Chapter 3
Epidemiology of Iodine Deficiency

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Abstract Global efforts to control iodine deficiency through the highly successful strategy of salt iodization have been in effect for over two decades. In 2016, urinary iodine concentration (UIC) data in school-age children are available for 127 countries: 15 countries are classified as iodine deficient, 102 have optimal iodine nutrition, and 10 have excess iodine intakes. This reflects tremendous global progress against iodine deficiency. Increasingly, countries are recognizing the importance of monitoring the iodine status in populations that are particularly vulnerable to the negative consequences of iodine deficiency, such as pregnant women. For the first time, global UIC data in pregnant women have been compiled and presented, based on surveys from 65 countries. The iodine intake in pregnant women is insufficient in 37 countries, and the main challenge is to further strengthen the delivery of salt iodization programs to ensure that iodized salt meets the iodine requirements of pregnant women.

Abbreviations

EAR	Estimated average requirement
IDD	Iodine deficiency disorders
ICCIDD	International Council for the Control of Iodine Deficiency Disorders
IGN	Iodine Global Network
PW	Pregnant women
SAC	School-age children
TGR	Total goiter rate
UIC	Urinary iodine concentration
WHO	World Health Organization
WRA	Women of reproductive age

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E.N. Pearce (ed.), *Iodine Deficiency Disorders and Their Elimination*,
DOI 10.1007/978-3-319-49505-7_3

Introduction

Iodine deficiency is the result of insufficient dietary iodine intake, which can lead to inadequate production of thyroid hormones and many adverse effects at all life stages, collectively known as iodine deficiency disorders (IDD) [1–3]. Thyroid hormones are particularly critical for fetal neurodevelopment, and severe iodine deficiency during pregnancy may result in maternal and fetal hypothyroidism and cognitive impairment in children, but the effects of mild-to-moderate iodine deficiency are less clear [4, 5]. Iodine deficiency during pregnancy remains a common cause of preventable cognitive impairment worldwide [6, 7]. The universality of iodine deficiency and its devastating impact on health and development have been at the root of global control efforts through salt iodization since the 1920s [8]. Yet, in spite of tremendous progress realized and achievement of high levels of program coverage in many countries, iodine deficiency remains a threat to global public health, with its greatest impact on infants and pregnant women [9].

Global Distribution of Iodine Deficiency

Iodine deficiency is an ecological phenomenon in many parts of the world [2]. Iodine distribution in the environment is wide but uneven, with the highest concentrations found in the oceans (45–60 μg/L) [10]. From the ocean surface, iodine volatilizes into the atmosphere and is returned to land with rain and snowfall [11]. In areas affected by past glaciation and denudation this cycle is slow, and iodine is only partially replenished [12]. In many regions, the loss of iodine from the topsoil is exacerbated by high rainfall, flooding, deforestation, and overgrazing by livestock. Crops grown in iodine-depleted soils typically do not contain enough iodine to cover the dietary needs of people and livestock. As a result, populations consuming them will become iodine deficient unless iodine is reintroduced into the food chain through deliberate efforts or public health programs, e.g., salt iodization [13].

A recognized clinical indicator of thyroid dysfunction, goiter was traditionally relied on to identify regions of low iodine intake [14]. High goiter rates were reported among populations living in mountain ranges and on alluvial plains, which led to the misperception that iodine deficiency was geographically confined to these areas [2]. With the increasing use of urinary iodine concentration (UIC), which reflects a broad range of iodine intakes, the global distribution of iodine deficiency has been better understood. It is now recognized that iodine deficiency may be present (albeit in milder forms) in regions without endemic goiter, in coastal areas, large cities, and industrialized countries, where it previously had been considered to be non-existent [2, 15]. Many of the worst affected regions are also the most heavily populated (Table 3.1) [16].

