

# The prevalence of iodine deficiency in women of reproductive age in the United States of America

Joseph G Hollowell<sup>1,\*</sup> and James E Haddow<sup>2</sup>

<sup>1</sup>Department of Pediatrics, University of Kansas Medical Center, 435 North 1500 Road, Lawrence, Kansas City, Kansas 66049, USA: <sup>2</sup>Division of Medical Screening, Department of Pathology, Women and Infants' Hospital, Providence, Rhode Island, USA

## Abstract

**Objective:** To review the iodine status of women as assessed through National Health and Nutrition Examination Surveys from 1971 to 2002.

**Design and Setting:** National normative estimates of iodine status of the civilian, non-institutionalized population in the United States of America.

**Subjects:** Women of reproductive age and pregnant women.

**Results:** In the United States of America, iodine began to be added to the diet in the 1920s. An excessive iodine intake was documented by the first National Health and Nutrition Examination Survey (NHANES I) in the 1970s which reported a median urinary iodine (UI) concentration of 320  $\mu\text{g l}^{-1}$ . In the NHANES III survey, conducted between 1988 and 1994, the median UI concentration had decreased to 145  $\mu\text{g l}^{-1}$ , while 14.9% of women aged 15–44 years and 6.9% of pregnant women had a UI concentration 50  $\mu\text{g l}^{-1}$ . The concentrations of serum T<sub>4</sub> and thyroid-stimulating hormone of women with a low UI concentration did not, however, indicate an iodine deficiency.

**Conclusions:** Further studies of the association between iodine excretion and biochemical and physiological changes should be undertaken to better understand women's needs for iodine and to develop criteria to monitor them in pregnancy. Because of the potential harm caused by iodine deficiency during pregnancy, we support the use of iodine supplements for all pregnancies while these data are being collected.

**Keywords**  
Iodine deficiency  
Women  
Pregnancy  
United States of America  
Urinary iodine  
NHANES

## Introduction

The role of maternally derived thyroxine (T<sub>4</sub>) in normal foetal development is now well established<sup>1</sup>, as is the need for an intake of iodine during pregnancy to meet both foetal requirements and the mother's increased demands to produce T<sub>4</sub><sup>2</sup>. In this paper, we first review iodine nutrition in the United States of America (USA) and then we examine data on the iodine status of women of reproductive age, including pregnant women, from a large cross-sectional population study, the third National Health and Nutrition Examination Survey (NHANES III). Using the limited data available from that study, we examine the relationships between thyroid function and iodine excretion in the urine. We also attempt to show that one cannot directly determine the magnitude of an iodine deficiency in a population from the proportion of subjects in a cross-sectional survey who excrete iodine in their urine below a certain concentration, e.g. <50  $\mu\text{g l}^{-1}$ .

Comprehensive reports have recently been published on the status of iodine nutrition of infants and pregnant and lactating women internationally<sup>3,4</sup>. This paper will address findings concerning women of reproductive age in the USA.

## Brief history of iodine nutrition in the USA

Iodised salt was introduced in the USA in 1922<sup>5,6</sup> and iodine also entered processed foods, including bread<sup>7</sup> and milk products<sup>8</sup>. The prevalence of goitre subsequently declined<sup>9,10</sup>. In the 1970s, the daily iodine intake ranged between 150 and 700  $\mu\text{g}$ <sup>11</sup>, with regional variations<sup>12</sup>. Within 50 years, iodine induced hypothyroidism, autoimmune thyroiditis and hyperthyroidism had become of more concern than iodine deficiency disorders<sup>13</sup>, and the population of the USA was thought to have an excessive iodine intake.

A study in 10 states in 1975 of 35 999 individuals found the goitre prevalence in all age groups to be 3.1%<sup>14</sup>. There was no association between having a goitre and a low urinary iodine (UI) concentration. Instead, a higher prevalence of goitre was documented among people with a high concentration of iodine in their urine. The median UI concentration in the study was 250  $\mu\text{g g}^{-1}$  creatinine, and <2% of subjects had a concentration below 50  $\mu\text{g g}^{-1}$  creatinine<sup>14</sup>.

Another study, of 7785 children aged 9–16 years in four areas of the USA, found an overall prevalence of palpable,

but not visible, goitre of 6.8%. No clinical or biochemical abnormalities were found. Children with goitre in localities with a high goitre rate tended to have a high UI concentration<sup>15</sup>.

