Report of the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) on the nutritional status of women of childbearing age, during pregnancy and lactation with respect to adequate iodine intake

Reference number: AESAN-2023-003

Report approved by the Scientific Committee in its plenary session on 6 June 2023

Working group

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Abstract

Iodine is an essential element involved in the synthesis of thyroid hormones, being essential for pre- and postnatal brain development and for cellular metabolism throughout life. On the other hand, iodine deficiency is one of the most easily preventable public health problems affecting the largest number of people in the world. The spectrum of deficit disorders is very broad, results in clinical symptoms of varying severity, and can lead to impaired brain function and development in the fetus and/or child. The World Health Organization (WHO) states that it is the major cause of preventable mental impairment.

Translated from the original published in the journal: Revista del Comité Científico de la AESAN, 37, pp: 105-151.

Therefore, adequate iodine nutrition is necessary, which is especially important in childhood, during pregnancy and lactation and in women of childbearing age who may want a pregnancy.

The most important sources of iodine are iodized salt, dairy products and fish. Iodine requirements increase during pregnancy and lactation, and the risk of deficiency increases, especially in women who do not consume iodized salt. The nutritional status of iodine in Spain is, in general, adequate; however, this situation may be due to the use of supplementation with drugs or food supplements that provide iodine, so it is necessary to evaluate the contribution through natural foods or iodized salt in our population.

In this context, the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) has carried out a review of the existing evidence on the nutritional status of iodine in our environment in women of childbearing age, pregnancy and lactation and the situations that may cause a higher risk of deficiency or toxicity.

Key words

Iodine, deficiency, pregnancy, lactation, woman, childbearing age, iodized salt.

Suggested citation

AESAN Scientific Committee. (Working group) Bretón, I., Díaz, A., Gil, Á., Recio, M. C., Vila, L. y Carlos, M.Á. Informe del Comité Científico de la Agencia Española de Seguridad Alimentaria y Nutrición (AESAN) en relación con la situación nutricional de la mujer en edad fértil, durante la gestación y la lactancia con respecto a la ingesta adecuada de yodo. *Revista del Comité Científico de la AESAN,* 2023, 37, pp: 105-151.

1. Introduction

Iodine deficiency (ID) is one of the most relevant preventable public health concerns affecting the largest number of people in the world (WHO, 2007a). The correct approach to this problem requires that special attention be paid to the diagnosis and its correction at a collective level, as a public health concern (Vitti, 2022).

The fundamental physiological role of iodine is the synthesis of thyroid hormones (De La Vieja et al., 2000), which are essential both for pre- and post-natal brain development and for the metabolism of all cells during life (Morreale de Escobar et al., 1987).

The spectrum of ID disorders (IDD) is very broad (Table 1) (Hetzel, 1983) (Niwattisaiwong et al., 2017) and, depending on whether the deficit is more or less severe, such disorders will be of greater or lesser extent (Zimmermann et al., 2008). ID can result in harmful and irreversible effects, such as impaired brain function and development in the foetus and/or child (Morreale de Escobar et al., 2004); some intelligence quotient (IQ) change has been observed even in moderate or mild ID (Levie et al., 2019). The World Health Organization (WHO) states that it is the major cause of preventable mental impairment (WHO, 2007a). Other disorders that may be associated with ID include decreased hearing threshold (Millon-Ramirez et al., 2019) or fertility (Mills et al., 2018). For all these reasons, adequate iodine nutrition is necessary, which is especially important in childhood, during pregnancy and breast-feeding, and also in women of childbearing age who may wish to become pregnant.

Table 1. Clinical consequences of iodine deficiency
Increased risk of thyroid disease: simple goitre, multinodular goitre, Hashimoto's thyroiditis, thyroid cancer
Hypothyroidism: growth and developmental delay, asthenia, intolerance to cold, heart and digestive disorders, cognitive impairment
Infertility, pregnancy problems, miscarriage, childbirth problems, post-partum depression
Foetal, newborn and infant neurological development disorders

Maintaining an adequate nutritional status of iodine is essential for women's health. Deficits in iodine intake can decrease fertility (Kuehn, 2018) and iodine requirements increase significantly during pregnancy and breast-feeding (Pearce et al., 2016), with maintaining adequate iodine intake during these periods is particularly important for neurocognitive development of the foetus, newborn and infant. Although women of childbearing age generally maintain an adequate intake of iodine, some women, particularly those who do not regularly consume dairy products, eggs, fish or iodized table salt, may not take enough to meet the increased needs during pregnancy and breastfeeding. This does not imply that pregnant or breastfeeding women should start taking or increase salt in their diet, but rather that they should ensure that any salt used in cooking or added to food at the table is iodized. On the other hand, pregnant or breastfeeding women may require additional iodine intake to achieve adequate iodine intake (DGA, 2020).

Different national and international organizations have established recommendations for iodine intake at different stages of life, including pregnancy and breastfeeding (Table 2). WHO (2007a) recommendations are probably the most influential internationally and include an iodine intake of 90 µg for children under 5 years of age; 120 µg for the population between 6 and 12 years of age and 150 µg for adolescents (over 12 years of age) and adults. During pregnancy and breastfeeding, the mother passes both thyroid hormones and iodine to the foetus and, in addition, during pregnancy, renal excretion of iodine is increased and salt intake is generally restricted, so it is necessary to increase iodine intake in these situations. For these reasons, as described below, in both cases WHO recommends a daily intake of 250 µg (WHO, 2007a) (Vitti, 2022). The European Food Safety Authority (EFSA), for its part, establishes recommendations for iodine intake (EFSA, 2014) for different stages of life, as well as the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN), which, in 2019, established a Recommended Nutritional Intake of iodine for the population (AESAN, 2019).

Table 2. Recommended iodine intake (µg) at different stages of life

Stages	**WHO (2007a)**	**EFSA (2014)**	**AESAN Scientific Committee (2019)**
0-6 months	-	-	70
7-11 months	-	70	80
<5 years	90	-	90
1-10 years	-	90	-
6-9 years	-	-	100
6-12 years	120	-	-
10-13 years	-	-	120
11-14 years	-	120	-
15-17 years	-	130	-
Adolescents (>12 years) and adults	150	-	150
≥18 years	-	150	-
Pregnancy	250	200	200
Breastfeeding	250	200	200

The most commonly used parameter for the study of iodine nutrition in a population is the analysis of urinary excretion or ioduria, which is a faithful marker of iodine intake, although its high variability limits its applicability for the study of iodine nutritional status individually, its greatest usefulness being in the study of the adequacy of iodine intake in populations. WHO considers a population to have adequate iodine nutrition when the median ioduria is between 100 and 199 µg/l (WHO, 2007b). In pregnant women, the median ioduria should range from 150 to 249 µg/l (ICCIDD, 2007), and in nursing mothers and children under 2 years of age it should be above 100 µg/l (ICCIDD, 2007).

Historically, Spain, like most European countries, has suffered intensely from the effects of iodine deficiency. However, in the last decade, a substantial and positive change has been observed with respect to the nutritional status of iodine. Two studies carried out on representative samples of the Spanish population demonstrate this change. A study conducted in more than 5000 people older than 18 years reported a median ioduria of 117 µg/l (Soriguer et al., 2011) and, in the one conducted in a child population, the median reached 173 µg/l (Vila et al., 2016). The criteria for adequate iodine nutrition were met in both cases (NGI, 2021). However, with respect to the adult population study, it should be noted, on the one hand, that a median of 117 µg/l implies that a significant part of the population has an ioduria below 100 µg/l, and on the other hand, that the median ioduria of women of childbearing age, although theoretically adequate, would be insufficient in the case of pregnancy.

In view of the above, it has been considered necessary to request the Scientific Committee of the AESAN to draw up a report on the nutritional status of women of childbearing age, pregnant and breastfeeding women with respect to adequate iodine intake in Spain.

2. Iodine and thyroid gland

2.1 Iodine and physiology of the thyroid gland

Iodine is an essential element for all mammals, essential for the proper structure and function of thyroid hormones, which is rapidly and almost completely absorbed in the stomach and duodenum. When iodine enters the blood flow, the thyroid gland concentrates it in amounts adequate for thyroid hormone synthesis and most of the remaining amount is excreted in the urine (Murray et al., 2008). The main thyroid hormone, T4 or thyroxine, contains approximately 65 % of body iodine (McDowell, 2003), while the concentration in tissues other than the thyroid is quite low, and the average iodine concentration in animal tissues, including the human species, is approximately 0.1 mg/kg (Jongbloed et al., 2002). In the body, almost all iodine is found in the extracellular fluid, where its concentration is 10-15 µg/l. The peripheral stores contain about 250 µg, a very small percentage of the total iodine in the body (Larsen et al., 1998).

Thyroid clearance of iodine is 10 to 20 ml/min, ranging from 3 ml/min after chronic iodine intake of 500-600 µg/day to 100 ml/min in case of severe iodine deficiency. About 20 % of the iodide that perfuses the thyroid gland is cleared each time it passes through the thyroid gland (Triggiani et al., 2009). The thyroid gland is able to trap iodide by means of a sodium-iodide symporter (NIS), expressed in the basolateral plasma membrane of thyrocytes, which actively transports iodide against electrochemical and concentration gradients, maintaining a concentration of free iodide 20 to 50 times higher than that of plasma (Triggiani et al., 2009), with the highest concentration gradient (100:1) in hyperthyroidism due to Graves' disease. Transport requires energy and oxygen (ATPase activity) (Triggiani et al., 2009). NIS expression is stimulated by the thyroid stimulating hormone (TSH) (Triggiani et al., 2009).

Iodide transport from the cytoplasm to the follicular lumen is passive and mediated by the apical iodide transporter (AIT), while the role of pendrin (Triggiani et al., 2009) remains unclear. Once transported into the thyroid, the iodide is oxidized and organizes or diffuses back into the extracellular fluid. TSH enhances the transport of iodide and its organification into iodothyroxine molecules. There is also an internal autoregulatory system by which the mechanism of iodide transport and its responsiveness to TSH vary inversely with the glandular organic iodine content. Thus, thyroid/plasma ratio increases when the thyroid gland is devoid of organic iodine or is stimulated by TSH. When the concentration of iodide increases in the extracellular fluid, the iodide transported to the thyroid decreases progressively (Triggiani et al., 2009). In other words, the amount of iodine undergoing organification shows a biphasic response to growing doses of iodine: at first increasing and then decreasing as a result of a relative blockage of organ binding. This decreasing performance of organic iodine from increasing doses of iodide is called the Wolff-Chaikoff effect (Wolff et al., 1949) and depends on the establishment in the thyroid of a sufficient concentration of inorganic iodide (Triggiani et al., 2009). Iodide transport in the thyroid depends on NIS expression, which increases in Graves' disease and autonomously functioning nodules and decreases after iodide overload, as well as in adenomas and carcinomas that appear as cold nodules on scintigraphy (Triggiani et al., 2009).