Table 3.1 Regions with naturally low soil iodine levels

Asia, including parts of China, India, Bangladesh, the Himalayan hillsides, and Indonesia
Africa, including the mountains of Morocco and Algeria (e.g., Atlas Mountains); much of west and central Africa (e.g., Nigeria, Cameroon, the Central African Republic, Democratic Republic of Congo), and some areas of East Africa (e.g., Uganda, Ethiopia)
Europe, including the European Alps and the Pyrenees, inland areas of England and Wales, Greece, and The Netherlands
South America, including the Andes and inland Brazil
Midwestern United States
Southern Australia
Highlands of New Guinea

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Global Monitoring of Iodine Nutrition

Collecting and reporting of national, regional, and global data on iodine status has been essential for estimating the current magnitude of iodine deficiency, tracking national progress and effectiveness of prevention strategies, and identifying population groups or pocket areas that may be at risk of insufficient or excessive iodine intakes [2]. Since 2005, the World Health Organization (WHO) has reported on the global iodine status to the World Health Assembly every 3 years, most recently in 2016 [17, 18]. All countries are advised to assess their population iodine status every 5 years, even if they have already achieved optimal iodine nutrition, to reinforce the importance of program sustainability, as well as to safeguard against program backsliding and re-emergence of iodine deficiency as a public health problem [2, 17, 19].

Biomarkers of Iodine Status

Since 2001, UIC in school-age children (SAC, aged 6–12 years) has been the main indicator of iodine status and has been considered a proxy for the general population. Criteria have been established based on the median UIC level to determine the iodine status of populations (Table 3.2) [2]. The shift from reliance on goiter to an objective biomarker of exposure has improved the availability and quality of nationally representative data. Unlike goiter, UIC reacts immediately to changes in iodine intake and is, thus, ideal for monitoring the impact of salt iodization programs [2, 20].

Table 3.2 Epidemiological criteria for assessing population iodine nutrition based on median urinary iodine concentrations (mUIC) of school-age children (≥6 years)[a] [2]

Median UIC (μg/L)	Iodine intake	Iodine nutrition status
<20	Insufficient	Severe iodine deficiency
20–49	Insufficient	Moderate iodine deficiency
50–99	Insufficient	Mild iodine deficiency
100–199	Adequate	Adequate iodine nutrition
200–299	Above requirements	Likely to provide adequate intake for pregnant/lactating women, but may pose a slight risk of more than adequate intake in the overall population
≥300	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases)

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[a] Applies to adults, but not to pregnant and lactating women

Global Databases on Iodine Nutrition

The WHO online Global Database on Iodine Deficiency is a repository of national and sub-national data from population-based surveys of iodine status conducted between 1960 and 2007 [21]. Although the mandate to track and report the global progress against iodine deficiency lies with WHO, since 2011 the collection of population data has been supported by the Iodine Global Network (IGN, previously known as the International Council for the Control of Iodine Deficiency Disorders, ICCIDD), a technical advisory group to the WHO on iodine nutrition [22]. The available studies and estimates can be accessed on the IGN's website, where they are regularly updated [23].

Methods to Estimate the Global Burden of Iodine Deficiency

To estimate the global status of iodine nutrition, national or sub-national UIC surveys with a population-based sampling frame and using accredited UIC analysis techniques are considered for inclusion. Nationally-representative UIC surveys are given priority over sub-national studies. Between 2003 and 2012, global estimates reported UIC data collected over the preceding 10 year period, while the 2016 estimates extend this time-frame to 15 years. In an effort to harmonize data reporting, the 2016 global estimate is the first to rely exclusively on data in school-age children (6–12 years) to estimate the iodine status in the general population (see Sect. 5 and Table 3.3). Previous global estimates included national UIC data from pre-school children, women of reproductive age, and adults when data in SAC were not available. But because the epidemiological criteria for assessing population iodine nutrition (in Table 3.2) were developed based on urine volumes and

Table 3.3 Trends in national iodine status and IDD monitoring over the period 1993–2016