The first NHANES survey conducted between 1971 and 1974 found a median UI concentration of  $320 \mu\text{g l}^{-1}$ . Among the overall study population, 2.6% of UI concentrations were  $<50 \mu\text{g per l}^{16}$ , findings similar to the Canadian national survey of 1969–72<sup>17</sup>.

Surveys from 1982 to 1991 during the Total Diet Study monitored the concentration of iodine in the food supply and showed a decline in iodine intake, although the authors argued that this did not represent a trend<sup>18</sup>. The decrease in iodine intake since 1984 could be explained by the reduction in the amount of iodine in milk and by the replacement of iodine with bromine salts during commercial bread production<sup>19</sup>. The total consumption of iodised salt, which is typically added in the USA as potassium iodide to give a concentration of  $77 \mu\text{g}$  iodine per of salt, was thought to be about 60% of all salt consumed<sup>20</sup>.

During NHANES III surveys from 1988 to 1994, the median UI concentration was  $145 \mu\text{g l}^{-1}$ , a decrease of more than 50% from the value of  $320 \mu\text{g l}^{-1}$  recorded during NHANES I<sup>16</sup>. This is shown in Fig. 1. There was also an increase in the prevalence of UI concentrations below  $50 \mu\text{g l}^{-1}$ : 11.6% in the 1988–94 survey compared with 2.4% between 1971 and 1974<sup>16</sup>. This is shown in Fig. 2. The prevalence of a UI concentration of  $<50 \mu\text{g l}^{-1}$  exceeded 20% only among women aged 40–59 years, for whom it was 23%<sup>16</sup>. The prevalence of a UI concentration of  $>500 \mu\text{g l}^{-1}$  decreased between surveys from 27.8 to 5.3% and the prevalence of a concentration of over  $1000 \mu\text{g l}^{-1}$ , from 5.3 to 1.3%<sup>16</sup>.

Using World Health Organisation (WHO) thresholds of more than a half of the population excreting  $>100 \mu\text{g l}^{-1}$  of UI and  $<20\%$  of the population excreting  $<50 \mu\text{g l}^{-1}$ , the data from NHANES III were interpreted to indicate

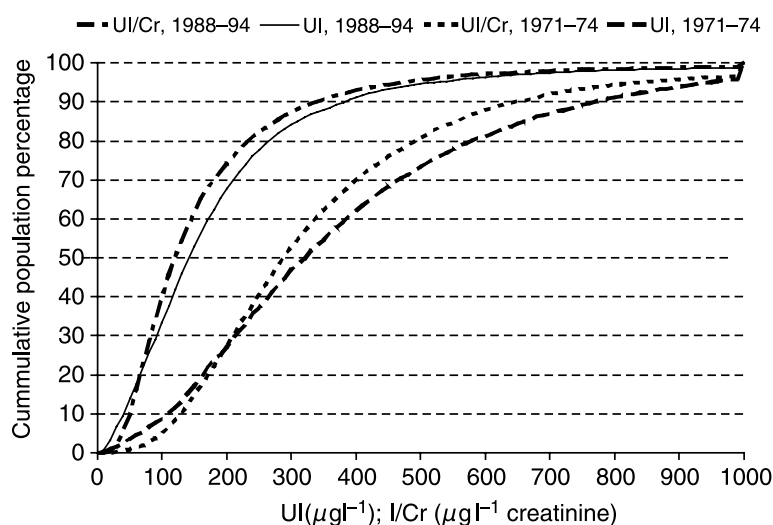
that iodine status of the population of the USA was adequate<sup>21</sup>. This was supported by Dr John Dunn in the accompanying editorial who emphasised the importance of continuing to monitor the iodine status of the population of the USA<sup>22</sup>.

Other reports gave a more cautious interpretation of the data and expressed concern that the USA population was entering the 21st century with an iodine deficiency<sup>23</sup>. An editorial<sup>24</sup> accompanying a paper on children born to women with hypothyroidism<sup>25</sup> warned that iodine deficiency was a possible reason for the thyroid deficiency observed in women, and could be an emerging cause of hypothyroidism in the USA.