2.2 Iodine deficiency disorders

ID is one of the most easily preventable public health problems and affects a large number of people in the world (WHO, 2007a). ID status is established when the intake of this element is not sufficient to meet the needs required for the adequate performance of the thyroid gland according to age and physiological state. For its prevention, special emphasis should be placed on diagnosis and its correction at a collective level, as a public health concern (Vitti, 2022). As described above, the fundamental role of iodine in the body is its participation in the synthesis of thyroid hormones (De La Vieja et al., 2000), which are essential both for pre- and post-natal brain development and for the metabolism of all cells throughout life (Morreale de Escobar et al., 1987).

The spectrum of IDD is very broad (Hetzel, 1983) (Niwattisaiwong et al., 2017) and, depending on whether the deficit is more or less severe, such disorders will be of greater or lesser extent (Zimmermann et al., 2008). WHO states that IDD is the major cause of preventable mental impairment (WHO, 2007a). Decreased hearing threshold (Millon-Ramirez et al., 2019) (Dineva et al., 2022) or fertility (Mills et al., 2018) are also some of the disorders that can be associated with ID. It is also worth considering that ID increases the risk of thyroid cancer caused by radioactive contamination, particularly in the paediatric population (Zimmermann and Galetti, 2015). Therefore, an adequate nutritional status of iodine must be maintained, which is especially important in childhood, during pregnancy and lactation and also in women of childbearing age who may wish to become pregnant.

2.3 Physiology of the thyroid gland in pregnant woman. Role of iodine in foetal brain maturation

Thyroid hormone (TH) metabolism undergoes remarkable changes in pregnant women, with up to a 50 % increase in TH levels. This means that iodine intake should be substantially increased in early pregnancy (WHO, 2007b).

Thyroid hormones play an essential role in growth and metabolic homeostasis in humans as well as in animals. By studying the severe neurocognitive impairment of patients with congenital hypothyroidism (CH) first, and through experimental animal studies, it has been shown that, already from the first weeks of embryonic development, the nervous system is highly sensitive to thyroid hormones.

The main effects of thyroid hormone deficiency on the development of the central nervous system (CNS), expressed in chronological order, are:

- Reduction of progenitor expansion.
- Deficits in neuronal migration.
- Delayed neuronal proliferation.
- Decreased expression of neuronal differentiation factors.
- Reduction of the thickness of the cortex.
- Cortical dysplasia.
- Abnormal cerebellar cortex.
- Worsening of dendrite and axon development.
- Decreased expression of proteins involved in synapse plasticity.
- Delayed myelination.

During pregnancy, maternally synthesized thyroid hormones cross the placental barrier via a specific transporter for thyroid hormones that appears to be more selective for T4. There it is converted to T3 by placental desiodases. Thus, maternal T3 can reach foetal tissues before maturation of the foetal thyroid gland occurs. In the CNS, T3 results from the *in situ* transformation of T4 due to the presence of desiodases with a specific distribution that are essential for tissue development and differentiation (Morreale de Escobar et al., 2000).

Experimental models represent very well what happens with foetal TH deficiency in humans. If the foetus is a carrier of a genetic deficiency in the hormone signalling pathway, if there is maternal hypothyroidism, or endocrine disruptors alter the availability of T3 and T4, it is going to cause an alteration in the achievement of psychomotor milestones and their neurological outcomes in children (Rovet, 2014).

However, these results are affected differently depending on the duration of exposure to thyroid hormone deficiency in the foetus. The early development of foetuses with congenital hypothyroidism is protected by maternal hormones. Therefore, the brain areas affected in this situation are those that develop in the later stages: spatial and associative memory, language and auditory processing, as well as attention and executive processing. Gross motor skills, visual processing, visual attention and event memory appear to be affected when thyroid hormones are lacking in the first trimester, as a consequence of iodine deficiency or maternal hypothyroidism. Human MRI studies also found differences in cortical abnormalities (thinning and thickening) between congenital hypothyroidism and maternal hypothyroidism, although further studies confirming these findings are needed (Lischinsky et al., 2016).

As shown in animal studies, a lack of thyroid hormones can lead to irreversible deficits in brain cytoarchitecture and development. Results from a Danish prospective study revealed an increased risk of seizure disorders, autism spectrum disorder, attention deficit disorder, hyperactivity and other psychiatric conditions among patients born to mothers with thyroid dysfunction (Andersen et al., 2014).

The most frequent causes of maternal thyroid hypofunction may be mainly iodine deficiency or autoimmune thyroid diseases.

Maternal hypothyroxinemia occurs when plasma TSH levels are normal, but T4 is abnormally low. It has been mainly associated with iodine deficiency, but an important new development is that other factors such as environmental disruptors, obesity, iron deficiency and impaired angiogenic factor (Dosio and Medici, 2017) may also be involved. Recent studies investigating the effects of hypothyroxinemia on foetal neurological development have generally reported a negative correlation, especially when it occurs during the first trimester (Rovet, 2014). However, data on the later stages of pregnancy are less consistent (Dosio and Medici, 2017).

A recent meta-analysis observed that maternal subclinical hypothyroidism and hypothyroxinemia are associated with an increased risk of impaired childhood cognitive development (OR (odds ratio): 2.14; 95 % CI (confidence interval): 1.20 to 3.83; p= 0.01, and OR: 1.63; 95 % CI: 1.03 to 2.56; p= 0.04, respectively). Maternal subclinical hypothyroidism and maternal hypothyroxinemia were not associated with attention deficit hyperactivity disorder, and their effect on autism risk was unclear (Thompson et al., 2018).

When the mother has subclinical hypothyroidism (SH) with thyroid autoantibodies, this can lead to a significant reduction in maternal TH supply to the foetus, especially in early pregnancy. Clinical studies in mothers with autoimmunity during pregnancy have revealed an association between high antibody titres and attention problems in children (Ghassabian et al., 2012). It must be noted that, after adjusting for TSH, this association was milder. The possible transient effect of maternal thyroiditis on the offspring or the autoimmune involvement of different pathways in foetal neurodevelopment could explain the different results in the literature.

3. Iodine sources

Iodine is a trace element that is naturally present in food or added to it, although it can also be part of food supplements and medicines.

Iodine is found in nature in several forms: inorganic sodium and potassium salts (iodides and iodates), inorganic diatomic iodine and organic monoatomic iodine (Patrick, 2008). The earth's soils contain varying amounts of iodine, which in turn affects the iodine content of crops and also animal foods. In some regions of the world, iodine-deficient soils are common, which increases the risk of iodine deficiency among people consuming food from those areas.

3.1 Food, naturally

Iodine is rarely found in nature in free form and generally occurs as iodide and iodate. Iodine minerals are found in igneous rocks and soils. It is released by weathering and erosion and, due to its solubility, is leached by rainwater into surface waters, the sea and oceans. Thus, the soil becomes increasingly poor in iodide (Triggiani et al., 2009). Older mountainous regions such as the Himalayas, the Andes and the Alps, the minor mountain ranges of Africa and flooded river valleys are among the most iodine deficient areas in the world. The elemental iodine released sublimates in the atmosphere due to its volatility and is precipitated by rainfall on the soil surface, where plants, which do not need this element, absorb small amounts of iodide. When the soil is poor in iodine, plants and animal tissues have a low content of this mineral and humans are exposed to iodine deficiency if the diet is based solely on food produced in these areas (Triggiani et al., 2009).

Vegetables generally do not provide adequate iodine in the diet (Lentze, 2001) (Krajcovicová-Kudlácková et al., 2003). In contrast, animal-based food (milk and dairy products, eggs, fish and meat) represent an important dietary source of iodine in human nutrition. The iodine content of animal tissues depends on the type of feed and iodine supplementation in the animal feed. Seaweed, shellfish and fish are rich in iodine because sea plants and animals can concentrate iodine from seawater. Freshwater contains less iodine than saltwater and so do fish living in rivers or lakes (Underwood and Suttle, 2001).

3.2 Food iodization

Processed foods may contain slightly higher levels of iodine if iodized salt or iodine-containing food additives, such as calcium iodate and potassium iodate, are added. Iodophors, used as sterilizing agents in the dairy industry, add iodine to the food chain.

According to WHO (2007a), salt iodization has been implemented in 40 European countries, being mandatory in 13 countries, voluntary in 16 and unregulated in the remaining countries. The amount of iodine added ranges from 10 to 75 mg/kg of salt, with most values within the range of 15 to 30 mg/kg. The iodine content in infant formulae and follow-on formulae is regulated by specific regulations (BOE, 2008).

3.3 Food supplements and medicines

Food supplements containing vitamins and minerals often provide iodine in the form of potassium iodide or potassium iodate, usually at a dose of 150 µg (NIH, 2020).

Iodine is also present in supplements containing seaweeds such as *Spirulina platensis*, *Chlorella pyrenoidosa* or *Fucus vesiculosus*. In these cases, the nutritional information on the labelling includes the significant amount of iodine in the supplement, although if iodine is part of the composition of the ingredient, for example, seaweed, the amount of iodine it provides may not be listed.

In 2004, the Spanish Agency of Medicines and Medical Devices (AEMPS) authorized the marketing of potassium iodide in Spain as a medicinal product for the prevention and treatment of iodine deficiency in pregnant and nursing women. These medicinal products provide between 100 and 300 µg of iodine, although not all are included in the funding of the National Health System.

Finally, it must be taken into account that there are other medicinal products that constitute a significant source of iodine, such as those containing amiodarone (antiarrhythmic drug) or topical antiseptics, such as povidone iodine or radiological diagnostic agents. For example, 200 mg of amiodarone contains 75 mg of organic iodine (Ylli et al., 2021), while iodinated contrast materials may contain an amount of this element reaching 18-45 g, for example, for performing a CT scan (Bednarczuk et al., 2021).