Iodine status	1993[a, b]	2003[c]	2007[d]	2011[e]	2015[f]	2016[g]
Iodine deficiency	113	54	47	32	25	15
Optimal iodine status[h]	8	67	76	105	116	102
Excessive iodine intake	0	5	7	11	13	10
Countries with data	121	126	130	148	154	127
National surveys	51	75	93	115	126	107
Sub-national surveys	70	51	37	33	28	20
Surveyed population group[i]	113	112	118	132	136	127
SAC only	8	12	11	16	18	–
Other	–	2	1	–	–	–
Unknown						
Total countries[j]	**183**	**192**	**193**	**193**	**194**	**194**

[a] Iodine status based on total goiter rate (TGR) in school-age children, classified as deficient if TGR >5%

[b] [14]

[c] [27]

[d] [28]

[e] [22]

[f] [33]

[g] [34]

[h] The optimal iodine status category includes countries with adequate and more than adequate iodine intakes (see Table 3.2) [2, 26]

[i] Iodine status based on the median UIC in school-age children or, where SAC data were not available, in another population group, for example pre-school children, adolescents, reproductive-age women, the general population, or a combination (see Table 3.2) [2]

[j] WHO member states

iodine concentration data in school-age children, their application in other population groups has been challenged [19, 24, 25]. Population UIC is typically not normally distributed, and the median of the UIC distribution is used instead of the mean to classify the countries' iodine status into different degrees of public health significance (Table 3.2). For the current analysis, the acceptable range of median UICs in school-age children (100–299 μg/L) has been presented as a single category of optimal iodine intake [26].

Between 2003 and 2011, efforts were made to estimate the number of iodine deficient individuals using the UIC distribution and the reported proportion of the population with UICs below 100 μg/L [27, 28]. The national prevalence of iodine deficiency was estimated by multiplying this proportion by the country's total population (of SAC and the general population), and the data were pooled for regional and global estimates [19, 22]. In recent years this approach has come under much criticism [19] because it assumes, incorrectly, that the UIC values reported in national surveys reflect habitual iodine intake and are, therefore, good markers of individual iodine status. In practice, this is not the case as UIC levels are highly variable from day to day, and iodine concentration in a single spot urine sample reflects only recent intake [29]. This method is likely to overestimate the real prevalence of iodine deficiency and has contributed to the erroneous perception that the global progress against iodine deficiency is slowing. In 2011, this approach led to an apparent paradox, where 74% of the children globally who were classified as iodine deficient were living in countries with an adequate median UIC, and only 26% were in countries classified as iodine deficient [19, 22]. Given this limitation, the WHO UIC median of 100 µg/L is the only meaningful metric of population iodine status, as even in countries with effective USI programs and adequate iodine intakes (i.e., median UIC ≥100 µg/L), there will be a proportion of individuals with a UIC below the 100 µg/L cut-off [19]. An alternative approach to estimating the prevalence of inadequate iodine intakes based on the estimated average requirement (EAR), and using repeat spot UIC samples to better characterize variations in iodine consumption, is currently being developed [19, 30]. In the meantime, global iodine status should continue to be reported as the number of countries with overall insufficient, adequate, and excessive iodine intake based on the recommended median UIC cut-off points.

Global Trends in Iodine Nutrition

The first comprehensive review of endemic goiter, undertaken in 1960 by WHO, estimated that iodine deficiency affected approximately 20–60% of the world's population, mostly in low- and middle-income countries [31, 32]. Before the 1990s, only a few countries in the world with previously documented goiter prevalence were considered iodine sufficient, mainly due to iodized salt programs and iodine in dairy products, including Switzerland, some Scandinavian countries, the USA, Canada, and Australia [1]. The first global estimate of the number of individuals at risk of iodine deficiency followed in 1993 [14]. Based on the total prevalence of goiter in more than 120 countries, around 1.57 billion people were estimated to be living in areas at risk of iodine deficiency, 12% of the population had palpable goiter, and 2% suffered from endemic cretinism [14, 31]. Based on a total goiter prevalence (TGR) >5%, 113 out of 121 countries with data were classified as iodine deficient. In subsequent years, many countries introduced and scaled up salt iodization programs, and estimates on the coverage of iodized salt at the household level and on population iodine status became more readily available [15]. Global estimates of iodine deficiency based on UIC were published in 2003, 2007, 2011, 2015, and 2016 [22, 27, 28, 33, 34]. The number of countries classified as iodine deficient has declined consistently over the past two decades, roughly halving every 10 years, and countries classified with severe deficiency (mUIC <20 µg/L) have not been recorded for more than a decade (Fig. 3.1 and Table 3.3). Salt iodization programs, strong political commitment, and engagement with the salt industry at the global, regional, and national level have all played a pivotal role in this achievement.

