





# Prevention and control of iodine deficiency in the WHO European Region adapting to changes in diet and lifestyle





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adapting to changes in diet and lifestyle

### Abstract:

lodine deficiency, especially mild deficiency, is still a widespread problem in the WHO European Region. Since the last WHO report on iodine deficiency in the Region was published 15 years ago, a wealth of new data on iodine status has become available, particularly concerning vulnerable population groups. This report reviews the iodine status in the WHO European Region, as well as current scientific knowledge on the consequences of mild iodine deficiency, dietary sources of iodine and the present effectiveness of iodine deficiency prevention measures. This report is also unique as it combines information sourced not only from scientific publications and public health reports, but also animal husbandry science and reporting, and the food industry.

### Keywords:

IODINE, IODINE INTAKE, IODINE DEFICIENCY, URINARY IODINE CONCENTRATION, SALT IODIZATION, MILK-IODINE CONCENTRATION, THYROID DISORDERS

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### Foreword

In an era marked by shifting dietary patterns and evolving lifestyle choices, ensuring optimal nutrition remains an ongoing challenge. As we confront the pervasive impact of overweight and obesity and diet-related noncommunicable diseases (NCDs) in the European Region, it becomes increasingly evident that we need to address the interconnectedness of various forms of malnutrition including both under- and over-nutrition.

This report sheds light on the critical issue of iodine deficiency in the Region, a significant component of the broader malnutrition landscape. Ensuring adequate iodine intake is paramount to promoting optimal health outcomes. As we examine the factors contributing to iodine deficiency detailed in this report, it becomes evident that our nutrition landscape is undergoing profound transformations. The rise of processed foods, the shift towards plant-based diets and changes in dairy consumption patterns all shape the iodine landscape, posing new challenges to public health initiatives.

For decades, consumption of milk and dairy products, as well as iodization of salt have stood as cornerstone strategies in the fight against iodine deficiency, safeguarding populations against the debilitating consequences of inadequate iodine intake. However, this report unveils a complex narrative, one where the efficacy of traditional approaches contends with the dynamic forces of modernity.

The coordination of stakeholders across the dairy industry, food production sector and governmental bodies (or equivalent) is essential in devising holistic approaches to ensure iodine adequacy. Coordinated action, informed by robust data and guided by the principles of equity and sustainability, is vital to overcoming the hurdles posed by evolving dietary patterns.

Recognizing salt reduction as a priority intervention to mitigate the burden of NCDs, and the use of salt as an optimal vehicle for iodine fortification, the report underscores the importance of integrating salt reduction strategies into broader public health initiatives.

The Special Initiative on NCDs and Innovation provides Member States of the WHO European Region with the support required to address the significant threat of NCDs, to bridge the gap between the challenges posed and actionable strategies to combat them.

Against this backdrop, it becomes imperative to chart a course forward that is both responsive to addressing the impact of emerging trends and grounded in evidence-based strategies.

The insights contained within this report serve as a call to action, urging policy-makers, health professionals and communities alike to redouble their efforts in safeguarding the health of our populations.

It is my sincere hope that this report will inform evidence-based policies and interventions, paving the way for healthier, more resilient communities across the Region.

### **Dr Gauden Galea**

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### Abbreviations

ADHD	attention-deficit/hyperactivity disorder			
Al	adequate intake			
ALSPAC	Avon Longitudinal Study of Parents and Children			
AR	average requirement			
BCI	bootstrapped confidence interval			
CI	confidence interval			
DRV	dietary reference value			
EFSA	European Food Safety Authority			
EU	European Union			
FFQ	food frequency questionnaire			
<u> </u> -	iodide			
ICP-MS	inductively coupled plasma mass spectrometry			
IGN	lodine Global Network			
INMA	Infancia y Medio Ambiente (Childhood and Environment)			
IQ	intelligence quotient			
IQR	interquartile range			
KI	potassium iodide			
KIO <sub>3</sub>	potassium iodate			
LT4	levothyroxine			
МоВа	Mother, Father and Child Cohort			
NIS	sodium iodide symporter			
NRV	nutrient reference value			
RNI	recommended nutrient intake			
RTK	rapid test kits			
Т3	triiodothyronine			
T4	thyroxine			
Tg	thyroglobulin			
TSH	thyroid-stimulating hormone			
UCC	urinary creatinine concentration			
UCE	urinary creatinine excretion			
UIC	urinary iodine concentration			
UIE	urinary iodine excretion			
UL	tolerable upper intake level			

### Executive summary

This report reviews the iodine status in the 53 Member States of the WHO European Region, and Kosovo, as well as current scientific knowledge on the consequences of mild iodine deficiency, dietary sources of iodine and the present effectiveness of iodine deficiency prevention measures. It also explores the economic impact of iodine deficiency in the current WHO European Region context.

The use of iodized salt as a vehicle for preventing iodine deficiency is a highly successful global public health intervention and has been implemented in most countries of the Region with remarkable impact. A century ago, large parts of the population of the Region were affected by endemic iodine deficiency due to severely iodine deficient diets. As a result of salt iodization, iodine deficiency disorders such as endemic goitre, clinical hypothyroidism and severe congenital iodine deficiency disorder (previously referred to as cretinism), once historically widespread, are now controlled.

However, iodine deficiency, especially mild deficiency, is still a widespread problem in the European Region, with consequences extending beyond potential effects on brain development early in life, to increased risk for goitre, thyroid nodules and hyperthyroidism in adults and the elderly, with a major impact on population health and the economy.

lodine status in school-age children is adequate in 26 of the 27 WHO European Region Member States, and Kosovo,<sup>2</sup> with data on urinary iodine concentration (n=28), largely due to salt iodization and dietary iodine from milk and dairy products. Salt iodization is implemented in 43 of 53 Member States, and Kosovo<sup>3</sup> (n=54). Iodization is mandatory in 29 Member States, and Kosovo,<sup>4</sup> (n=30) and voluntary in 13. Progress towards optimal iodine nutrition in some Member States is deteriorating, especially in those with voluntary salt iodization, and iodine intake needs improvement to prevent iodine deficiency and ensure optimal iodine nutrition in all population groups.

lodization of salt remains the main strategy to ensure adequate iodine intake in the WHO European Region. A key finding is that milk and dairy products are also important sources of iodine in many western and central European countries, especially for children. Yet consumption of milk and dairy products is declining among adolescents and adults, heightening their risk of iodine deficiency. Iodine status in adults and pregnant women is less than optimal in several countries with voluntary or no salt iodization.

Foods produced or cooked outside the home, such as bread, processed meats or ready-to-eat meals, are now the main sources of salt in many countries of the WHO European Region (70–80% of total); yet, recent market surveys found that a low proportion of salt in processed food products (e.g. 9% in Germany and 34% in Switzerland) was iodized.

<sup>1</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

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<sup>3</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>4</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

In countries with voluntary or no iodization, commonly consumed foods are often produced with non-iodized salt. The shift towards plant-based dairy alternatives, particularly among women, is concerning from an iodine nutrition perspective, especially in countries relying on milk as a source of iodine, as most dairy alternatives do not contain iodine. Overall, lifestyle choices and dietary trends, including more frequent use of processed foods and the switch to plant-based diets and dairy alternatives, are contributing to a persistent, and in some countries an increased, proportion with insufficient iodine intakes.

Routine iodine status surveillance using nationally representative population-based studies is lacking in most countries and in many the most recent data is more than 10 years old. Data frequently comes from universities, medical experts and research centres, often with little support, or recognition, from health authorities.

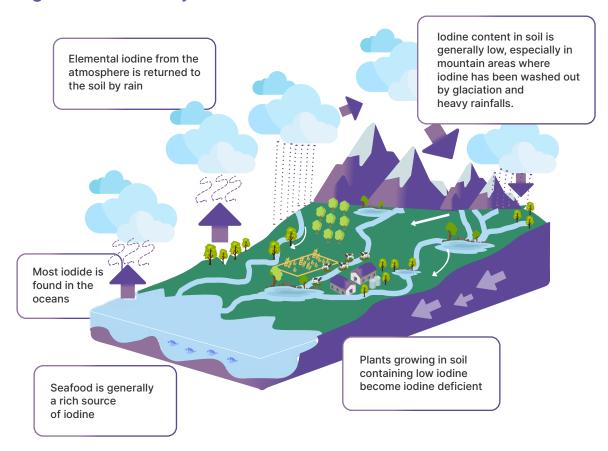
Poor knowledge about the consequences of iodine deficiency among the public, health authorities, health professionals and food producers is a barrier to improving iodine intake. There is little understanding that advice to reduce salt intake for health reasons is compatible with use of iodized salt.

Since the publication of the last WHO report on iodine deficiency in the WHO European Region 15 years ago, much new data has become available, including information about vulnerable population groups. The present report uniquely combines information sourced not only from scientific health and nutrition publications and public health reports, but also from animal husbandry science and reporting and the food industry.

### Chapter 1. Introduction

lodine (as iodide, I<sup>-</sup>) is an essential trace element that must be supplied by the diet. Its primary physiological function is as a component of the thyroid hormones thyroxine (T4) and triiodothyronine (T3) (1). Iodine deficiency is due to the lack of iodine in the soil and groundwater leading to low innate of iodine content in locally grown foods and drinking water (2) (Fig. 1.1). Iodine deficiency was historically widespread in most parts of Europe (3), especially in mountain areas where glaciation and heavy rainfalls have caused low soil iodine content. The geological characteristics of the soil are largely unmodifiable and the control of iodine deficiency must be a continuous process.

Fig. 1.1. The iodine cycle



Source: adapted with modification from Fuge & Johnson (2015) (2).

The first indications of endemic goitre due to iodine deficiency and severe intellectual disability due to congenital iodine deficiency disorder (previously referred to as cretinism) in Europe date back to the Roman empire and the Middle Ages (4). In the worst affected areas of Europe, goitre was present in up to 50% of newborns and nearly all school children, hearing disability was common and as many as one in 10 to one in 200 infants were born with severe intellectual disability (photographs 1.1 and 1.2) (5, 6). Intellectual disability was so frequent in some regions that the term "cretin of the Alps" appears in the common vocabulary of several European languages.



Source: Michael Bruce Zimmermann.

### Photograph 1.1.

Woman with myxedematous congenital iodinedeficiency disorder (previously referred to as myxedematous cretinism), intellectual disability and dwarfism

(Italy, 1980)

### Photograph 1.2.

Man with goitre from an endemic goitre region in Sicily

(Italy, 1980)



Source: Michael Bruce Zimmermann.

WHO recommends the addition of iodine to all food-grade salt for the prevention of iodine deficiency (7). Boussingault was the first to propose that iodized salt would correct and prevent goitre in 1833 (8) and Switzerland the first country to introduce iodized salt as a public health strategy in 1922 (6). Success was rapid: goitre prevalence and incidence of intellectual disability due to iodine deficiency fell drastically within a decade (6).

In the late 1980s, a report of 27 countries published by the European Thyroid Association indicated continuing high goitre rates in countries with both voluntary (Bulgaria, Germany, Italy, Spain and Türkiye), and mandatory (Austria, Hungary, Poland and the former Yugoslav Republic of Macedonia) salt iodization (9). In addition, higher neonatal thyroid stimulating hormone (TSH) concentration and transient effects on newborns' thyroid function due to low iodine intake were detected at routine clinical neonatal screening for congenital hypothyroidism (9). In 1993, WHO estimated that, based on the total goitre prevalence, 97 million people in the WHO European Region were affected by iodine deficiency (10). In the same year, WHO recommended national monitoring of iodine status using urinary iodine concentration (UIC), a proxy biomarker for current iodine intake (Section 5.1) (11). In 2007, WHO reported UIC data in school-age children from 40 European Union (EU) Member States, applicant countries and European Free Trade Association countries (12). The situation had improved substantially compared to 1993 (10) and 21 countries were now documented as iodine sufficient (12). However, this report confirmed persistent inadequate iodine intakes, and 11 countries were classified as mildly iodine deficient, most of them in central Europe (12). WHO urged Member States to establish regular national monitoring of iodine status in the population using UIC, ideally every five years (12, 13). In 2015, the EU funded the EUthyroid research project with partners from 22 Member States and five additional countries (Iceland, Israel, Norway, Switzerland and the former Yugoslav Republic of Macedonia) (14). The results identified knowledge gaps and hurdles to optimizing iodine intake in the region (8, 15-19).

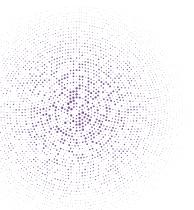
Salt iodization policies have now been adopted by most European Region countries. Thanks to the introduction of iodized salt, goitre and intellectual disability due to severe iodine deficiency are no longer endemic in the previously affected regions. However, mild iodine deficiency continues to be a nutritional challenge in the Region. The "classic" iodine deficiency disorders are the result of severe iodine deficiency and are only the tip of the iceberg of potential health consequences of dietary iodine inadequacy. Longstanding mild iodine deficiency increases the risk of thyroid diseases. Unfortunately, complacency and the absence of visible clinical signs have led to a widespread perception that iodine deficiency is no longer a public health concern in the European Region. As for any successful public health intervention, the collective memory of the clinical consequences of iodine deficiency and the reasons behind salt iodization may fade.

Strategies to reduce mild iodine deficiency or maintain adequate iodine intake require sustained commitment by health authorities. In countries with historical occurrence of severe iodine deficiency, adequate iodine intake must be maintained and iodine deficiency prevention and control programmes should be viewed as long-term or permanent.

This report reviews and presents updates on the following issues for the 53 Member States of the WHO European Region, and Kosovo:<sup>5</sup>

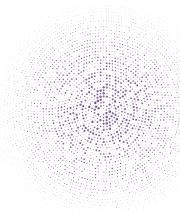
- health consequences of mild iodine deficiency, to better define its magnitude in the European Region and the benefits of its control;
- different national (and equivalent) approaches to combating iodine deficiency;
- regulation of iodized salt, sales of iodized salt, and the use of iodized salt in households and in processed food in the Region;
- the role of milk and dairy products as sources of dietary iodine;
- national (and equivalent) policies of dietary iodine supplementation for pregnant and lactating women and data on the current use of pre- and postnatal iodine containing dietary supplements;
- current iodine status based on UIC data in school-age children, adults and pregnant women using nationally representative (or equivalent) cross-sectional studies conducted during the last 15 years; and
- sustainable strategies to improve monitoring iodine status in the WHO European Region and methods to provide more reliable assessment and better identify iodine deficiency.

Because of dietary and lifestyle changes, variation in national salt iodization regulations, and lack of understanding of iodine nutrition in the European Region context, progress toward optimizing iodine intake may be stalling or even declining in some countries. If adequate iodine intake in the Region is not maintained, iodine deficiency disorders will return, resulting in economic loss.



<sup>5</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

## Chapter 2. Methods



This report presents data for 53 Member States of the WHO European Region, and Kosovo.<sup>6</sup> Data are from published literature, including that published in local languages. All data collected are from the years 2008–2023, except when otherwise indicated; in such cases, the period of reporting is duly acknowledged.

### 2.1 lodine in the diet

### 2.1.1 lodine intake and contribution of food groups

A 2022 systematic review of iodine intake in Europe (from dietary assessment methodology) examined the total iodine intake (from food and supplements) and the contribution of food groups (20). For the purposes of this report, the data were reviewed and extended to include the 53 Member States of the WHO European Region, and Kosovo.<sup>7</sup>

### 2.1.2 Systematic review of milk-iodine concentration

A systematic review of milk-iodine concentration was conducted for data from European Region countries, using the search terms "(milk AND iodine) AND (concentration OR content) AND (cow OR bovine)" (21). Four citation databases (Embase, PubMed, Scopus and Web of Science) were searched to identify relevant literature on milk-iodine concentration in the Region from data published in January 2006–December 2022. In addition, European Region online national food composition databases were searched for milk-iodine concentration. When comparing milk-iodine concentration values between countries, results from conventional milk and all-season values were used where possible (for data from food composition databases, it was assumed that if the farming method was not stated, the value was from conventional milk). Furthermore, preference was given to studies that reported the use of a certified reference material for the laboratory measurement of milk-iodine concentration, as this indicates that results are accurate.

<sup>6</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)

<sup>7</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

### 2.2 Salt iodization

### 2.2.1 Legislation and regulations

Information on legislation and regulation of salt iodization was obtained from the Global Fortification Data exchange (GFDx) (22) and a literature search, and was provided by IGN national coordinators, WHO country office colleagues and national counterparts in Member States of the European Region between April 2023 and April 2024 (Web annex A).

### 2.2.2 lodized salt production, import, sales and coverage at the household level

Information on iodized salt production and sales in western and central Europe was obtained from EUsalt, an association of 28 salt producers (section 6.1.2.1). The data were provided by the 26 member companies who produce in the European Region and compiled by the EUsalt secretariat. Two member companies who do not produce in the European Region were not included in the analysis.

Producers were asked to provide information on the proportion (%) of iodized vs. non-iodized salt of the total production of edible salt supplied to countries in the European Region. Each producer provided data for their three main markets (Fig. 2.1). The data represents salt sales during 2022 or 2023 (most recent information available).

Country

Industrial

Retail

Non-iodized

Non-iodized

Non-iodized

Fig. 2.1. Information on sales of iodized salt provided by members of EUsalt

Source: authors.

<sup>&</sup>lt;sup>a</sup> <25% of daily salt consumed is from discretionary sources (e.g. household salt) (23).

 $<sup>^{\</sup>rm b}$   $\geq$  75% of daily salt consumed is from foods made outside the home (e.g. processed food, food from large kitchens and canteens (23)).

Of the 26, eight reported no production of food-grade salt and 10 did not respond to the inquiry. Salt sales data are presented for the remaining eight companies, who sell salt to 13 countries in the European Region. Company names were anonymized and coded for this publication. For reporting purposes, one large company was split into three codes. Salt imported into the EU was not considered in the report.

For seven countries of eastern Europe and central Asia (section 6.1.2.1) data on iodized salt production and/or import was provided by representatives of the salt industry, IGN national coordinators and through literature search.

Data on household coverage of iodized salt and the level of iodine in household salt was obtained from nationally representative nutritional surveys, multi-indicator cluster surveys and demographic health surveys. Information from the United Nations Children's Fund global database (24) was updated with new national studies obtained by literature searches and provided by IGN national coordinators.

### 2.3 Dietary iodine supplements

Information on national recommendations of dietary supplementation with iodine in the preand postnatal period, was obtained from relevant websites of national authorities and medical associations and the European Board and College of Obstetricians and Gynaecology and IGN national coordinators between March 2023 and December 2023. A comprehensive systematic literature search conducted in PubMed and Web of Science between January 2023 and January 2024 identified relevant studies reporting the use of dietary iodine supplements using the search terms "Pregnancy AND UIC AND *country*", "Pregnancy AND iodine supplement\* AND *country*" and "Pregnancy AND supplement\* AND *country*" where the *country* was replaced with the corresponding country.

### 2.4 lodine status

### 2.4.1 Data collection, literature searches and data sources

Nationally representative country data on UIC in school-age children, adults (and specifically women) and pregnant women were obtained from a variety of resources, as described below.

- A search of the WHO Micronutrients Database, part of the WHO Vitamin and Mineral Nutrition Information System (25), was conducted. The database compiles UIC data from cross-sectional studies conducted in population groups. Studies selected had to have a cross-sectional and population-based sampling frame and be nationally or regionally representative or representative for the first administrative level of the country where the study took place.
- ◆ A comprehensive systematic literature search was conducted in MEDLINE, EMBASE, Web of Science and Scopus between January 2022 and January 2024 to identify relevant new studies using the search terms "iodine deficiency", "urinary iodine concentration", "monitoring".

- Hand searching of reference lists of original articles and relevant reviews was conducted.
- Specific data requests were sent to IGN national coordinators in selected countries. as well as to WHO Country Office colleagues and national counterparts in Member States of the WHO European Region between April 2023 and April 2024.

### 2.4.2 Data inclusion criteria

For each country, the most recent UIC data was selected for three population groups, applying the following criteria:

- The study included school-age children and adolescents (6−15 years of age), adults (> 15 years of age, women and men), and/or pregnant women. If no studies were conducted in school-age children (6−12 years), data from studies in adolescents (13−19 years) were selected. Data for adults from both sexes were included. If data for both sexes were not available, data were selected in the following order of priority: 1) women only (> 15 years of age); 2) non-pregnant non-lactating women of reproductive age (15−49 years); 3) women of reproductive age (15−49 years).
- Studies selected had to have been conducted between 2008 and 2023, have had a cross-sectional and population-based sampling frame, and have been nationally representative.
- ✓ In the absence of national data, regional or first administrative level data were used when the population sample from the subnational region was described and considered homogeneous to the rest of the population. However, data were included only when three or more regional or first administrative-level surveys were carried out in different locations in a country during the analysis period. The survey results were pooled into a single summary measure, using a weighted sample size for each survey.
- A minimum sample size of at least 100 was used for the UIC collection.
- Standard, validated data collection techniques and laboratory methodologies were used such as studies collecting spot urine samples and 24 hour urine collections.
- The study must have used the Sandell-Kolthoff method or inductively coupled plasma mass spectrometry (ICP-MS) to measure UIC.
- The study reported median, mean and/or geometric mean UIC in μg/L (interquartile range (IQR) and/or bootstrapped confidence interval (BCI) were included if available);
- The complete study report was available, or a summary presenting sufficient data to judge the inclusion criteria above.

### 2.4.3 Classification of iodine status

lodine status for each population group was determined based on the median UIC and classified as iodine deficient (mild, moderate and severe), optimal, or at risk of adverse health consequences (13) (Table 5.1).

## Chapter 3. lodine in health and disease

### 3.1 lodine metabolism

Dietary iodine is absorbed as  $I^-$  in the small intestine via the sodium iodide (Na<sup>+</sup>/ $I^-$ ) symporter (NIS) (26). Absorption is rapid and nearly complete (27). The chemical form or composition of the diet does not affect bioavailability. If iodine intake is adequate, 5–25% of absorbed iodine is actively taken up by the thyroid via the NIS transporter for the synthesis thyroid hormones (1, 26, 28). T4 and T3 are produced in the follicles of the thyroid gland and released into the bloodstream (29). Biosynthesis is controlled by the hypothalamic-pituitary-thyroid axis via TSH in a negative feedback loop (30). Thyroidal iodine uptake and production of T4 and T3 begin as early as 10–12 weeks of gestation (26, 31). Before this, maternal thyroid hormones are provided via the placenta to the fetus (32).

Dietary iodine not taken up by the thyroid is removed from circulation and excreted, primarily via urine. At adequate iodine intake and normal thyroid function, approximately 90% of the absorbed dietary iodine is excreted in the urine within 24 hours after consumption (1). Small amounts may be lost in faeces and sweat (1, 33). During lactation, iodine is also excreted into breast milk (34, 35).

### 3.2 Physiological role of thyroid hormones

Thyroid hormones regulate cellular metabolism in virtually all tissues at any life stage. In the peripheral tissues, T4 is converted to the metabolically active form T3 via deiodinase enzymes (36). T3 binds to nuclear thyroid hormone receptors and regulates expression of a wide range of genes controlling numerous fundamental physiological processes, including metabolism, development and maturation of the central nervous system, the musculoskeletal system and the lungs (37, 38). In the brain, T3 regulates neurocognitive development by regulating neuronal proliferation and migration, glial differentiation and myelination of axons in the central nervous system (37).