4. Iodine intake

4.1 Recommendations for iodine intake in pregnancy and lactation. Methods for the study of iodine nutrition

As discussed in the above section, the daily intake of iodine recommended by the WHO is 90 µg for children under 5 years of age, 120 µg for the population between 6 and 12 years of age and 150 µg for adolescents (over 12 years of age) and adults (WHO, 2007a). During pregnancy and breastfeeding, there is an increase in iodine requirements due to several factors. First, maternal thyroxine production can be increased by up to 50 %, which, according to Delange (2007), can result in an approximate increase in iodine requirements of about 50 µg/day. There is also a transfer of iodine and thyroxine to the foetus, which, in total, Delange estimates at about 50 µg/day of iodine. Finally, there is an increase in renal iodine clearance, although this same author questions its real effect since there are clear disagreements in the literature. In the case of breastfeeding, the passage of iodine into breast milk should be considered. In total, this author estimates the increase in requirements at 100 µg/day of iodine, which added to the requirements of the adult population results in a recommendation of 250 µg/day. Based on this, a WHO Technical Committee established the recommendation of a daily intake of 250 µg (WHO, 2007a) (Vitti, 2022) for both pregnant and breastfeeding populations. Although there is a certain unanimity on the part of different organisms when establishing the requirements of 150 µg/day of iodine in the adult population, there are substantial differences when they are established for the population of pregnant or nursing women. EFSA (2014) proposes an adequate iodine intake during pregnancy of 200 µg, in women with adequate pre-pregnancy nutritional iodine status. The difference with respect to the WHO recommendation lies in the estimate of iodine that is transferred from the mother to the foetus. The calculation on which WHO (Delange, 2007) is based assumes an average transfer of 50 µg/day and, in contrast, in EFSA's calculations it is only 4 µg/day. The American Institute of Medicine (IOM, 2001) makes a recommendation for pregnant women that is lower than that of the WHO (220 *versus* 250 µg/day), which, according to Delange, it is because they do not consider the increase in T4 production during pregnancy. The difference is most marked in the recommendations set out in the Nordic Nutrition Recommendations (NNR, 2022), which in the case of pregnancy indicate an increase of 25 µg/day, based on the same principles used by Delange. The paper assumes that renal clearance is increased by 30-40 % and that iodine transfer to the foetus is about 7 µg/day, according to a 1984 study by Delange (Delange et al., 1984), being much lower than that calculated by Delange himself in 2007 (Delange, 2007). There is no measurement of the increase in maternal thyroxine synthesis. The Spanish Federation of Nutrition, Food and Dietetics Societies (FESNAD) (2010) establishes recommendations similar to those made by the NNR (2022) based on recommendations from Ireland and France. The AESAN Scientific Committee, for its part, in 2019, based on the reference literature, establishes Nutritional Reference Intakes similar to those of EFSA (Table 3).

The most widely used parameter for the study of the nutritional iodine status of a population is the analysis of its urinary excretion or ioduria, which is a good marker of recent iodine intake, since its intestinal absorption is 92 % and, in healthy iodine-sufficient adults, more than 90 % is excreted in the urine within 24-48 hours (Zimmermann, 2012). The collection of 24-hour urine is difficult to implement in epidemiological studies, so a urine sample is usually analysed, extrapolating to 24 hours, if the ioduria/creatinuria ratio is included. The analysis of ioduria expressed in µg/l also correlates with iodine intake. In any case, these techniques are highly variable and not very accessible in the clinical practice, so their usefulness for the study of the nutritional status of iodine in individuals is limited and they are used especially for the study of populations. WHO considers a population to have adequate iodine nutrition when the median ioduria is between 100 and 199 µg/l (WHO, 2007b). In pregnant women, the median ioduria should range from 150 to 249 µg/l (ICCIDD, 2007), and in nursing mothers and children under 2 years of age it should be above 100 µg/l (ICCIDD, 2007). Median ioduria values below 100 µg/l in children and adults indicate insufficient iodine intake in the population, although iodine deficiency is not classified as severe until the median ioduria is below 20 µg/l. More recently, thyroglobulin measurement has been proposed as a marker of iodine deficiency (Stinca et al., 2017).

Table 3. Summary of daily iodine requirements for pregnant and nursing women according to different agencies and associations (iodine values expressed in µg/day)

Factors inducing an increase in iodine requirements	IOM (2001)		WHO (2007a)**		EFSA (2014)		NNR (2022)		FESNAD (2010)		AESAN Scientific Committee (2019)	
	Pregnant	Infant	Pregnant	Infant	Pregnant	Infant	Pregnant	Infant	Pregnant	Infant	Pregnant	Infant
Increased thyroxine synthesis	Not included		50-100		44							
Passage of iodine from mother to foetus	EAR= 75	-	50-75	-	4	-	25	-	25	-	50	-
Increased renal iodine clearance	Not included		Not included		Not included							
Passage to breast milk	-	EAR= 114	-	75-200	-	60	-	50	-	50	-	50
Requirements in adult population (>20 years)	RDA= 150*	RDA= 150*	RNI= 150	RNI= 150	RNI= 150	RNI= 150	RI= 150	RI= 150	IDR= 150	IDR= 150	INR= 150	INR= 150
Total recommended	**RDA= 220**	**RDA= 290**	**RNI= 250**	**RNI= 250**	**AI= 200**	**AI= 200**	**RI= 175**	**RI= 200**	**IDR= 175**	**IDR= 200**	**INR= 200**	**INR= 200**

*EAR 95 µg/day ± 2 SD = RDA 150; **Data based on Delange (2007) calculations.

AI: Adequate Intake; EAR: Estimated Average Requirements; DRI: Dietary Reference Intake; RNI: Reference Nutritional Intakes; RDA: Recommended Dietary Allowance; RI: Recommended Intake; RNI: Recommended Nutrient Intake.

4.2 Current status of iodine nutrition in Spain

Historically, Spain, like most European countries, has suffered intensely from the effects of iodine deficiency. However, the last decade has seen a substantial and positive change with regard to iodine nutrition. Two studies carried out on representative samples of the Spanish population demonstrate this change. A study conducted in more than 5000 people older than 18 years showed a median ioduria of 117 µg/l (Soriguer et al., 2011) and in the one conducted in a child population the median reached 173 µg/l (Vila et al., 2016). In both cases, the criteria for adequate iodine nutrition are met (IGN, 2021). However, with respect to the adult population study, it should be noted, on the one hand, that a median of 117 µg/l implies that a significant part of the population has an ioduria below 100 µg/l, and on the other hand, that the median ioduria of women of childbearing age, although theoretically adequate, would be insufficient in the case of pregnancy. There is no nationwide study on iodine nutrition in the pregnant population.

In the last decade, there have been several local or regional studies assessing the nutritional status of iodine in pregnant women in Spain, which show disagreeing results (Santiago et al., 2013) (Velasco et al., 2013) (Menéndez et al., 2014) (Torres et al., 2017) (Ollero et al., 2020) (González-Martínez et al., 2021) (Melero et al., 2021) (Murillo-Llorente et al., 2021) noting that the median ioduria ranges from 57 to 242 µg/l (Table 4).

Table 4. Intake of iodized salt and use of iodized medicinal products and food supplements in the first trimester of pregnancy in Spain. Data from the last decade

Reference	Population	Number of pregnant women included	Median ioduria* (µg/l)	Percentage of women consuming iodized salt (%)	Percentage of women receiving potassium iodide (%)
Santiago et al. (2013)	Jaén	131	109	31.9	Randomization
Velasco et al. (2013)	Málaga	233	126	42.2	83.3
Menéndez et al. (2014)	Asturias	173	197	46.8	50.8
Torres et al. (2017)	Catalonia	945	172	35.7	46.8
Murillo-Llorente et al. (2021)	Valencia	261	57	49	70.5
Ollero et al. (2020)	Pamplona	400	242	55.3	98.5
González-Martínez et al. (2021)	Oviedo	318	171.5	51.1	87.08
Melero et al. (2021)	Madrid	2523	123**	40.5	8,7*** 57

*Adequate iodine nutrition of a pregnant population is considered when the median is greater than 150 µg/l. **Estimated average daily iodine intake. ***Pre-pregnancy.

5. Prevention of iodine deficiency

5.1 Prevention Strategy of the World Health Organization (WHO)

WHO (2007a) proposed the following program for the control and eradication of iodine deficiency:

1. Status analysis (Prevalence of iodine deficiency and iodine consumption study).

2. Dissemination of the results and benefits of the eradication of "Iodine Deficiency Disorders" among health professionals and the population.
3. Planning of a public health program with multidisciplinary teams of experts and representatives of the Public Health Departments.
4. Involvement of political agents.
5. Implementation of the program (training of professionals, involvement of the salt industry and public awareness campaigns).
6. Periodic evaluation and monitoring.

The WHO considers that the best method for the prophylaxis of iodine deficiency is the use of iodized salt because it is the most easily accessible food for the entire population. In addition to being effective, prophylaxis by salt iodization is safe and cost-effective (WHO, 2014).

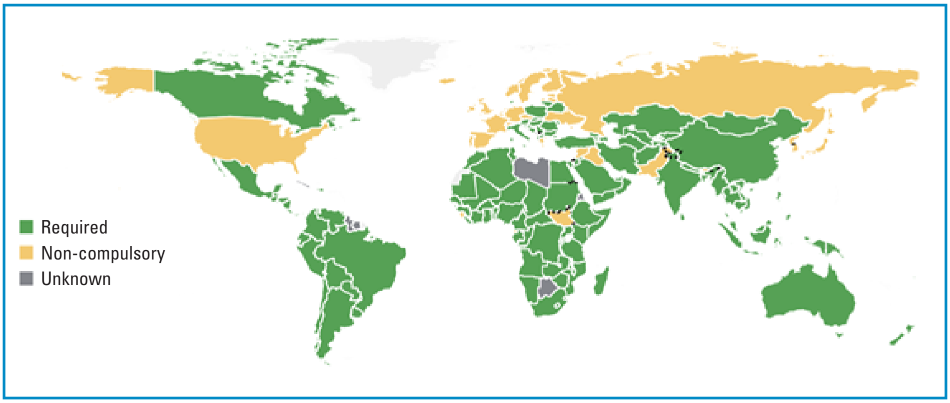

Figure 1. Map showing the mandatory use of iodized salt in the world. **Source**: (GFDx, 2023).

5.2 Strategies to prevent iodine deficiency in Europe

As far as Europe is concerned, strategies for the prevention of iodine deficiency are mainly linked to the supply, access and consumption of iodized salt by the population and are articulated through six major challenges (WHO, 2007a):

- Strengthen the monitoring and evaluation of national iodine deficiency prevention and control programs in European Union (EU) countries, including monitoring of the iodine status of national populations.
- Ensure sustainable implementation of Universal Salt Iodization (USI) in all EU countries by harmonizing relevant legislation and regulations.
- Ensure adequate quality control and quality assurance procedures to strengthen the traceability of iodine-enriched foods, especially salt iodization, from producer to consumer.
- Increase awareness among political leaders and health authorities on the social and public health dimensions of iodine deficiency and the need to implement and maintain programs for its control.