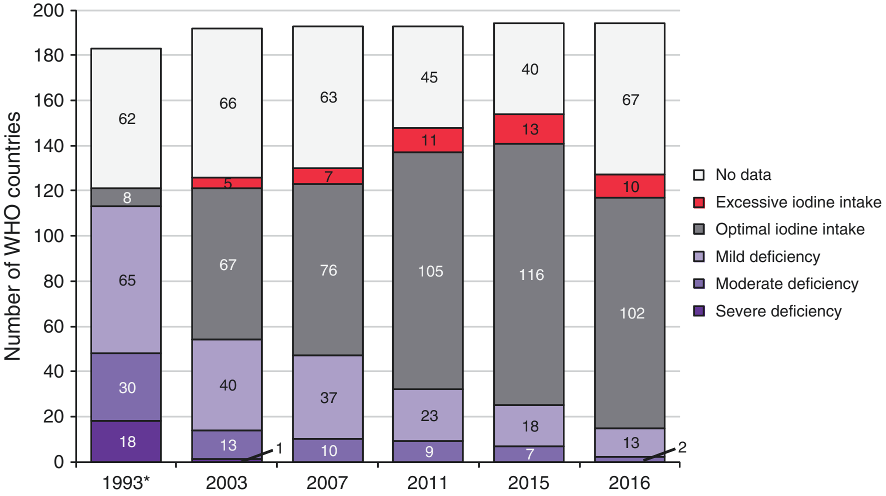

Fig. 3.1 The number of iodine deficient WHO countries has consistently declined between 1993 and 2016 [14, 27, 28, 22, 33, 34]
*In 1993, iodine deficiency is defined using total goiter rate >5%; in 2003–2016 it is defined based on median UIC in school-age children (Table 3.2)

Current Global Iodine Status

School-Age Children

The 2016 global estimate of iodine nutrition, based on surveys of school-age children conducted between 2002 and 2016, shows that the iodine intake is insufficient in 15 countries, sufficient in 102, and excessive in 10 countries (Table 3.3 and Fig. 3.2) [34]. Among the 15 countries with insufficient intake, only two are classified as moderately deficient and 13 as mildly deficient. The dwindling number of countries with insufficient iodine intake, from 32 in 2011 and 25 countries in 2015 to 15 countries in 2016 [22, 33, 34] is mainly a reflection of continuing progress to improve the coverage of iodized salt at the national level. However, the stricter data inclusion criteria applied in 2016 (see Sects. 3.3 and 3.4) have meant that eligible UIC surveys are available for fewer countries: 126 countries in 2016 compared with 154 countries in 2015, and 148 countries in 2011. This represents a drop in global population data coverage from 98.2% of 6–12 year-olds in 2015 to 93.3% in 2016, and it may confound trend analysis (Fig. 3.1). At the same time, many countries continue to sustain or strengthen their iodine monitoring efforts. Since 2015, 18 new nationally-representative surveys in SAC have been reported[1]. In 2016, there is considerable regional variation in population data coverage, ranging from more than

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[1] These include Bangladesh, Burkina Faso, China, Ecuador, Egypt, Ethiopia, Indonesia, Japan, Panama, Paraguay, Peru, Spain, Sri Lanka, Switzerland, Uruguay, Venezuela, Vietnam, and Yemen.

