

COMMENTARY

EUthyroid2: The next step towards the elimination of iodine deficiency and preventable iodine-related disorders in Europe and beyond

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Abstract

European iodine fortification programmes are heterogeneous and in some countries ineffective. A key problem with iodine nutrition is the low awareness of iodine deficiency-related risks common in the general population and among women of reproductive age. The major objective of EUthyroid2 is to improve the low awareness of IDD risks in adolescents and young women. The aim is to identify best practice models for accessing and disseminating information to increase awareness and improve iodine status, thereby establishing a foundation for young women to improve their own thyroid function, their general health and that of their offspring. To achieve this, EUthyroid2 will build on existing infrastructures and expertise established by the consortium during the initial EUthyroid project.

All interventions tested will be tailored to specific regions and populations. EUthyroid2, by identifying the most effective intervention tools, will establish a solid foundation for paving the way for future national awareness campaigns.

Keywords: iodine deficiency; prevention; intervention studies

Introduction

Thyroid disorders are a major cause of morbidity in Europe, particularly in women, and iodine status is one of the main determinants of thyroid function. Iodine deficiency disorders (IDDs) affect the entire life cycle, and women and children are especially vulnerable. Iodine deficiency during pregnancy may increase the risk of developmental impairment of the offspring (1). Adults living in iodine-deficient regions carry a high risk of goitre, thyroid nodules and hyperthyroidism. Subclinical hyperthyroidism, as a common and frequently undiagnosed IDD, is tightly associated with an increased risk of mortality, cardiac arrhythmias and coronary heart disease (2). The effects of iodine deficiency impose tremendous costs on the healthcare systems of affected regions (3), but can be easily prevented by iodine fortification of table salt and livestock feed and the consumption of dietary sources, such as seafood, eggs, milk, and dairy products.

The adverse effects, although well established, receive surprisingly little publicity. Addressing iodine deficiency through public health initiatives and ensuring adequate iodine intake is essential for preventing IDDs and reducing their impact on individual and public health in Europe.

Based on the prevalence of IDD and the significant impacts on health, the EUthyroid consortium was established in 2015 to pave the way towards an iodine sufficient European population. The first EUthyroid project evaluated existing IDD prevention programmes in Europe and created critical infrastructures to conduct valid monitoring studies. Standardised measurements of urinary iodine concentration in regional and nationwide studies demonstrated that iodine deficiency in pregnancy was widespread in Europe, with 64% of studies in pregnancy revealing an iodine status that was below WHO recommendations (4).

The EUthyroid consortium conducted a Delphi survey among experts from 36 countries and different fields of work, which demonstrated that the main barriers against an optimum iodine supply of general populations comprise challenges in the fields of knowledge and information, implementation and management, communication and cooperation, political support, and differences between the European countries (5). Consequently, the EUthyroid consortium released the Krakow Declaration on Iodine in 2018 to call on national governments and health authorities to monitor and evaluate iodine fortification programmes regularly

and to increase the awareness of populations to risks related to iodine deficiency (6).

Although the Krakow Declaration on Iodine was endorsed by 78 organisations, European iodine fortification programmes are still heterogeneous with concerning their principle (mandatory or voluntary), iodine carriers (iodide or iodate), kind of iodised food (e.g. salt, bread, dairy products, milk alternatives, chocolate, and/or cattle and poultry feed), and monitoring and evaluation procedures (none, irregular or regular) (7). The nearly complete absence of public information campaigns represents a major reason for the low awareness of IDD risk in European populations, particularly in countries with iodine fortification programmes based on the voluntary principle. Sustained activities addressing political and medical decision-makers, healthcare professionals and the general public are needed.

A key problem with iodine nutrition is the low awareness of iodine deficiency-related risks common in the general population and among women of reproductive age. For example, studies demonstrated that only 2% of pregnant women in Puerto Rico (8), 8.3% in Shanghai (9), 20% in Northern Ireland (10), 25% in Scotland (11), and 26% in Norway (12) were aware that they need increased iodine intake during pregnancy or knew about the potential risks of iodine deficiency for the foetus. These are alarming data, particularly because knowledge of the importance is tightly and positively associated with the iodine status of pregnant women (13).

Against this background, it is surprising that the policy-makers often fail to see the need for intervention. The question arises, how can this vicious circle be broken?