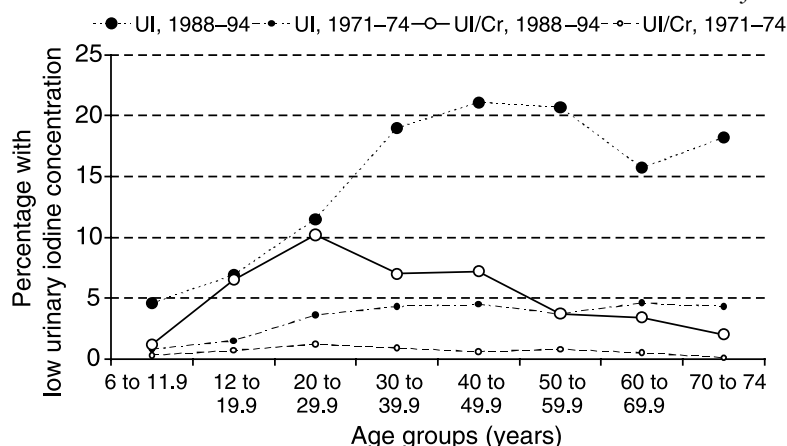
Using data from these two surveys done between 1971–74 and 1988–94, it was not possible to know if the USA was experiencing a trend of decreasing iodine intake that would continue, or whether a change had already occurred and the intake had stabilised. No further decrease in UI concentration was found when the two phases of NHANES III from 1988 to 1991 were compared with 1991–94<sup>16</sup>. The stability of the median UI concentration over the 6 years of sampling during NHANES III was reinforced by data released from NHANES 2000, which showed a median UI concentration of  $161 \mu\text{g per l}^{-1}$ <sup>26</sup>. The median values recorded in these surveys are shown in Fig. 3. Data on the UI concentration recorded in surveys from 2001 to 2002 in the USA showed the median to be  $168 \mu\text{g per l}^{-1}$ <sup>27</sup>. This suggests that the decrease seen in 1988–94 did not represent a trend, but had already occurred and was stabilised as reported by Pennington and Schoen<sup>18</sup>.

## Subjects and methods

The NHANES surveys are designed to give national, normative estimates of the health and nutritional status of



**Fig. 1** The cumulative prevalence of urinary iodine concentration (UI) and  $\text{UI g}^{-1}$  creatinine in people aged 6–74 years in the USA in the NHANES I survey (1971–74) and in NHANES III (1988–94). The concentrations of UI and UI/Cr both decreased by more than 50% between surveys. Adapted from reference 16.



**Fig. 2** The percentage of females in the United States by decade of life with urinary iodine (UI) concentrations  $<50 \mu\text{g l}^{-1}$  or  $<50 \mu\text{g UI g}^{-1}$  creatinine (Cr) in the NHANES 1 survey (1971–74) and in NHANES III (1988–94). In the later survey, greater proportions of females in all decades of life have lower iodine values than in the first survey. This is especially true for women aged 40–59 years, and more than 20% of women fall into this category. The pattern of  $\text{UI g}^{-1}$  Cr is different from UI alone: the highest proportion of values in that category (10%) is among women aged 20–29 years. Adapted from reference 16.

the civilian, non-institutionalised population of the USA. The NHANES III survey was conducted from 1988 to 1994<sup>28</sup>. Descriptions of how samples were collected and laboratory methods have been described previously<sup>29</sup>. Assays were done for UI concentration, thyroid-stimulating hormone (TSH) and thyroxine ( $\text{T}_4$ ).

Data on UI concentration were available for 5405 women of reproductive age, defined as 15–44 years inclusive, of whom 348 were pregnant. Data on UI and TSH were available for 4929 of these women; 312 were pregnant. Data were also collected on age; race or ethnic origin classified as white non-Hispanic, black

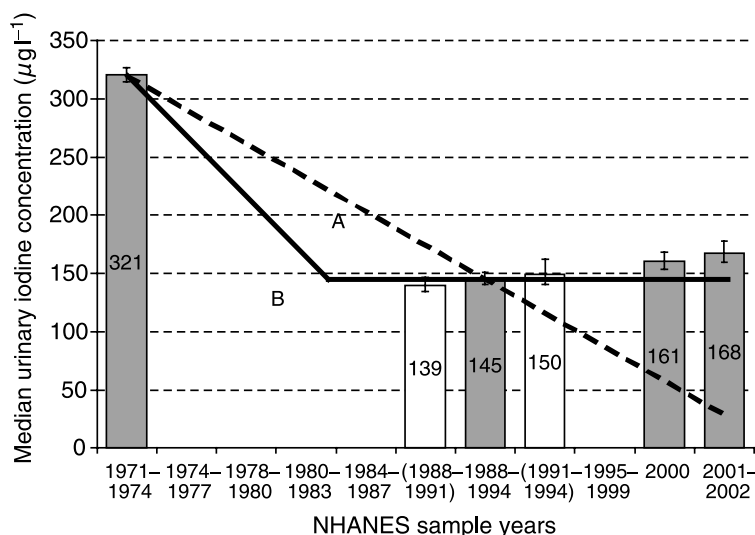
non-Hispanic, Mexican-American and remaining groups; and region of the country, divided into the north-east, mid-west, south and west.

