ethnic diversity with many women of Subcontinental, Asian and Middle Eastern background. People born overseas represent a greater proportion of the local area than seen in NSW and Australia overall (Table 5).²⁷⁻²⁹ Consequently there is cultural varia-

tion in diet and consumption of sliced bread was relatively low in this group overall. Less than one third of women surveyed ate bread daily. The frequency of bread consumption according to ethnicity is presented in Table 6. Similarly, iodised salt intake was also low. These two measures of salt and bread enrichment are the most widely adopted on a global level to correct iodine deficiency. Public health initiatives such as the mandatory iodine fortification of bread may be less effective in ethnically diverse populations, and there appears to be a need for new strategies.

Iodine status has improved in Australia, but levels remain suboptimal in a large proportion of women of childbearing age, despite public health measures. Although the median UI concentration in this population was

Table 5. Basic demographic data comparing the population of Western Sydney, specifically the area served by the hospital, to data reflecting NSW and Australia

	Westmead (within City of Parramatta) ²⁷	NSW ²⁸	Australia ²⁹
Median age (y)	33.5	37.9	37.4
Median income (excluding government pensions and allowance) (AUS Dollar \$)	43528	44780	44940
Overseas born population (%)	51.4	31.4	30.2
South East Asia (%)	4.7	3.6	3.3
North east Asia (%)	10.8	3.7	2.5
Southern and Central Asia (%)	11.8	2.5	2.3
Sub-Saharan Africa (%)	1.1	1	1.3
North Africa and Middle East (%)	7	2.3	1.4
Oceania and Antarctica (excluding Australia) (%)	2.9	2.5	2.8
North-West Europe (%)	2.9	5.4	6.7
Southern and Eastern Europe (%)	2.7	3.3	3.2
Education level			
Post school qualifications (% of population age 15 and over)	60.2	57.2	55.9
Post school qualifications – with postgraduate degree (%)	7.5	4.3	3.6

Demographic data is compared between the city of Westmead (the location of the hospital in which the study was conducted), New South Wales (the state in which Westmead is found) and Australia. This compares city, state and nationwide data.

Table 6. Frequency of bread consumption according to ethnicity

Ethnic group	Every day n (%)	A few days a week n (%)	Once/ week n (%)	Less than once/ week n (%)	Never n (%)
Caucasian	15 (31.9)	24 (51.0)	2 (4.3)	4 (8.5)	2 (4.3)
Indian Subcontinental	4 (25.0)	6 (37.5)	3 (18.8)	3 (18.8)	0 (0.0)
Chinese/ SE Asian	3 (18.8)	7 (43.8)	3 (18.8)	3 (18.8)	0 (0.0)
Middle Eastern	5 (41.7)	2 (16.7)	2 (16.7)	1 (8.3)	2 (16.7)
Eastern European	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)
Pacific Islander	1 (33.3)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)
African	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	29 (29.9)	41 (42.3)	12 (12.4)	11 (11.3)	4 (4.1)

Subjects were asked to rate their intake of dietary iodine sources according to Likert Scale 1 (Every Day) through to 5 (Never). This table compares bread consumption (the most commonly consumed dietary iodine source) according to ethnicity.

regarded as sufficient by WHO criteria, the proportion of women meeting criteria for iodine deficiency is concerning. Lack of awareness of the associated health consequences, and poor adherence to iodine containing supplements appear to be contributing factors. Dietary intervention is limited in an increasingly diverse ethnic society. The findings from this research support other studies suggesting that a lack of knowledge regarding this problem remains an issue. Promotion of information in the pre-pregnancy domain regarding iodine supplementation needs to be amplified to protect foetal development. New strategies and further attention to education are warranted. Consideration of a national survey may be justified.

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AUTHOR DISCLOSURES

The authors declare they have no conflicts of interest.

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