### 3.3 Health effects of mild iodine deficiency

### 3.3.1 Physiological adaptation

The thyroid gland uses several mechanisms to regulate iodine uptake, storage and excretion to preserve normal thyroid hormone synthesis (29). If dietary iodine intake is low, the thyroid adapts to deficiency by increasing iodine uptake (1, 27). In individuals with chronic iodine deficiency, the iodine uptake can be as high as 80% (1, 27). Iodine can be accumulated in the

thyrocytes and is primarily stored bound to thyroglobulin (Tg) (26, 29). This iodine reserve may be utilized during periods of low intake. In adults, the average thyroidal iodine store amounts to approximately 5–20 mg, but there are large individual differences depending on previous habitual iodine intake (1). In severe iodine deficiency, the iodine content of the thyroid can fall to < 20  $\mu$ g.

Circulating Tg is the first biomarker of thyroid stimulation triggered by iodine inadequacy (29, 39-41). Normal TSH and thyroid hormone levels persist as long as compensatory mechanisms maintain normal thyroid hormone synthesis. A relative increase of thyroidal T3 secretion may also be a response to low intake resulting in more efficient use of available iodine stores (42).

### 3.3.2 Thyroid dysfunction and thyroid disorders

Health consequences of inadequate iodine intake are mediated through the effects on thyroid function and the thyroid hormone's actions on target organs. The association between iodine intake and thyroid disease is U-shaped and adverse health consequences are reported at both inadequate and excessive intakes (43, 44). The effects depend on the degree of iodine deficiency or excess, as well as the timing and duration of exposure (43, 45).

If physiological homeostatic mechanisms are overwhelmed by iodine deficiency, TSH concentrations begin to increase. As a result, subclinical hypothyroidism (elevated TSH along with normal T4 and T3) increases. If iodine deficiency is severe and persists, overt hypothyroidism (elevated TSH, low T4, and, more rarely, low T3) may develop.

In mild iodine deficiency the compensatory thyroid mechanisms maintain normal thyroid hormone levels. However, persistent mild iodine deficiency results in chronic thyroidal hyperstimulation (43). Persisting stimulation increases thyroid growth and oxidative stress, promoting mutagenesis and the occurrence of thyroid nodules in adult and elderly populations (46, 47).

Goitre prevalence is associated with age in children exposed to mild iodine deficiency (48). In some European Region countries with incomplete coverage of iodized salt, children may be protected from mild iodine deficiency to some extent due to the relatively high iodine content of dairy products. However, consumption of dairy products generally declines during adolescence (49), as reflected in lower median UIC by age (15, 50). This reduced consumption of dairy products may increase the risk of iodine inadequacy and thyroidal hyperstimulation. Other determinants, such as smoking, dietary habits, pregnancy and seasonal variations, may further aggravate the risk of iodine deficiency (51). In iodine-deficient European pregnant women (Spain, United Kingdom), milk intake is negatively associated with Tg concentration (52, 53).

### 3.3.2.1 Goitre and thyroid nodules

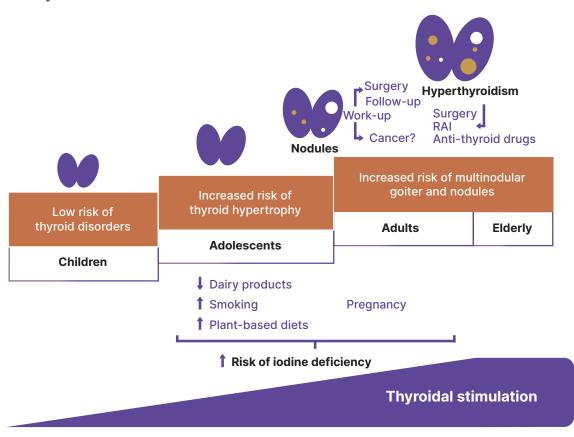
The main consequences of mild iodine deficiency are the structural modifications of the thyroid induced by thyroidal hyperstimulation and characterized by hypertrophy and thyroid nodules (54) (Fig. 3.1). Thyroid nodules may appear in enlarged thyroids (multinodular goitre) or normal-sized thyroid glands. Autonomously functioning nodules frequently result in hyperthyroidism in adult and elderly populations (54, 55).

The risk of cancer in thyroid nodules is about 5%, but the risk is lower in hyperfunctioning nodules (56). An elevated prevalence of thyroid nodules in the adult population represents a burden for the health system, as medical tests are required to exclude the few malignant cases each time a thyroid nodule is detected.

### 3.3.2.2 Hyperthyroidism

Hyperthyroidism is a common chronic health condition, with the prevalence of overt hyperthyroidism (low TSH and high T3 and/or T4) up to 1.4% and subclinical hyperthyroidism (low TSH and normal T3 and T4) also up to 1.4% worldwide (57). Many cases remain undiagnosed and the prevalence of undiagnosed hyperthyroidism in the European Region has been estimated to be as high as 1.7% (58). In iodine replete populations, Graves disease is the most common cause of hyperthyroidism. However, toxic nodular goitre is the second most frequent cause and is more common in iodine-deficient populations (57).

Fig. 3.1. Effects of mild iodine deficiency on thyroid function over the life cycle<sup>a</sup>



RAI: radioiodine therapy.

<sup>&</sup>lt;sup>a</sup> Yellow circles indicate hyperfunctioning nodules and white circles indicate hypofunctioning nodules. *Source*: authors.

The incidence of the various subtypes of hyperthyroidism is age dependent and increases in the elderly in iodine deficient regions (55). Prevalence of overt hyperthyroidism as high as 2.9% has been reported in a mildly iodine deficient region in Italy, mainly due to toxic nodular goitre (59). This is more than twice as high as the total prevalence of 1.3% (0.5% overt and 0.7% subclinical hyperthyroidism) observed in iodine-sufficient countries (60).

Untreated hyperthyroidism can cause cardiac arrhythmias, raises the risk of heart failure and cardiac morbidity, cognitive impairment in elderly subjects, osteoporosis and sarcopenia, and adverse pregnancy outcomes (57, 61-63). In addition, hyperthyroidism, because of its cardiac effects, can be life-threatening, and is typically more challenging to treat than hypothyroidism.

Radioiodine therapy, anti-thyroid drugs and surgery are the most frequent treatments for toxic nodular goitre or hyperfunctioning solitary nodules (57, 64). Diagnosis and treatment of these preventable disorders are burdens for patients and the health system.

Introduction of iodine fortification and correction of iodine deficiency may increase the incidence of hyperthyroidism, but this increased incidence is typically transitory and decreases over time to a lower level than before fortification (65-68).

3.3.2.3 European cohort studies investigating effects of iodine intake on thyroid function A Danish cohort (DanThyr) study investigated the incidence of thyroid disease over 21 years (Table 3.1) before and after iodine fortification (mandatory iodization at 13 mg/kg in 2000, which increased to 20 mg/kg in 2019) in one area with mild iodine deficiency (Copenhagen) and another area with moderate iodine deficiency (Aalborg) (69, 70). Before iodine fortification, Aalborg had a higher goitre prevalence and higher incidence of hyperthyroidism, but lower frequency of hypothyroidism than Copenhagen (69, 71, 72). After iodine fortification, iodine intake improved in both areas. Aalborg went from moderately to mildly deficient, although Copenhagen remained mildly deficient (73). Four years after salt iodization, thyroid volumes decreased in younger age groups, but higher thyroid volumes persisted in subjects over 40 years; the decline was larger in Aalborg than Copenhagen (74). The increase in iodine intake in both regions abolished the age-dependent difference in thyroid volume (75). Thyroid multinodularity increased in Aalborg after the transition from moderate to mild iodine deficiency and remained stable in Copenhagen (76). Six years after iodine fortification, the incidence of hyperthyroidism increased in both locations and all age groups, but the increase was highest in young adults (77). After 21 years, incidence of hyperthyroidism decreased in both areas to levels below the baseline values observed before salt iodization (66). A similar transient trend in increased hyperthyroidism was observed in pregnant women (68).

The incidence of hypothyroidism increased in young and middle-aged adults in Aalborg seven years after iodine fortification but remained stable in Copenhagen (78). However, 17 years after iodine fortification, an increase in hypothyroidism incidence also occurred in Copenhagen (67). In both regions, the increases in hypothyroidism were only seen among young and middle-aged subjects but not among subjects older than 60 years.

In summary, data from the Danish cohorts suggest that correction of iodine deficiency decreases thyroid volume and the incidence of hyperthyroidism in adults in the long term at the expense of a slight increase in the incidence of hypothyroidism. The cohort study illustrates the importance of monitoring the effects of a salt iodization programme on thyroid health and diseases.

**Table 3.1.** European cohort studies investigating effects of iodine status on thyroid function, neurocognitive and obstetric outcomes

Country	Cohort (n)	Period	Population	Median UIC (IQR) μg/L	Outcomes		
Adult population							
Denmark	DanThyr C1a, n=4 649 C2, n=3 570 C1b, n=4 174	C1a: 1997–2016 C2: 2004–2005 C1b: 2008–2010	Women aged: 18–22, 25–30, 40–45, 60–65 years Men aged: 60–65 years	Aalborg: 53 (30, 90) Copenhagen: 68 (30, 112) Overall: 61 (34, 101)	<ul><li>UIC</li><li>Thyroid function</li><li>Thyroid volume</li><li>Thyroid diseases</li></ul>		
Pregnant wo	omen/children						
Norway	MoBa Pregnant women, n=95 243 Children, n=114 754	1999–ongoing	1st trimester UIC, thyroid function in a subsample (n= 2 910) lodine intake assessed by FFQ at 22 weeks	68 (35, 116)	<ul> <li>Cognitive function</li> <li>Obstetric outcomes</li> </ul>		
United Kingdom	ALSPAC Pregnant women, n=14 541 Children, n=13 998	1991–ongoing	All trimesters UIC Iodine/ creatinine ratio	1st trimester: 91 (54, 143) Overall: 96 (57, 153)	<ul><li>Cognitive function</li><li>Obstetric outcomes</li></ul>		
United Kingdom	Born in Bradford (n=6 971)	2007–2010	26–28 weeks UIC lodine/ creatinine ratio	76 (46, 120)	<ul> <li>Obstetric outcomes</li> <li>Neurocognitive outcomes</li> <li>Thyroid function in subset</li> </ul>		
Spain	INMA Pregnant women, n=3 174 Children, n=2 939	2004–ongoing	All trimesters UIC Iodine/ creatinine ratio	Overall: 128 (75, 213)	<ul> <li>Neurocognitive outcomes</li> <li>Obstetric outcomes</li> <li>Thyroid function in subset</li> </ul>		
Netherlands	Generation R Pregnant women, n=7 145 Children, n=1 525	2017–ongoing	All trimesters UIC lodine/ creatinine ratio	Overall: 159 (90, 275)	<ul> <li>Neurocognitive outcomes</li> <li>MRI in offspring</li> <li>Obstetric outcomes</li> <li>Thyroid function in subset</li> </ul>		

ALSPAC: Avon Longitudinal Study of Parents and Children; C1a: Cohort study from Aalborg (Al) and Copenhagen (Cp); C1b: Follow-up of C1a cohort; C2: Cohort from Al and Cp after iodine fortification; FFQ: food frequency questionnaire; INMA: Infancia y Medio Ambiente; MoBa: Mother, Father, and Child Cohort; MRI: Magnetic resonance imaging.

Source: authors.

### 3.3.3 Neurodevelopment

Pregnancy increases the dietary requirement for iodine and pregnant women are particularly vulnerable to iodine deficiency (13). The consequences of iodine deficiency are not directly caused by a lack of iodine, but indirectly due to inadequate synthesis of thyroid hormones by the mother and the fetus.

Severe iodine deficiency can reduce thyroid hormone levels in the brain and impair neurodevelopment when exposure occurs in the womb and during early childhood (79, 80). Two systematic reviews confirmed the benefits of correcting severe iodine deficiency (81, 82). The first systematic review looked at 89 studies on the provision of iodized salt to populations and estimated a 72-76% reduction in risk for low intelligence (defined as intelligence quotient (IQ) < 70) and an 8.2-10.5 point overall increase in IQ (81). The second review suggested that iodine-sufficient children have a 6.9-10.2 point higher IQ than iodine-deficient children (82).

Pregnant women exposed to mild iodine deficiency typically maintain thyroid hormone concentrations within normal reference ranges throughout pregnancy (83), although at the expense of experiencing thyroidal hyperstimulation, as indicated by elevated Tg concentrations (84). Studies providing iodine supplements to mildly iodine deficient pregnant women show reduced Tg concentrations, but without affecting thyroid hormone concentrations in mothers and newborns (85-89).

This suggests that pregnant women may be able to physiologically adapt to mildly low iodine intakes during pregnancy to maintain adequate thyroid hormone production and normal fetal development. The effects of mild iodine deficiency on fetal brain development are still uncertain (83, 90-93). A meta-analysis found no overall effect of iodine supplements in women with mild iodine deficiency on fetal neurodevelopment up to 6 years of age (83). The evidence is limited by the small number of trials, the fact that in one trial, women in one of two study sites were not exposed to iodine deficiency at baseline (86), and that two trials were statistically underpowered (one was stopped early) (94, 95). The evidence base is too poor to conclude whether iodine supplementation of euthyroid mildly iodine-deficient pregnant women is beneficial for child neurodevelopment.

The lack of effect of mild iodine deficiency on pregnant women's thyroid hormone levels leaves few mechanistic options to explain why mild iodine deficiency impairs child neurodevelopment. Two large randomized controlled trials, conducted in an iodine-sufficient (96, 97) and a mildly iodine deficient population (98) showed no benefits on child neurodevelopment in mothers treated with levothyroxine (LT4) for subclinical hypothyroidism and/or hypothyroxinemia starting in the second trimester, although both trials have been criticized for initiation of therapy after the first trimester (96-98).

A randomized controlled trial of iodine supplementation in Albanian children corrected moderate iodine deficiency and improved thyroid function and cognitive performance in school-age children (99). Another trial conducted in New Zealand suggests that correction of mild iodine deficiency can also improve cognitive performance of children (100). The Tg concentration decreased after iodine supplementation in this trial, but no modification of thyroid hormones was observed in supplemented children (100, 101).

The trials in pregnant women and children have a crucial design limitation stemming from the difficulty in including individuals who are iodine deficient. The use of the population median UIC to classify the subjects included in a trial as iodine deficient is problematic because the median UIC does not necessarily apply to all subjects, and it is likely that many subjects included in a trial are not iodine deficient, adding uncertainty to the conclusions.

### 3.3.3.1 European cohort studies investigating effects of iodine intake on obstetric outcomes and child neurodevelopment

Five European observational cohort studies in pregnant women investigated the effects of iodine intake and/or status on obstetric outcomes and child neurodevelopment (Table 3.1). The cohorts were originally established for other purposes and UIC and thyroid function parameters were measured in a subsample of the participants.

The MoBa study (Table 3.1) conducted in Norway, a country with mild to moderate iodine deficiency in women of reproductive age, investigated several obstetric and child neurodevelopmental outcomes in almost 80 000 mother-child pairs. Iodine intake was not associated with impaired thyroid function in pregnant mothers, however there was an inverse relationship between UIC and T3 and T4 (102). Nevertheless, the investigators reported an association between insufficient maternal iodine intake (from FFQ) and reduced fetal growth, an increased risk of preeclampsia, and subfecundity (103). Further, suboptimal maternal iodine intake was associated with child language delay, behaviour problems and reduced fine motor skills at 3 and 8 years of age (104). No association was found between insufficient maternal iodine intake and a clinical diagnosis of attention-deficit/hyperactivity disorder (ADHD) in the offspring, though there was an association between low iodine intake and a higher ADHD symptom score (from questionnaires completed by mothers) (105, 106). No evidence was found for a protective effect of iodine supplementation during pregnancy on child outcomes (104, 106), though there was some evidence that starting a supplement after 12 weeks gestation was associated with lower T4 (102). These findings may suggest that production of thyroid hormones is temporarily impaired with an iodine-containing supplement in pregnancy, though the data are limited by the fact that the supplement was a multivitamin/mineral preparation. The conflicting results between iodine intake, iodine status and thyroid function may be explained by the limitations of iodine assessment in an individual, resulting in imprecise estimates. In addition, maternal thyroid measures do not provide an estimate of the transfer of iodine across the placenta to supply the fetus.

**The ALSPAC cohort study**, in the United Kingdom (**Table 3.1**), reported an association between inadequate iodine status (urinary iodine/creatinine ratio) during early pregnancy (< 13 weeks gestation) and an increased risk of suboptimal scores for verbal IQ at age 8 years and reading accuracy and comprehension at age 9 years (107). Unlike the MoBa cohort study, low maternal iodine status was not associated with adverse obstetric outcomes (108). ALSPAC used measures of iodine status from a single spot-urine sample, whereas MoBa had longer-term measures of iodine intake (from an FFQ).

**The Born in Bradford cohort study** measured iodine status at 26–28 weeks' gestation and found no overall association with child neurodevelopment at 4–7 years (109). The exposure measure was made later in pregnancy than the ALSPAC cohort and used school-based educational assessments (i.e. not IQ or other tests performed by psychologists). Born in Bradford reported a positive association between iodine status in pregnancy and birthweight, and a greater risk of small-for-gestational-age, but no associations with other pregnancy outcomes (110).

**The INMA cohort**, in Spain (Table 3.1), included pregnant women with overall deficient iodine intakes (with the exception of women from one region of the Basque Country (111). The investigators reported an association between low maternal UIC and lower cognitive scores in childhood (4–5 years). The study did not find an association between iodine supplements during pregnancy and children's cognition and motor abilities at 1 and 4–5 years of age (112, 113), although in most women the iodine supplement was part of a multivitamin and mineral preparation, which limits conclusions.

**The Generation R study cohort** is based in Rotterdam, the Netherlands (Kingdom of the) (**Table 3.1**), an iodine-sufficient country, and pregnant women in this cohort are also classified as iodine sufficient (114, 115). Urinary iodine/creatinine ratios (< 10th percentile) during early pregnancy were associated with impairment of executive functioning in children at 4 years of age, but the association was not explained by low dietary iodine intake or thyroid hormone concentrations (116). In a subsequent publication based on the same cohort, the authors did not find a relationship between maternal low UIC and children's non-verbal IQ or language comprehension in children at 6 years of age (115). This is most likely because statistical power was too low to detect differences between groups (as most women were iodine sufficient). However, higher UIC in pregnancy was associated with an increased risk of neonatal hyperthyroidism (117).

A subsequent meta-analysis of individual participant data from three cohorts (ALSPAC, Generation R and INMA), which pooled and harmonized data, reported an association between urinary iodine/creatinine ratio and mean verbal IQ (114). Again, no mechanistic explanation was reported as there was no association between urinary iodine/creatinine ratio and maternal thyroid function (114). The association was only statistically significant at < 14 weeks' gestation, which supports the earlier study in just the ALSPAC cohort, which was restricted to the first trimester (< 13 weeks); it may suggest that any effect of mild iodine deficiency is in early pregnancy. Analysis of the same pooled data showed no evidence of an association between iodine status during pregnancy and child ADHD or autistic traits (92).

In summary, the data from cohort studies suggests that mild iodine deficiency in pregnancy may affect outcomes in the pregnancy and/or offspring, but the evidence is inconclusive, as it is weak owing to the observational nature of the studies and risk of residual confounding.

### 3.4 Health effects of iodine excess

Not only iodine deficiency but also iodine excess increases the risk of thyroid diseases, and the association between iodine intake and risk of thyroid diseases is U-shaped (43, 44, 118).

The effects of iodine excess on the thyroid are multiple (119). An acute overload of iodine can block the synthesis of thyroid hormones, known as the Wolff-Chaikoff effect (44, 119). This is a transient effect lasting about 24 hours and is without long-term consequences (119). Chronic exposure to iodine excess is associated with an increased prevalence of thyroid autoimmune diseases, hypothyroidism, hyperthyroidism and even goitre. In children, thyroid volume increases when the median UIC is above 500 µg/L (120).

Hypothyroidism and autoimmune thyroid diseases are more frequent in populations with iodine excess (121-123). Data from Chile and China show that the frequency of anti-thyroid peroxidase and anti-Tg antibodies are 10-times higher in areas with iodine excess (median UIC of  $634 \mu g/L$ ) compared to areas with lower iodine intake or mildly iodine-deficient regions (121, 124). In Chile, the population has been exposed to iodine excess for more than 20 years due to high iodine levels in salt, and the prevalence of hypothyroidism is high in adults, including pregnant women (122, 123).

lodine excess occurs when foods with naturally high iodine content are consumed (Section 4.3.2). The iodine content in the diet or drinking water is high in, for example, Japan (125, 126) and some regions of China (127, 128). Iodine excess may also occur if the iodine content of salt is too high or if the content is poorly monitored. Several previously iodine-deficient countries have been affected by iodine excess when fortifying salt at levels that are too high (122, 123). In the European Region, current iodine levels in salt (Web annex A) do not pose a risk for iodine excess.

### 3.5 Key messages

- Normal thyroid hormone synthesis (euthyroidism) is typically ensured over a broad range of iodine intake, thanks to physiological adaptation to variations in iodine intake.
- Mild iodine deficiency results in chronic thyroidal hyperstimulation. Populations exposed to mild iodine deficiency have a higher prevalence of individuals with increased thyroid volume, thyroid nodules, multinodular goitre and hyperthyroidism, particularly in adults and the elderly. Untreated hyperthyroidism increases the risk of cardiac arrhythmias, heart failure, osteoporosis and adverse pregnancy outcomes, as well as cognitive impairment in older people.
- Correction of mild iodine deficiency decreases the prevalence of hyperthyroidism, which
  may be a life-threatening condition. Improved iodine intake may be associated with a
  small and transient increase in the prevalence of hypothyroidism, but this condition is
  easier to treat than hyperthyroidism.
- The effects of iodine deficiency on neurodevelopment are mediated through fetal exposure to low thyroid hormone concentration. Mild iodine deficiency does not typically cause maternal hypothyroidism. While the evidence for neurodevelopmental effects of mild iodine deficiency is insufficient from randomized controlled trials, evidence from the cohort studies is suggestive of negative consequences on obstetric and neurodevelopmental outcomes. These are of public-health concern, although the evidence is weak owing to the observational nature of the studies. In many studies, it is uncertain whether women are truly iodine deficient, as the classification is based on UIC, which is not suitable for individuals.
- Correction of mild iodine deficiency in children may improve their cognitive performance.

## Chapter 4. lodine in the diet

### 4.1 Dietary reference values for iodine intake

Dietary reference values (DRVs) for iodine by population group, established by WHO and the European Food Safety Authority (EFSA), are presented in Table 4.1 (12, 129). The recommended nutrient intake (RNI) is set to meet the iodine requirements of nearly all (97.5%) healthy individuals in a population and can be used to assess individual nutrient adequacy (130). RNI may be used as a comparison with the mean iodine intake in a population (mean intake should be > RNI), but cannot be used to report the percentage with inadequate intake (i.e. it is not correct to report the percentage with intake < RNI) (130). For reporting of the proportion of a population with inadequate intake, the average requirement (AR) is needed (i.e. the habitual intake estimated to meet the physiological requirement of half (50%) of healthy individuals of a specific life stage) (131, 132). For the AR cut-point method, nutrient intake is considered to be adequate when < 2–3% of the population have usual intakes below the AR (130, 133, 134). AR has been estimated by WHO (133), in the United States of America by the National Academy of Medicine (previously Institute of Medicine) (135) and in the Nordic countries (136), but not by EFSA (129).

The lack of scientific data to define reference values has led to large differences in DRVs for iodine between countries in the European Region (20). There is no evidence that physiological iodine requirements vary between populations and harmonization of nutrient reference values is warranted (132, 137, 138).