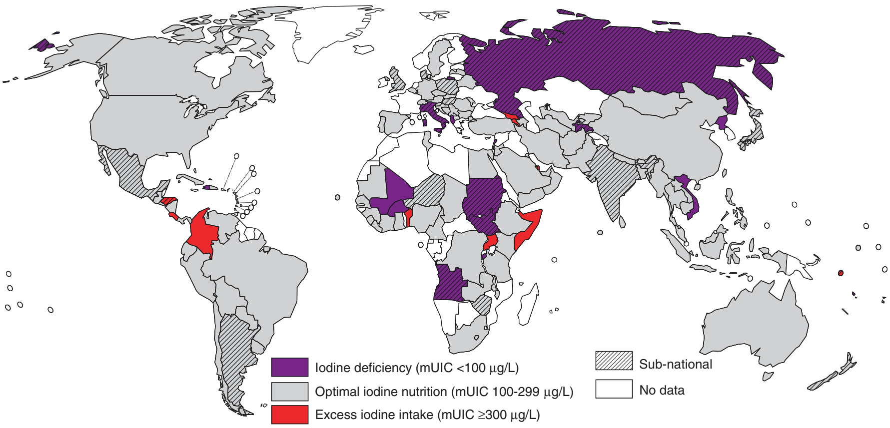

Fig. 3.2 Iodine nutrition based on the median urinary iodine concentration (mUIC) in school-age children, by country in 2016 [34]

99% in the Americas, where salt iodization and national iodine nutrition monitoring programs have been very well-implemented and effective, to approximately 80% in Europe, where iodine nutrition surveillance and prophylaxis are heterogeneous, with many countries lacking regulatory support.

Although the proportion of sub-national surveys is steadily decreasing, in 2016 they cover around 27% of the world's SAC population in 20 countries (Table 3.3). Sub-national UIC surveys are commonly carried out to provide a rapid assessment of iodine status in the population in pre-selected areas, but due to a lack of sampling rigor and adherence to basic principles of randomization, they may over- or underestimate the burden of iodine deficiency at the national level and should be interpreted with caution [1, 22].

Re-emergence of Iodine Deficiency

When iodine deficiency control programs lapse in areas that were previously considered iodine sufficient, the risk of IDD reappears, and such countries require remedial action to revitalize and strengthen the sustainability of their USI programs [35]. Like many countries which pledged to eliminate iodine deficiency at the 1990 World Summit for Children, Vietnam mandated salt iodization in the 1990s. By 2005, adequately iodized salt was reaching more than 90% of households in Vietnam, and the country was declared as iodine sufficient (with a median UIC in SAC of 139 µg/L in 2003) [22]. However, Vietnam downgraded the USI program to voluntary in 2005. The household coverage of iodized salt and the iodine status in SAC declined as a result, but the ongoing monitoring detected these declines and led to renewed efforts to reinstate the program in 2016 [36].

Vietnam's experience highlights the fact that prevention of iodine deficiency is an ongoing process, which necessitates long-term political commitment and sustainable implementation.

Australia and New Zealand are frequently cited as examples of industrialized countries where a change in dairy farming practices led to a re-appearance of iodine deficiency, when iodine-containing sterilizers were replaced with other chemicals, and the consumption of milk, the primary source of iodine in the diet, declined at the same time [37, 38]. To address these decreases in iodine intake, both countries mandated the use of iodized salt in commercially baked bread in 2009, and more recent surveys in SAC have confirmed that the iodine status has improved.

Excess Iodine Intake

Iodine excess occurs when the iodine intake is too high, generally as a result of over-iodization of salt (addition of too much iodine to salt at the point of production due to poor quality control or high iodization standards) or high intake of iodine from other sources, including iodine in local water supplies [39]. A high population intake of iodine, manifesting as a median UIC ≥300 μg/L, was reported in five countries in 2003, seven countries in 2007, and 10 countries in 2016 [27, 28, 34]. This gradual upward trend demonstrates the importance of regular monitoring of iodine status to detect not only inadequate but also excessive iodine intakes, and to better understand the sources of iodine in the diet [22]. It is important to note, however, that the benefits of correcting iodine deficiency far outweigh the health risks associated with excess.