- Educate the public on the need to prevent iodine deficiency through the consumption of iodized salt, thereby also increasing consumer awareness and demand.
- Consider iodine supplements for the most susceptible groups (pregnant women and young children) when there is insufficient iodized salt and take into account public health policies to reduce salt consumption.

For this purpose, the EU proposes a political strategy with the development of the above points focused on the eradication of iodine deficiency (WHO, 2007a):

1. Assessment of iodine status

In this section, it is considered key to have a recent iodine database of the population on which to base and thus be able to implement a program to control iodine deficiency in the population.

2. Application of USI (Universal Salt Iodization)

There is universal agreement on the application of iodized salt programs in terms of USI since almost all European countries have iodized salt that guarantees such programs in terms of quality and sustainability within the framework of the legislation on this product in each country. It is emphasized that most of these programmes are voluntary so that information and awareness of the problem of iodine deficiency should be consistent and not interrupted by political or social ups and downs. A current conditioning factor is the decrease in salt intake for health reasons (high blood pressure) and the differences in iodized salt content of foods in different countries and in national regulations and legislation.

Therefore, a future strategy lies in the harmonization of legislation and regulations on iodization and the uniformity of criteria for iodine addition processes in foods.

3. Special attention to infants and pregnant women

The focus is on iodine supplements for pregnant and breastfeeding mothers so that the foetus, newborn or infant does not suffer brain damage or thyroid hormone problems that may be caused by iodine deficiency and may lead to irreversible neurointellectual damage in the future.

4. Application of alternative strategies to correct iodine deficiency

Adequate application of the USI is essential for the iodine deficiency control program; however, it is key that all countries apply it in an adequate and consistent manner for an adequate adjustment of the amounts of iodine especially in pregnant women, infants and children using salt iodization, supplements with iodized oil or other products containing micronutrients including iodine.

5. Monitoring and evaluation

Monitoring is key to the eradication of iodine deficiency; therefore, the strategy is based on monitoring the status of iodine levels and thyroid function using median ioduria, as well as neonatal screening of TSH as a measure of brain damage, with the collaboration of all countries, in order to compensate and standardise analytical capabilities.

On the other hand, it is considered essential to monitor the introduction of the use and application of iodized salt in households and in the food industry in order to monitor iodine consumption and possible excess consumption, which is also a health risk.

6. Legislation

It is indicated that there is a need for legislation on salt iodization, mechanisms for continuous monitoring of such legislation, as well as information strategies on the need for the use of iodized salt to convince consumer populations that are sceptical of these programs and prefer products that provide natural salt, which is not iodized.

7. Economic impact

Iodine control programmes have been shown to be very cost-effective and have an impact on economic productivity and national neurointellectual capabilities, but such studies are very scarce, so their promotion is needed.

8. Promotion and partnership

Develop a promotion, education and communication approach on the importance of preventing iodine deficiency aimed at the public, national health authorities and the food industry.

In line with these strategies developed by the EU is the Krakow Declaration launched in 2018 by the EUthyroid Consortium (EUthyroid Consortium, 2018), which highlights the threat of iodine deficiency disorders to people's global health and the diversity of adverse effects leading to a significant burden on public health systems. Furthermore, it is stated that such disorders receive little attention from legislators, opinion leaders and the public, thus showing concern in the political interest of public health strategies against iodine deficiency disorders in European populations (Vila et al., 2020).

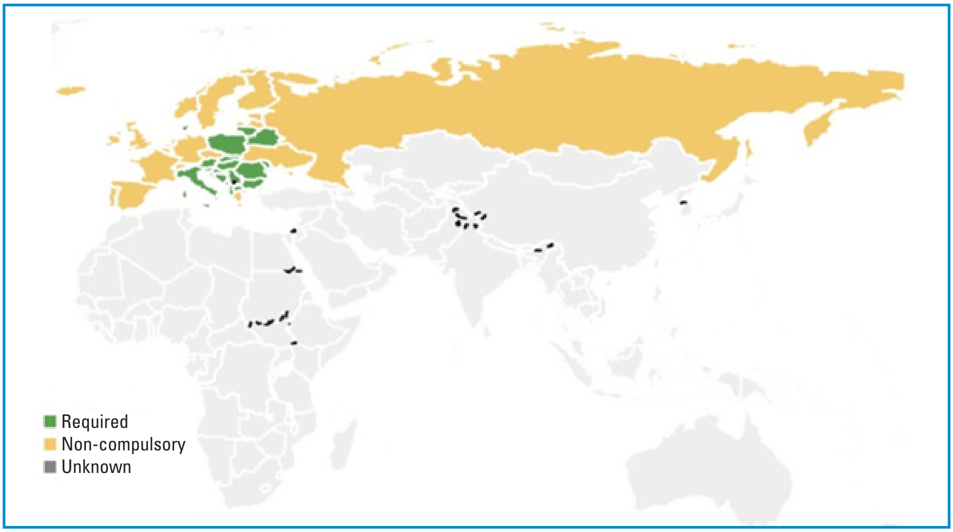

Figure 2. Map showing the mandatory use of iodized salt in Europe. **Source**: (GFDx, 2023).

The following table (Table 5) shows the strategies carried out in relation to iodized salt in some EU countries, as well as the regulations covering them.

Table 5. Salt iodization strategies in the European Union countries

Country	Mandatory salt iodization	Regulations	Description
Austria		Federal Table Salt Trade Act (Table Salt Act) StF: BGBI 112/1963 (as amended by the Federal Law of July 22, 1999)	Mandatory iodization of table salt was first regulated by this law in 1963 and in 1990 increased from 10 mg/kg to 20 mg/kg in the form of potassium iodide or potassium iodate. In 1999, the law was further amended and, since then, the total iodine content in iodized salt has been at least 15 mg and up to 20 mg per kg of table salt. The note "iodized" and the iodization form should appear on food labelling. Only iodized table salt may be used in bakery and confectionery products
Bulgaria		Decree 23, of 30 January, 2001, on the requirements for the composition and characteristics of salt for food purposes. Decree 148 of 23 July, 2010, amending and supplementing the Decree on the requirements for the composition and characteristics of salt for food purposes	The regulations establish levels of potassium iodate in feed salt of 28-55 mg/kg. Only salt enriched with potassium iodate may be used for food purposes
Croatia	Yes	Salt Ordinance (NN 70/2019)	Amount of iodine that salt for human consumption should contain: 15-23 mg iodine per kilogram of product. The use of iodized salt is mandatory in the food industry except in cases where salt cannot be iodized for technological reasons and/or when the food production process does not allow the use of iodized salt. In these cases, the warning will appear on the labelling: "Non-iodized salt. Adequate iodine intake is necessary for the normal functioning of the body"
Czech Republic	No	Decree No. 398/2016 Sb. on requirements for spices, edible salt, dehydrated products, condiments, cold sauces, dressings and mustard	Table salt with iodine: 27±7 mg of iodine per kg of salt. Although the use of iodized salt in the food industry is not mandatory, it is a fairly common practice
France	No	Order of 24 April, 2007 on nutritional substances that can be used for the supplementation of salts intended for human consumption. Directive 2002/46/EC, of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. Order of May 9, 2006 on the nutrients that may be used in the manufacture of food supplements.	Food grade salt, not intended for the food industry, may be iodized by the addition of potassium iodate, sodium iodate, sodium iodide or potassium iodide, in the proportion of 15 to 20 mg/kg (expressed as iodine) under a number of conditions laid down in the standard

Table 5. Salt iodization strategies in the European Union countries

Country	Mandatory salt iodization	Regulations	Description
Germany	No	Additive Approval Ordinance 1981 (ZZulV 1981) Ordinance on the Transition to the New Additives Law (ZRÜV) 1998. 1998 Additive Approval Ordinance	Iodized table salt is legally marketed as "iodized table salt". The iodine content, including the natural content, should be at least 15 mg/kg and up to 25 mg/kg. Only sodium iodate and potassium iodate compounds are allowed for iodination
Greece	No	National Food and Beverage Code	The potassium iodate content in salt should be 40-60 ppm. Although universal salt iodization is not mandatory in this country, this measure has been implemented for decades as a strategic prophylactic measure against iodine deficiency in the population
Hungary	Yes	Decree 37/2014 (April 30) on nutritional health standards for public catering. Standard No. MSZ-01-10007 on edible salt (sodium chloride)	Only iodized table salt in accordance with MSZ-01-10007 may be used for the preparation of meals offered in public catering. If the iodine content of drinking water used for food preparation exceeds the permissible limit, the head of the public agency concerned may grant an exemption from compliance with the above obligation in a procedure initiated at the request of the interested party. The application of Standard No. MSZ-01-10007 entitled "Edible salt (sodium chloride)" is not mandatory; however, if the food industry refers to it, it must comply with its provisions. According to this standard, iodized salt is salt enriched with potassium iodide (KI) or potassium iodate (KIO_3). (Potassium iodide (KI) content in the case of iodized salt, maximum 25.0 mg/kg; KI content in the case of iodized salt, expressed as KIO_3, maximum 32.2 mg/kg)
Lithuania	Yes	Order No V-1639 of the Ministry of Health of the Republic of Lithuania of 9 July 2021 on the use of table salt containing iodine in the production of food products (TAR, 09-07-2021, No. 15687)	Table salt must contain 20-40 mg/kg iodine when used in food production to compensate for iodine deficiency; only table salt containing 20-40 mg/kg iodine may be used in the production of bread and bakery products and in the production of foods supplied by mass catering companies. Table salt containing 20-40 mg/kg of iodine sold at retail must be labelled appropriately and in accordance with the regulations
Montenegro	Yes	Official Gazette of Montenegro, No. 010/20 of 28 February, 2020, on the quality of salt for consumption and industrial production	An amount of 20-30 mg of iodine (potassium iodate) is established in the salt