Tolerable upper intake level (UL) has also been set for different populations, and differs between authorities. UL is defined by EFSA as the maximum daily intake of a nutrient that is unlikely to be of risk, and values for iodine are shown in **Table 4.1**. A harmonized UL for iodine in adults of 600  $\mu$ g/day was recently proposed based on the EFSA recommendation (132, 139). It is important to note that the EFSA UL does not apply to iodine-deficient populations, where there may be increased sensitivity to iodine.

### 4.2 Assessing iodine intake from dietary assessment

Estimation of iodine intake through dietary assessment methodology rather than with UIC data provides another source of information on iodine in the population. As with all nutrients, the assessment of iodine through dietary assessment methodology (e.g. FFQs or food diaries) is challenging for three reasons. Firstly, there is high day-to-day variability, as some iodine-rich foods (such as fish) are consumed episodically so assessment over a short period may underestimate intake. Secondly, discretionary salt intake (i.e. added during cooking and/or at the table) including any iodized salt, is hard to capture accurately. Third, food composition databases contain inaccuracies and missing data, including on variability in the iodine concentration of foods (142, 143). However, despite limitations, dietary assessment can be used to estimate the dietary iodine contribution from different food groups.

**Table 4.1.** Recommendations for iodine intake ( $\mu g/d$ ) by age or population group according to WHO and EFSA

WHO <sup>a,b</sup>				EFSA°		
Age or population group	RNIª (µg/day)	AR⁵ (µg/day)	Upper limit <sup>b</sup> (µg/day)	Age or population group	Al (μg/day)	Upper limit <sup>d</sup> (µg/day)
Infants				Infants		
0-12 months	90	-	_	7-12 months	70	_e
Children				Children		
1–5 years 6–12 years	90 120	64 87	200 300	1-3 years 4-6 years 7-10 years	90 90 90	200 250 300
Adolescents				Adolescents		
13-17 years	150	107	600	11-14 years 15-17 years	120 130	450 500
Adults				Adults		
≥ 12 years	150	107	1100	18-70 years	150	600
Pregnant				Pregnant		
	250	143	500		200	600
Lactating				Lactating		
	250	143	500		200	600

Al: adequate intake.

Source: authors.

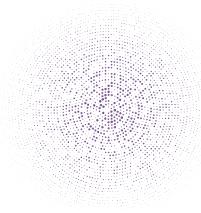
<sup>&</sup>lt;sup>a</sup> Adapted from WHO (2004, 2007) and Andersson et al. (2007) (12, 140, 141).

<sup>&</sup>lt;sup>b</sup> Adapted from Allen et al. (2006) *(133)*. Correction factor AR is obtained by dividing the RNI for a given population subgroup by the conversion factor 1.4.

<sup>&</sup>lt;sup>c</sup> Adapted from Agostoni et al. (2014) (129).

d EFSA (2006) (139).

<sup>&</sup>lt;sup>e</sup> Upper limit not set by EFSA for infants < 12 months due to a lack of data.



At current iodine levels in salt in the WHO European Region, there is no risk for iodine excess.

### 4.2.1 Iodine intake in the WHO European Region

Of the European Region's 53 Members States, and Kosovo<sup>8</sup> (*n*=54), 26 have national nutrition survey data (48%), but data on iodine intake obtained using dietary assessment methods were only available in 15 countries for adults (28%) and 13 countries for children (24%). Furthermore, data on both iodine intake and the contribution of different food sources were only available from 10 countries in adults and five countries in children (see **Web annex C** for full details).

Fig. 4.1 summarizes total iodine intake for adult men and women separately, by country; iodine intake is compared against the recommended adult intake of 150  $\mu$ g/day (see Table A.3.2 in Web annex C for details). The data do not include intake from iodized salt, so may be an underestimate for some countries. Iodine intake was < 150  $\mu$ g/day in both men and women in seven countries (six shown in Fig. 4.1, and Lithuania where data are combined), and > 150  $\mu$ g/day in just three countries. When looking at differences between men and women, iodine intake was consistently lower in women. In 11 of the 14 countries with data for men and women (78%), iodine intake was < 150  $\mu$ g/day in women, but in five of those countries, intake in men was > 150  $\mu$ g/day (Fig. 4.1). This suggests that women are more at risk of low iodine intake than men overall, and within a country women may have low intake of iodine, while intake in men may be sufficient.

<sup>8</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

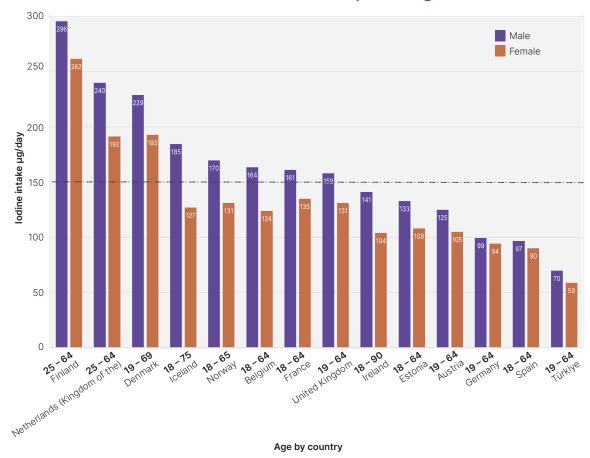


Fig. 4.1. lodine intake (obtained using dietary assessment methods) in adult men and women in the WHO European Region<sup>a</sup>

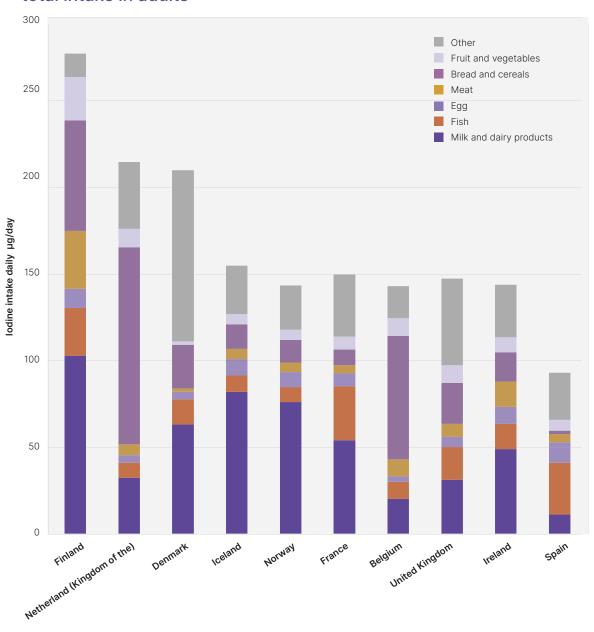
 $^{\circ}$  Data from Bath et al. (2022) (20) but simplified to combine data from all adults (> 18 years), not by small age brackets. Data from Lithuania not shown as not available by sex (mean intake in adults: 31  $\mu$ g/day). Black dashed line shows the adult recommended intake (150  $\mu$ g/day). Source: authors, with data from Bath et al. (2022) (20).

# 4.3 Food sources of iodine

Drinking water typically contains a low concentration of iodine (<  $10 \mu g/L$ ) in most parts of the WHO European Region. In certain geographical locations, groundwater may be high in iodine due to marine influences (e.g. Denmark) (144) or due to contamination of drinking water from natural springs with high iodine content, as observed in the Ural region of the Russian Federation (145). In such settings, ground water consumption may cause excess iodine intake (44), as described in the Ural region (median UIC of 719  $\mu g/L$  in school-age children) (145).

In many countries of the European Region, iodized salt provides a supply of iodine in the diet (See Section 5.1), but in countries without strong salt iodization programmes, knowledge of dietary sources is important. Fig. 4.2 shows the contribution of different food groups (milk/dairy, fish, eggs, meat) to total iodine intake in adults for countries that have national iodine-intake data (see Table A3.2 in Web annex C for country details and contributions to children's intake).

Fig. 4.2. Contribution of foods to total iodine intake as a proportion of total intake in adults



Source: authors, with data from Bath et al. (2022) (20).

#### 4.3.1 Animal-based foods

The main dietary sources of iodine in many countries are animal-based (20, 146, 147), especially in children (148). A review of European sources of iodine in the diet showed that animal-based foods contribute 82% of total iodine intake in children in Norway and 73% in children in the United Kingdom, and in adults provide 65% and 61% respectively (Fig. 4.2) (20).

#### 4.3.1.1 Milk and dairy products

Of the animal foods, milk and dairy products provide the largest contribution (Fig. 4.2) – for example providing 53% of adult intake in Ireland, and over a third of adult intake in Denmark, Finland, Norway and the United Kingdom (20). Milk and dairy products are sources of dietary iodine due to dairy-farming practices, such as iodine supplementation of feed (149-151), which were originally motivated by the deleterious impact of iodine deficiency on cattle health and milk yield, without consideration of population iodine status.

However, the per capita consumption of cows' milk and dairy products is declining in many countries (152-154) and there is a shift towards plant-based alternatives, particularly among women (Section 7.5.3).

#### 4.3.1.1.1 Milk intake as a predictor of iodine status

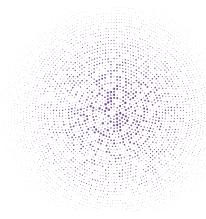
In the United Kingdom, milk intake is associated with iodine status in school-age children, adolescents, women of reproductive age and pregnant women. For example, in adolescent girls (14–15 years of age; n=737), milk intake was positively associated with UIC, with the lowest median UIC being in the group that did not consume milk (62  $\mu$ g/L) (50).

In Denmark, intake of milk was significantly associated with iodine excretion and reduced milk-iodine concentration may explain the decrease in UIC in women between 2004 and 2008 (155). While the use of supplements and consumption of iodine-rich food did not change in this period, milk-iodine concentration was lower in 2013 compared with previous years, explaining, at least partially, the decrease in urinary iodine excretion (UIE). These findings suggest that milk intake is needed to maintain adequate iodine intake, and the situation in Denmark is probably similar to many European Region countries where milk is an important source of iodine.

In pregnancy, determinants of iodine status were investigated in three European cohorts (ALSPAC, INMA, Generation R) (156) and milk and dairy product intake were predictors of iodine status in all three cohorts.

#### 4.3.1.2 Fish

Fish and other seafood are naturally rich in iodine, but the contribution to total iodine intake is generally limited due to infrequent consumption in many countries (157, 158). Fish contributes a relatively high amount to adult iodine intake in Iceland and Spain, at 47% and 32% respectively, but in other European countries fish makes a smaller contribution (Fig. 4.2; Table A3.2, Web annex C).



As the trend for plant-based diets grows, with the increased popularity and availability of plant-based alternatives to key sources of iodine (milk, dairy, fish), coordinated action is needed to ensure appropriate fortification of alternative milk and dairy products with iodine.

# 4.3.2 Plant foods, including dairy alternatives

In many parts of the European Region, particularly in mountainous regions, iodine levels in soil and groundwater are low (2). The iodine content of plants and crops depends on the iodine content of the soil in which they are grown and plant foods such as fruits, vegetables and cereals are therefore typically poor sources of iodine (20, 159).

Certain seaweed types contain large amounts of iodine as they concentrate iodine from seawater and can even be a potential source of excess (157, 160). Indeed, kelp supplements are not recommended, as the recommended dose along with the variability in iodine concentration, can lead to excess iodine intake. However, there is also a question of the bioavailability of iodine from seaweed as a meal, with data from Norway and the United Kingdom suggesting that the iodine is less bioavailable than an iodine supplement (of potassium iodide) (161, 162).

#### 4.3.2.1 Bread and cereals

Bread and cereals, with a naturally low iodine content (i.e. without iodized salt), provide less than 10% of adult iodine intake in countries such as Ireland and Norway. By contrast, bread and cereals can contribute over 50% of total iodine intake in adults when iodized salt is used for their production (e.g. in Belgium and the Netherlands (Kingdom of the); (Fig. 4.2) (see Section 6.1.4 for details on iodized salt in bread).

#### 4.3.2.2 Plant-based dairy alternatives

Data from several countries of the European Region, including Norway and the United Kingdom, have shown that in contrast to cows' milk, plant-based alternative drinks (e.g. oat or soy) contain very little iodine unless fortified (i.e. just 2.1% of the value of United Kingdom cows' milk (163). This is important as the majority of milk-alternative drinks on the market are not currently fortified with iodine, although they are fortified with other nutrients such as calcium. A United Kingdom market survey in 2020 found that just 28% of non-organic milk alternatives on the market were fortified with iodine compared to 88% that were fortified with calcium (164). Furthermore, the market for plant-based alternatives is expanding into other dairy products, such as alternatives to yoghurts and cheese. Currently, the proportion of these products that are fortified with iodine is lower than in milk alternatives (164). The lack of iodine fortification, and the low iodine content of unfortified plant-based dairy alternatives, means that consumers are at risk of low iodine intake if they switch from cows' milk products (see Section 7.5.3).

# 4.4 Variability in milk-iodine concentration across the European Region

There is considerable variability in milk-iodine concentration across the Region. For the purposes of this report, milk-iodine concentration data from European Region countries has been reviewed through a systematic review (see Section 2.1.2) (21).

#### 4.4.1 Results

Data on milk-iodine concentration are available for 25 countries in Europe (Table A3.3, Web annex C), and the variation is shown in Fig. 4.3. lodine concentration in milk ranged from 33  $\mu$ g/kg (in Slovenia) to 499  $\mu$ g/kg (in Latvia). Eighteen countries had milk-iodine concentration below the threshold required by the EU to label milk as a source (i.e. 22.5  $\mu$ g/100 g; see Section 4.5.1). However, this labelling threshold is based on 100 g providing 15% of the adult RNI, and therefore milk with a lower concentration would still be a good source for children. The seven countries where milk would have sufficient iodine to label it as a source were: Austria, Croatia, Czechia, Ireland, Italy, Latvia and the United Kingdom.

Data in six countries were based on results that did not report use of a certified reference material in the laboratory analysis, and therefore there is uncertainty as to the quality of the data. In two countries the data were from one season only, and in a further five countries the season was not stated. Furthermore, the sample size in some countries was small. Therefore, the overall dataset on milk-iodine concentration in Europe is of variable quality.

# 4.4.2 Factors affecting milk-iodine concentration

Milk-iodine concentration is affected by factors such as use of iodine-fortified cattle feed, iodine-containing disinfectants (iodophors) and goitrogens in cattle feed (150, 165, 166). The current EU regulations permit a maximum of 5 mg iodine/kg dry matter for dairy ruminants, but 2 mg/kg is recommended where possible (167). EFSA considered the case to reduce the maximum to 2 mg iodine/kg, but Member States, including Belgium, Finland and the United Kingdom, raised concerns that this lower value may reduce milk-iodine concentration and could worsen iodine deficiency in their countries (168). Historically, the limit was 40 mg/kg but this was reduced to 10 mg/kg in July 1996 (169), and then reduced again to 5 mg/kg in 2005 (170).

There is a linear relationship between feed-iodine concentration and milk-iodine concentration (171). However, the carry-over of iodine from the cattle feed into milk is reduced in the presence of goitrogenic substances, such as rapeseed (which contains glucosinolates, which are metabolized to thiocyanate, a competitive inhibitor of iodine via the sodium-iodide symporter (found in the mammary gland)). Experimental evidence has shown that the inclusion of rapeseed in cattle feed lowers milk-iodine concentration by up to 50% (172). These factors may result in considerable variation by season and dairy-production system (i.e. organic or conventional milk).

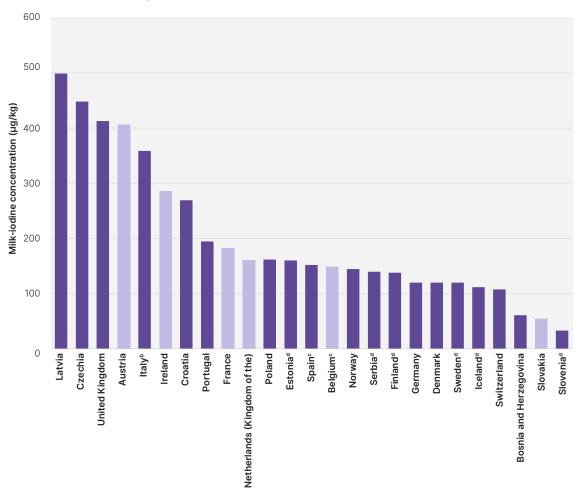
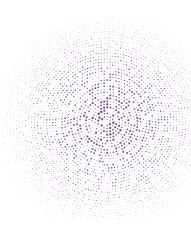


Fig. 4.3. Variability in milk-iodine concentration in 25 countries across the European Region<sup>a</sup>

<sup>&</sup>lt;sup>d</sup> Food composition database value: farm system and season not stated. *Source*: authors, data in Table A3.3, **Web annex C**.



Because of the importance of dairy to iodine sufficiency in the Region, regulations for animal feeds and milk-iodine concentrations should be part of iodine deficiency prevention programmes. The dairy industry needs to be involved in efforts to ensure iodine adequacy in many countries.

<sup>&</sup>lt;sup>a</sup> Pale purple bars indicate that the study did not report a certified reference material with the laboratory analysis and therefore there is uncertainty around method accuracy.

<sup>&</sup>lt;sup>b</sup> Summer milk only.

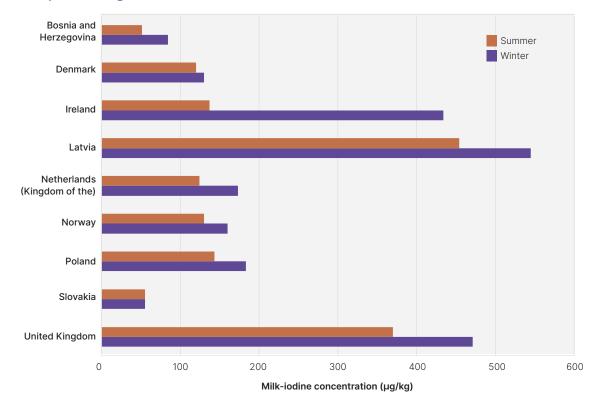
<sup>&</sup>lt;sup>c</sup> Autumn/winter milk only.

#### 4.4.2.1 Seasonal variation

The data from the systematic review showed that milk-iodine concentration is higher in winter than summer months in all but one country that had data from both seasons (the difference ranges from 0 to 297  $\mu$ g/kg; Fig. 4.4; Table A3.3, Web annex C). The higher iodine in winter milk is partly because of greater use of mineral-fortified feed in winter months, but also due to potential differences in goitrogenic load in winter and summer forage (150, 163). Fresh forage is grazed in the summer, which may reduce carry-over of iodine into milk due to a higher goitrogenic load. In the winter, the conserved forage (silage) has a lower goitrogenic potential because the lower pH may reduce the goitrogenic potential of the feed, resulting in greater carry-over of iodine into milk in the winter months (173).

This seasonal variation in milk-iodine concentration can affect iodine status, especially in countries with a high reliance on milk and dairy products to supply iodine. Studies in the United Kingdom have shown that iodine status is higher in the winter than in the summer in pregnant women and in children aged 8–10 years (174, 175). Furthermore, there is an interaction between season and milk intake, such that the effect of season on iodine status was greater in the highest consumers of milk (175).

Fig. 4.4. Iodine concentration of conventional milk by season in European Region countries



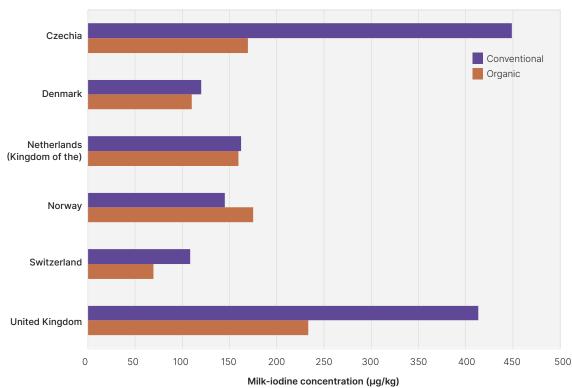
Source: authors, data in Table A3.3, Web annex C.

#### 4.4.2.2 Variation between organic and conventional milk

Whether milk is produced on organic or conventional farms may lead to variation in milkiodine content. The data from the systematic review showed that organic milk was lower in iodine in five out of six countries (difference ranged from 30  $\mu$ g/kg higher to 280  $\mu$ g/kg lower; Fig. 4.5) (21). The lower iodine concentration in organic milk is likely to be as a result of two factors, first the restrictions on cattle feed, and second the high pasture content of the diet (150, 163, 176-178). The EU organic regulations stipulate that at least 60% of the feed on organic dairy farms must be fresh or conserved forage (179, 180), thus limiting the amount of mineral-fortified concentrates that can be given to cattle. Organic dairy farming is more reliant on the iodine content of the soil and forage, which can be low. Secondly, the pasture content of organic feed is higher, with more grazing than on conventional farms, including white clover (which is used in organic farming as a natural nitrogen-fixer), and certain strains are goitrogenic (containing linamarin and lotaustralin, which are metabolised to thiocyanate). Studies have shown that there is an inverse relationship between pasture grazing and milk-iodine concentration (181).

Changes to farming practice can increase iodine concentration in organic milk – analysis of milk produced in the United Kingdom from 2019 found no overall difference in iodine content between organic and conventional milk (though it is still lower in the summer, which may relate to goitrogenic components in summer feed) (181, 182). This is likely as a result of changes to farming practice on organic farms, after a project to increase milk-iodine concentration to match that of conventional milk (183).





<sup>&</sup>lt;sup>a</sup> Countries included if there was data on season-average values of organic and conventional milk. Source: authors, data in Table A3.3, Web annex C.

# 4.5 Food labelling and iodine

#### 4.5.1 Foods labelled as a source of iodine

In EU regulations, to be labelled as a source of a nutrient, the food must provide 15% of the adult nutrient reference value (NRV) in 100 g; the NRV for iodine is 150  $\mu$ g/day according to the Annex to Regulation (EU) No 1169/2011 (184), so the food must have a minimum of 22.5  $\mu$ g/100 g. This explains why many milk-alternative drinks are fortified at this concentration. To be considered as a "high source" of a nutrient, the food must provide twice that as the "source" level (i.e. 30% of the NRV (or 45  $\mu$ g/100 g).

#### 4.5.2 Permitted health claims

If foods meet the threshold to be labelled as a "source" then there are six permitted health claims that can be used in relation to iodine (Table 4.2).

Table 4.2. Nutrition and health claims that relate to iodine

	Permitted claim	Conditions	EFSA opinion reference	Legislation
Nutrient claim	Source of iodine	15% adult NRV	NA	Annex to Regulation (EC) No 1924/2006 (185)
	High in iodine	30% adult NRV		
	lodine contributes to normal cognitive function			Commission Regulation (EU) 432/2012 of 16/05/2012 (186)
	lodine contributes to normal energy- yielding metabolism			
Health claims	lodine contributes to normal functioning of the nervous system	Food must be	2010;8(10):1800	
	lodine contributes to the maintenance of normal skin	at least a "source"		
	lodine contributes to the normal production of thyroid hormones and normal thyroid function			
	lodine contributes to the normal growth of children		Q-2008-324	Commission Regulation (EU) No 957/2010 of 22/10/2010

Source: authors.