The data were analysed using SUDAAN software (Research Triangle Institute, NC, USA) in which sample weights were applied to account for the complex survey design.

## Results

### Urinary iodine concentration

The median UI concentration of women of reproductive age in the period 1988–94 was significantly lower than in



**Fig. 3** The median urinary iodine concentration (UI) of the United States population at NHANES surveys between 1971 and 2002 with 95% confidence intervals. The open bars present data for the two phases of NHANES III in 1988–91 and 1991–94; there was no difference between the medians and the shaded bar between them is the overall median for the whole NHANES III survey (1988–94)<sup>16</sup>. Subsequent surveys, which had fewer samples, showed the UI (median UI,  $161 \mu\text{g l}^{-1}$  in 2000<sup>26</sup> and  $168 \mu\text{g l}^{-1}$  in 2001–02<sup>27</sup>) not to be lower, and possibly higher, than in 1988–94 (median UI  $145 \mu\text{g l}^{-1}$ ). The data between 1971–74 and 1988–94 created the concern for a downward trend, represented by the dashed line (A), which has not materialised, whereas the continuous line B represents is believed to have occurred: the decrease had levelled off prior to 1988–94 as reported by Pennington and Schoen<sup>18</sup> and as suggested by the two phases of NHANES III. Adapted from reference 36.

1971–74, and the prevalence of women with a UI concentration  $<50 \mu\text{g l}^{-1}$  was higher, among both pregnant and non-pregnant women (Table 1). In 1988–94 the median UI of pregnant women was  $140.5 \mu\text{g l}^{-1}$  (95% CI 124.3–180.2). This was higher than the median UI concentration of  $126.6 \mu\text{g l}^{-1}$  for non-pregnant women (95% CI 120.1–135.1). Mexican-American and black, non-Hispanic women had higher median concentrations than white, non-Hispanic women, whether pregnant or not (Table 2). Non-pregnant women from the south had a higher median UI concentration than women in the other regions, but pregnant women from the west had the highest median concentration (Table 3). Non-pregnant women aged 15–24 years had a higher median UI concentration than women of other ages. This pattern was not seen in pregnant women. There was considerable variation among the subgroups in the USA available for analysis. In pregnant, white, non-Hispanic women and women aged 15–19 and 30–34 years, the median UI concentrations were above  $100 \mu\text{g l}^{-1}$ , but the lower 95% confidence limits fell below 100.

### Thyroid-related hormones

The highest mean TSH concentration was found in pregnant and non-pregnant, white, non-Hispanic women. The lowest concentrations were found in pregnant and non-pregnant black, non-Hispanic women. Among non-pregnant women, the prevalence of women with a TSH value  $>4.5 \text{ mIU l}^{-1}$  was highest in Mexican-American women (5.1%) and lowest in black, non-Hispanic women (0.7%); among pregnant women, however, the prevalence was lowest in Mexican-American women. The concentration of total  $T_4$  was similar among all races and ethnic groups of pregnant women, but was slightly higher in Mexican-American women than the rest.

### Relationship between urinary iodine concentration and thyroid-related hormones

To evaluate the association between the concentration of UI and thyroid-related hormones, data were analysed for all women of reproductive age. For this analysis, the UI concentrations were divided into three ranges: 0–99, 100–299, and  $300 \mu\text{g l}^{-1}$  and above. Table 4 shows the geometric mean and mean concentrations of TSH and  $T_4$ ,

respectively, by pregnancy status for each of the three groups of UI concentration. A high value of TSH is defined as  $>4.5 \text{ mIU l}^{-1}$ . A low concentration of UI in women of reproductive age does not appear to be associated with a thyroid deficiency, as measured by the concentration of TSH or  $T_4$ .