Iodine Status and Trends in Pregnant Women

During pregnancy, the daily requirement for iodine increases from 150 μg in non-pregnant women to 250 μg to account for increased renal clearance of iodine and to cover the needs of the developing fetus [40]. In a population of pregnant women, a median UIC <150 μg/L indicates that iodine intake is insufficient, and a median UIC of 500 μg/L or higher indicates that iodine intakes are excessive (Table 3.4) [2, 41]. The increased requirement puts pregnant women and their offspring at higher risk of iodine deficiency than the general population, particularly if the availability of iodine in the diet is poor [42]. Recent studies indicate that pregnant women may be at risk of iodine deficiency even when school-age children in the same area are maintaining adequate iodine intakes [43–48]. As such, there is growing awareness of the need to monitor the iodine status of pregnant women through national surveys and to make programmatic adjustments to ensure that their needs are met.

Table 3.4 Epidemiological criteria for assessing iodine nutrition based on median and/or range of urinary iodine concentrations (UIC) in pregnant women [2]

Median UIC (μg/L)	Iodine intake	Iodine nutrition status
<150	Insufficient	Iodine deficiency
150–249	Adequate	Optimal
250–499	Above requirements	–
≥500	Excessive[a]	–

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[a] In excess of the amount required to prevent and control iodine deficiency

In 2016, recent surveys (conducted between 2002 and 2016) in pregnant women cover a third of the world's countries (65 out of 194 WHO member states) [34]. By comparison, only 42 countries had data on the iodine status of pregnant women in 2006 according to the WHO Global Database on Iodine Deficiency [20, 21]. Figure 3.3 shows the global status of iodine nutrition in 2016 based on surveys in pregnant women. Although the 65 surveys are distributed across all six WHO regions, 28 (43%) cover more than a half of the European region (Table 3.5). Data coverage is also reasonably high (6 out of 11 of countries) in South-East Asia. The lowest coverage is in Sub-Saharan Africa, where only 17%, or 7 out of 39 countries have data. It should be noted that fewer than a half of the country estimates are based on nationally representative surveys, which adds uncertainty to the data and highlights the need to systematically expand national iodine monitoring to include pregnant women.

The iodine status of pregnant women is sufficient in 23 countries, which in a majority of cases can be attributed to long-standing salt iodization programs. In these countries, the median UIC is generally lower in pregnant women compared to SAC, as seen in China (198 μg/L in SAC vs. 155 μg/L in PW in 2014), Thailand (237 μg/L in SAC vs. 156 μg/L in PW in 2014), Mongolia (171 μg/L in SAC vs. 152 μg/L in PW in 2010), and Indonesia (223 μg/L in SAC vs. 172 μg/L in PW in 2013). However, this is expected given physiological adaptations associated with pregnancy, including increased renal clearance of iodine and greater urine volume.

At the same time, the iodine intake is classified as low in 37 out of the 65 countries with available data. Globally, a number of countries are reporting adequate iodine intakes among SAC coupled with inadequate intakes in pregnant women, such as in the Philippines (mUIC of 168 μg/L in SAC vs. 105 μg/L in PW in 2013), Sri Lanka (164 μg/L in SAC vs. 113 μg/L in PW in 2010), and Belgium (113 μg/L in SAC vs. 124 μg/L in PW) [34]. A previous US NHANES reported a median UIC among 6–11 year-old children to be above 200 μg/L, but only 125 μg/L in pregnant women [49]. In Europe, three-quarters of countries report inadequate iodine intakes among pregnant women, and only 11% of countries among school-age children [34]. This emerging trend clearly highlights the need to make adjustments in the USI strategy to ensure that the dietary needs of pregnant women are met, but also to better understand how to interpret UIC data in this population group.