# 4.6 Key messages

- Dietary intake recommendations for iodine should be harmonized between WHO, EFSA and countries of the WHO European Region, and ARs should be established for all population groups to allow appropriate interpretation of dietary iodine adequacy and inadequacy.
- lodine intake comes from many different sources in the diet in the population of the European Region, including iodized salt and milk products.
- Milk and dairy products are important dietary sources of iodine intake in many countries, although there is considerable variability in milk-iodine concentration across the Region.
- Considering its importance as a dietary source of iodine, there is a need for regulation of iodine concentration in milk, to reduce variability by season and farming practice.
- The shift towards plant-based alternatives to milk and dairy products is of concern, especially in countries that are reliant on milk as a source of iodine. Most of these alternative products are not fortified with iodine and therefore do not replace the iodine from cows' milk. With increased popularity and availability of plant-based alternatives, coordinated action is needed to ensure appropriate fortification of alternative milk and dairy products with iodine.
- All food-grade salt should be fortified with iodine. This includes salt used in households and processed foods, particularly products destined for the domestic market, such as bread, bakery-derived products, meat and meat products.

Chapter 5.

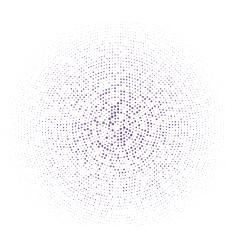
Assessment and monitoring of population iodine status

# 5.1 Urinary iodine concentration

lodine status in populations is assessed in cross-sectional studies by measuring UIC in casual spot-urine samples or 24 hour urine collections (13, 134). Most dietary iodine is excreted in urine within 24 hours of consumption and UIC reflects current iodine intake from all dietary sources. WHO recommends regular UIC monitoring in the population, ideally every five years (13).

lodine deficiency and excess in populations is defined by comparing population median UIC to thresholds defined by WHO (13). Epidemiological criteria are outlined in Table 5.1 (13). However, the thresholds for adults, pregnant women and infants are under debate (35, 134, 187) (Section 5.1.2) and are currently being reviewed by WHO. To obtain a reliable assessment of iodine status in a specific population based on median UIC requires a study sample size of approximately 500 (188, 189). Due to the high intra- and inter-variability of iodine intake, UIC cannot be used to assess individual iodine intake or to diagnose iodine deficiency (188, 189). Consequently, studies collecting a single UIC cannot determine the percentage of iodine-deficient subjects, a frequent misuse and misinterpretation of UIC data. During lactation, breast milk iodine concentration may be a more reliable biomarker of iodine status than UIC (35, 190).

UIC can be measured by the Sandell-Kolthoff method and ICP-MS. A comparative study of European UIC data observed analytical differences in UIC between laboratories (15), stressing the importance of external quality control for the analysis.



Countries should take advantage of national health and nutrition surveys and surveillance systems, including those for sodium intake, as well as using health facilities (such as maternity centres) to measure urinary iodine concentration.

**Table 5.1.** Epidemiological criteria for assessment of iodine nutrition in a population based on median or range of median UIC

lodine intake	lodine nutrition	School-age children	Adults	Pregnant women		
		Median UIC μg/				
Insufficient	Severe iodine deficiency	< 20 µg/L	Not defined	Not defined		
	Moderate iodine deficiency	20-49 μg/L	Not defined	Not defined		
	Mild iodine deficiency	50-99 μg/L	< 100 µg/Lª	< 150 µg/Lª		
Adequate	Optimum	100-299 μg/L <sup>b</sup>	≥ 100 µg/L	150−249 µg/L°		
Excessive	Risk of adverse health consequences	≥ 300 µg/L	Not defined	≥ 500 µg/L <sup>d</sup>		

<sup>&</sup>lt;sup>a</sup> UIC thresholds for severity of iodine deficiency have not been defined.

## 5.1.1 Population group for monitoring

lodine status can be monitored in any population group, but WHO recommends surveillance in school-age children, adults and/or pregnant women as a first priority (13). Monitoring in the same population group over time may help to better detect changes in iodine intake and facilitate trend analysis.

UIC was conventionally monitored in children aged 6–12 years as school-based studies were logistically feasible and children were considered representative of the general population (13, 191). However, the logistical conditions for school-based studies in the European Region have changed in recent years. Motivating schools, parents and children to participate in population-based studies has become challenging and recent studies have faced low response rates (187, 192), which biases study representativity and interpretation of results. Further, children may have higher milk consumption compared to other population groups and studies in children may not be representative of the general population, as previously assumed.

Whenever possible, UIC should be included in national health and nutrition studies, health studies assessing noncommunicable diseases, or be measured along with urinary sodium concentration in national surveillance for sodium intake. Surveillance of sodium intake is typically done by collecting 24 hour urine in adults, and many countries have successfully combined measurement of sodium and iodine. This is a cost-effective choice as additional costs associated are mainly analytical expenses for UIC.

<sup>&</sup>lt;sup>b</sup> Range of median UIC from Zimmermann et al. (2013) (39).

<sup>°</sup> Median UIC of 250–499µg/L indicates iodine intake above the requirement (13).

<sup>&</sup>lt;sup>d</sup> The term "excessive" means in excess of the amount needed to prevent and control iodine deficiency. Chronic exposure to iodine excess is associated with an increased prevalence of thyroid autoimmune diseases, hypothyroidism, hyperthyroidism and even goitre (Section 3.4). *Source*: WHO (2007) (13).

Reports of emerging iodine deficiency in many countries of the Region have prompted UIC studies in pregnant women, a population group particularly vulnerable to iodine deficiency. Over the past decade there has been a shift towards iodine status assessment in pregnant women (Section 7.1). Pregnant women can be sampled at regular antenatal care in permanent health facilities such as gynaecological practices and/or obstetric clinics during a given timeframe.

#### 5.1.2 Influence of urine volume

Spot urine samples may vary in dilution depending on the individual's hydration state at the time of sample collection (193-196). Low urine volumes may overestimate iodine intake and mask iodine deficiency, whereas large volumes may underestimate intake (193, 195).

The current WHO median UIC threshold defining adequate iodine intake ( $\geq 100~\mu g/L$ ) was originally defined for children based on the association between median UIC and goitre prevalence and the recommended average iodine intake of 120  $\mu g/day$  (120  $\mu g/day \times 0.90$  (90% excretion) / urine volume of 1.0 L/day  $\approx 100~\mu g/L$ ) (13, 134). The WHO median UIC threshold in adults of 100  $\mu g/L$  corresponds to an intake of about 150  $\mu g/day$  (RNI), based on the assumption that the average urine volume is 1.5 L/day (13). However, several recent European studies report larger average urine volume in adults, of around 1.9–2.1 L/day (147, 197-199). At a urine volume around 2 L/day, median UIC corresponding to the recommended daily average iodine intake of 150  $\mu g/day$  would be 70  $\mu g/L$ , lower than the current WHO threshold (Table 5.1). In pregnant women, a median UIC as low as 110  $\mu g/L$  may reflect an adequate average iodine intake of  $\geq 250~\mu g/day$ . Consequently, a median UIC in adults and pregnant women below the WHO median UIC thresholds ( $< 100~\mu g/L$  and  $< 150~\mu g/L$ ) may not necessarily indicate iodine deficiency, and this has implications for the interpretation of the data reported in UIC studies (Section 7.2).

# 5.1.3 Estimating iodine intake from UIC

It is possible to estimate the daily iodine intake and the prevalence of inadequate intake from UIC measured in 24 hour urine collections or spot urine samples by accounting for urine volume (134). The AR cut-point method involves two steps (131). First, a repeat spot urine sample is collected in a subsample of 25% of the study population and used to account for the intra-individual variability in iodine intake (134). Second, the daily iodine intake may be estimated either by collecting urine over 24 hours and expressing the iodine as 24 hour UIE ( $\mu$ g/day) (200) or by measuring urinary creatinine concentration (UCC) in spot urine samples (201-203). The UIE as  $\mu$ g iodine/g creatinine can be calculated from the UIC:UCC ratio (193, 200, 202, 204, 205) by multiplying the ratio by population-specific reference ranges for 24 hour urinary creatinine excretion (UCE) (201, 206) (Fig 5.1 1a). Reference values for daily creatinine excretion should preferably be from the same population (202). The obtained UIE may be used to estimate iodine intake, using the assumption that  $\geq$  92% of dietary iodine is excreted (135, 162, 207, 208) (Fig 5.1 1b).

Using the AR cut-point method (131), the prevalence of inadequate and/or excessive iodine intakes may be estimated as the proportion of individuals with iodine intakes lower than the AR (134). Iodine deficiency may be considered a public health concern in the studied population if > 3-10% have intakes below AR, but more data are needed to define the criteria.

# Figure 5.1. Equations used to estimate iodine intake from UIC

1a)

Estimated UIE (µg/day) = UIC (µg/L) / UCC (g/L) × UCE reference values (µg/day)

1b)

lodine intake (µg/day) = estimated UIE (µg/day) / 0.92

Data on the prevalence of iodine inadequacy, in addition to the median UIC, can improve the interpretation of iodine status, as demonstrated in several studies conducted in the European Region (134, 187, 194) and elsewhere (209). In Switzerland, a national study in Swiss adults collected 24 hour urine samples (average urine volume was 2.0 L) and observed a median UIC of 76  $\mu$ g/L, suggesting iodine deficiency, based on the WHO threshold (147) (Table 5.1). However, the prevalence of inadequate iodine intake estimated using the AR cut-point method was 2% in men and 14% in women (147). Another national study in Swiss children reported adequate iodine intake based on the median UIC (127  $\mu$ g/L), but the estimated prevalence of inadequate iodine intake (< 65  $\mu$ g/day) was 5.4% (187). In German adults with a median UIC of 54  $\mu$ g/L, the prevalence of iodine inadequacy using the AR cut-point method in spot urine samples was estimated at 33% (194).

The data suggest that information on urine dilution and estimation of the prevalence of inadequacy is particularly advantageous in countries with borderline iodine intakes. It provides a more reliable assessment of the mean/median iodine intake, estimates the distribution of habitual intakes and identifies the extent of the risk of iodine inadequacy. This method can be used as a complement to the conventional reporting of median UIC.

# 5.2 Thyroglobulin measurement parameters

# 5.2.1 Tg concentration in whole blood or serum

Tg measured in blood is a biomarker of population iodine status indicating increased thyroid activity and/or volume (13). Tg is synthesized by follicular cells in the thyroid and is a precursor for the production of thyroid hormones (29). Blood levels of Tg are low at adequate iodine intakes but increase in iodine deficiency and excess (39, 210-212). In iodine-deficient populations, elevated Tg concentrations normalize in response to iodine repletion (210). However, an elevated Tg concentration is not specific to iodine deficiency and the role of other determinants is not fully understood (29, 213). The intra-individual variability in blood Tg concentration is also high (214). However, Tg can be a useful population marker of thyroid activity when evaluating change in iodine status within a study, for example in an randomized controlled trial providing iodine supplements. Absolute levels in cross-sectional studies are more difficult to interpret. Tg may be used as a complement to UIC, but should not replace UIC as the main biomarker of population iodine status.

Tg concentration can be measured in serum, plasma or whole blood extracted from dried blood spots (215, 216). The reference ranges for Tg vary between analytical methods and assays (217, 218) and study/survey data measured using two different assays cannot directly be compared. A certified reference material can be used to improve the standardization between methods, but does not entirely overcome the problem. Further, Tg antibodies may interfere with the analysis (218). Adequate iodine intake in populations may be indicated by a low prevalence of elevated Tg (< 3%) (i.e. concentrations above the reference range).

### 5.2.2 Neonatal TSH

In most countries of the European Region, all newborns are routinely screened for congenital hypothyroidism by measuring TSH in whole dried blood samples on filter paper collected 2–5 days after birth (219). The purpose of neonatal screening is to identify newborns with congenital hypothyroidism and initiate prompt treatment with LT4 to prevent irreversible neurodevelopmental delay and optimize developmental outcomes (220, 221). Congenital hypothyroidism is suspected when elevated TSH is detected at screening (generally  $\geq$  20 mIU/L, but some countries apply lower thresholds depending on the method used) (219-221).

TSH data from national screening programmes may also be used to identify populations at risk of iodine deficiency (13, 222-224). Exposure to iodine deficiency during pregnancy and/or after birth may increase the infant's thyroidal iodine turnover, resulting in thyroid hyperstimulation and mildly elevated neonatal TSH (224). A prevalence of mildly elevated neonatal TSH (> 5 mlU/L) in > 3% of a population may indicate iodine deficiency (13, 222-224). Prevalence increases with severity of deficiency (224) and decreases as iodine status improves (225). Although elevated neonatal TSH may be a good indication of moderate to severe iodine deficiency during pregnancy, the sensitivity of neonatal TSH to mild iodine deficiency is poor (226, 227). Lowering the threshold of elevated TSH has been proposed to better identify populations exposed to mild iodine deficiency (228-231). Trends in neonatal TSH over time may reflect changes in iodine status and may provide complementary information on population iodine nutrition in the European Region (227, 228, 230, 231), but more data are needed.

# 5.2.3 Surveillance of thyroid disorders

A few countries in the European Region collect clinical data on the incidence of thyroid disorders related to iodine deficiency (**Table 5.2**) in national health registers (e.g. Armenia, Azerbaijan, Belarus, Kyrgyzstan, Russian Federation, Sweden and Ukraine). Routine use of health statistics on goitre incidence is built into existing public health systems for monitoring of health indicators and does not require additional financial resources or organizational efforts. In Belarus, following successful implementation of regulations on the mandatory use of iodized salt in the food industry (adopted in 2001), median UIC increased from  $68 \mu g/L$  to  $191 \mu g/L$  (232) and the goitre incidence decreased almost four-fold between 1998 and 2007 (**Fig. 5.1**). In the Russian Federation, with low population coverage with iodized salt, the incidence of goitre in children (0–14 years old) remained stable between 2009 and 2015 (233). In Sweden, adequate iodine intake has been reported in school children (median UIC  $125 \mu g/L$  (234)) and no cases of "iodine-deficiency goitre (E01)" were recorded in children and adolescents between 1998 and 2018 (235).

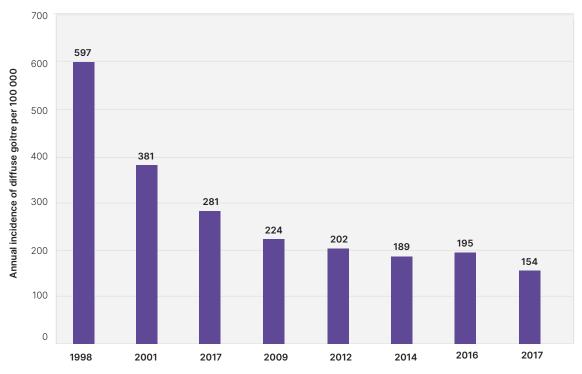
However, trends in goitre morbidity obtained from national health registers should be interpreted with caution as goitre incidence may depend more on the existing clinical practices for detecting goitre and may not be indicative of changes in iodine nutrition of the population.

**Table 5.2.** Iodine-deficiency related thyroid disorders and allied conditions (ICD-10)

ICD-10 code	Disease condition
E.01.0	lodine-deficiency related diffuse (endemic) goitre
E.01.1	lodine-deficiency related multinodular (endemic) goitre
E.01.2	lodine-deficiency related (endemic) goitre, unspecified
E.01.8	Other iodine-deficiency related thyroid disorders and allied conditions

ICD: International Classification of Diseases. *Source*: WHO (2019) *(236)*.

Fig. 5.2. Incidence of diffuse goitre in children and adolescents (0–18 years) in Belarus in 1998–2017



Source: Mokhort et al. (2018) (232).

# 5.3 Key messages

- UIC measured in spot or 24 hour urine collections reflects recent iodine intake from all dietary sources and is the most suitable biomarker to assess population iodine status.
- The current WHO median UIC threshold defining adequate iodine intake (≥ 100 μg/L) was originally defined for children and later extended to adults. However, the median UIC thresholds recommended for adults (100 μg/L) and pregnant women (150 μg/L) may underestimate the iodine intake and be inconsistent with the recommended average iodine intake of 150 μg/day for adults and 250 μg/day for pregnant women due to high urine volume in many European Region adult populations (typically on average ~ 2 L/day).
- Median UIC above the threshold for iodine sufficiency does not preclude iodine deficiency in some groups/individuals in the population. Methods to estimate the prevalence of inadequate iodine intake have been proposed. In countries with borderline iodine intakes, accounting for intra-individual variability in iodine intake by collecting a repeat urine sample in 25% of the study participants and correction for urine volume by measuring urinary creatinine can provide useful additional information for a more reliable assessment of iodine status.
- UIC can be measured in national nutrition studies, studies monitoring sodium intake, or stand-alone iodine studies. Surveillance through permanent sentinel health facilities such as obstetric care may also be an option.
- It is recommended that national iodine status be monitored in at least one population group every five years.

Chapter 6.

# Strategies to prevent and control iodine deficiency

# 6.1 Salt iodization

Fortification of salt with iodine is the preferred public health strategy for the prevention and control of iodine deficiency (7). This WHO recommendation is based on the principle that, if most salt consumed is iodized, salt iodization provides enough iodine to meet the dietary requirements in all population groups, including pregnant women, lactating women and breastfed infants with high dietary requirements (7, 13, 237). Numerous studies demonstrate the effectiveness of iodized salt and confirm adequate iodine status in all population groups if the coverage is high (81, 191, 238).

Salt iodization was first introduced in Switzerland (in 1922) and has been successful for more than 100 years (6, 239). Several countries of the European Region initially implemented iodized salt in areas affected by severe iodine deficiency and endemic visible goitre. In the 1950s, salt iodization was made mandatory in countries of central and eastern Europe (Austria, Bulgaria, Poland, Romania, the Union of Soviet Socialist Republics (USSR), Yugoslavia) (240). However, with reduction of endemic goitre in the 1960s and 1970s monitoring waned, public interest decreased, resources were reallocated to other health issues and iodine deficiency re-emerged. In the 1990s, salt iodization was revived in many countries of the European Region and the production and trade of iodized salt increased with resulting improvement in iodine status (241).

# 6.1.1 Legislation and regulations

Salt iodization is currently implemented in most Member States of the WHO European Region, and Kosovo<sup>9</sup> (Table 6.1, Web annex A). National policies (or equivalent) are regulated by legislation (national law, or equivalent) or regulatory acts of governments/ministries of health/public health authorities (Table 6.1).

Salt iodine fortification is mandatory in more than half of the Member States and Kosovo<sup>10</sup> (n=30/54). In 21 out of these 30, all salt for human consumption (discretionary salt and salt used by the food industry) must be iodized. Of these 21, a few exempt certain types of salt from mandatory regulations (e.g. sea salt in Slovenia), or certain processed foods (salt for artisanal soft cheese production in Armenia). In 9 of the 30, mandatory iodization applies to salt for specific foods and/or distribution channels (for example bread, **Table 6.1**).

<sup>9</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>10</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

Salt iodization is voluntary in 13 countries (i.e. both iodized and non-iodized salt may be available and no mandatory legislation exists with regard to production, import or distribution of iodized salt (Table 6.1)). In countries with voluntary salt iodization, food business operators have the freedom to choose between iodized salt and plain salt in food production. Regulations for salt iodization are not available in five countries (Table 6.1).

**Table 6.1.** Member States (and Kosovo)<sup>[1]</sup> with mandatory, voluntary and no/unknown legislation or regulation for salt iodization in the WHO European Region

Mandatory	(n=30)	Voluntary (n=13)	Noª or unknown <sup>b</sup> ( <i>n</i> =11)
All salt for human consumption ( <i>n</i> =21)	Salt for specific foods and/or distribution channels (n=9)		
Albania	Austria <sup>c</sup>	Belgium	Andorra <sup>b</sup>
Armenia	Belarus <sup>d</sup>	Czechia	Cyprus⁵
Azerbaijan	Denmark <sup>e</sup>	Finland	Estonia <sup>b</sup>
Bosnia and Herzegovina	Hungary <sup>f</sup>	France	Iceland <sup>a</sup>
Bulgaria	Italy <sup>g</sup>	Germany	Ireland <sup>a</sup>
Croatia	Republic of Moldovad,g	Greece	Israela
Georgia	Poland <sup>h</sup>	Latvia	Luxembourg <sup>b</sup>
Kazakhstan	Portugal <sup>f</sup>	Netherlands	Malta <sup>a</sup>
Kyrgyzstan	Russian Federation <sup>f</sup>	(Kingdom of the)	Monaco⁵
Lithuania		Norway	San Marino <sup>b</sup>
Montenegro		Spain	United Kingdom <sup>a</sup>
North Macedonia		Sweden	
Romania		Switzerland	
Serbia		Ukraine	
Slovakia			
Slovenia			
Tajikistan			
Türkiye			
Turkmenistan			
Uzbekistan			
Kosovo <sup>[1]</sup>			

<sup>&</sup>lt;sup>a</sup> No national policy.

<sup>&</sup>lt;sup>b</sup> Unknown national policy.

<sup>&</sup>lt;sup>c</sup> Mandatory for the production of bread and bakery products.

<sup>&</sup>lt;sup>d</sup> Required for the production of all processed foods, except seafood and cheese.

e Required for household salt and salt included in bread and general bakery products intended for sale in Denmark.

f Must be used in mass catering (education, health and social welfare facilities).

<sup>&</sup>lt;sup>9</sup> Shops must sell both iodized and non-iodized salt, but are required to only provide non-iodized salt on specific request

<sup>&</sup>lt;sup>h</sup> Only table salt requires mandatory iodization.

<sup>&</sup>lt;sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

Source: authors. More information in Web annex A.

In the past 10 years several countries updated and strengthened their salt iodization requirements (Web annex A). Albania (in 2020) and Uzbekistan (in 2015) revised the legislation requiring the use of iodized salt in the food industry, resulting in increased iodine intake in school children. In Uzbekistan, the revised law for salt iodization abolished the previous requirement to provide non-iodized salt to people with "contraindications" to iodized salt; now all salt intended for human consumption must be iodized. In Bosnia and Herzegovina (in 2012) and in Montenegro (in 2020), potassium iodate (KIO<sub>3</sub>) was made compulsory for salt iodization and the iodine level was increased from 12–18 mg/kg to 20–30 mg/kg. In the Republic of Moldova (in 2022), the iodine level of salt was increased to 25–40 mg/kg while use of iodized salt was made mandatory in the baking industry and public catering. In the Russian Federation, a new regulation (adopted in 2020) requires mandatory use of iodized salt in school canteens and kindergartens as well as other social and educational institutions. Denmark revised the level of iodine in salt from 13 to 20 mg/kg in 2019. Norway revised the maximum allowed level of iodine in salt from 5 to 20 mg/kg in 2024.

#### 6.1.1.1 lodine compounds and level of fortification

Potassium iodide (KI),  $KIO_3$ , sodium iodide (NaI) and sodium iodate (NaIO $_3$ ) are permitted for salt fortification (Web annex A). These fortificants cause no sensory changes to salt or food and the bioavailability is high (242).

Salt iodine fortification should provide the adult RNI of 150  $\mu$ g/day (7). The average amount of iodine added to salt should be adapted based on: 1) estimated average salt consumption (g/day); and 2) iodine losses estimated based on local conditions of production, climate, packaging and storage (30% generally assumed) (7). At a salt intake of 5–10 g salt per day, the recommended iodine level is 20–40 mg/kg salt, with the assumption that the salt contains at least 15 mg iodine/kg salt at the household level (7).

In eastern Europe and central Asia only  ${\rm KIO_3}$  is used for salt fortification and the normative for iodine content is 40 ± 15 mg/kg, with the exception of the Republic of Moldova (25–40 mg/kg). In western and central Europe the normative amounts of iodine in salt range from 15 mg/kg to 60 mg/kg ( $\leq$  65 mg/kg for bread salt in the Netherlands (Kingdom of the)) (Web annex A). While the components to use for iodine fortification are harmonized by European Commission Regulation No 1925/2006 (184) the differentiation that countries apply to the permissible levels of these components in salt, leads de facto to a patchwork of rules across the European Union. Depending on the type of the compound (potassium iodide or iodate) added to salt, food products can be barred from entering certain countries. Harmonization of the fortification requirements and the use of iodized salt in food production would ensure free trade by applying the principle of mutual recognition.