Because of the concern expressed in a recent publication that ‘... 7.6% of the pregnant women in the USA are still affected by moderate to severe iodine deficiency’<sup>3</sup>, data were analysed for 23 pregnant women with a UI concentration of  $<50 \mu\text{g l}^{-1}$ , seven of whom also had an iodine concentration of  $<50 \mu\text{g g}^{-1}$  creatinine. Their TSH concentrations ranged from 0.15 to  $4.0 \text{ mIU l}^{-1}$  and their  $T_4$  concentration from  $45.0$  to  $243.2 \text{ nmol l}^{-1}$  ( $3.5$ – $18.9 \mu\text{g dl}^{-1}$ ). Only one of the women had a  $T_4$  concentration  $<128.7 \text{ nmol ml}^{-1}$  ( $<10 \mu\text{g dl}^{-1}$ ) and a TSH concentration  $>2.5 \text{ mIU l}^{-1}$  ( $T_4$   $124 \text{ nmol l}^{-1}$  ( $9.6 \mu\text{g dl}^{-1}$ ), TSH  $4.0 \text{ mIU l}^{-1}$ , UI  $26 \mu\text{g l}^{-1}$  and UI/Cr  $85.2 \mu\text{g g}^{-1}$  creatinine).

### Discussion

The NHANES III survey provides a representative sample of the population of the USA who can be classified according to the WHO thresholds for assessing iodine status. The WHO thresholds are based on the median UI concentration of school-aged children and the proportion with values  $<50 \mu\text{g per l}^{21}$ . The NHANES III data for women of reproductive age gave a median UI concentration of  $128 \mu\text{g l}^{-1}$ , with 14.9% of values  $<50 \mu\text{g l}^{-1}$ . For a published report on the iodine status of children in countries with sufficient iodine, nutrition values were included from NHANES III that were much higher than expected because they represented the entire population of the USA, 70% of which was older than 20 years of age<sup>30</sup>. In a recent publication, data from NHANES III were presented on 6460 children aged 6–17 years that gave a median UI concentration of  $197.4 \pm 1.0 \text{ SE } \mu\text{g l}^{-1}$ , with  $4.2 \pm \text{SE } 0.4\%$  of values  $<50 \mu\text{g per l}^{27}$ . These values for school-aged children are consistent with values reported from other countries with adequate iodisation programmes<sup>30</sup>. The fact that children excrete a higher concentration of iodine in fasting urine samples than older persons should be considered when applying the

**Table 1** The median concentration and standard error (SE) of iodine in the urine women of reproductive age (15–44 years inclusive) in the USA measured in 1971–74 (NHANES I) and 1988–94 (NHANES III), and the percentage (SE) with a urinary iodine concentration  $<50 \mu\text{g l}^{-1}$ . Adapted from reference 16.

	NHANES I (1971–74)			NHANES III (1988–94)		
	<i>n</i>	Median UI $\mu\text{g l}^{-1}$ (SE)	% $<50 \mu\text{g l}^{-1}$ (SE)	<i>n</i>	Median UI $\mu\text{g l}^{-1}$ (SE)	% $<50 \mu\text{g l}^{-1}$ (SE)
Total	5279	294 (10)	3.9 (0.5)	5405	128 (4)	14.9 (1.1)
Pregnant	208	327 (35)	1.0 (0.6)	348	141 (14)	6.9 (1.9)
Not pregnant	5071	293 (10)	4.0 (0.5)	5057	127 (4)	15.3 (1.2)

**Table 2** The median urinary iodine (UI) concentration of women of reproductive age (15–44 years inclusive) by pregnancy status, ethnic origin and race in the NHANES III survey in the USA, 1988–94.

Study groups	Sample	Population	Median UI ( $\mu\text{g l}^{-1}$ )	95% confidence intervals	
				Upper	Lower
All women					
White, non-Hispanic	1609	42 487 075	123.7	117.0	131.6
Black, non-Hispanic	1865	8 239 795	133.7	129.6	139.3
Mexican-American	1931	9 551 618	139.2	122.8	166.4
Total	5405	60 278 488	128.0	120.9	136.4
Pregnant					
White, non-Hispanic	84	2 416 959	132.2	61.4	265.8
Black, non-Hispanic	110	503 819	155.5	143.9	192.5
Mexican-American	154	489 814	142.7	106.4	192.0
Total	348	3 410 592	140.5	124.3	180.2
Not pregnant					
White, non-Hispanic	1525	40 070 116	123.0	115.3	130.6
Black, non-Hispanic	1755	7 735 976	131.3	126.4	137.5
Mexican-American	1777	9 061 804	139.1	123.0	165.4
Total	5057	56 867 896	126.6	120.1	135.1

median and low values to an older population. It is possible that additional guidelines, based on new studies, are needed when assessing the iodine status of adults, including pregnant and lactating women.