Objectives

The major objective of EUthyroid2 is to improve the low awareness of IDD risks in adolescents and young women. The aim is to identify best practice models for accessing and disseminating information to increase awareness and improve iodine status, thereby establishing a foundation for young women to improve their own thyroid function, their general health and that of their offspring.

To achieve this, EUthyroid2 will build on existing infrastructures and expertise established by the consortium during the initial EUthyroid project.

All interventions tested will be tailored to specific regions and populations.

The intervention studies

Implementation studies and community-based randomised-controlled trials will be conducted with the objective of increasing IDD-related awareness in adolescents and young, non-pregnant women up to age of 24. The interventions are multimodal and will be performed in two settings in the study regions.

The selection of potential European regions for intervention studies was based on results from the initial EUthyroid project (4). Inclusion criteria were the existence of iodine deficiency either in the general population (median urinary iodine excretion: <100 µg/L), in women of reproductive age (median urinary iodine excretion: <100 µg/L) or in pregnant women (median urinary iodine excretion: <150 mmol/L). Among the candidate countries, the Republic of Cyprus, Poland, Norway, Slovenia, and two regions of the United Kingdom (England and Northern Ireland) were selected to conduct the interventions. In addition, Germany met the inclusion criteria and will add interventions by in-kind contribution. As requested by the grant call, the EUthyroid2 consortium was then supplemented by Bangladesh and Pakistan as two low- and middle-income countries with evidence for iodine deficiency in the general population (14, 15).

The interventions will be conducted in two settings, the educational setting and the healthcare setting. In the educational setting, pupils aged 13–17 years in secondary schools, high schools and vocational schools will be targeted in six regions. Sample size calculations revealed that, within each region, at least 22 classes (with an average of 11 pupils per class) of each type of schools (basic, medium, and high education) will need to be recruited for study site, aiming for 750 pupils in total. The interventions will be implemented within all classes. Different implementation approaches will be used in each school, tailored to the specific context of that school. This means that the study design will compare different implementation approaches, based on pre- and post-intervention measurements, but omit a control group as such. The focus lies on process evaluation and feasibility, intending to have a clear indication of the most effective tools and promising approaches to increase IDD awareness among students. On clinicaltrials.gov, the interventions are registered under NCT06769009.

In the healthcare setting, there will be two levels of intervention implementation in five regions. First, EUthyroid2 will increase the professionals' awareness and engender behavioural change in the professional's practice and counselling process. With the exception of Pakistan, where young doctors agreed to get involved, the target staff will be healthcare professionals and trainees rather than physicians, as these personnel have the first

direct contact with patients. In addition, they often have more time resources to offer. Second, EUthyroid2 will increase awareness in young women via a change in personnel action and health education, ultimately aiming to support behavioural change in terms of women's own nutrition. According to power analyses in a cluster randomised-controlled trial, at least ten clusters (healthcare settings, with at least 30 women recruited in each) per region will need to be randomised to either the intervention or control arm, with an assumed final follow-up cluster size of a mean of 30 and a range of 20–40, resulting in 180–200 participants with complete data per site. In the control group, the same measurements will be performed as planned for the intervention group and general information material on health. Once the intervention are finalised, also the control group will get access to all study materials.

For both the educational and the healthcare setting, process evaluation according to the RE-AIM framework will be implemented, allowing to assess reach, effectiveness, adoption, implementation and maintenance of the intervention (16). To achieve the necessary data basis, a parallel convergent mixed methods approach is applied, in which interviews with key stakeholders, assistants, participants, teachers, students, and regional interventionists are combined with surveying and analysing documentation of intervention delivery in the regions.

In all studies, a basic set of data will be obtained before and on two occasions after intervention. To measure short-term effects, the first follow-up will be conducted 2 to 4 weeks after the intervention. To measure longer-term effects, a second and final follow-up will be performed 6 to 8 months after the intervention, when the outcomes will be measured. All measurements will also be done in the control groups. Change in awareness regarding iodine-related risks will represent the primary outcome, while the change in the median urinary iodine excretion will be the secondary outcome in the healthcare setting. In addition to the outcome measuring instruments, further information will be collected to characterise the study populations and to observe further effects of the interventions (Table 1).