# 6.1.2 Production, import and sales of iodized salt

The European Region is the second largest salt-producing region in the world, after China. Food-grade salt is a crystalline product obtained from sea water, underground rock salt deposits or natural brine. According to Codex Alimentarius, the content of sodium chloride (NaCl) in food-grade salt will not be less than 97% on a dry matter basis, exclusive of additives (243). About 7% of total salt production is used for nutritional purposes, whereas the main applications for salt are in chemical industries and de-icing of roads in the winter (244).

In the majority of counties in the European Region, iodized salt is manufactured in large modern factories with production management systems focused on food quality and safety, such as ISO 9000 series, ISO 22000 series, Hazard Analysis and Critical Control Points, or Good Manufacturing Practices. Compliance with regulatory standards is generally high in the Region, apart from Tajikistan and Uzbekistan where iodized salt is produced by a large number of small and medium size enterprises (241).

#### 6.1.2.1 Western and central Europe

Most salt consumed in western and central Europe ( $\geq 75\%$ ) comes from industrially processed foods (23). While supporting data is limited, low use of iodized salt in the production of these foods is believed to be a major cause of inadequate and/or declining iodine intake in many countries. This report, for the first time, has attempted to provide information on the relative proportion (%) of sales of iodized vs. non-iodized salt from producers in western and central Europe.

Data was obtained from members of EUsalt, an association of salt producers selling significant volumes of salt in the Region (Section 2.2.2). Eight of 26 EUsalt member companies responded to the inquiry, eight did not produce food-grade salt and 10 did not respond. Two member companies who do not produce in the European Region were not included in the analysis. The data compiled by EUsalt provide unique insight into the sales of iodized salt in selected countries. Fig. 6.1 presents information on the proportion (%) of iodized vs. non-iodized salt sold for retail and food industry for the eight EUsalt members who responded, selling to 13 countries in the European Region in 2022 or 2023. For producers selling to more than one country, data for the three countries with the largest volumes were provided. The proportion of industrial salt which is iodized ranges from 0% to 49% and is low (< 20%) in nine of the 13 countries (Fig. 6.1). The proportion of retail salt that is iodized varies widely from 0% to 100%, but is generally higher than for industrial salt (Fig. 6.1). The results confirm the perception that coverage of iodized salt, particularly industrial salt, may not be adequate in some countries.

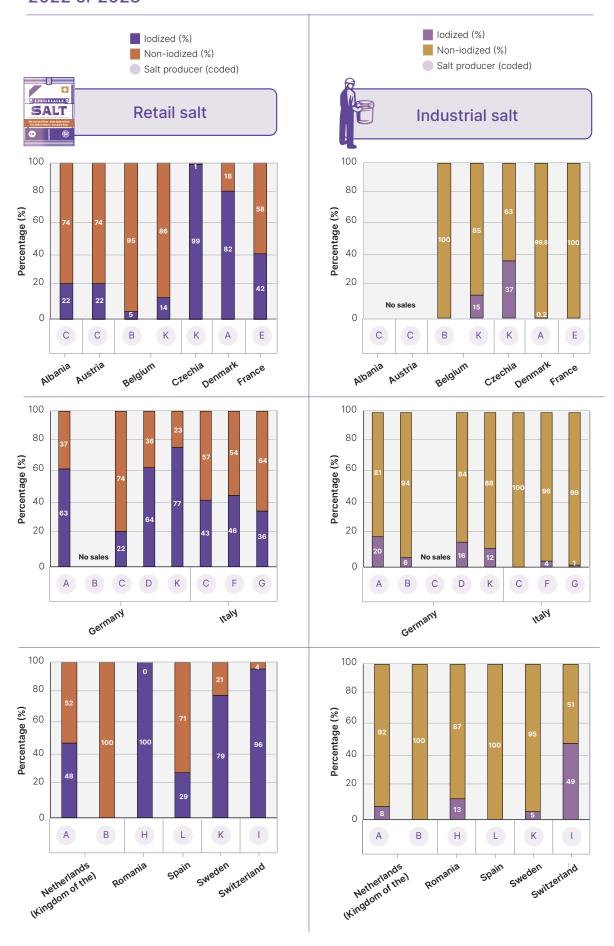
There are some limitations with the data presented. The response was incomplete and salt producers who are not members of EUsalt are not represented, for example, in Albania, where most salt is locally produced and coverage of iodized household salt is high (82%). Lack of information about the market share for the reporting companies may over- or underestimate the total sales of iodized salt. In Austria, Denmark and the Netherlands (Kingdom of the), regulations require use of iodized salt in bakery products and a higher proportion of iodized salt than reported is expected. It is possible that the low use of industrial salt reported by the current data underestimates the true total proportion of iodized industrial salt.

A further limitation is the lack of information on the proportion of salt produced for retail and industry use. Information from Switzerland shows that 73% of all food-grade salt was used by the food industry and 27% sold in retail trade (personal communication, Swiss Saltworks AG, 2023). In total, 61% of all food-grade salt was iodized: almost all retail salt (96%) and half of industry salt (49%).

Despite limitations, the data presented raise concerns about potential poor coverage of iodized salt in western and central Europe. The results confirm the need for more data and suggest that information on sales of iodized salt may be a new approach for programme monitoring. Addressing the conflict of interest between the importance of public health and the reluctance of businesses to share information due to commercial competition or legal constraints is a complex but crucial issue in addressing the problem of iodine deficiency in the European Region.

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Fig. 6.1. Sales of retail and industrial salt by 8 members of EUsalt in 2022 or 2023<sup>a</sup>



<sup>&</sup>lt;sup>a</sup> Data was obtained from salt producers that are members of EUsalt (section 2.2.2). Salt producers are coded as A–L, with one large company coded with three letters.\_ Source: authors, with data obtained by EUsalt for this report (2024).

#### 6.1.2.2 Eastern Europe and central Asia

For seven countries in eastern Europe and central Asia (**Table 6.2**), the penetration of iodized salt was calculated based on annual production/import of iodized salt against its potential demand, the population size and per capita salt intake derived from national studies measuring 24 hour sodium excretion (245).

In Armenia and Turkmenistan, almost all salt produced nationally and imported was iodized. Annual iodized salt production in Kazakhstan reached 253 600 tonnes in 2018, fully covering the potential domestic demand and with over 100 000 tonnes exported to neighbouring countries. Production and/or import of iodized salt did not meet the potential demand in Uzbekistan (28%), Tajikistan (34%) and the Republic of Moldova (45%). In Georgia, which has no domestic salt production, imports of iodized salt were higher than the potential demand.

**Table 6.2.** Production and/or import of iodized salt against the potential demand in seven countries of eastern Europe and central Asia

Country	Year	Population (millions)	Annual production and/or import (tonnes) <sup>a</sup>	Annual potential demand (tonnes) <sup>b</sup>	Penetration of iodized salt (%)
Armenia	2022	2.777	12 471	12 694	98
Georgia	2022	3.748	34 640	18 218	190°
Kazakhstan	2018	19.606	253 600	121 590	208 <sup>d</sup>
Republic of Moldova	2022	3.435	4 732	10 500	45
Tajikistan	2022	10.143	18 642	54 725	34
Turkmenistan	2018	6.516	36 000	35 365	102
Uzbekistan	2022	35.684	55 000	192 060	28

<sup>&</sup>lt;sup>a</sup> Country information on production and/or import of iodized salt was provided by representatives of the salt industry, IGN national coordinators and other experts.

Source: authors.

# 6.1.3 lodized salt coverage at household level

Population coverage of iodized salt has conventionally been monitored at the household level (13). Previous guidelines (13, 246) recommended that household iodized salt should contain at least 15 mg iodine/kg salt to be considered "adequately" iodized, and the target for mandatory salt iodization programmes was 90% or more of households using adequately iodized salt (13, 247). However, household salt is only one part of the intended total iodized salt supply and many countries achieved adequate iodine status despite having household coverage below 90%.

<sup>&</sup>lt;sup>b</sup> Annual consumption of salt and potential demand for iodized salt was calculated based on population size and per capita salt intake derived from national studies measuring 24 hour sodium excretion.

<sup>°</sup> Import of iodized salt.

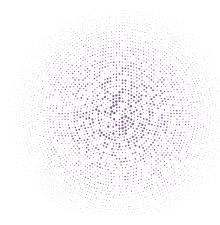
<sup>&</sup>lt;sup>d</sup> lodized salt is exported to neighbouring countries.

Rapid test kits (RTKs) have been widely used to assess the presence and, in some cases, the adequacy of iodine content in salt. RTKs consist of small bottles containing a stabilized starch/acid-based solution. The presence of iodine is indicated by a blue/purple stain that develops when the solution is dropped onto a sample of salt containing iodine. However, evaluation of their performance shows that RTKs are reliable only to distinguish between the presence and absence of iodine in salt, but not to determine the level of iodine. Validated quantitative laboratory methods, such as iodometric titration, the Sandell-Kolthoff method, iCheck or the WYD Checker, are used for measuring iodine content in household salt (247, 248).

Data on household use of iodized salt over the past 15 years (2008-2023) are available from 20 Member States of the WHO European Region, and Kosovo<sup>11</sup> (n=21) (**Table 6.3**). In six of these, RTKs were used while in 13 iodine content of salt was determined by quantitative methods. For these Member States, and Kosovo,<sup>12</sup> total coverage vs. coverage with adequately iodized salt (> 15 mg/kg) is presented in **Table 6.3**. In Portugal, a recent study analysed iodized salt supermarket sales from 2010 to 2021 from a major retailer (25% of the market share), identifying the proportion of iodized salt in total salt sales and its distribution (249). In Italy and Switzerland household coverage was assessed using questionnaires.

More than 90% coverage of households with iodized salt was reached in 11 out of 12 Member States, and Kosovo, <sup>13</sup> with mandatory salt iodization (n=13) (i.e. requiring iodization of all salt for human consumption). Household surveys in Albania, Tajikistan and Uzbekistan revealed lower iodized salt coverage in rural areas, certain geographical zones and among poorer and less educated population groups (250-252). In countries with > 90% household coverage (Armenia, Georgia, North Macedonia) such differences were absent (253-255).

In Belarus and the Republic of Moldova, despite the absence of mandatory iodization of table salt, household coverage with iodized salt was reasonably high (81% and 77%, respectively) (232, 256). In the Russian Federation, average household coverage with iodized salt was generally low (20%), with the exception of the previously severely iodine deficient Tuva region that reached 95% coverage thanks to a regional prevention programme (257, 258). In Portugal, only 11% of retail (supermarket) salt was iodized (249).



Salt iodization remains the main strategy to ensure adequate iodine intake in the European Region. Lifestyle choices and dietary trends, including increasing use of processed foods and the switch to plant-based diets and dairy alternatives, are contributing to persistent, and in some countries increased, insufficient iodine intakes.

<sup>11</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>12</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>13</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

**Table 6.3.** Household coverage with iodized salt in countries of the WHO European Region, and  $Kosovo^{[1]}$ 

Member States,	Level of survey	Year of survey	Household coverage with iodized salt		
and Kosovo <sup>[1]</sup> (References)			Questionnaire/ market studies	Presence of iodine by RTK (%)	Presence of iodine/ level of iodine > 15 mg/kg salt by quantitative methods (%)
Mandatory iodization	on of all salt fo	or human c	onsumption		
<b>Albania</b> (Ylli et al., 2022) (250)	National	2021	-	_	82/68
Armenia (Hutchings et al., 2019) <i>(253)</i>	National	2017	-	-	93/93
Azerbaijan (UNICEF, 2013) (259)	National	2013	-	94	-
Georgia (Gerasimov & van der Haar, 2017) (254)	National	2017	-	-	95/95
Kazakhstan (Sharmanov, Tazhibayev & Ospanova, 2011) (260)	Regional	2011	-	91	-
Kyrgyzstan (UNICEF, 2021) (261)	National	2021	-	_	98/76
Montenegro (Institute of Public Health, Montenegro, 2021) (262)	National	2020	-	-	100/81
North Macedonia (Kostova et al., 2020) (255)	National	2016	-	_	100/98
<b>Serbia</b> (van der Haar et al., 2011) <i>(240)</i>	National	2007	-	-	100/68
Tajikistan (UNICEF, 2017) (264)	National	2021	-	-	37/13
Turkmenistan (UNICEF, 2016) (252)	National	2018	-	100	-
Uzbekistan (Rohner et al., 2020) (251)	National	2017	-	-	65/20

## Table 6.3 contd

Member States,		Year of	Household coverage with iodized salt		
and Kosovo <sup>[1]</sup> (References)		survey	Questionnaire/ market studies	Presence of iodine by RTK (%)	Presence of iodine/ level of iodine > 15 mg/kg salt by quantitative methods (%)
Kosovo <sup>[1]</sup> (National Institute of Public Health Kosovo, 2018) (263)	Area	2018	-	-	100/96
Mandatory iodizatio	n of salt for s	specific food	s and/or distribut	tion channels	
Belarus <sup>a</sup> (Mokhort et al., 2018) <i>(232)</i>	National	2018	-	-	81/81
Italy <sup>b</sup> (De Angelis et al., 2023) <i>(265)</i>	National	2015– 2019	72	-	-
Republic of Moldova <sup>c,d</sup> (D'Elia et al., 2019) (256)	National	2016	-	-	77/57
Russian Federation <sup>c</sup> (Troshina et al., 2021) (257, 258)	Regional	2008– 2020	_	20	-
Voluntary salt iodiza	ation				
<b>Belgium</b> (Vandevijvere et al., 2012) <i>(48)</i>	National	2010– 2011	-	37	-
Portugal (Machado et al., 2023) (249)	National <sup>e</sup>	2010– 2021	11 <sup>e</sup>	_	_
Switzerland (Fischer et al., 2023) (187)	National	2020– 2022	87	-	85/81
Ukraine (Tronko, Kravchenko & Bondar, 2022) (266)	National	2012	_	21	-

<sup>&</sup>lt;sup>a</sup> Required for the production of all processed foods, except seafood and cheese.

<sup>&</sup>lt;sup>b</sup> Requires shops to sell both iodized and non-iodized salt and to only provide non-iodized salt on specific request.

<sup>&</sup>lt;sup>c</sup> Must be used in mass catering (education, health and social welfare facilities).

<sup>&</sup>lt;sup>d</sup> Mandatory for the production of bread and bakery products.

<sup>&</sup>lt;sup>e</sup> Market survey of household salt sold in supermarkets.

<sup>&</sup>lt;sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999). *Source*: authors.

# 6.1.4 lodized salt use in processed foods

Industrially processed foods account for an increasing proportion of total salt intake in all countries of the WHO European Region. Foods produced or cooked outside the household, such as bread or processed meat products are the main sources of salt in many countries of the WHO European Region (70–80% of the total amount of salt consumed) (23). This "hidden" salt used in food production should also be iodized to ensure adequate population iodine nutrition (7).

The use of iodized salt in processed foods varies between countries. In 20 Member States, and Kosovo<sup>14</sup> (*n*=21) with mandatory salt iodization, all salt containing foods (with few exceptions) must be produced with iodized salt. Targeted mandatory iodization of salt for specific foods (for example bread, **Table 6.1**, **Box 1**) is applied in four countries (Austria, Belarus, Denmark and the Republic of Moldova). In five other countries, mandatory iodization is applied to retail salt (Italy, Poland) or school meals (Hungary, Portugal, Russian Federation).

# **Box 1.** Case study: Denmark – mandatory iodized salt in bread/bakery products

Voluntary use of iodized salt in Denmark started in 1998 at a salt iodine concentration of 8 mg/kg (household salt and salt for food production), but the use of iodized salt in food production did not improve. Therefore, a programme mandating iodization of household salt and salt used in bread production began in 2000 at an iodization level of 13 mg/kg. Data suggesting low iodine intake in pregnant women (279, 280) led the Danish food authorities to increase the iodine fortification level from 13 to 20 mg/kg in 2019.

lodine is currently also allowed to be added to salt used in some food categories (including potato products, crisp bread and pizza dough). Food producers can apply for the addition of iodine to new categories. Approvals are based on a risk assessment that takes iodine intake from other food categories into account.

Modelling of iodine intake from industrialized processed foods showed that bread and bakery products with iodized salt are major sources of iodine in countries of eastern Europe and central Asia with mandatory salt iodization programmes (Armenia, Belarus, Georgia, Republic of Moldova), providing approximately 32–50% of the adult RNI for iodine (267). Bread consumption is relatively high also in the Russian Federation and in Ukraine. If adults were assumed to be consuming only bread from bakeries where all the bread is baked with iodized salt at the minimum acceptable level of 25 mg/kg, bread would provide approximately 37% in the Russian Federation and 32% in Ukraine of the adult RNI for iodine (268).

<sup>14</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

The relative contribution of other salt-containing industrialized processed foods (e.g. meat products, cheese, pickles, etc.) to iodine intake is much lower (269-272).

In countries with voluntary salt iodization, food business operators have the freedom to choose between iodized and plain salt in food production. In Belgium (since 2009), iodized salt has been used in bread-making at a concentration of 10–15 mg/kg salt (273) (Box 2), while in the Netherlands (Kingdom of the) bakery salt (for all bakery products) must contain a maximum 65 mg KI/kg (274). In the Netherlands (Kingdom of the), a slice of bread (40 g) provides 20  $\mu$ g iodine (in contrast to 3  $\mu$ g iodine/40 g slice in the United Kingdom) (275)). Estimates suggested that 95% of all bread and 1% of all pastries and cookies contained iodized bakery salt (274). Iodized salt at lower levels ( $\leq$  25 mg/kg) was estimated to be used in 40% of all pizzas and 0.5% of other specific food groups.

# **Box 2.** Case study: Belgium – agreement between Ministry of Health and bakeries

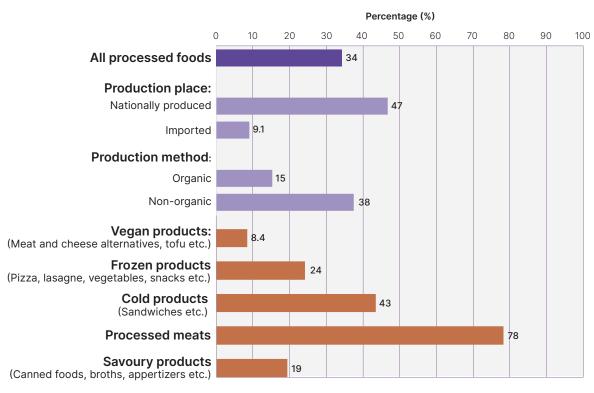
Salt iodization is allowed in Belgium, but there is no specific law regulating the iodine content of salt, only a law regulating the maximum iodine content of foods (15% of the adult NRV). The Belgian Health Council, a federal scientific body, recommends that salt be fortified with iodine at 15 mg/kg salt.

Against this legal backdrop, in 2009, at the instigation of the Ministry of Health, the bakery industry agreed to replace cooking salt with iodized salt (15 mg/kg) for products destined for the domestic market. The signatory parties monitor and report on the application of the agreement.

In 2010–2011, a survey on iodine nutrition showed that school children no longer suffered from iodine deficiency, as had been the case in previous surveys. Fortifying bread with iodized salt may have helped to correct iodine deficiency in Belgian children.

Overall, this approach suggests that the lack of a specific law on salt iodization is not always an obstacle to optimizing iodine intake. The absence of a legal framework can also be an opportunity for action.

Over recent years, the addition of iodized salt has become less popular among food business operators. Recent market surveys from Germany and Switzerland found overall low coverage of iodized salt in processed food products – 9% in Germany and 34% in Switzerland (276-278). In Switzerland, the proportion of iodized salt in meat and meat products is high (78%), whereas vegan products rarely contain iodized salt (8%) (Fig. 6.2) (278).



**Fig. 6.2.** Proportion of iodized salt in processed foods in Switzerland<sup>a</sup>

#### 6.1.4.1 Challenges for the use of iodized salt in processed foods

While use of iodized salt by the food industry could be increased across the WHO European Region to improve and sustain optimum iodine status, there are several challenges and barriers related to regulatory structures, particularly in the EU countries with voluntary legislation.

Current food labelling laws are discouraging food business operators from using iodized salt in compound foods. According to current EU regulation (184), compound ingredients when used in processed foods must identify all their ingredients on the food label, unless there are specific exemptions. lodized salt is a compound ingredient consisting of salt and an iodine substance with a chemical name that may alienate some consumers. A food label declaring that the product contains "iodized salt" without specific indication of the chemical form of iodine would be more consumer friendly. Food business operators argue that such a regulatory change would provide an incentive to use iodized salt without compromising on consumer acceptance of their products.

Food business operators trading their products across borders in the European Region must also comply with national legislation and regulation for salt iodization in each country. Some countries mandate iodized salt only for specific food groups, or require mandatory registration or approval of products made with iodized salt before placing them on the market. This

<sup>&</sup>lt;sup>a</sup> Market study of 750 processed foods in Switzerland in 2021–2022. Source: Federal Food Safety and Veterinary Office (2022) (278).

regulatory burden increases the complexity in the supply chain and has consequently led to the preferred use of non-iodized salt. A concept of mutual recognition of different national legislation and acceptance of products following the rules of another country may provide more legal certainty for food business operators and remove barriers to intracommunity or international trade.

#### 6.1.5 Use of iodized salt in school meals

In four countries of the WHO European Region (Hungary, Portugal, Republic of Moldova and the Russian Federation) iodized salt is mandatory for the preparation of school meals, as well as for catering in other educational, medical and social institutions. This strategy provides a significant contribution to the dietary iodine requirement. A recent study in Portugal showed that at least one main meal (lunch or dinner) prepared with iodized salt is sufficient to reach the recommended daily iodine intake (90  $\mu$ g/day) (281). Similar estimations were made in the Tyumen region of the Russian Federation (282). The use of iodized salt for preparation of salt-containing meals in preschool educational institutions fully covered the iodine requirements of children aged 3–7 years. The use of iodized salt in school breakfast meals provides 23–37% of the RNI of iodine in rural areas and 15–26% of the RNI in children aged 7–11 years living in urban areas (282).

lodized salt in school meals has been implemented in other countries without mandatory regulations. In Italy, 78% of school canteens used iodized salt, with almost complete use (90–97%) in South Tyrol, Sicily and Tuscany regions (265).

# 6.1.6 Estimating consumption of iodized salt using 24 hour urine collections

To estimate the share of iodized salt from all dietary salt sources (discretionary salt and salt in processed foods), urinary sodium and iodine concentrations can be measured in studies collecting 24 hour urine. By multiplying the urinary concentration of sodium and iodine by the urine volume, the daily urinary excretion of sodium and iodine can be calculated. In regression analysis of the two parameters, the proportion of iodized salt out of all salt consumed can be estimated.

Large population-based studies in Germany and Switzerland using this approach estimated that only 28% and 45% of all salt consumed was iodized, respectively (146, 147, 283) (Fig. 6.3).