Table 5. Salt iodization strategies in the European Union countries

Country	Mandatory salt iodization	Regulations	Description
Netherlands	No	Decree on the addition of micronutrients to food products of 24 May, 1996 (Stb. 1996, 311)	Iodine compounds may be present in the following foods and beverages (according to the conditions specified in the standard): a. In bread, bread substitutes and other bakery products, only by the addition to such products of bakery salt containing not more than 65 mg of iodine per kg of salt. b. In other foodstuffs and beverages: up to a content of not more than 25 mg of iodine per kg of salt. The latter shall not apply to unprocessed products and beverages with an alcohol content exceeding 1.2 % by volume as referred to in Article 4 of Regulation (EC) No. 1925/2006
Poland	Yes	Regulation of the Minister of Health of 16 September, 2010 on fortification substances added to food (Law Review 2010, No. 174, item 1184)	Salt intended for human consumption must be fortified with potassium iodide or potassium iodate so that 100 g of table salt contains 2.3 mg of iodine (± 0.77), corresponding to 30 (± 10) mg of potassium iodide or 39 (± 13) mg of potassium iodate in 1 kg of table salt
Portugal	No	General Directorate of Education. Circular No. 3/ DSEEAS/DGE/2013 - guidelines on school menus and cafeterias. Guideline No. 011/2013 General Directorate of Health on: iodine intake in women during preconception, pregnancy and breastfeeding	Mandatory use of iodized salt in school cafeterias. Recommendation of iodine supplementation in the form of potassium iodide (150-200 µg/day) for women during preconception, pregnancy and breastfeeding
Romania	Yes	National Government Agreement No. 568/2002 on iodine fortification of salt for human consumption, animal feed and food industry	Mandatory iodization of salt for human consumption, animal feed and the food industry

Table 5. Salt iodization strategies in the European Union countries

Country	Mandatory salt iodization	Regulations	Description
Slovak Republic	Yes	Decree of the Ministry of Agriculture of the Slovak Republic and the Ministry of Health of the Slovak Republic of March 15, 2004 No. 608/8/2004-100 issuing the Chapter of the Slovak Food Code on a particular ingredient of foodstuffs (fortification of edible salt with potassium iodide and potassium iodate). Decree No. 309/2015 of the Ministry of Agriculture and Rural Development of the Slovak Republic on snacks, edible salt, dehydrated foods, soup preparations and condiments	Iodized table salt: a mixture of sodium chloride with potassium iodide or potassium iodate. The maximum allowable amount of potassium iodide or potassium iodate in iodized edible salt after conversion to potassium iodide is 35 mg/kg. The lowest amount of potassium iodide or potassium iodate in iodized table salt after conversion to potassium iodide is 15 mg/kg
Spain	No	Royal Decree 1424/1983, of 27 April, 1983, approving the Technical-Health Regulations for the production, circulation and sale of edible salt and brine	Special salts: These are those consisting of refined salt, to which various substances authorized by the General Directorate of Public Health have been added and which will be declared on the labelling of the containers. Among them we can distinguish: Iodized salt: Salt to which potassium iodide, potassium iodate or another iodized derivative authorized by the General Directorate of Public Health has been added at the appropriate proportion so that the finished product contains 60 mg of iodine per kg of salt, with a tolerance of 15 %
Sweden	No	-	The Swedish Food Agency encourages the food industry to use iodized salt, as it is not mandatory.
Switzerland	No	RS 817.022.32 - Ordinance of the Swiss Federal District of 16 December, 2016 on the addition of vitamins, mineral salts and certain other substances to foodstuffs	Enrichment of salt with iodine in the range of 20-40 mg/kg as iodide or iodate is allowed. Labelling: the use of iodized salt is permitted in processed foods but must be declared. The Federal Food Safety and Veterinary Office (FSVO) monitors salt levels in bread, but also iodized salt in bread. This encourages industries to use it

Regarding risk assessment on iodine deficiency, in several EU countries, including, for example, Germany (BFR, 2021, 2022), Portugal (Limbert et al., 2012) (Costa Leite et al., 2017) (Ferreira et al., 2021) (Pinheiro et al., 2021) (Carvalho et al., 2022) (Lopes et al., 2022) (Matta Coelho et al., 2022), Netherlands (Verkaik-Kloosterman et al., 2017) (Bath et al., 2022), Greece (Zois et al., 2003) (Koukkou et al., 2017), Poland (Trofimiuk-Müldner et al., 2020), Estonia, Hungary, Montenegro or Spain (Soriguer et al., 2012) (Vila et al., 2016), studies have been carried out on iodine intake in the population, especially in groups considered at risk for iodine deficiency, such as pregnant and breastfeeding women and children. In some cases, studies have analysed the relationship between the consumption of iodized salt (population-based surveys) and urinary iodine levels in these at-risk groups, as well as the relationship between iodized salt consumption and its impact on iodine deficiency diseases or disorders. Furthermore, in some countries, such as the Netherlands (Vellinga et al., 2022), France (ANSES, 2018), Austria (AGES, 2021) or Spain (AESAN, 2012, 2021b), risk assessment reports have been drawn up on the consumption of seaweed and the risk that excessive iodine intake through these foods may pose.

In addition, public institutions responsible for food safety in various EU countries, such as Bulgaria, the Czech Republic, Germany, Greece and Switzerland, among others, have developed different communication strategies and actions to promote information, education and health promotion in the field of nutrition, in particular, on adequate iodine intake, especially in pregnant and nursing women, in order to raise public awareness of the risks and consequences of both iodine deficiency and excess, through the media, the websites of official bodies or by distributing information material through health professionals.

As a safe and effective strategy for the prevention and control of iodine deficiency disorders, WHO recommends fortifying all food-grade salt used in households and food processing with iodine (WHO, 2014, 2022). Moreover, it states, not only that this strategy is compatible with measures aimed at reducing sodium intake in order to reduce blood pressure and the risk of cardiovascular disease, but that these are cost-effective measures of great public health benefit (WHO, 2022, 2023).

Although WHO recommends that iodized salt should be universally used, Spain, like many other countries, opted for voluntary consumption. In Spain, the marketing of iodized salt was authorized in April 1983 by Royal Decree 1424/1983 (BOE, 1983). This approved the technical-health regulations for the production, circulation and sale of edible salt and brines, which defined iodized salt as salt to which "*potassium iodide, potassium iodate or another iodized derivative authorized by the General Directorate of Public Health has been added, in the appropriate proportion so that the finished product contains 60 milligrams of iodine per kilogram of salt, with a tolerance of 15 percent*". This concentration exceeds that of other European countries, with the exception of the salt used in the Netherlands for bread production (Gerasimov, 2009). This facilitates the recommendation to reduce salt consumption (AESAN, 2022) (WHO, 2023) while advising the consumption of iodized salt, so that a minimum amount, around 2 g, would cover the iodine needs of a large part of the population.

The voluntary use of iodized salt requires campaigns to explain to the population the need to consume this type of salt instead of common or sea salt. These campaigns should be included in a public health programme, as indicated by WHO (2007a). In Spain, the marketing of iodized salt was authorized, but it was not accompanied at that time by an information campaign that could have a significant impact on the population, nor was it translated into specific actions at the state level for the implementation of the guidelines proposed by the WHO. In 2003, the Interterritorial Council of the National Health System approved resolutions recommending the consumption of foods rich in iodine, such as fish, dairy products and iodized salt (CISNS, 2003). It also indicated the importance of ensuring adequate iodization of pregnant or breastfeeding women through the provision of potassium iodide. The exclusive use of iodized salt was also recommended in school canteens in all autonomous regions (CCAA), but this has not been generalized (Vila et al., 2020). Although excellent material was produced and an important distribution was made, the action was one-time and did not last long. In 2004, the Directorate General of Pharmacy and the Spanish Medicines Agency authorized the marketing of potassium iodide as a medicinal product, to be administered to pregnant and breastfeeding women, and included in the public financing of the National Health System. The approval of this medicinal product allowed and allows to protect a large part of pregnant women from IDD in Spain. In 2004, the General Directorate of Public Health, in agreement with the working group on Iodine Deficiency Disorders of the Spanish Society of Endocrinology and Nutrition (SEEN), carried out an awareness and information campaign aimed at health professionals, pregnant women and the general population.

In 2006, at the proposal of the Ministry of Labour and Social Affairs, the Council of Ministers approved the National Strategic Plan for Children and Adolescents 2006-2009, which included, in the list of measures: "*Promote actions for the prevention of spina bifida and eradication of iodine deficiency disorders, to prevent the serious consequences that this deficiency causes in children and adults*" (MTAS, 2006).

On the other hand, the transfer of health care competencies to the different autonomous regions has allowed them to implement Public Health Programmes for the prevention of ID; however, their role has been very unequal. In Asturias, the Basque Country, Catalonia and Galicia, clearly defined Public Health Programmes have been carried out, although it is worth noting that Asturias has been the autonomous region in which the plans for the prevention and control of ID have been maintained almost up to the present day. A noteworthy action was the mandatory use of iodized salt in school canteens in the autonomous regions of Andalusia, Galicia and Asturias (Vila et al., 2020). In other autonomous regions such as Andalusia, Aragon, Extremadura or Madrid, isolated actions have been carried out that are not included in an integrated Public Health Program. Finally, it should be noted that some autonomous regions, such as Cantabria and La Rioja, lack epidemiological studies.

6. Iodine consumption in Spain and other European countries

6.1 Iodized salt

As in other European countries, salt iodization and its use is voluntary in Spain. Approximately 10 years ago, two studies were carried out to estimate its consumption in the Spanish population. In the Di@bet study, conducted on more than 4000 adults, iodized salt consumption was observed among 43.9 % of the population evaluated (Soriguer et al., 2012). Subsequently, an iodized salt consumption of 69.8 % was observed in the Tirokid study (Vila et al., 2016), conducted in a child population aged 6-7 years. The difference between the two results may be due to the fact that in the Dia@bet study the survey was conducted in an outpatient clinic. In contrast, in the Tirokid study, the survey was completed by the parents at home and it was emphasized that they should look at the label on the package of the salt they consumed. Although in the Tirokid study the sample size was not calculated for the analysis by autonomous regions, iodized salt consumption ranged from 59.6 % in the Region of Madrid to 80.4 % in Aragón. The vast majority of results, overall for Spain or by autonomous region, are far from the WHO (2007a) recommendation: more than 90 % of households should consume iodized salt.

With respect to iodized salt consumption among the pregnant population, there is no study that covers the entire Spanish territory. In the last decade, several studies have been published that illustrate its consumption (Table 4) in some provinces or autonomous regions, which show that it ranges from 32 to 55 %, far from the WHO recommendation. There is no recent information on the situation of breastfeeding women. A study conducted in Catalonia reported a significant increase in the use of iodized salt from the first to the third trimester (from 35.7 % to 87.6 %) when midwives were involved in education (Torres et al., 2020). If changes are made during pregnancy, they are likely to persist after delivery. However, there are no data on this subject in our environment.