The intake of iodine recommended for pregnant women by the Food and Nutrition Board (FNB) of the US Institute of Medicine (IOM) is  $220 \mu\text{g day}^{-1}$ , which corresponds to a UI concentration of  $150 \mu\text{g per l}^{31}$ . The NHANES III median UI value in pregnant women was  $141 \mu\text{g per l}^{16}$ . This has contributed to a heightened concern about iodine nutrition during pregnancy in the USA.

In a study of 100 pregnant women in Boston, USA, the UI concentration was consistent with adequate iodine nutrition as defined by the WHO, but 49% of the women had values which fell below the IOM recommendation for pregnancy<sup>32</sup>. The authors pointed out that, although cretinism is not a problem in the USA, an inadequate iodine intake may have subtle effects on foetal development<sup>33</sup>.

Data on infants and lactating women in the USA are not readily available. A study in 1983 found that the concentration of iodine in breast milk samples from 16 subjects ranged from 21 to  $281 \mu\text{g kg}^{-1}$  with an average of  $142 \mu\text{g per kg}^{33}$ . Pearce and Braverman in Boston reported a median iodine concentration of  $157 \mu\text{g l}^{-1}$  (mean  $208 \mu\text{g l}^{-1}$ ) in breast milk samples collected from 27 women<sup>34</sup>. There was no correlation between the concentration of iodine in breast milk and in urine<sup>34</sup>. Among the 27 women, 44% of breast milk samples contained insufficient iodine to meet the infant's needs when calculated using the IOM recommendation of  $110 \mu\text{g day}^{-1}$  for infants aged 0–6 months and  $130 \mu\text{g day}^{-1}$  for infants aged 7–12 months<sup>34</sup>. Semba and Delange concluded that, to meet the FNB recommendations, breast milk should contain  $100\text{--}200 \mu\text{g l}^{-1}$  of iodine<sup>35</sup>.

Because of the current uncertainty about iodine status during pregnancy and lactation, even in populations believed to have adequate iodine nutrition, recommendations are being proposed that iodine supplements should be given during those periods and in anticipation of pregnancy. At a workshop on the thyroid gland and pregnancy, Dr John Dunn of the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) proposed the following statement which was endorsed by Dr Francois Delange (ICCIDD), Dr Bruno de Benoist (WHO) and Dr Ian Darnton-Hill (UNICEF): *Iodine nutrition needs to be included in any assessment of the impact of maternal thyroid status on the foetus. Efforts to promote optimal iodine nutrition in pregnancy are essential. Strong consideration should be given to including adequate iodine ( $150 \mu\text{g}$  or more daily) in all vitamin/mineral preparations used in pregnancy*<sup>36</sup>. Data from NHANES III indicate that the intake of supplementary iodine by pregnant and lactating women averaged  $158 \mu\text{g}$  (median  $128 \mu\text{g}$ ) per day<sup>31</sup>.

In a study of pregnant women in New England, Mitchell and colleagues found that the serum thyroglobulin concentration was neither increased in women with a normal TSH concentration, nor was the thyroglobulin concentration different from that of normal, non-pregnant women<sup>37</sup>. In thyroid-deficient women, thyroglobulin and TSH values were higher, and the free  $T_4$  concentration was lower. This was interpreted to mean that iodine nutrition was adequate in this population of pregnant women<sup>37</sup>.

In order to assess whether there was evidence of iodine deficiency in the United States population, an analysis of the NHANES III data by logistic regression examined the relationship between iodine deficiency assessed by UI concentration and thyroid-related hormones, using a model that included age, region, sex and UI concentration. The study showed that only a

**Table 3** Median urinary (UI) concentration of women of reproductive age (15–44 years inclusive) by whether pregnant or not, region and age group in the NHANES III survey in the USA, 1988–94 (\*insufficient data).