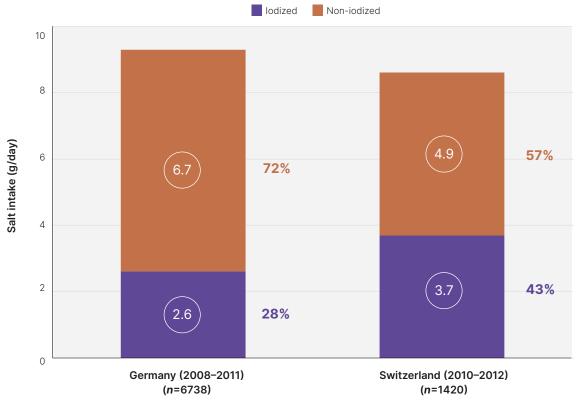


Fig. 6.3. Contribution of iodized salt to total salt intake (median values) in adults in Germany and Switzerland

Source: adapted with permission from Esche, Thamm & Remer (2020) (146).

# 6.1.7 Effects of adjusting the salt iodine content

Many countries in Europe introduced salt iodization in the 1950s at iodine levels around 10 mg/kg (6, 284). This level of fortification reduced goitre prevalence and controlled severe intellectual disability due to iodine deficiency (cretinism), but was not sufficient to meet the recommended dietary iodine intake (6, 284). Increasing the level of fortification effectively improves the iodine intake in countries with mandatory salt iodization, as demonstrated in Croatia. The level of fortification was increased from 10 mg/kg salt (which it had been since 1953) to 25 mg/kg of salt in 1996.

The median UIC in school children was below 100  $\mu$ g/L before the change in salt iodine content (285), but increased to 140  $\mu$ g/L in 2002 (286) and stabilized at 250  $\mu$ g/L in 2009 (287) and 2014–2019 (288).

Belarus, the Russian Federation and Ukraine increased salt iodization levels from 10–30 mg/kg to 25–55 mg/kg in 1998. Subsequently, other members of the Commonwealth of Independent States increased and harmonized salt iodine levels at 25–55 mg/kg, adopted mandatory salt iodization and reached optimal iodine status of the population (289). Similarly, all countries

of the former Yugoslavia (except Serbia) increased the salt iodization level from 12–18 mg/kg to 20–30 mg/kg in the first two decades of the 21st century to sustain adequate iodine status of all population groups, including pregnant women (241).

Other countries increased the salt iodine content in small steps (e.g. Denmark (Box 1) and Switzerland (Box 3)). In the Netherlands (Kingdom of the), iodine content is higher in bakery salt compared to all other salt (Web annex A). Since 1984, mandatory iodization of salt used in bread baking was replaced by voluntary addition regulated via a covenant between the Ministry of Health and industrial bakeries. In 2008, the level of fortification was increased (from 39 mg/kg, as it had been since 1960) and iodized bakery salt now has a maximum level of 65 mg iodine/kg salt. For all other food, iodized salt with a maximum of 25 mg/kg may be used. The iodine intake of the Dutch population (7–69 years) remained adequate after correction of iodine levels in salt, although it has decreased since 2008 (274).

Increasing the salt iodine content may be less effective in countries with voluntary salt iodization if the proportion of iodized salt is low or incomplete (Box 3). Only modest improvements in median UIC were observed in Switzerland after increasing the level of fortification from 15 mg/kg to 20 mg/kg (1998) and 25 mg/kg (2014) (Box 3). In Sweden, the median UIC in school children (125  $\mu$ g/L, 95% bootstrapped CI: 120, 130  $\mu$ g/L) is comparable to that in Switzerland (127  $\mu$ g/L, 95% bootstrapped CI: 119, 140), despite a fortification that was twice as high (50 mg/kg vs. 25 mg/kg, Web annex A).

Salt iodine levels may also be adjusted downwards in cases of excessive intake. In Armenia (mandatory legislation), salt iodine content was lowered from 50  $\pm$  15 mg/kg to 40  $\pm$  15 mg/kg in 2005 after a national survey observed excessive iodine intakes in school-age children (median UIC 313  $\mu$ g/L) (290). This change effectively reduced the iodine intakes, and the median UIC in school-age children fell to 242  $\mu$ g/L (IQR: 203, 289  $\mu$ g/L) in 2016 (253).

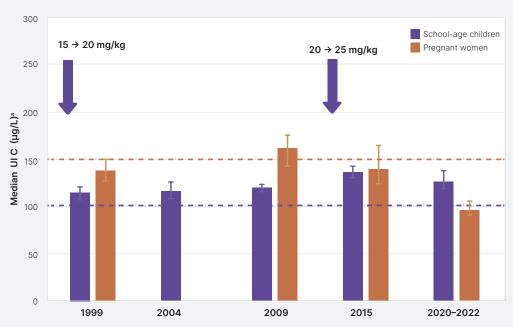
# **Box 3.** Case study: Switzerland – effects of adjusting salt iodine content

lodization of salt was introduced in Switzerland in 1922 and implemented as a voluntary national programme in 1952 (6). The level of iodine fortification was increased in a stepwise fashion, from 3.75 mg/kg initially to 7.5 mg/kg in 1962, 15 mg/kg in 1980 and 20 mg/kg in 1998. Between 2006 and 2017 regulations allowed 20–30 mg/kg. The current regulation allows 20–40 mg iodine/kg salt (291). The Swiss Saltworks, owned by the 26 cantons (states) and the Principality of Liechtenstein, holds a monopoly to extract salt in the country and must produce both iodized and non-iodized salt. A fixed level of fortification is implemented on the recommendation of the Federal Department of Home Affairs.

## Box 3 contd

lodine status has been monitored in nationally representative cross-sectional spot UIC studies of 6–12-year-old children and pregnant women every five years since 1999, supported by funding from the Federal Food Safety and Veterinary Office (Fig. 6.4) (187). The first three national UIC studies indicated adequate iodine intake in children but at the lower end of the recommended optimal range, and low or borderline adequate iodine intake in pregnant women (292). In 2010–2012, nationally representative sodium studies collecting 24 hour urine in adults observed adequate iodine intake in men, but insufficient intake in 14% of Swiss women (147, 148, 293). Low iodine intake was also observed in lactating women and infants (292).

Fig. 6.4. Nationally representative UIC in school-age children and pregnant women in Switzerland by year following increased salt iodine concentration



<sup>&</sup>lt;sup>a</sup> Data are presented as median with 95% bootstrapped CIs. The dotted lines indicate adequate iodine nutrition according to WHO median UIC thresholds (Table 5.1). The arrows indicate increased salt iodine concentration.

Source: adapted from Fischer et al. (2023) (187). Effectiveness of increasing the salt iodine content from 20 to 25 mg/kg

#### Box 3 contd

In an attempt to improve the iodine intake in the Swiss population, the salt iodine concentration was increased from 20 to 25 mg/kg in January 2014 (291). In 2015, the effectiveness of increasing the salt content by 5 mg/kg was evaluated nationally based on UIC. Iodine intake improved modestly in children. Five to six years later, the median UIC remained stable in children, but the proportion of children with inadequate habitual iodine intake had decreased from 10% to 5% (187). However, the intervention had no effect in women of reproductive age and pregnant women (148); in fact, in the same period, UIC in pregnant women declined (187). Diet alone was not meeting the iodine requirements in one third of pregnant women.

## Why did iodine intake not improve?

The median UIC in Swiss children, women and pregnant women (Fig. 6.4) is lower compared to countries with the same level of fortification (25 mg/kg) but where salt iodization is mandated (191). The estimated average salt intake is 6.1 g/day in children, 7.4 g/day in adult women and 9.9 g/day in adult men, well above international recommendations (148, 294). If all salt were iodized, salt would provide approximately 150 µg/day in children, 185 µg/day in women and 250 µg/day in men. However, only 61% of all food-grade salt sold in Switzerland is iodized (Swiss Saltworks AG, personal communication, 2023). Population-based studies collecting 24 hour urine in adults estimate that 40% of the salt consumed is iodized (Fig. 6.3) (147, 148, 293). Bread is one of the main sources of salt in the Swiss diet and most bakeries (87%) use iodized salt (295) as do most households (> 80%) (187). However, a recent market survey showed that only one third of all types of convenience foods sold in Switzerland are produced with iodized salt (Fig. 6.2) (278).

The data demonstrate the poor effectiveness of increasing the salt iodine level by 5 mg/kg if the coverage of iodized salt is incomplete. Improving coverage is likely more effective, possibly in combination with a higher level of fortification.

### 6.1.8 Compatibility with recommendations to reduce salt intake

Sodium intake in the European Region is well above WHO recommendations, in both children and adults (296). In almost all countries, men consume more salt than women, ranging between 5.4 and 18.5 g for men and 4.3 and 16.1 g for women (296). Generally, western and northern European countries have the lowest average salt intake, while eastern European and central Asian countries have the highest (296).

WHO recommends that adults consume no more than 5 g of salt (or 2 g of sodium) per day to reduce the risk of cardiovascular diseases (297). In 2013, the World Health Assembly agreed to a global target of a 30% reduction in population salt intake by 2025 (298). As part of WHO's support and technical leadership for the prevention and control of noncommunicable diseases, the WHO Regional Office for Europe has developed guidance to support Member States either to initiate or accelerate existing efforts to reduce salt intake (299). While national strategies to reduce salt intakes are gaining momentum (300), based on trend analysis over the period 2010–2019, sodium intake will likely only reduce minimally at current rates (301).

Policies for salt iodization and reduction of salt to < 5 g/day are compatible, and the two need to be carefully aligned (7, 302). Both are aimed at improving public health, and can reinforce each other. They include common elements, including programme monitoring via urine collection and engagement with the food and salt industries (302). This provides an opportunity to share and leverage resources and approaches to be more effective and efficient (302). As salt intakes fall, iodine levels in salt can be increased to adjust for the recommended reduction in dietary salt to < 5 g/day (289, 302, 303). Monitoring of sodium (salt) intake and iodine intake at the country level using urinary sodium and iodine excretion/concentration can easily be combined and is needed to adjust salt iodization over time as necessary to ensure that individuals consume sufficient iodine despite reduction of salt intake (7).

Optimal intake of each requires: full implementation of universal salt iodization, as recommended by WHO and the United Nations Children's Fund (UNICEF); effective implementation of salt reduction policies including regulation of salt levels in processed foods; and increasing iodine levels in salt as salt intakes are reduced. Integrating communication and advocacy strategies can help to increase understanding of the importance of maintaining optimal iodine levels while reducing salt and to ensure coordinated messaging (302). It is particularly important that these communication messages are distributed across all channels including through health-care professionals.

Despite WHO reassurances that salt reduction and salt iodization programmes can be harmonized (302), there is resistance from some health-care professionals and advisors in countries with strong salt-reduction programmes. Concerns have been raised that programmes to reduce dietary salt could adversely affect programmes to prevent iodine deficiency, and, conversely, that using salt as a vehicle for fortification could encourage higher salt intakes (304). The United Kingdom was one of the first (in the early 2000s) to introduce policy and legislation for salt reduction, and their approach has been adopted by other countries worldwide. As such, many medical professionals, dietitians and nutritionists are reluctant to endorse iodized salt messages (305, 306). Sodium/salt reduction policies may therefore be a barrier to implementation in some countries.

## 6.1.9 Educational activities and information campaigns

Poor knowledge about iodine nutrition and the health consequences of iodine deficiency among the general population, health authorities, health professionals and food producers represents a barrier to optimizing iodine intake in the European Region (307). The proverb "out of sight, out of mind" epitomizes the situation, including in countries previously affected by severe iodine deficiency.

Education and training for relevant people in ministries of health/public health authorities, health professionals and the general public could help to fill this knowledge gap. In Italy, a nationwide informative campaign on the use of iodized salt was recently launched by the Ministry of Health's General Directorate of Food Hygiene, Safety and Nutrition, together with a panel of experts at the Italian National Institute of Health as part of the nationwide 2007 strategy for reducing sodium intake in the population (265). The slogan "use less salt, but iodized" was promoted. German authorities launched a campaign in 2023 to raise awareness about the importance of adequate iodine intake for health. They drew attention to the persistence of iodine deficiency in Germany and the difficulties of obtaining sufficient iodine intake from locally produced food due to the low iodine content in the soil. The campaign promotes iodized salt to optimize iodine intake without increasing total salt consumption.

An EU-funded public health research project, EUThyroid2, launched through Horizon Europe, started in 2023, with the aim of developing best practice models for reaching young people, especially young women, to improve awareness of their iodine status (308). The project brings together epidemiologists, endocrinologists, nutritionists, health economists and communications specialists from a broad range of educational institutions and countries. The interventions take place in two settings: ambulatory care and educational, and were developed to ensure effectiveness and appropriateness for audiences in different geographic areas. Building on the findings of the first EUThyroid consortium, which identified limitations in awareness of iodine nutrition in Europe, EUThyroid2 is set to implement community-based trials and intervention studies in multiple countries, including Cyprus, Poland, Norway, Slovenia, the United Kingdom, Bangladesh and Pakistan.

## 6.2 Dietary iodine supplementation

## 6.2.1 Pregnancy and lactation

WHO recommends iodine supplementation during pregnancy and lactation in situations where salt iodization fails (i.e. in populations with poor coverage of iodized salt) and when the iodine intake in the general population is insufficient, or there are subgroups with risk of very low iodine intake (237,309). The European Thyroid Association provides a more general recommendation and recommends that all women who are pregnant or lactating take 150 µg iodine/day as a supplement (310).

Reports of low UIC in pregnant women have led health authorities in several countries of the European Region to recommend iodine supplementation during preconception, pregnancy and lactation, although recommendations differ between countries throughout the Region and information for many countries is missing (Web annex D). Portugal, for example, officially recommends a supplement of 150–200 µg/day (as potassium iodide) in the preconceptual period, and during pregnancy and lactation (311). In other countries, professional societies (such as those of endocrinologists, obstetricians or nutritionists) recommend iodine supplements during pregnancy, although in others guidelines for prenatal supplementation do not mention iodine at all (Web annex D). In some countries, such as Norway, the recommendation for iodine supplementation only applies to certain groups (e.g. those with low intake of iodine-rich foods); in others, the guidance is to consult obstetricians or dietitians about the subject. Besides pregnant women, lactating women are included in some of the recommendations, and a few countries include women who are planning a pregnancy (Web annex D).

While there are official recommendations for iodine supplementation during pregnancy in some countries, it is important to consider whether these are followed. Studies that have investigated the proportion of women taking iodine supplements vary in quality and representativeness; for example, many of them are local, not national, studies, or they do not detail the amount of iodine in the supplement (Web annex D). Nevertheless, such studies give an idea about the situation and indicate possible hurdles and opportunities (e.g. when looking at the low use of iodine supplements before conception).

In countries that have official (i.e. governmental) recommendations, the use of iodine supplements varies from around 3.5% of women in Iceland to up to 74% in Spain (Web annex D). Conversely, in countries without national recommendations, such as Denmark, up to 84% of pregnant women take iodine supplements in pregnancy, suggesting that practice and official policy are not always linked.

Data from Portugal show that after the introduction of the recommendation for iodine supplementation in pregnancy in 2013 (for up to 200  $\mu$ g/day), the median UIC increased (from 68 to 107  $\mu$ g/L) and the proportion with UIC < 50  $\mu$ g/L decreased from 38% to 18% (312). In Switzerland, use of iodine supplements in pregnancy was associated with higher UIC (129  $\mu$ g/L vs. 81  $\mu$ g/L) and lower Tg (23  $\mu$ g/L vs. 29  $\mu$ g/L) (187).

Ideally, iodine stores should be optimized prior to pregnancy, rather than relying on iodine supplementation once pregnancy has been confirmed, especially as there is some evidence (albeit weak) that there are negative effects on thyroid function and child neurodevelopment with an abrupt increase in iodine intake through supplements at the start of pregnancy, especially in those with habitually low intake (104). However, as many pregnancies are unplanned (up to 50%), it may not be possible to ensure adequate intake in the preconception period for all, especially in countries that do not have iodized salt supplying iodine to the general population. Therefore, iodine supplementation (at doses of around 150  $\mu$ g/day) may help to meet iodine requirements during pregnancy if the dietary iodine intake is low.

## 6.3 Key messages

- Salt iodization as a public health strategy to prevent iodine deficiency has been implemented in 43 of the 53 Member States of the WHO European Region, and Kosovo<sup>15</sup> (n=54); programmes are mandatory in 30 and voluntary in 13. Five Member States have no regulations, and in six the regulations are not known.
- If most salt consumed is iodized, salt iodization effectively ensures adequate iodine intake in all population groups.
- The coverage of iodized salt is high and satisfactory in the majority of Member States, and Kosovo, 16 with mandatory salt iodization in WHO European Region, whereas it is incomplete in many with voluntary regulations.
- Processed foods, such as bread or meat products, are the principal sources of salt in the diet, and dietary iodine intake can be improved by increasing the proportion of iodized salt in such food products. Current food labelling laws are discouraging food business operators from using iodized salt and adaptations are needed.
- Because of export barriers, the food industry prioritizes use of iodized salt for products intended for the local market, such as bread and meat-derived products. Recommendations to increase iodine fortification of processed foods need to integrate this preference for iodine fortification of products for the local market.
- The recommendation for populations to reduce salt intakes is compatible with the use of iodized salt for the prevention of iodine deficiency, but the two policies need to be carefully aligned. The reduction of salt consumption can be compensated by increasing the iodine content in salt.
- lodine intake and status should be optimized prior to pregnancy and this is possible with consumption of iodized salt. National (or equivalent) recommendations for iodine supplementation in pregnancy and lactation vary across the Region. WHO recommends supplementation in populations with partial or no salt iodization and inadequate iodine intake. Targeted, not blanket, iodine supplementation (approximately 150 μg/day) may be useful for pregnant women and other groups with low dietary iodine intake.

<sup>15</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>16</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

## Chapter 7.

# lodine status in the WHO European Region

## 7.1 Data availability of national (or equivalent) iodine status

The impact and effectiveness of national (or equivalent) policies aimed at preventing iodine deficiency, including any modifications made, should be evaluated in representative population-based UIC studies, ideally every five years (13). During 2008–2023, nationally representative (or equivalent) UIC studies conducted in children aged 6–15 years, adults and/or pregnant women were available in 38 of the 53 Member States of the European Region, and Kosovo<sup>17</sup> (n=54) (Fig. 7.1, Web annex B). Half of the countries, and Kosovo, conducted iodine status studies in more than one population group over the 15 year time-period (Fig. 7.2).

Nationally representative (or equivalent) UIC studies in school-age children are available in half of Member States, and Kosovo, 19 but many (29%) of these are more than 10 years old (Fig. 7.1). A few countries (e.g. Tajikistan, Uzbekistan) assessed UIC in preschool children (6–59 months old) in household-based studies along with women of reproductive age, but the data is not included in this report.

In adults, iodine status has been assessed nationwide (or equivalent) in 22 of the 53 Member States, and Kosovo<sup>20</sup> (n=54) by measuring UIC in spot urine or 24 hour urine collections (**Fig. 7.1** and **Web annex B**). UIC has been included in national health and nutrition studies (e.g. Ireland, Tajikistan, Ukraine, the United Kingdom, Uzbekistan), health studies assessing noncommunicable diseases (e.g. Finland, Italy and Spain), or was measured along with urinary sodium concentration in national surveillance for sodium intake (e.g. Belgium, Lithuania, Moldova, Switzerland (**Web annex B**)). Kyrgyzstan, Latvia, Lithuania, Tajikistan and Ukraine have conducted nationally representative studies in adults within the last five years. However, in 10 out of 22 countries with data in adults, the studies are now older than 10 years (**Fig. 7.1**).

Reports of low UIC in several countries of the WHO European Region prompted authorities and researchers to conduct iodine studies in pregnant women, a population group particularly vulnerable to iodine deficiency (309, 313). Since 2007, 23 Member States, and Kosovo<sup>21</sup> (n=24) in the Region have conducted representative studies in pregnant women, the majority (18/24) were done within the last 10 years (Fig 7.1, Web annex B).

<sup>17</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

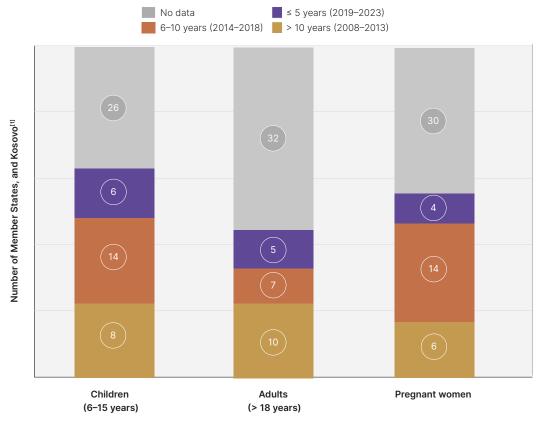
<sup>18</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>19</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>20</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>21</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

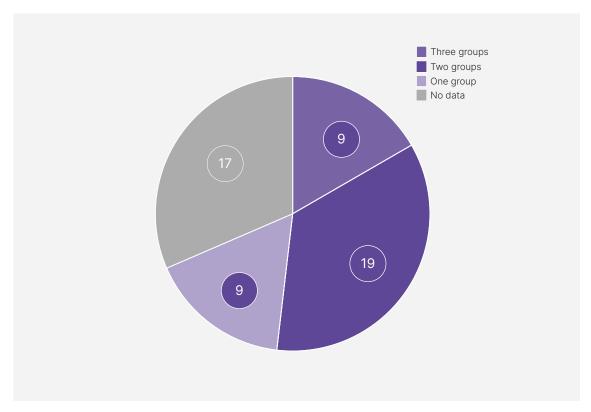
Fig. 7.1. Number of Member States, and Kosovo,<sup>[1]</sup> with nationally representative (or equivalent) UIC studies in children 6–15 years, adults and pregnant women conducted in 2008–2023 in the WHO European Region



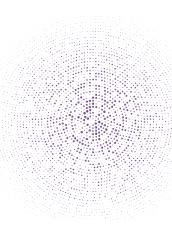
<sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999). Source: authors.

The data summarized in this report show heterogeneous iodine status monitoring across the Region. Iodine status is assessed in different population groups and many studies are old. Seventeen countries have no nationally representative UIC data for any population group and the current iodine status is uncertain. Only a handful countries have established regular iodine status surveillance supported by public funding (e.g. Switzerland and the United Kingdom) (187, 314) and routine monitoring systems are lacking in most countries. Data frequently comes from universities, medical experts and research centres, often with little support, or recognition, from health authorities. Local or regional cross-sectional or cohort studies are available in several countries, which offer valuable additional information. However, political commitment, funding and new strategies for representative population monitoring of iodine status are needed.

Fig. 7.2. Number of Member States, and Kosovo, [1] in the WHO European Region assessing iodine status using UIC in one or more population groups (children 6–15 years, adults and/or pregnant women) during 2008–2023



<sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999). Source: authors.

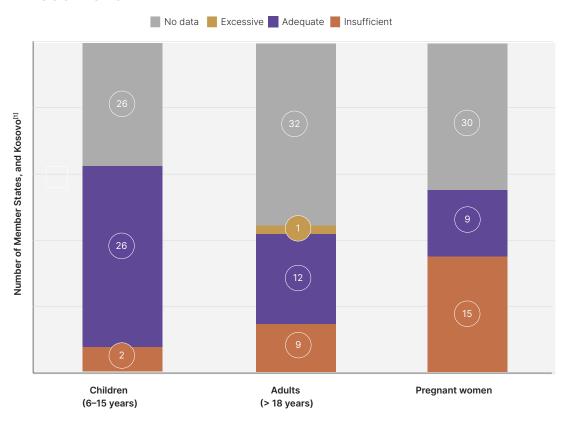


Routine iodine status surveillance using nationally representative population-based studies is lacking in most countries and in many the most recent data is more than 10 years old. Data frequently comes from universities, medical experts, and research centres, often with little support or recognition from health authorities. Only Switzerland and the United Kingdom publicly fund regular population iodine status monitoring. In eastern European and central Asian countries (except Kazakhstan and the Russian Federation) surveys have only been conducted with external support from donor agencies, making future monitoring unsustainable.