In summary, iodized salt consumption in Spain, for the most part, is lower than the WHO recommendations, both in the general population and specifically in the pregnant population. On the other hand, as mentioned above, the concentration of iodine in salt is one of the highest in Europe (60 ppm), which means that with a limited salt intake (around 2 g) the necessary iodine requirements can be met.

An undervalued and extremely important aspect is the quality of salt iodization. There are few data on this subject in Spain, but a study published in 1999 (Donnay et al., 1999) is noteworthy, in which 27 packages of iodized salt obtained from different stores in the province of Cuenca were studied. Accepting an iodine content of 60 mg iodine per kg of salt as adequate, with a tolerance of 15 %, 60 % of the "iodized salt" was found to be under-iodized and 25 % was found to be over-iodized. This study was carried out after observing that iodine deficiency persisted even after an intensive campaign to promote taking iodized salt instead of common or non-iodized salt. More recently, a study reported at the European Congress of Endocrinology (albeit unpublished) (Arosa et al., 2017) analysed 162 samples of salt packages from different autonomous regions and reported that 67 % of salts containing iodide were out of range (51-60 µg/g); for those containing iodate, the percentage of inadequacy was 43 %. In addition to the problems caused by deficient salt iodization, iodine losses that may occur due to poor storage in the home or different types of cooking should also be considered. With this regard, when promoting the change from common salt to iodized salt, information should also be provided on how to reduce iodine losses from iodized salt.

There are no data in our environment on the use of iodized salt by the food industry, which must appear as such on the labelling, in accordance with Regulation (EU) No. 1169/2011 (EU, 2011).

6.2 Milk and dairy products

Milk and dairy products mean an important iodine intake in the European population due to their relevance and frequency of consumption of these foods. Iodine content in milk varies considerably from one country to another, which is probably due to differences in agricultural practices. For example, UK milk has a relatively high iodine concentration (427 µg/l) compared to other countries: it provides 85 µg of iodine per glass of milk (200 ml), which constitutes approximately 57-34 % of the WHO recommended iodine intake for adults (150 µg/day) and pregnant women (250 µg/day), respectively (WHO, 2007a) (Witard et al., 2022).

In Europe, the average consumption of milk and dairy products in adults ranges from 180 to 450 g/person/day (Table 6) (Van der Reijden et al., 2017).

Table 6. Total consumption of milk and dairy products in the adult population of selected European countries and their contribution to the recommended daily allowance of iodine for adults

Country and year of survey	Average per capita consumption of dairy products	Contribución a las necesidades diarias de yodo (%) con respecto a las recomendaciones de la OMS (2007a)
Lower total dairy consumption	**<300 g/day**	
France (2014; 2015)	184	13-26
Italy (2005; 2006)	190	13-27
Germany (2012; 2013)	191	13-27
Switzerland (2014; 2015)	215	15-31
United Kingdom (2008; 2012)	239	16-34
Ireland (2011)	268	18-38
Sweden (2010; 2011)	280	19-40
Increased total dairy consumption	**≥300 g/day**	
Denmark (2003; 2008)	324	22-46
Netherlands (2012; 2014)	352	24-50
Finland (2007)	357	24-51
Spain (2006)	379	26-54
Norway (2010; 2011)	382	26-54
Iceland (2002)	393	27-56

The contribution of milk and dairy products to the recommended daily intake of iodine ranges from 13 % to 40 % at lower dairy intakes (<300 g/day) and 22 % to 64 % at higher dairy intakes (≥300 mg/day). Therefore, milk and dairy products probably play an important role as sources of iodine in many countries. On the other hand, it is worth bearing in mind that in most countries cheese intake accounts for only 5-10 % of the total intake of milk and dairy products (Van der Reijden et al., 2017).

In recent years, a reduction in the consumption of milk and dairy products has been observed in children and adolescents in several countries, including Spain. Other studies also observed that the intake of milk and dairy products decreases with age, and men tend to take a slightly higher amount than women. However, these patterns were not conclusive for all countries (Fernandez et al., 2017) (Van der Reijden et al., 2017).

A recent review carried out in the United Kingdom (Witard et al., 2022) highlights that the consumption of milk and dairy products contributes 51 % of the total iodine intake in British children aged 4 to 10 years. In contrast, 27 % of girls aged 11-18 years have been reported to have low iodine intake (NDNS, 2018) and pregnant women are classified as deficient, especially if they do not receive iodine supplements (Bath et al., 2015). In this study, milk intake was found to be significantly associated with iodine status in pregnant women (median iodine:creatinine ratio in women with a milk intake of 140 *versus* 280 ml/day: 72 *versus* 150 µg/g), whereas shellfish intake was not. Other studies in adolescent females also show an association between iodine nutritional status and milk intake, but not other foods, such as fish (Mullan et al., 2020).

The fact that milk intake is lower in adults than in children is problematic for the assessment of the population as a whole. WHO recommends the evaluation of iodine nutritional status in the population by evaluating school-age children. This may lead to an overestimation of iodine intake if other particularly vulnerable population groups, such as pregnant women, have a lower intake of dairy products.

6.3 Other foods

A systematic review was published in 2022 (Bath et al., 2022) that includes a total of 57 previous published investigations, which included, in turn, 22 national-level epidemiological studies and 35 local studies evaluating iodine intake at the national level in child population aged ≤10 years (n= 11), 11 to 17 years (n= 12) and adults (n= 15). In the case of pregnant women, data were only available at the local level. The role of 8 food groups as sources of iodine was evaluated: 1) milk and dairy products; 2) fish; 3) cereals; 4) eggs; 5) meat and poultry; 6) fruits, vegetables and potatoes; 7) beverages, including alcoholic beverages; and 8) miscellaneous (which includes condiments and may include iodized salt if declared). This review reported that, although the main source of natural iodine in foods is milk and dairy products, there are also sources of iodine from other foods such as fish, and bread in some countries through the use of iodized salt. This fact puts individuals in the population who avoid these foods, such as vegans, vegetarians and people with gluten or lactose intolerance, at risk of iodine deficiency.

The consumption of iodine from foods other than iodized salt and dairy products, and, therefore, its contribution to the diet, depends largely on the country considered, the age group, and the gender in each country. Specifically, although milk contributes more than half of the iodine intake of children in Norway and the United Kingdom and more than one third of the intake of adults in Finland, Norway, the United Kingdom and Ireland, in Belgium and Ireland bread and cereals contribute between 49 and 59 % of iodine intake (children and adults) due to the use of iodized salt in bread. If iodized salt is not used in these products, the contribution is reduced to 12 % of the total in the United Kingdom and only 2 % in Spain for adults. It should also be highlighted that fish contributes 47 % of iodine to the adult diet in Iceland, 32 % in Spain (AESAN, 2015) and 21 % in Norway, but in the other countries it contributes <15 %. In children, fish contributes 18 % of the intake in Norway, but contributes 10 % in countries such as the United Kingdom.

Finally, eggs are an important source of iodine in adults in Spain, contributing 13 % (AESAN, 2011). In other countries, eggs provide 2-7 % of iodine intake (Bath et al., 2022).

6.4 Nutrition and health claims for iodine-containing foods

The labelling, format and advertising of an increasing number of foodstuffs contain nutrition and health claims. The primary objective of the European legislation regulating it is to ensure a high level of consumer protection and to make it easier for consumers to choose the healthiest option among different foods. In addition, European regulations ensure that nutrition and health claims are truthful, clear, reliable and useful to the consumer. The claims are voluntary, i.e., they are not part of the mandatory statements that must appear on food labelling. However, if a food operator decides to use them, it must do so in compliance with the conditions of use established for each of them and, in addition, they must comply with rules clearly established in the current regulations. In general, it is important to know that all nutrition and health claims that are authorized have previously undergone a procedure in which it has to be demonstrated that they are based on robust scientific data that are evaluated by EFSA and authorized at the European level (AESAN, 2021a).

In accordance with the provisions of Regulation (EC) No. 1924/2006 on nutrition and health claims made on foods (EU, 2006), the following nutrition claims relating to iodine may be used on foods that meet the conditions of use set out in that European standard and summarized below (Table 7).

Table 7. Nutrition claims for iodine-containing foods

Nutrition declaration	Conditions of use of the declaration
Source of iodine	A claim that a food is a "source of iodine", and any claim likely to have the same meaning for the consumer, may only be made if the product contains 22.5 µg of iodine per 100 g or 100 ml in the case of food other than beverages, and 11.25 µg of iodine per 100 ml in the case of beverages
High iodine content	A claim that a food is "high in iodine", and any other claim likely to have the same meaning for the consumer, may only be made if the product contains at least twice the value of the "iodine source"
Contains iodine	A food may only be claimed to "contain iodine" under the conditions corresponding to the claim "source of iodine"

Regarding health claims for iodine-containing foods, Regulation (EU) No. 432/2012 establishing a list of authorized health claims made on foods (EU, 2012), indicates that the health claim (Table 8) may be used on those foods that are "Source of iodine" or where "High in iodine" or "Contains iodine" is labelled, as set out in Regulation (EC) No. 1924/2006 (EU, 2006).

Table 8. Health claims for foods containing iodine
Iodine contributes to normal cognitive function
Iodine contributes to normal energy metabolism
Iodine contributes to the normal functioning of the nervous system
Iodine contributes to the maintenance of normal skin conditions
Iodine contributes to normal thyroid hormone production and normal thyroid function
Iodine contributes to the normal growth of children

6.5 Iodine supplements

The importance of iodine in pregnancy and the difficulty of ensuring an adequate nutritional status in all pregnant women, with the risk to foetal health that a possible deficiency entails, could justify, in some cases, giving supplements with this element, either in the form of a food supplement or as a medicine.

The authorization by the AEMPS in 2004 of medicinal products with potassium iodide as an active ingredient for pregnant and breastfeeding women was a very significant change in the prevention of iodine deficiency in this population. However, as the iodine nutrition of the population improved (Soriguer et al., 2012) (Vila et al., 2016) the dilemma of the need for universal supplementation, i.e.: to all pregnant women *versus* individualized supplementation targeting at-risk populations with low iodine intake, was raised. In 2014, the SEEN working group on Disorders related to Iodine Deficiency and Thyroid Dysfunction, with some disagreement within it, published a position paper advocating universalization (Donnay et al., 2014). Shortly before, in 2012, as a result of a workshop on this topic, the Bilbao Document (Jalón et al., 2012) was produced, which advocated individualization. Also in 2014, in the "Guía de práctica clínica de atención en el embarazo y puerperio" (Clinical Practice guideline for the management of pregnancy and post-partum period) published by the Ministry of Health, Social Services and Equality, the following recommendation was made: *"Pharmacological supplements during pregnancy with potassium iodide at doses of 200 µg/day is suggested for women who do not reach the recommended daily amounts of iodine intake with their diet (3 servings of milk and milk derivatives + 2 g of iodized salt)"*. (MSSSI, 2014).