Region	Pregnant women					Non-pregnant women					
	Age group	Sample size	Population	Median UI ( $\mu\text{g l}^{-1}$ )	95% CI		Sample size	Population	Median UI ( $\mu\text{g l}^{-1}$ )	95% CI	
					Lower	Upper				Lower	Upper
All women											
15–19	64	452 530	143.2	89.0	243.8	910	8 211 598	163.1	149.2	177.8	
20–24	119	1 175 585	127.3	111.0	196.1	829	9 036 883	130.9	123.7	147.7	
25–29	79	804 535	168.7	128.2	208.5	787	8 878 923	119.1	108.1	134.2	
30–34	64	776 590	104.2	91.4	179.5	863	10 111 732	120.2	112.0	134.9	
35–39	19	114 009	166.6	141.8	421.4	865	10 656 869	114.8	100.0	131.8	
40–44	3	87 344	*	*	*	803	9 971 891	115.0	104.1	132.2	
Total	348	3 410 592	140.5	124.3	180.2	5057	56 867 896	126.6	120.1	135.1	
North-east											
15–19	5	95 388	64.1	*	*	116	1 695 270	141.6	113.6	275.5	
20–24	9	226 177	236.1	83.1	365.3	124	2 346 123	107.8	100.0	131.2	
25–29	6	113 919	127.9	101.7	154.1	102	1 921 815	89.3	79.5	123.7	
30–34	11	160 017	104.7	*	*	89	1 605 360	113.0	97.0	168.3	
35–39	2	6281	*	*	*	119	2 297 556	119.0	93.1	231.7	
40–44	0	0	*	*	*	105	1 871 249	133.9	86.6	169.2	
Total	33	601 782	131.1	95.8	278.5	655	11 737 372	114.8	103.2	136.5	
Mid-west											
15–19	7	63 407	362.7	147.5		168	1 761 540	150.6	130.7	189.9	
20–24	23	275 564	125.3	75.8	164.5	127	1 567 142	150.0	124.6	171.6	
25–29	12	171 497	130.2	110.4	209.1	152	2 308 662	124.6	115.1	147.0	
30–34	13	180 862	92.6	76.0	149.3	185	2 586 679	100.9	79.5	114.0	
35–39	4	35 078	*	*	*	165	2 347 801	100.2	77.3	128.3	
40–44	1	3785	*	*	*	156	2 496 203	106.9	88.6	143.1	
Total	60	730 193	128.6	111.4	196.5	953	13 068 027	119.2	113.0	126.8	
South											
15–19	30	228 347	141.0	130.5	249.9	408	3 024 899	175.9	156.0	187.2	
20–24	53	478 319	118.2	92.6	153.9	362	3 620 190	134.4	122.0	168.2	
25–29	35	303 995	217.2	130.7	261.6	320	2 935 470	139.3	115.3	165.8	
30–34	15	222 386	98.5	*	312.3	366	3 270 005	133.7	127.6	144.8	
35–39	5	21 896	421.0	85.5	*	354	3 516 736	131.7	110.9	162.6	
40–44	0	0	*	*	*	354	3 657 515	109.5	95.5	138.0	
Total	138	1 254 943	131.8	118.6	207.8	2164	20 024 815	137.9	129.6	148.5	
West											
15–19	22	65 388	125.3	71.6	282.0	218	1 729 888	159.6	142.2	172.9	
20–24	34	195 524	186.2	101.9	187.8	216	1 503 429	139.0	105.6	183.9	
25–29	26	215 124	168.4	74.8	169.7	213	1 712 976	124.6	95.0	178.8	
30–34	25	213 325	147.6	64.0	216.0	223	2 649 688	139.5	93.5	180.0	
35–39	8	50 754	134.6	99.1	*	227	2 494 777	96.5	65.4	137.3	
40–44	2	83 559	*	*	*	188	1 946 924	118.5	100.0	144.4	
Total	117	823 674	169.9	127.7	276.4	1285	12 037 682	129.3	103.8	157.3	

high UI concentration of more than  $1000 \mu\text{g g}^{-1}$  creatinine was associated with a TSH concentration  $>4.5 \text{ mIU l}^{-1}$ . There was no significant difference in the proportion of study subjects with TSH values  $>4.5 \text{ mIU l}^{-1}$  in association with a low UI concentration<sup>38</sup>. Another analysis of data from the NHANES III survey using a different statistical technique also failed to show evidence of iodine deficiency when defined using the concentrations of  $T_4$  and TSH. In that study, the lower range of iodine concentrations, when adjusted for creatinine concentration, was associated with a low TSH concentration. When grouped by decile of iodine concentration, with approximately 1400 study subjects per decile, the median total  $T_4$  measurements ranged between  $110.7$  and  $113.3 \text{ nmol l}^{-1}$  and show no trend.