## 7.2 Current national (or equivalent) iodine status

lodine intake in school-age children is overall adequate in 26 out of 27 Member States, and Kosovo, with data (n=28), while the intake is documented as insufficient in two (**Fig. 7.3** and **Fig. 7.4**). UIC data in adults (> 15 years) indicate overall adequate iodine intake in 12 out of 22 Member States with data (**Fig. 7.4**), but insufficiency in nine using the median UIC threshold of 100  $\mu$ g/L (13). However, the interpretation of iodine status using this median UIC threshold is uncertain due to the urine volume in European Region adults (**Section 5.1.2**). Several of the UIC studies in adults collected 24 hour urine and documented urine volume of around 1.9–2.1 L/day (Italy, Lithuania, Switzerland) (147, 198, 199), suggesting underestimation of the iodine status using the WHO UIC threshold. In 23 Member States, and Kosovo, with representative UIC data in pregnant women (n=24), the data suggest the iodine intake is adequate in nine and insufficient in 15 (**Fig. 7.4**). In Armenia, the iodine intake is estimated to be more than adequate/excessive in adults.

Fig. 7.3. lodine intake in children 6–15 years, adults and pregnant women in the WHO European Region assessed by median UIC in nationally representative (or equivalent) cross-sectional studies in 2008–2023

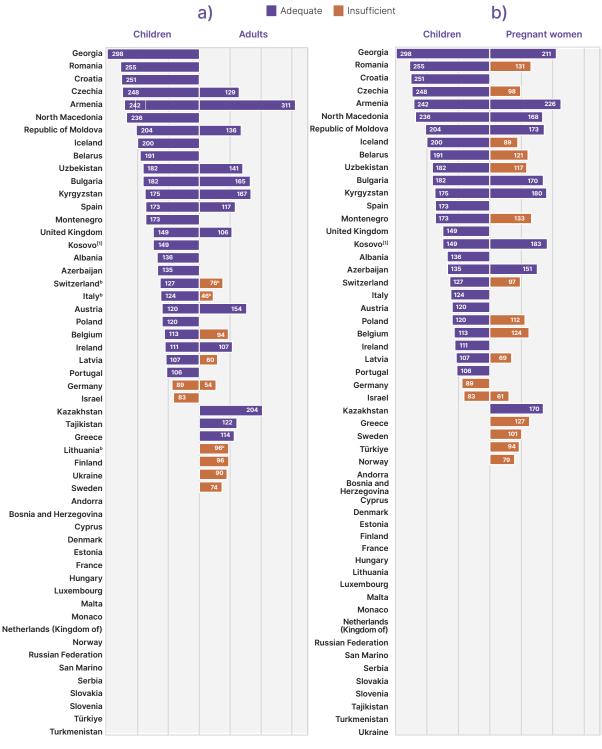


<sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999). Source: authors.

<sup>22</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

<sup>23</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

Fig. 7.4. Median UIC in school-age children (6–15 years) and a) adults (> 15 years), and b) pregnant women in the WHO European Region obtained in nationally representative (or equivalent) cross-sectional studies in 2008–2023<sup>a</sup>



<sup>&</sup>lt;sup>a</sup> Median UIC above and below the WHO thresholds for iodine inadequacy is indicated in green and red, respectively. Grey indicates excessive iodine intake.

<sup>&</sup>lt;sup>b</sup> Studies collected 24 hour urine and observed urine volume of 1.9–2.1 L/day (147, 198, 199), suggesting an underestimation of the iodine status using the WHO UIC threshold.

<sup>&</sup>lt;sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999). Source: authors.

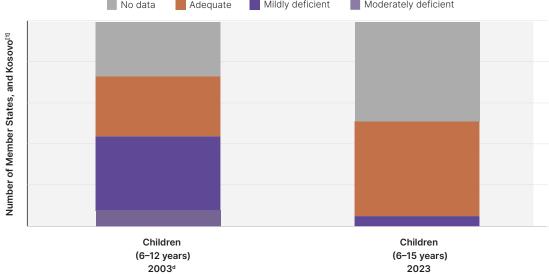
## 7.3 Trends in iodine status

Nationally representative UIC studies in school-age children for the WHO European Region were compiled for the first time in 2003 (315). Since then, iodine status has improved considerably and the number of Member States, and Kosovo,<sup>24</sup> with overall inadequate iodine intake in school-age children decreased from 23 in 2003 to two in 2023 (Fig.7.5).

A WHO review of iodine status based on median UIC in school-age children for 40 countries in western and central Europe conducted in 2007 showed moderate iodine deficiency in one country (Albania), mild iodine deficiency in 10 countries and adequate iodine status in 21 countries (12). Another review conducted for 12 countries of eastern Europe and central Asia in 2009 demonstrated mild iodine deficiency in two countries (the Russian Federation and Ukraine), adequate status in eight countries and excessive iodine intake in two countries (Armenia and Georgia) (240). Additional publications have collated European UIC studies, including local and regional studies (15).

In 2023, no country (or area) in the WHO European Region was affected by moderate iodine deficiency or excessive iodine status. School-age children are mildly iodine deficient in two countries: Israel with no previous UIC data and Germany where iodine status deteriorated. Local, regional and/or state level studies in the Russian Federation and Ukraine indicate that iodine status had not improved (Web annex B). A recent national study in Tajikistan reports low UIC in 6–59 month old children, also suggesting deteriorating iodine intakes (Web annex B).





<sup>&</sup>lt;sup>a</sup> The categories indicate iodine intake based on median UIC obtained in cross-sectional studies (Table 5.1).

<sup>&</sup>lt;sup>b</sup> Compilation of UIC data in 2003 and 2023 is based on UIC studies conducted 15 years prior to the year of review and many studies are old (Fig. 7.1).

<sup>&</sup>lt;sup>c</sup> Adapted from Andersson et al. (2005) (316).

<sup>[1]</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

Source: authors.

<sup>24</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

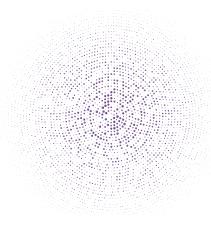
## 7.4 Impact of salt iodization on iodine intake in different population groups

### 7.4.1 Mandatory salt iodization

Between 2008 and 2023, UIC studies were conducted in 16 of 20 Member States, and Kosovo, with mandatory salt iodization in the European Region (n=21) (Table 7.1). In most, iodized salt was used for the production of processed foods and by 80–90% of households (Table 6.3). The level of iodine in salt ranged from 15 to 65 mg/kg (Web annex A). The UIC data confirms that the iodine intake is typically adequate in school-age children, adults and pregnant women if most salt consumed is iodized ( $\geq$  25 mg/kg) (Table 7.1), demonstrating the effectiveness of mandatory salt iodization (13).

The median UIC is below the WHO threshold in Lithuanian adults but the iodine intake was estimated to be ~200  $\mu$ g/day when accounting for the average urine volume (2.1 L/day) (202). The median UIC in pregnant women is below the WHO UIC threshold in Montenegro, Romania, Türkiye and Uzbekistan (Table 7.1). In these countries, the production of iodized salt is low (Table 6.2) and household coverage is poor (Table 6.3). In Montenegro, the legislation was revised and the level of fortification was increased in 2020 (Section 6.1.1). In Türkiye, the use of iodized salt is mandatory for household salt, but voluntary for the production of processed foods and salt iodization is not universal. In Uzbekistan, the coverage of iodized salt is low (tables 6.2 and 6.3) despite mandatory legislation. In Tajikistan, a recent study found adequate UIC in women of reproductive age, but low UIC in children aged 6–59 months (317). Despite mandatory salt iodization in Tajikistan since 2002, the programme is poorly enforced. There are problems with production and distribution of quality iodized salt and the coverage is low (317) (Table 6.3).

No recent UIC studies matching inclusion criteria are available for Bosnia and Herzegovina, Serbia, Slovakia, Slovenia and Turkmenistan.



Data shows that in countries (or areas) where the use of iodized food-grade salt in households and processed foods is mandatory, particularly in domestic products such as bread, bakery goods and processed meats, population iodine status is generally adequate.

<sup>25</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

**Table 7.1.** Median UIC (µg/L) in school-age children (6–15 years of age), adults ( $\geq$  15 years) and pregnant women in Member States of the WHO European Region, and Kosovo<sup>[1]</sup> with mandatory, voluntary and no regulation of salt iodization<sup>a</sup>

Member States, and Kosovo <sup>[1]</sup>	Population group (Median UIC (µg/L))			
	School-age children (6-15 years)	Adults (≥ 18 years)	Pregnant women	
Mandatory salt iodization of all salt for human consumption (n=21)				
Georgia	<b>298</b> (IQR: 224, 374)	-	<b>211</b> (IQR: NA)	
Romania	<b>255</b> (IQR: NA)	-	<b>131</b> (IQR: NA)	
Croatia	<b>251</b> (IQR: 157, 371)	-	_	
Armenia	<b>242</b> (IQR: 203, 289)	<b>311</b> (IQR: 244, 371)	<b>226</b> (IQR: 209, 247)	
North Macedonia	<b>236</b> (IQR: NA)	-	<b>168</b> (IQR: NA)	
Bulgaria	<b>182</b> (IQR: 119, 245)	<b>165</b> (IQR: NA)	<b>170</b> (95% BCI: 161, 177)	
Kyrgyzstan	<b>175</b> (95% BCI: 172, 190)	<b>167</b> (95% BCI: 158, 175)	<b>180</b> (95% BCI: 146, 198)	
Montenegro	<b>173</b> (IQR: NA)	-	<b>133.3</b> (IQR: NA)	
Albania	<b>136</b> (95% BCI: 142, 161)	-	-	
Azerbaijan	<b>135</b> (IQR: NA)	-	151	
Uzbekistan	> 100 (IQR: NA)	<b>141</b> (95% BCl 132, 151)	<b>117</b> (95% BCI: 102–140)	
Kazakhstan	_	<b>204</b> (IQR: NA)	<b>170</b> (IQR: NA)	
Tajikistan	-	<b>122</b> (IQR 89, 149)	-	
Lithuania	-	<b>96</b> (IQR: NA) <sup>b</sup>	-	
Türkiye	_	-	<b>94</b> (IQR: 52, 153)	
Bosnia and Herzegovina	-	-	-	
Serbia	-	-	-	
Slovakia	-	-	-	
Slovenia	-	-	-	
Turkmenistan	_	_	_	
Kosovo <sup>[1]</sup>	<b>149</b> (95% BCI: 144, 153)	-	<b>183</b> (IQR: NA)	
Mandatory salt iodization for specific foods and/or distribution channels (n=9)				
Republic of Moldova	<b>204</b> (IQR: 130, 302)	<b>136</b> (IQR: NA)	<b>173</b> (IQR: NA)	
Belarus	<b>191</b> (IQR: NA)	-	121 (IQR: NA)	
Italy	<b>124</b> (IQR: 77, 188)	<b>46</b> (IQR: 23-88) <sup>b</sup>	-	
Austria	<b>127</b> (IQR: NA)	<b>154</b> (IQR: NA)	-	
Poland	<b>120</b> (74, 166)	-	<b>112</b> (95% BCI 98, 124; IQR 44, 179)	
Portugal	<b>106</b> (IQR: NA)	-	-	
Denmark	-	-	-	

### Table 7.1 contd

Member States, and Kosovo <sup>[1]</sup>	d Population group (Median UIC (μg/L))			
	School-age children (6-15 years)	Adults (≥ 18 years)	Pregnant women	
Hungary	-	-	-	
Russian Federation	-	_	_	
Voluntary salt iodization ( <i>n</i> =13)				
Czechia	<b>248</b> (IQR: NA)	<b>129</b> (IQR: NA)	<b>98</b> (IQR: NA)	
Spain	<b>173</b> (118–237)	<b>117</b> (IQR: 69, 165)	-	
Switzerland	<b>127</b> (95% BCI: 119, 140; IQR 87, 194)	<b>76</b> (IQR: NA) <sup>b</sup>	<b>97</b> (95% BCI: 90, 106; IQR: 45, 187)	
Belgium	<b>113</b> (95% BCI: 110, 117; IQR: 72, 154)	<b>94</b> (IQR: 68, 133)	<b>124</b> (IQR: 73, 213; 95% BCI 118, 131)	
Latvia	<b>107</b> (IQR: 61, 154)	<b>60</b> (IQR 38-94)	<b>69</b> (IQR 54, 93)	
Germany	<b>89</b> (IQR: 55, 120)	<b>54</b> (IQR: 25, 83)	-	
Greece	-	<b>114</b> (IQR: NA)	<b>127</b> (IQR: NA)	
Finland	_	<b>96</b> (IQR: 55, 138)	-	
Ukraine	-	<b>90</b> (95% BCI: 84, 96)	-	
Sweden	-	<b>74</b> (IQR: NA)	<b>101</b> (95% BCI: 95, 108; IQR: 61, 182)	
Norway	-	_	<b>79</b> (IQR: 47-132)	
France	_	_	-	
Netherlands (Kingdom of the)	-	-	-	
No or unknown salt iodization policy ( <i>n</i> =11)				
Iceland	<b>200</b> (20th, 80th quartiles: 90, 320)	-	<b>89</b> (95% CI: 42, 141)	
United Kingdom	<b>149</b> (IQR: NA)	<b>106</b> (IQR: NA)	-	
Ireland	<b>111</b> (IQR: 72, 165)	<b>107</b> (IQR: 70, 161)	-	
Israel	<b>83</b> (IQR: 5å2, 127)	-	<b>61</b> (IQR: 36, 97)	
Andorra	-	-	-	
Cyprus	-	-	-	
Estonia	-	-	-	
Luxembourg	-	-	-	
Malta	-	-	-	
Monaco	-	-	-	
San Marino	-	_	-	

BCI: bootstrapped confidence interval; NA: not available.

Source: authors.

<sup>&</sup>lt;sup>a</sup> Colours indicate if the iodine intake is adequate (purple), inadequate (orange) or excessive (grey) based on median UIC using the WHO thresholds (13) (Table 5.1). More details on the original studies are available in Web annex B. <sup>b</sup> Studies collected 24 hour urine and observed urine volume of 1.9–2.1 L/day, suggesting an underestimation of the

iodine status using the WHO UIC threshold.

[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

## 7.4.2 Mandatory salt iodization for specific foods and/or distribution channels

Nine European Region Member States have mandatory salt iodization policies for specific foods and/or mass catering (education, health and social welfare facilities) (Section 6.1.1, Table 6.1). In most of these, iodine intake is overall adequate in school-age children although it is generally lower than in those with mandatory universal salt iodization (Table 7.1). Member States that have mandated the use of iodized salt in processed foods (Belarus) or in the baking industry (Austria and Republic of Moldova) typically achieve adequate iodine intake. In Italy, the availability of iodized salt in food shops and supermarkets (coarse salt and table salt) is mandatory, whereas non-iodized salt can be sold at customer request (Web annex A). The law permits, but does not require, the use of iodized salt in the food industry and communal eating areas, including school canteens. A recent nationwide study showed that 78% of school canteens used iodized salt and the iodine intake in children is adequate (265), whereas another study suggests mildly deficient intakes in Italian adults (median UIC was 46  $\mu$ g/day, but the iodine intake was ~100  $\mu$ g/day accounting for the urine volume of 1.9 L per 24 hours) (199).

In the Russian Federation and Portugal, iodized salt must be used in mass catering (education, health and social welfare facilities), but the household coverage of iodized salt is generally low (below 20%). No national survey has been conducted in the Russian Federation; data from regional surveys conducted in 2008–2023 show that median UIC differ substantially between regions across the country in school-age children and pregnant women (**Web annex A**). Iodine status was optimal in larger cities (Moscow, Novosibirsk, St. Petersburg, Tyumen) while mostly inadequate in other regions, especially in rural areas (318). A new sanitary regulation (adopted in 2020) requires mandatory use of iodized salt in school canteens and kindergartens as well as other social and educational institutions. In Poland, the use of iodized salt is mandated for table salt only. Iodized salt for the production of processed foods is voluntary and restricted.

Two countries recently revised their salt iodization policy and the available studies were conducted before the revision and may not reflect the current situation. In the Republic of Moldova, the salt iodine level was increased (to 25–40 mg/kg) in 2022 and iodized salt was made mandatory for the baking industry and public catering. Denmark revised the level of iodine in salt from 13 to 20 mg/kg in 2019, but no recent median UIC data matching inclusion criteria are available. Recent national data is lacking for Hungary.

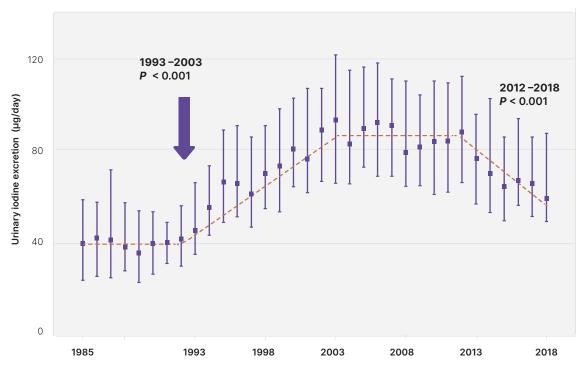
## 7.4.3 Voluntary salt iodization

Salt iodization is voluntary in 13 countries of the WHO European Region. In six of the countries, iodine intake is documented sufficient in one or more population groups (**Table 7.1**). However, in several countries median UIC fluctuates around the threshold in adults (< 100  $\mu$ g/L) and/or in pregnant women (< 150  $\mu$ g/L), suggesting borderline iodine inadequacy. Median UIC in pregnant women is < 150  $\mu$ g/L in all seven countries with available data (**Table 7.1**). Compared to countries with mandatory salt iodization, coverage of iodized salt in food production is lower and often incomplete (**Section 6.1.4**).

Several countries have been reporting decreasing iodine intakes over the past 10-15 years (15, 148, 319). In Germany, the iodine intake decreased in children and is currently inadequate (319) (Fig. 7.6). In adults, the median UIC was  $54 \,\mu g/L$  and the prevalence of iodine inadequacy was estimated at 33% when accounting for urine volume (194). Several salt producers report low sales of iodized salt to the food industry and decreasing iodine intakes may be due to reduced use of iodized salt in processed foods (319). It is possible that other countries are following the same trend, but recent data and trend data are lacking in most countries.

In Ukraine, two recent national surveys indicate iodine deficiency in adults, one in non-pregnant non-lactating women in 2021 using spot urine (median UIC 90  $\mu$ g/L) and another study in 2019 collecting 24 hour urine in adult men and women (median UIC 75  $\mu$ g/L and estimated daily iodine excretion of 110–115  $\mu$ g/day) (266) (Web annex A). At the time of this report, salt production was suspended in Ukraine because the major salt producer is located in the area of Donetsk region of Ukraine under the temporary military control of the Russian Federation. Edible salt is instead imported (mainly from Poland, Romania and Türkiye) but detailed information is not available.

Fig. 7.6. Trends in 24 hour UIE ( $\mu$ g/day) measured in German children (n=677, 2600 repeated samples) in 1985–2018 (participants of the DONALD study)<sup>a</sup>



<sup>&</sup>lt;sup>a</sup> Germany introduced nationwide iodine fortification of table salt in 1981. The purple arrow indicates the legislative decree in 1993 allowing iodized salt in bakeries and butchers as well as in commercial food production. The 24 hour UIE (µg/day) data is presented as median (IQR); P values indicate time periods with statistically significant time trend. *Source*: Remer et al. (2022) (319).

In Swiss adults, the median UIC was also below the WHO threshold (76  $\mu$ g/L) (147). However, the estimated median iodine intake was 132  $\mu$ g/day in women and 174  $\mu$ g/day in men (147) when accounting for urine volume (2.0 L) (sections 5.1.3 and 7.5). The iodine intake was estimated to be inadequate in 14% of women, but only in 2% of men (147). Median UIC suggests insufficient iodine intake in pregnant women in all countries with data, and Kosovo<sup>26</sup> (Table 7.1, Section 7.5.2).

Data obtained by dietary assessment can also complement the results of urinary monitoring. For example, according to dietary intake, average intake is above the RNI in Denmark and Finland (Section 4.2.1). Although there are limitations to dietary assessment, if iodized salt is incorporated in the food-table values used (as was the case in Denmark and Finland), then it is possible to build a more complete picture of countries' iodine status/intake.

In conclusion, among countries with voluntary salt iodization, the overall iodine intake is insufficient in Germany and Ukraine. In six countries available UIC data suggest adequate iodine intake in one or more population groups, whereas UIC data indicate mild iodine deficiency in other population groups. Subgroups with inadequate iodine intake may be present in all countries, particularly in population groups with low consumption of milk and dairy products. However, most of the studies are old and only two countries (Germany and Switzerland) have assessed the prevalence of iodine inadequacy. More recent data are needed to assess the extent of iodine inadequacy in these countries.

### 7.4.4 No salt iodization policy

Four countries (Iceland, Ireland, Israel and the United Kingdom) have no salt iodization policies. The population in Israel is exposed to mild iodine deficiency, whereas the iodine intake is overall adequate in the other three countries. The data suggest that the iodine intake in countries of western Europe likely also comes from dietary sources other than salt, such as milk and dairy products. The population in Iceland has historically had adequate iodine intake thanks to high consumption of fish. lodine intake remains adequate in children, but recent data suggest changing dietary patterns and iodine deficiency in pregnant women (320). In Ireland, dietary data suggest 26% of the general adult population and 77% of women of reproductive age have iodine intakes below the AR (321). Local UIC studies also suggest inadequate iodine intake (40, 322). In Israel, milk and dairy products are iodine rich, but the consumption is not sufficient to ensure adequate iodine intake (323, 324). In the United Kingdom, although national data from children (4–18 years) and adults (19–64 years) shows iodine adequacy, when the national data are restricted to women of reproductive age (16-49 years), they are classified as deficient according to their median UIC (98 µg/L) (314) (Box 4). Furthermore, there was a decrease in median UIC in this group between 2013 and 2019 (from 117 µg/L to 98 µg/L). There are a number of studies of iodine status in United Kingdom pregnant women (from 12 areas of the country) and all show that the group is classified as deficient (median UIC < 150  $\mu$ g/L).

<sup>26</sup> All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

## **Box 4.** Case Study: United Kingdom – no salt iodization policy

The United Kingdom is a country where iodine deficiency was historically common. In the 1800s the country had endemic goitre and in the early 1900s, a goitre belt was described that extended through England and into parts of Northern Ireland, Scotland and Wales (5).

Goitre was eradicated in the United Kingdom, not through an iodized-salt programme, but through an increase in milk-iodine concentration (for cattle rather than human health) as well as a general rise in milk consumption (e.g. through advertising milk for general health). Between the 1950s and the 1980s, iodine intake increased three-fold and was sufficient to eradicate goitre; it was subsequently assumed that iodine deficiency was not a problem in the United Kingdom. However, it is important to note that this was not an official iodine fortification policy, and there is no regulation or monitoring of milk-iodine concentration.

The problem with reliance on milk and dairy products to eradicate goitre in the United Kingdom is that this is a situation that is vulnerable to changes in either milk-iodine concentration, or milk consumption. Indeed, there has been a decline in milk intake since the 1970s, and in recent years there has been increased popularity of milk-alternative drinks, especially among women of childbearing age. As these unfortified drinks do not replace the iodine from cows' milk, groups in the population who consume them, or those who have low intake of milk and dairy products are likely to be iodine deficient. There have been case reports of goitre in children and adults in the United Kingdom who follow a dairy-free diet (325). The fact that overall the United Kingdom is classified as iodine sufficient may mask deficiency in groups, and may not be sustainable.