Iodine can also be administered through food supplements containing vitamins, minerals and trace elements that usually provide a dose of 150 µg of iodine.

WHO recommendations regarding iodine supplements during pregnancy (WHO, 2007c) are established according to the iodine nutrition status of each country:

- Category 1: 90 % of families have been consuming iodized salt for more than 2 years. All salt is iodized. Median ioduria >100 µg/l:
  Universal supplementation is not required.
- Category 2: 20-90 % of families consume iodized salt and not all salt is iodized. Median ioduria <100 µg/l:
  Supplement.
- Category 3: <20 % of families consume iodized salt and it is not easily accessible. Median ioduria <20 µg/l:
  Supplement.

In the same document, the following comment is worth noting: *"However, the Consultation recognized that it has limitations as the prevalence of households reached by iodized salt at the national level may mask variations within countries between regions or districts: some may have achieved universal salt iodization, but this may not be the case at the national level, while some regions or districts may not have reached universal salt iodization even though the country has. In other words, the policy on iodine supplementation for pregnant women and young children should be adjusted as far as possible to take into account such variations within the country. This may require an assessment of iodized salt coverage before designing a supplementation program"* (WHO, 2007c).

The data available in Spain indicate that the situation in our country is between Category 1 and Category 2: the median ioduria of the adult and child population is higher than 100 µg/l (according to the adult Dia@bet study): 117 µg/l (Soriguer et al., 2012) and according to the Tirokid study: 173 µg/l (Vila et al., 2016)), although iodized salt consumption does not reach the levels recommended by WHO (more than 90 % of households should consume iodized salt) (WHO, 2007a). The data included in Table 4 show that less than half of pregnant women consume iodized salt and that more than 70 % receive iodine supplements. Therefore, it is likely that the supplements are largely responsible for the adequacy of iodine nutritional status.

The benefit of iodine supplements for pregnant women in areas with mild or moderate iodine deficiency, a situation in most of the autonomous regions of Spain, has also been extensively discussed. Table 9 shows a summary of the meta-analyses and systematic reviews published on the subject. As can be seen, the literature shows a significant disagreement about the benefit of potassium iodide supplements. When this type of disagreement exists in the literature, it seems that the best option may be the good clinical judgement of the professionals.

Table 9. Meta-analysis and systematic reviews on the effect of iodine supplements in pregnant women in areas with mild to moderate iodine deficiency

Effect	**Reference**	**No. of studies**	**Conclusions on iodine supplements**	**Summary**
Effect on neurocognitive development	Machamba et al. (2021)	8	It may improve poor psychomotor development	++
	Nazeri et al. (2021)	5	No evidence of improved growth or neurological developmental outcomes in infants	NS
	Dineva et al. (2020b)	3	No effect on the cognitive development of the children. Not enough evidence to support supplementation in these areas	NS
	Levie et al. (2019)	3	Verbal IQ effect if supplements are initiated in the first trimester (ioduria values >150 µg/g creatinine)	++
	Harding et al. (2017)	14	There were insufficient data to draw meaningful conclusions	NS
	Taylor et al. (2013)	4	Discrete improvement in cognitive function in children aged 6 to 18 months	+
	Zhou et al. (2013)	8	Lack of quality of evidence	NS
	Bougma et al. (2013)	20	IQ improves by 7.4 points (supplements *versus* non-supplements)	+++
	Trumpff et al. (2013)	5	Weak evidence of benefit on neurocognitive development	+
Effect on the maternal gland	Dineva et al. (2020b)	7 2	Decreased thyroglobulin or maternal thyroid volume. Decrease in maternal TSH	++ +
	Taylor et al. (2013)	7	Improved maternal thyroid function	+

NS: not significant; IQ: intelligence quotient; +,++ and +++ refer to the severity of the effect: mild, moderate and high, respectively.

In summary, iodized salt consumption at homes in Spain does not reach the level recommended by WHO. However, the iodine nutritional status, estimated through ioduria, is adequate in the general population and especially in children. Most likely (and especially among the school population) dairy products have contributed to these results (Soriguer et al., 2012) (Vila et al., 2016).

The studies conducted in Asturias (Menéndez et al., 2014) and Jaén (Santiago et al., 2013) report that, in cases where iodized salt consumption was observed during the year prior to pregnancy, adequate iodine nutrition was achieved without the need for iodine supplements. In a study conducted in Catalonia (Torres et al., 2017) the concomitance of iodized salt consumption and a daily dairy intake equal to or greater than 2 servings was also sufficient to achieve adequate iodine nutrition. However, iodized salt consumption is probably not the predominant factor in pregnancy. Not all studies in pregnant women show adequate median ioduria (Melero et al., 2021). In a survey conducted in Madrid (Melero et al., 2021) it was observed that only 23.9 % of pregnant women had an estimated iodine intake of more than 150 µg/l; 40.5 % of women used iodized salt and 58 % consumed 2 or more servings of dairy products.

7. Iodine deficiency and excess risk situations

7.1 Risk of iodine deficiency

Based on the data discussed above, the iodine nutrition of pregnant women in Spain is highly variable (Table 4). It should be noted that some of the results are favourably biased by the (desired) effect of iodine supplements. However, if this supplementation did not exist, most probably part of the pregnant population in our country would suffer mild to moderate iodine deficiency. There is no statewide study to support this claim; however, an approach can be made by considering the Di@bet study (Soriguer et al., 2012), in which the median ioduria among women of childbearing age was 114 µg/l. This median, theoretically adequate for the population of non-pregnant women (>100 µg/l), would be clearly deficient for the same women in case of pregnancy (>150 µg/l). Also noteworthy are the results of an unpublished study conducted by the AESAN, based on the National Food Survey on the Adult, Elderly and Pregnant Population (ENALIA-2) (AESAN, 2015), which estimated an average iodine intake of 62 µg/day among the population of women aged 18 to 30 years (n= 67); of 79 µg/day among those aged 31 to 50 years (n= 124) and of 76 µg/day in pregnant women (n= 144), an amount below the recommended amount.

Along these lines, what scenarios would be associated with a risk of iodine deficiency in pregnant or nursing women? We would understand that there is a risk of deficiency when the intake of iodine is lower than the recommended intake according to the WHO (Recommended Nutrient Intake: 250 µg/l) (WHO, 2007a) or according to EFSA (2014) or AESAN (2019) when the intake is below the "adequate intake" (<200 µg/l).

Establishing risk scenarios for iodine deficiency is complex since its sources are diverse, as is the iodine content of the different food groups and their combination may be excessive and difficult to consider. A recent study (Dineva, 2020a) compares three cohorts of pregnant women in Europe (Netherlands, United Kingdom, Spain) who had a complete dietary survey in addition to ioduria analysis. The study shows that dairy products are the only food group that is positively associated with ioduria in all three cohorts. In the Spanish cohort, the impact of dairy products on ioduria is greater than that observed in the other two cohorts and, in addition, fish and iodized salt also contribute significantly to ioduria. In Spain, these three food groups have characteristics that differ from those of other countries. On the one hand, the iodine content of milk, which can reach an average of 259 µg/l, represents a significant iodine intake for the population (Soriguer et al., 2011). On the other hand, the iodine content of salt is one of the highest in Europe (60 ppm) (BOE, 1983).

In order to assess the risk of deficiency, theoretical scenarios have been created based on the frequency of consumption of foods that constitute the fundamental source of iodine.

The scenarios presented have some limitations: the iodine content of some foods, such as fish, is variable; information on the use of iodized salt by the food industry is limited; excessive consumption of processed foods in which iodized salt has not been used may limit iodine intake, even if the salt used in food preparation at home is iodized. Other aspects that have not been included in the elaboration of these scenarios are seasonal changes in the iodine content of dairy products (Arrizabalaga et al., 2020), the effect of cooking on iodine loss from iodized salt or the type of preservation.

i. Scenario 1: Minimal risk of iodine deficiency:

   a) A woman who has been consuming iodized salt and dairy products (2 or more servings per day) for more than 1 year and also consumes regularly other foods that are a significant source of iodine, including fish.

   b) A woman who has been consuming iodized salt for more than 1 year, but has a low/no consumption of dairy products or other iodine-rich foods.

   "Scenario 1a" undoubtedly guarantees an adequate iodine intake.

   A recent study carried out by Torres et al. (2020) shows how, independently, milk, iodized salt and iodine supplements favourably impact ioduria. Other studies report how iodized salt alone is able to achieve adequate ioduria levels (Santiago et al., 2013) (Menéndez et al., 2014) (Torres et al., 2017) (González-Martínez et al., 2021). It is also relevant that the consumption of iodized salt is done at least one year before pregnancy to ensure that the gland has good iodine stores at the beginning of pregnancy (Santiago et al., 2013).

   However, very few women would be part of this scenario in Spain. Different studies show a low consumption of iodized salt at the beginning of pregnancy: 33 % in Jaén, 36 % in Catalonia and 40.5 % in Madrid (Santiago et al., 2013) (Torres et al., 2017) (Melero et al., 2021). In Catalonia, only 14 % of pregnant women consumed iodized salt and 2 or more servings of dairy per day (Torres et al., 2017).

ii. Scenario 2: Moderate risk of iodine deficiency:

   A woman who consumes 2 or more servings of dairy products per day and other iodine-rich foods at least one year before the onset of pregnancy, but does not use iodized salt.

   There is some disagreement about the risk of iodine deficiency in this group.

   Most studies have primarily evaluated the role of dairy products as the main source of iodine. Studies conducted in Catalonia (Torres et al., 2017, 2020) show, in the multivariate analysis, that, independently, consuming 2 or more servings of dairy products is associated with adequate ioduria in case of pregnancy. Some other study supports this finding (Soriguer et al., 2012) (Bath et al., 2015). However, the two studies conducted in Asturias show that the effect of adequate ioduria is attributable only to iodized salt and not to dairy products (Menéndez et al., 2014) (González-Martínez et al., 2021). The seasonal changes discussed above can also substantially modify the iodine content in milk. In the study by Arrizabalaga et al. (2020) the milk analysed in winter shows an average iodine level of 241 µg/l and in the summer-autumn it is 162 µg/l.

iii. Scenario 3: High risk of iodine deficiency:

   A woman with no consumption of foods that are a significant source of iodine and who does not use iodized salt.