The median TSH values, however, ranged from a low of  $1.30 \text{ mIU l}^{-1}$  in the lowest iodine decile to  $1.60 \text{ mIU l}^{-1}$  in the highest iodine decile<sup>39</sup>.

In the current study, a similar trend was seen in women of reproductive age when comparing the UI concentration with the TSH concentration, but it did not achieve statistical significance.

In the NHANES III survey, as described elsewhere<sup>40</sup>, we believe that an otherwise normal individual may excrete a concentration of iodine  $<50 \mu\text{g l}^{-1}$  at the time of study, but this value does not necessarily reflect the long-term pattern for that individual. At other times, the same individual may ingest excessive amounts of iodine and thyroid function remains normal. As we show here, the NHANES data represent the status of a population and is not designed to



**Table 4** The geometric mean and standard error (SE) of the concentration of serum thyroid-stimulating hormone (TSH); the percentage of women with TSH concentrations  $>4.5 \text{ mIU l}^{-1}$  with the SE of the prevalence; and the serum thyroxine concentration, by pregnancy status in the NHANES III survey of women aged 15–44 years inclusive in the USA, 1988–94, with the statistical significance of differences between groups.

Variable Study group			Urinary iodine ranges ( $\mu\text{g l}^{-1}$ )			Statistical significance		
			0–99.9	10–299	300 +			
			Total	1	2	3	1–2	1–3
TSH ( $\text{mIU l}^{-1}$ )								
All women	<i>N</i>	4929	1591	2642	696			
	Geometric mean	1.33	1.31	1.32	1.45	NS	NS	NS
	SE geometric mean	0.03	0.04	0.03	0.06			
Pregnant	<i>N</i>	312	80	174	58			
	Geometric mean	1.14	1.23	0.97	1.55	NS	NS	NS
	SE geometric mean	0.10	0.15	0.13	0.72			
Not pregnant	<i>N</i>	4617	1511	2468	938			
	Geometric mean	1.35	1.32	1.35	1.44	NS	NS	NS
	SE geometric mean	0.03	0.04	0.03	0.06			
% with TSH $>4.5 \text{ mIU l}^{-1}$								
All women	<i>N</i>	4929	1591	2642	696			
	Prevalence (%)	2.76	2.18	2.98	3.53	NS	NS	NS
	SE prevalence	0.45	0.47	0.68	1.25			
Pregnant	<i>N</i>	312	80	174	58			
	Prevalence (%)	1.33	0.00	0.19	6.15	NS	NS	NS
	SE prevalence	1.11	0.00	0.19	5.67			
Not pregnant	<i>N</i>	4617	1511	2468	638			
	Prevalence (%)	2.85	2.28	3.15	3.27	NS	NS	NS
	SE prevalence	0.49	0.49	0.74	1.25			
Thyroxine ( $\text{T}_4$ ) ( $\text{nmol l}^{-1}$ )								
All women	<i>N</i>	4929	1591	2642	696			
	Mean	119.9	119.3	120.0	120.7	NS	NS	NS
	SE mean	1.0	1.3	1.3	2.0			
Pregnant	<i>N</i>	312	80	174	58			
	Mean	147.1	145.4	150.2	141.7	NS	NS	NS
	SE mean	2.5	5.0	3.8	3.4			
Not pregnant	<i>N</i>	4617	1511	2468	638			
	Mean	118.2	118.1	118.2	118.5	NS	NS	NS
	SE mean	1.1	1.4	1.5	2.2			

label individuals or specific subgroups as definitively abnormal. When a subgroup, such as women of reproductive age, is demonstrated to be affected by moderate or severe iodine deficiency, immediate remedies would be indicated for the entire population. The data at hand do not support the conclusion that the group of pregnant women, or any other group in the USA, is deficient in iodine.

The WHO thresholds are based on UI concentrations correlated with goitre rates in school children. These measurements have been used to estimate the adequacy of iodine nutrition in children and then generalised to estimate the iodine status of the population. The time has come to establish similar guidelines and criteria for other age groups or biological states, such as pregnancy. These criteria should be derived by relating the UI concentration of each subgroup with physiological outcomes, such as the goitre rate, the serum thyroglobulin concentration or, perhaps some other sensitive biological outcome. Until this is done, the estimated risk for the subgroup being studied may not be understood and could be inaccurate. Until such research is completed, we support the use of iodine supplements by all

pregnant women because of the potential harm of iodine deficiency during pregnancy.

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