## 7.5 Population groups at particular risk of iodine deficiency

Achieving iodine adequacy for all is essential. One of the challenges with the current use of median UIC for assessment of iodine status is that it defines and classifies nutritional iodine status at the population level (i.e. for the whole population). However, the reported national (or equivalent) median UIC does not necessarily apply to all individuals and does not inform about the extent of iodine inadequacy in the population (Section 5.1.3).

In practical terms, in a population that is overall mildly iodine-deficient, some individuals will have an iodine intake at the lower end of the distribution with potentially more severe health consequences. If a country (or area) is classified as overall sufficient, there is likely still a proportion (and in some cases a relatively high proportion) with low, or very low, intake of iodine. This is especially true in countries (or areas) without mandatory salt iodization policies. In some countries (or areas) there is evidence for re-emergence of goitre in some groups (e.g. in the United Kingdom among pregnant women and those following dairy-free diets), despite overall adequate iodine intakes at the national (or equivalent) level (326). In such situations, improving iodine intake in the whole population would reduce the proportion of people with low intake (including severely low intake), as a result of the distribution of iodine intake shifting to the right (i.e. increasing). Methods to better identify the proportion of a population with deficiency are available (Section 5.1.3), but are not widely applied.

### 7.5.1 Adolescents and adults

Adequate iodine intake in adolescent girls and women of reproductive age is particularly important to ensure sufficient iodine stores in order to help meet the higher requirements in pregnancy. However, among the population of the European Region, there is evidence of iodine deficiency in adolescents (50, 327) and adults (Section 7.4). These groups are at a greater risk of iodine deficiency than children, particularly in countries with no or voluntary salt iodization. In such populations, milk and dairy products are important sources of iodine and adolescents and adults consume less than children.

## 7.5.2 Pregnant women

Within the adult population, pregnant women represent a vulnerable group. During pregnancy, the iodine requirement increases due to increased thyroid hormone production, renal iodide loss and iodide transfer to the fetus (328). Iodine deficiency triggers an increase in thyroid iodine uptake during pregnancy. This compensatory mechanism may lead to increased thyroid volume not only in pregnant women but also in newborns (84, 87). Indeed a United Kingdom study of pregnant women found palpable goitre in 36% (n=89; median UIC 135  $\mu$ g/L) (326). Pregnant women starting pregnancy with low iodine status may remain iodine deficient throughout pregnancy despite starting iodine supplements in early pregnancy (41), suggesting that iodine deficiency should be corrected in women of childbearing age, therefore avoiding the need for a supplement.

## 7.5.3 Consumers following a predominantly plant-based diet

A vegan diet completely eliminates all animal-based foods. A systematic review and metaanalysis showed that vegans have a low iodine intake and status, and an increased risk of iodine deficiency (329). Plant-based diets are increasingly advocated for environmental reasons, and while less strict than a vegan diet, they emphasize reducing consumption of meat, milk and dairy products, owing to their contribution to carbon emissions. Governments in the European Region have published targets for reduction in meat and dairy intake, for example the United Kingdom Climate Change Committee has targets for a 20% reduction in meat and dairy by 2030 and a 35% reduction by 2050. Diets that limit dairy products and replace them with plant-based alternatives may result in an inadequate iodine intake. A study using data from the United Kingdom National Diet and Nutrition Survey (years 7–9; 2014–2017) showed that individuals who exclusively consumed (largely unfortified) plant-based milk alternatives had a lower iodine intake (94  $\mu$ g/day vs. 129  $\mu$ g/day) compared to exclusive cows' milk consumers (330). The iodine status in the group exclusively consuming plant-based milk alternatives was significantly lower than those consuming cows' milk (median UIC: 79  $\mu$ g/L vs. 132  $\mu$ g/L) and classified them as iodine deficient. A dietary modelling study has used national dietary data in the United Kingdom to examine the effect of replacing cows' milk with plant-based alternatives on population iodine intake; the results show that for all population groups, iodine intake would fall if replacement was with plant-based milk alternatives fortified at 0–22.5  $\mu$ g/100 mL (i.e. the current market values) (331).

As outlined in **Section 4**, animal products provide the majority of the iodine in the diets of many countries (or areas) in the European Region. **Fig. 7.7** shows that the foods with the highest iodine content are all animal-based and therefore if these foods are replaced with plant sources, iodine content of the diet will fall. Consumers following a predominantly plant-based diet may be at increased risk of deficiency. As shown in **Fig. 7.7**, this is especially the case in countries without a strong iodized salt policy, or iodine fortification of plant-based sources such as bread. It is therefore important that the impact on iodine status is considered in the growing narrative for populations to reduce their intake of animal-based foods for environmental reasons.

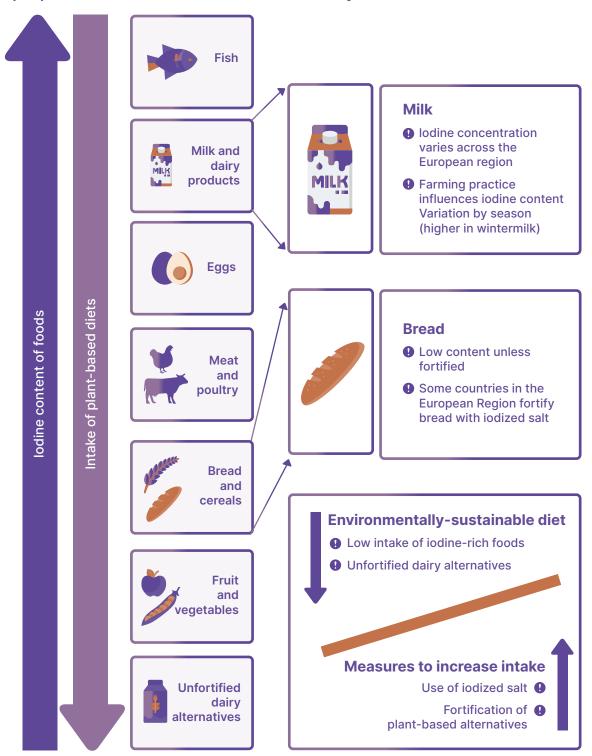
The EAT-Lancet diet was proposed in 2019 (332) as a planetary health diet – one that would reduce environmental impact but provide key nutrients; however, iodine was not specifically mentioned in the report. It may have been assumed that iodized salt would ensure adequate intake, but this is not likely in all countries (or areas). The EAT-Lancet diet includes a moderate amount of milk, fish and eggs, and the total iodine content of the diet has been estimated at 128  $\mu$ g/day, or 85% of the adult RNI (164); if unfortified plant-based alternatives are used instead of milk, the diet would provide just 54  $\mu$ g/day or 36% of the adult RNI.

Fig. 7.7 highlights the potential risk of iodine deficiency with environmentally sustainable (i.e. plant-based) diets, because of low iodine content of plant foods. However, there are measures that can be used to reduce the risk of low iodine in plant-based diets, including appropriate fortification of plant-based dairy alternative products (such as soya/oat drinks), and greater coverage of iodized salt, or fortification of other staple plant-based foods (such as bread). In addition, while industry catches up with the fortification of plant-based products on the market, there may need to be a personalized approach to individuals following a plant-based diet, where a suitable iodine supplement is used to ensure adequate iodine intake, especially in countries (or areas) that do not yet have widespread coverage of iodized salt.

## 7.5.4 Equity in iodine intake

Globally, iodine deficiency is more prevalent in geographically remote areas and lower-income groups, especially in countries (or areas) with limited access to iodized salt. This pattern has been observed in eastern Europe and central Asia. Lower median UIC has been recorded in rural areas compared to urban areas in women of reproductive age in Uzbekistan (333) and in pregnant women in the Republic of Moldova (334). In Uzbekistan, the median UIC in women was adequate in urban areas  $(148 \mu g/L)$  whereas for women residing in Namangan and Samarkand regions, as well as those from the poorest households nationwide, median UIC was below optimal (333). In contrast, in North Macedonia, where high levels of household coverage with adequately iodized salt have been sustained for decades, no statistically significant differences in the median UIC were found between children from low and high income households (255).

Fig. 7.7. Schematic of food sources, highlighting the risk with a diet proposed for environmental sustainability



Source: authors.

In Italy, the opposite trend was observed and the median UIC in school-age children was lower in urban areas, compared rural areas (265). Median UIC in school-age children living in households that used iodized salt was higher than in households not using iodized salt (138  $\mu$ g/L vs. 111  $\mu$ g/L, p < 0.001), but the difference was small and the iodine intake overall adequate, probably due to use of iodized salt in school canteens (265). In the United Kingdom, because of an absence of salt iodization, there is variability in iodine intake and status between groups as a result of the variation in intake of iodine-rich food sources. Studies have shown that iodine status in pregnancy (urinary iodine/creatinine ratio) is positively associated with maternal age, education (107) and socioeconomic status (335).

## 7.6 Key messages

- UIC studies in the WHO European Region indicate overall adequate iodine intake in school-age children, largely due to a combination of salt iodization and iodine provided by milk and dairy products. The number of countries classified as iodine deficient based on median UIC in school-age children decreased from 23 in 2003 to two in 2023.
- Mandatory salt iodization ensures adequate iodine intake in all population groups, except in a few countries where programmes are poorly enforced.
- lodine inadequacy is mainly of concern in countries with voluntary salt iodization or no policy, where only a small percentage of all salt consumed is iodized, particularly in women of reproductive age and pregnant women. Recent studies suggest falling iodine intakes in some countries with voluntary salt iodization.
- The classification of a population with "mild" iodine deficiency based on the median UIC may be misleading as there will be a proportion with more severe deficiency (i.e. at the tail of the intake distribution). Studies correcting UIC for urine volume and estimation of the prevalence of inadequacy, show that there is a proportion (and in some cases a relatively high proportion) with low, or very low, intake of iodine.
- Routine iodine status surveillance using nationally representative (or equivalent) population-based UIC studies is lacking in most countries of the European Region, and many countries have outdated data (> 10 years old). Regular information on national (or equivalent) iodine status is needed and monitoring should prioritize the adult population (particularly women of reproductive age), adolescents and/or pregnant women. Regular sentinel monitoring through health facilities or obstetric care may be a feasible alternative to national surveys. Political commitment, funding allocation and new strategies for representative population monitoring of iodine status are needed.
- UIC in school-age children may no longer represent iodine status for the general population in the European Region since the intake of cows' milk and dairy products (good sources of iodine) is higher in children than in adults, and in some countries iodized salt is mandatory for food preparation in school canteens, but not for household salt or for salt used by the food industry.

Chapter 8.

Positive economic impact of the prevention of iodine deficiency

The low soil iodine content in countries of the European Region led to a lack of dietary iodine and was responsible for severe iodine deficiency in the 19th century. Today, despite suboptimal iodine intake in many countries of the Region, iodine consumption has improved compared with the 1980s, when goitre was endemic and subclinical hypothyroidism in neonates was frequent in many countries (336). As the ecological situation will persist, iodine fortification programmes require a sustained commitment by health systems in every country in the Region.

## 8.1 Severe iodine deficiency

Correction of iodine deficiency is cost-effective if fortification programme costs are lower than those associated with the consequences of deficiency. The negative economic impact is most apparent in severely iodine deficient populations with a high prevalence of endemic goitre, neurocognitive deficits and severe intellectual disability (133, 337, 338). The costs are related to the negative impact on productivity due to neurocognitive impairment, and in such settings the estimated cost-benefit ratio of iodine fortification ranges between 1:26 and 1:400 (12, 133).

The 2008 Copenhagen Consensus of economic experts, guided by consideration of economic costs and benefits, ranked salt iodization third in a list of more than 30 initiatives to promote global welfare at a cost of US\$ 0.05 per person per year. A favourable cost-benefit ratio was reported in studies carried out in several severely iodine deficient countries (Bolivia, Ecuador and India) (339). However, most information on the economic impact of severe iodine deficiency is found in synopses, symposium summaries and monographs, while country studies are limited. Despite the lack of high quality cost-benefit analysis, it is well accepted that iodine fortification prevents production losses associated with neurocognitive impairment and is cost-effective in severely iodine deficient populations.

## 8.2 Mild iodine deficiency

The economic impact of strengthening iodine fortification programmes goes beyond reducing health-care costs by preventing the disorders associated with mild iodine deficiency, and thus the cost of treatments. Lack of awareness by medical and health authorities in the Region, fragile iodine fortification legislation and changing dietary patterns may lead to reductions in iodine intake over time, as demonstrated in Germany and the United Kingdom (50, 319), with the associated costs of iodine deficiency.

The principal argument for optimizing iodine intake in mildly iodine deficient populations is to prevent thyroid nodular diseases, goitre and hyperthyroidism (340) (Section 3.3.2). Most cases of goitre in mildly iodine deficient regions are not visible on examination and must be detected by ultrasound. The health benefit of correcting mild iodine deficiency has been

clearly demonstrated in several countries. In Switzerland, incidence of hyperthyroidism decreased significantly following correction of mild iodine deficiency (341), but the study did not assess cost-effectiveness. In Denmark, prevalence of both solitary and multiple thyroid nodules was lower 11 years after mandatory iodine fortification (76).

Few studies assess the economic impact of mild iodine deficiency in the European Region but all point to a societal benefit for prevention (8, 17, 18, 342-344). None of the studies collected data aimed specifically at assessing the cost-effectiveness of correcting mild iodine deficiency, but are rather based on modelled estimates. The estimated levels of economic benefit of preventing mild iodine deficiency vary between studies due to model design, implicit expected benefit and the national economic context. In contrast to severe iodine deficiency, the consequences of mild deficiency on human health are less well defined (Section 3.3), and this may affect the accuracy of the estimates. Iodine deficiency is one of many risk factors for thyroid disorders and potential intellectual disability. Cost-benefit assessments use the best available scientific estimate of the relative risk of developing potential health consequences of iodine deficiency. Cost-benefit analysis is also greatly impaired by the lack of national data recording thyroid diseases associated with mild iodine deficiency, including nodular thyroid disease and hyperthyroidism. In addition the quality of the data on thyroid diseases in national registries is highly heterogeneous in the Europe Region, precluding comparisons (16). Establishment of a European Region registry of thyroid diseases specifically associated with mild iodine deficiency is needed to assess the costbenefit of mild iodine deficiency correction more accurately. The lack of prevalence data for iodine deficiency is a further challenge for reliable cost-benefit analysis.

A recent assessment using a decision-analytic model designed to evaluate the benefits and harms of iodine deficiency prevention in Germany suggests that iodine fortification of salt increases quality-adjusted life expectancy (17, 18). The data suggest that reduction of goitre and thyroid nodules prevalence by salt iodization is cost-saving. The studies also reviewed other health outcomes including intellectual disability, hypothyroidism, stillbirths/miscarriages, thyroid cancer and mortality. However, evidence of causality between mild deficiency and some of these health outcomes, such as intellectual disability, is weak (Section 3.3.3) and the effect sizes of relative risk uncertain (81). Consequently, inclusion in cost-benefit analysis of the potential improvement in intellectual capability brought about by correcting mild iodine deficiency is poorly supported by scientific data. Estimation of the risk of hypothyroidism, stillbirths/miscarriages and thyroid cancer due to mild iodine deficiency in cost-benefit models is also challenging due to the lack of clinical data. Inclusion of these outcomes may lead to an overestimation of the cost-savings achieved by mild iodine deficiency correction.

In the United Kingdom, correction of mild iodine deficiency by iodine supplementation in pregnant women was reported to be cost saving (342). As in Germany, this evaluation was based on the assumption that iodine supplementation of mildly iodine deficient pregnant women improves the IQ of children born to those mothers. Authors of both studies refer to Germany and the United Kingdom as having mildly to moderately iodine-deficient populations, but data on iodine status shows that both regions are mildly iodine deficient, rather than moderately (15, 50). The combination of "mildly to moderately iodine deficient" should probably be avoided when referring to a specific region because the health consequences of mild and moderate iodine deficiency differ.

In a study in Belgium, it was assumed that correcting mild iodine deficiency would decrease the prevalence of thyroid nodular diseases by 38% over a period of 4–5 years, saving at least 14 million euros annually (343). One limitation of this study is that data on the prevalence of thyroid nodules was not drawn from Belgium, but from Denmark and there may be a difference in prevalence between countries. Cost savings arising from better cognition and higher productivity, and reduction in the costs associated with work disability were not included in the study. This led to a more conservative – and probably more reliable – estimate of cost-saving potential.

The economic benefits of salt iodization in the European Region were estimated by applying a regression model derived from observational data on the relationship between the total goitre rate assessed by palpation and median UIC using data from 43 countries (344). The model was used to estimate hypothetical national total goitre prevalence from the current median UIC. Reduction of goitre prevalence due to salt iodization in 2019 was estimated at 60%, compared to the situation in 1993, preventing 70 154 cases of goitre. The total goitre rate may, however, underestimate the impact of mild iodine deficiency as many subjects without palpable goitre may have nodular thyroid disease, which can only be detected by ultrasound. As well as a reduction of the goitre rate across the Region, the authors suggested a potential reduction in cognitive deficits and improved future earnings potential. In addition, applying the regression model to newborns, the relationship between total goitre rate and median UIC derived from child and adult populations likely overestimates the prevalence of palpable goitre in newborns across the Region.

In Denmark, the cost to health services of thyroid diseases increased after iodine fortification, arising principally from hormone replacement therapy and thyroid surgery (345). However, the changes in the incidence of thyroid diseases after iodine fortification do not completely explain the increase in treatment cost. Other determinants may modify the incidence of thyroid diseases and may also affect treatment costs, such as changes in clinical practice, new treatment guidelines and increased diagnostic rates, which have already been observed with the increasing use of thyroid ultrasound. These limitations should be considered when interpreting data. This illustrates the limitations of a national registry to accurately assess the impact of iodine fortification alone on attempts to achieve cost-savings in treatment of thyroid diseases. This study shows that reliable evaluation of the costs and benefits of preventing mild deficiency, even using an accurate national registry, is more difficult than anticipated.

Ironically in the Europe Region, while many pregnant women are at risk of iodine deficiency, there is recognition that farm animals, including dairy cows, benefit from adequate iodine intake for the prevention of negative effects of deficiency. Animals bred in areas with iodine deficient soils and fed with rapeseed (a common animal feed) containing goitrogens (naturally occurring substances that can interfere with the function of the thyroid gland) have impaired reproduction and productivity (346). In fact, iodine fortification of animal feed is a well-established practice in the European Region, delivering adequate iodine intake across all sectors of the livestock industry.

In summary, salt iodization has prevented endemic goitre and cognitive deficits in those regions where iodine deficiency was severe, with clear economic benefits. At present, iodine intake is still suboptimal in large parts of the European Region and mild iodine deficiency is responsible for an avoidable high frequency of thyroid nodules and hyperthyroidism. Further evidence is needed to understand the extent to which reducing the frequency of these

diseases translates into cost savings. Cost-analysis models should preferably include evidence-based benefits to strengthen the advocacy message for preventing mild iodine deficiency. A conservative approach to estimating the economic impact of mild iodine deficiency in the Region would have the advantage of being more accurate and compelling.

The cost-benefit ratio for preventing mild iodine deficiency in the European Region is plausibly favourable, considering the very low cost of an iodine fortification programme – in Germany it was estimated at approximately 11 (euro) cents per person per year (18). Beyond the economic impact of mild iodine deficiency, the challenge is to also prevent any return to the situation which existed in the 1980s, when endemic goitre and subclinical hypothyroidism in neonates were frequent. Because of differing regulations on iodine fortification across the Region, and the lack of understanding of iodine nutrition in the Region, we cannot take for granted that progress toward optimizing iodine intake, or even maintenance of current iodine status, will continue.

## 8.3 Key messages

- Salt iodization (and/or indirect fortification of milk and dairy products) prevents endemic goitre and cognitive deficits due to severe iodine deficiency, with clear economic benefits. If adequate iodine intake is not maintained in the European Region, iodine deficiency disorders will return and be associated with economic loss.
- A favourable cost-benefit ratio for preventing mild iodine deficiency in the European Region is plausible, considering the low cost of iodine fortification programmes.
- Cost-benefit analysis of optimizing iodine intake is challenging as data on the relative risk of clinical consequences of mild iodine deficiency is limited and data on the prevalence of iodine deficiency is lacking. Further, changes in the incidence of thyroid disease after iodine fortification are not the only factor determining the cost of treatment, but also changes in clinical practice, new treatments and increased frequency of diagnostics procedures.
- The cost-analysis models of correcting iodine deficiency in the European Region should include only undisputed potential benefits, thereby increasing the relevance of the advocacy message for optimizing iodine intake of the Region's population.

## Chapter 9. Ways forward

### Ensuring sustainability of salt iodization

- Ministries of health and/or public health authorities should actively review, implement, maintain and strengthen policies and programmes aimed at controlling iodine deficiency, such as adopting mandatory salt iodization policies to improve sustainability; working with specific food producers (e.g. the bakery industry) to use iodized salt for domestic food products; and eliminating regulatory barriers to the use of iodized salt.
- Salt reduction and salt iodization policies and messaging must be integrated ("Use less salt but make sure it is iodized") and take advantage of possible synergies in data collection.
- Education and training for health professionals, salt producers and the food industry, and communication to the public would improve knowledge about iodine nutrition, the consequences of deficiency and the need for iodine in the diet.

## Recognizing the importance of milk and dairy products for adequate iodine intake

- Because of the importance of dairy products to iodine sufficiency in the Region, regulations for animal feeds and milk-iodine concentrations should be part of iodine deficiency prevention programmes. The dairy industry needs to be involved in efforts to ensure iodine adequacy in many countries.
- As the trend for plant-based diets grows, with increased popularity and availability of plant-based alternatives to key sources of iodine (milk, dairy, fish), coordinated action is needed to ensure appropriate fortification of alternative milk and dairy products with iodine.

## Monitoring iodine status

- More regular information on national (or equivalent) iodine status is needed and monitoring should include the adult population (particularly women of reproductive age), adolescents and/or pregnant women. Political commitment, funding allocation and new strategies for population monitoring of iodine status are needed.
- Countries (and areas) should take advantage of national (or equivalent) health and nutrition surveys and surveillance systems, including those for sodium intake, as well as using health facilities (such as maternity centres) to measure UIC.
- More research is needed on the association between iodine status and thyroid disorders. Current estimates suggest that salt iodization is highly cost effective, but more studies on the cost-effectiveness of salt iodization vs. treatment of thyroid disorders would be useful.

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## List of web annexes

- 1. Prevention and control of iodine deficiency in the WHO European Region: adapting to changes in diet and lifestyle. Web annex A: legislation and/or regulation for salt iodization in the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2024 (https://iris.who.int/handle/10665/377743).
- 2. Prevention and control of iodine deficiency in the WHO European Region: adapting to changes in diet and lifestyle. Web annex B: nationally representative (or equivalent) cross-sectional studies in the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2024 (https://iris.who.int/handle/10665/377744).
- 3. Prevention and control of iodine deficiency in the WHO European Region: adapting to changes in diet and lifestyle. Web annex C: dietary data for the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2024 (https://iris.who.int/handle/10665/377745).
- 4. Prevention and control of iodine deficiency in the WHO European Region: adapting to changes in diet and lifestyle. Web annex D: iodine supplementation in pregnant women in the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2024 (https://iris.who.int/handle/10665/377746).



## The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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