   Not consuming dairy products and, most especially, not consuming iodized salt is associated with iodine deficient nutrition (Menéndez et al., 2014) (Torres et al., 2017, 2020) (González-Martínez et al., 2021).

Women who do not consume iodized salt and follow a vegan diet, who do not consume dairy, fish or other animal sources of iodine, have been found to have an increased risk of iodine deficiency (Eveleigh, 2020) (Koeder, 2022), if not supplemented with other sources of iodine.

The effect of smoking may increase the risk of iodine deficiency. The risk of iodine deficiency in infants born to smoking mothers is especially noteworthy, due to the inhibitory effect of tobacco on NIS. This involves a marked decrease in iodine uptake by the mammary gland, with a subsequent decrease in its concentration in breast milk (Andersen, 2015). Smoking has not been found to increase the risk of iodine deficiency during pregnancy (Torres et al., 2020); however, it is recommended that pregnant women do not smoke or stay in environments with tobacco smoke (passive smoking).

Other factors, such as the educational level and socioeconomic status, can also influence iodine intake. In the Di@bet study, it was observed that the uneducated population used less iodized salt than the group with primary or secondary education (OR (odds ratio): 1.73; 95 %; CI (confidence interval): 1.39-2.16) or university education (OR: 2.23; 95 %; CI: 1.71-2.92) (Soriguer et al., 2012). Also, in the study carried out by Melero et al. (2021) in Madrid it was reported that pregnant women with a lower educational level consumed less iodine. Dairy and fish consumption was also lower in the population with a lower socioeconomic status (FEN, 2013).

In summary, the consumption of iodized salt and dairy products would guarantee an adequate iodine intake in the population of pregnant women and also during the nursing period. Iodized salt, when used well before pregnancy, by itself, is able to provide an adequate amount of iodine. Some studies also attribute this property to dairy products, although they are subject to more variations. The percentage of women who regularly use iodized salt and also consume 2 or more daily servings of dairy products is very low. The prevalence of iodized salt use, as a whole, is significantly higher, but far from the 90 % recommended by WHO (2007a). In the study carried out by Melero et al. (2021) only 35 % of the women surveyed consumed 2 or more daily servings of dairy. This study estimated that only 25 % of women exceeded an intake of more than 150 µg per day of iodine before pregnancy (Melero et al., 2021). Excluding potassium iodide supplements, most pregnant women in Spain have a mild to moderate deficit. Low iodine intake in women is a situation that the White Paper on Nutrition in Spain already considered a threat (FEN, 2013).

7.2 Risk of excess iodine

Most of the population is able to adapt to excess iodine. Initially, due to the Wolff-Chaikoff effect (Wolff et al., 1949), the excess iodine causes a blockage of iodine uptake to resume, after a few days, the normal functioning of the gland through the "escape" phenomenon. If this fails and the blockage persists, hypothyroidism may be induced. This problem may occur more frequently among the population with Hashimoto's thyroiditis, although some studies note a marked increase in the prevalence of hypothyroidism in areas with a high iodine intake (Markou et al., 2001). It appears that, in the foetus, the "escape" phenomenon is not sufficiently effective until about 36 weeks, making it more vulnerable to hypothyroidism should the mother take excess iodine (Thomas and Collett-Solberg, 2009) (Connelly et al., 2012).

EFSA (2014), based on the opinion of the Scientific Committee for Food, establishes, as maximum tolerable dose of iodine, the intake of 600 µg/day, both for adult and pregnant population. They recognize that this figure is approximately half of the 1100 µg/day indicated by the IOM (2001) as the maximum tolerable dose. They calculate this figure based on dose-response studies of short duration and with a low number of participants. These studies observed that intakes of 1700-1800 µg/day would induce a greater elevation of TSH under intravenous Thyrotropin-Releasing Hormone (TRH) stimulation (Gardner et al., 1988) (Paul et al., 1988). At the lowest concentration at which adverse effects were observed, the following were observed,1700 µg/day, an "Uncertainty Factor" of 1.5 was applied, resulting in 1100 µg/day, which was estimated as the cut-off point to define the maximum tolerable dose of iodine. A WHO expert committee (2007c) states that intakes above 500 µg/day provide no additional benefit and should be avoided. Although there is no major evidence defining safe upper limits (Eastman et al., 2019), some studies associate an increased risk of subclinical hypothyroidism in pregnant women with iodurias with values above 500 µg/l (Shi et al., 2015) (Corcino et al., 2019) and even in women with iodurias between 250 and 500 µg/l (Shi et al., 2015). A study conducted in a Spanish population reported an increased risk of hyperthyrotropinemia (TSH>3 mIU/l) among women receiving supplements of iodine 200 µg (Rebagliato et al., 2010). Along these lines, the study by Moleti et al. (2011) observed higher TSH levels in women who received iodine than in women who had been consuming iodized salt for more than 2 years. However, they did not observe an increased rate of hypothyroxinemia. The TSH increase was attributed to a transient stunning effect on the thyroid gland as a result of the sudden increase in daily iodine intake in women with mild to moderate deficiency, highlighting the importance of adequate iodine nutrition well before pregnancy. It is likely that Rebagliato's results are due to the same process. More recently, a meta-analysis (Katagiri et al., 2017), which included 5 studies with pregnant women, did not observe any conclusive association between iodine excess and subclinical hypothyroidism.

As can be seen, there is some disagreements as to how much iodine intake may be harmful to pregnant woman; however, WHO experts consider that exceeding 500 µg/day is not necessary as it would not provide any additional health benefit and, in theory, may be associated with impaired thyroid function (WHO, 2007c). The same document describes the iodine nutrition of a pregnant population as "more than adequate" when the median iodine levels are between 250 and 499 µg/l. As discussed, EFSA sets this limit at 600 µg/day (EFSA, 2014).

The following is a description of the main situations in which excess iodine may be present:

1. In Scenario 1 above, where the risk of deficiency is minimal, supplements of iodine 150 or 200 or 300 µg, by means of medicinal products or food supplements, could approach or exceed 500 µg of iodine. Thus, especially in Scenario 1a, it would not be necessary or appropriate to administer iodine beyond the amount provided by natural foods or fortified foods (iodized salt).
2. Excess iodine from the consumption of seaweed has been associated with an increased prevalence of hypothyroidism and goitre (Markou et al., 2001). The iodine content of algae can be very high, reaching values of up to 7088 µg/g dry weight (Romarís-Hortas et al., 2009). The most extreme value was observed in *kombu* seaweed, coinciding with the analysis conducted by AESAN (2019). According to a study conducted in Norway in which they analysed the iodine

content of different seaweed products available on the Norwegian market, it was observed that the iodine content was highly variable, and in the labelling, the declaration of iodine content was found to be inadequate or inaccurate in several of them (Aakre et al., 2021).

In the report drawn up by the AESAN Scientific Committee in 2012 (AESAN, 2012) on the evaluation of the risk associated with the consumption of macroscopic algae with high iodine content, it was concluded that, although at that time the consumption of this type of algae was not significant in the Spanish population, it would be advisable to adopt 2000 mg/kg dry weight as the maximum limit of iodine content of edible algae, regardless of the species.

More recently, AESAN has published recommendations for consumers on the consumption of seaweed due to its iodine content (AESAN, 2021b), among which the following stand out:

- People with thyroid dysfunction or taking iodine-containing medicinal products should avoid consuming food containing seaweed, especially *kombu* species *(Laminaria japonica; Saccharina japonica*), due to the high levels of iodine in their composition.
- In the absence of sufficient data to measure the risk in the child population due to the iodine content of seaweed, it is recommended to avoid its consumption by children, as well as by pregnant or breastfeeding women.

In summary, if we accept as excess iodine intakes above 600 µg/day, following the EFSA proposal, the consumption of seaweeds with high iodine content can greatly exceed this threshold. A hypothetical risk of excess could also occur in the case of administration of iodine, in the form of medicinal products or food supplements, to women included in Scenario 1a described above. The harmful effect of excess iodine is especially focused on people with thyroid autoimmunity, which is mostly expressed as hypothyroidism.

Conclusions of the Scientific Committee

- Iodine is an essential element for the synthesis of thyroid hormones and must be taken at adequate amounts. Pregnancy and breastfeeding are periods particularly sensitive to iodine deficiency, since thyroid hormones are essential for the development and maturation of the foetus and newborn brain.
- The main dietary sources of iodine are iodized salt, milk and dairy products and fish. In Spain, as in some European countries, salt iodization is voluntary. The iodine content of iodized salt in our country is one of the highest in Europe (60 ppm), which would allow the recommended daily intake of iodine to be reached with a low consumption of iodized salt.
- In women of childbearing age, pregnant or breastfeeding, the use of medicines or food supplements with iodine guarantees an adequate intake of this nutrient, although the regular intake of small amounts of iodized salt per day would also allow the iodine requirements to be met.
- The nutritional status of iodine in Spain is, in general, adequate, although it should be taken into account that the use of medicines or food supplements that provide iodine is largely responsible for this situation. A low consumption of dairy products or not using iodized salt would

significantly increase the risk of iodine deficiency in pregnant or breastfeeding women. As for iodized salt, studies carried out in Spain show that its consumption in households is still below the 90 % recommended by the WHO.

- The universal use of iodized salt, in households and in the food industry, would be a very useful tool to achieve adequate iodine nutrition in the general population and especially in women of childbearing age, during pregnancy and lactation. The use of iodine-containing medicinal products or food supplements during pregnancy or breastfeeding should be considered only in at-risk populations that do not receive sufficient iodine intake from the diet.
- Iodine intake above 600 µg/day should be avoided. Women of childbearing age, pregnant or nursing women who regularly use iodized salt, consume 2 or more daily servings of dairy products and also consume iodine-containing medicines or food supplements may exceed this figure. Likewise, in this case, the consumption of seaweeds with a high iodine content or food supplements that include this type of seaweeds in their composition should be avoided.
- The inclusion in food labelling of authorized nutrition and health claims related to iodine intake could be a useful tool to promote an adequate and informed choice of those foods containing iodine that meet the legally established criteria for making such claims. This could contribute to the improvement of nutritional status with respect to this element, in particular in the most vulnerable populations.

Acknowledgements

The authors would like to thank the representatives of the EFSA focal points for their contribution to this report by providing relevant information on iodine fortification of foods in their respective countries.

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