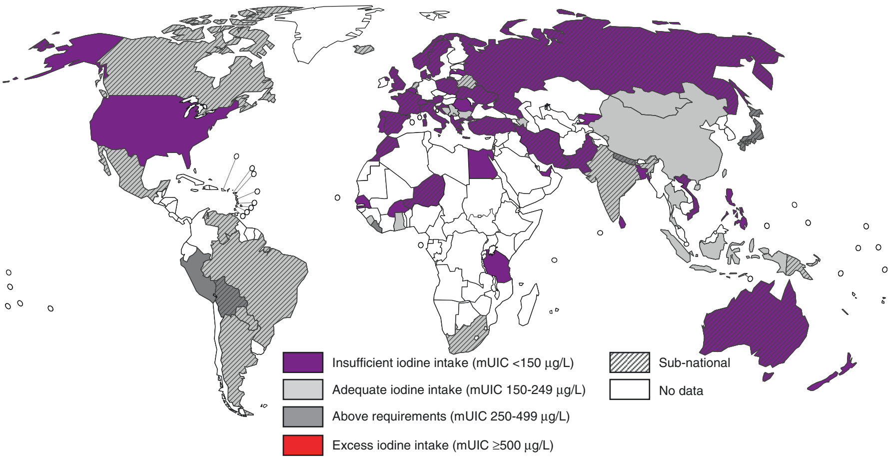

Fig. 3.3 Iodine nutrition based on the median urinary iodine concentration (mUIC) in pregnant women, by country in 2016 [34]

Table 3.5 Classification of iodine status in pregnant women (PW) based on the median urinary iodine concentration (UIC) [2] in 2016, by country [34]

		Iodine status in PW			Survey administrative level		
WHO Region	Total countries[a]	Iodine deficiency	Optimal	Above require-ments	National	Sub-national	Countries with no data
Sub-Saharan Africa	47	4	3	1	6	2	39
Americas	35	1	6	2	2	7	26
Eastern Mediterranean	21	5	1	0	3	3	15
Europe	53	21	7	0	11	17	25
South East Asia	11	2	3	1	4	2	5
Western Pacific	27	4	3	1	4	4	19
Total	**194**	**37**	**23**	**5**	**30**	**35**	**129**

[a] 194 WHO Member States

WHO/UNICEF recommend iodine supplementation of all pregnant women in countries where salt iodization is not feasible or incomplete [40]. Iodine supplementation of pregnant and lactating women has been recommended by scientific societies and regulatory bodies in Australia [15], USA and Canada [50], and Europe [51, 52], but it has not been widely adopted. Randomized controlled trials investigating the effects of iodine supplementation on pregnant women exposed to mild-to-moderate iodine deficiency are lacking, and its long-term benefits and safety in this group are unclear [5].

Remaining Challenges

Although USI programs have been implemented in more than 140 countries, and around 75% of households globally have access to adequately iodized salt [53, 54], some countries and sub-groups within countries continue to be at risk of sub-optimal iodine intakes. Despite ongoing efforts to improve access to iodized salt for all populations, disparities in household coverage have been reported at the sub-national level, where coverage could vary between rural and urban areas, or between the poorest and the richest socio-economic strata. In an analysis of iodized salt coverage amongst 11 low- and lower-middle-income countries in 2010, the coverage of iodized salt in urban areas was 8.7% higher than in rural areas, and 19.3% higher in the richest than in the poorest quintile in low-income countries [9]. A recent national survey in the Philippines suggests that such inequity may translate into a significantly lower iodine status among the rural poor [55]. Advocating the importance of iodine to national governments, encouraging the salt industry to iodize all salt for human consumption, and the food industry to use iodized salt in the manufacture of processed foods and condiments are all critical actions needed to ensure progress towards the global elimination of iodine deficiency. While overall program performance may be satisfactory, it is imperative to focus on reaching disadvantaged groups, particularly pregnant women and those of lower SES, in order to ensure that the entire population is protected from IDD.

Acknowledgments We thank Vincent Assey, Karen Codling, Nita Dalmiya, Gregory Gerasimov, Izzeldin Hussein, Pieter Jooste, John Lazarus, Gary Ma, Qian Ming, Chandrakant S. Pandav, Elizabeth Pearce, Eduardo A. Pretell, Ekaterina Troshina, and Michael B Zimmermann for providing recent country data on iodine status. We also thank Karen Abbott for help in compiling data on the iodine status in pregnant women.

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