Before data collection, institutional committees of the participating sites will give their ethical approval. All participants will give their informed consent. For underage participants, also the informed parental consent will be obtained.

Dissemination

As a public health project, EUthyroid2 is not only science but will also serve our societies. Therefore, dissemination of findings to various sectors of our countries and the EU will be of utmost importance.

Table 1 Overview of data collected within EUthyroid2. Estimated dietary iodine intake is assessed using food frequency questionnaires adapted to the dietary habits in the different countries. Process evaluation will be conducted through interviews with stakeholders after intervention.

	Intervention setting			
	Healthcare		Educational system	
	Before intervention	After intervention	Before intervention	After intervention
Demographics	X		X	
Socioeconomics	X		X	
Education	X		X	
Myths	X	X	X	X
(Iodine) nutrition	X	X	X	X
Current pregnancy (as exclusion criterion)	X	X		
Thyroid disease	X	X	X	X
Awareness	X	X	X	X
Urinary iodine	X	X		
Process evaluation	X	X	X	X

There is still a critical need to raise awareness of the risks of iodine deficiency among all sectors of the European society, in particular, the crucial need for iodine during pregnancy to protect the children’s brain development. While the main focus of EUthyroid2 will be on adolescents and young women in particular, it will seek, through its findings, to raise awareness of the problem among various audience sectors, including both large-scale and more specifically targeted groups.

An overarching and compelling effort from project’s inception will be to reach adolescents and young people in the target countries, and more broadly throughout Europe and beyond, with messages about the importance of iodine for health. As adolescents are activists and familiar with modern communication methods, early messaging will focus on the importance of nutrition, and in particular iodine nutrition for their own health and that of their future offspring.

The main users of the EUthyroid2 project outcomes will be the scientific community and policymakers from regional and national governments and the EU.

In addition, EUthyroid2 will target healthcare providers, national or regional institutions and bodies involved in IDD prevention and monitoring, including public health offices, patient organisations, and medical practitioners. EUthyroid2 will also engage the interested public with targeted activities to raise public awareness in support of the goal of a euthyroid world. All dissemination activities will be centrally supported by an online presence with a project website (<https://euthyroid2.eu/>) serving as the primary hub, complemented by with regular posts and articles on various social media platforms, such as LinkedIn and X. Main dissemination activities will be published only after the completion of the interventions to not interfere with the studies.

Project structure

The project is structured in six work packages (WPs), which are tightly interlinked with each other (Fig. 1). In WP2, experts in the field of public health interventions will define methods to improve the IDD-related

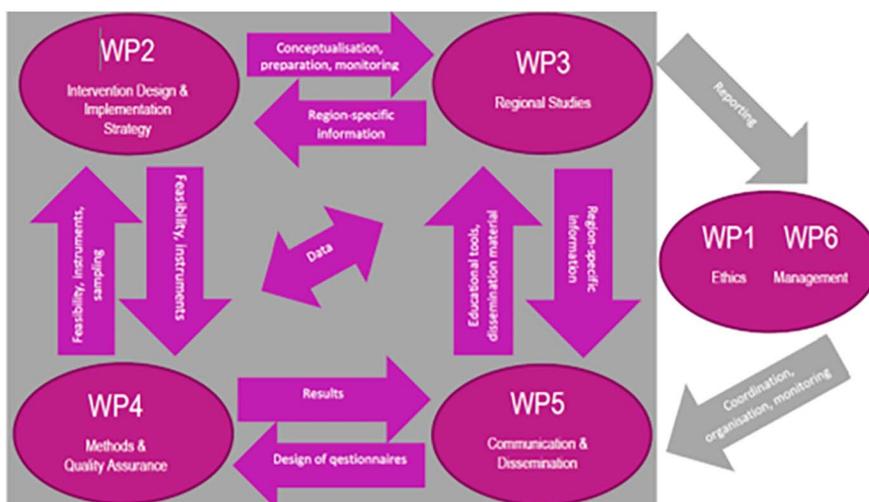


Figure 1 EUthyroid2 work package structure, interactions and interdependencies.

awareness in adolescents and young women. WP2 will oversee and support WP3, which will perform the intervention studies in healthcare and schools in eight regions. WP4 will also support WP3 by defining instruments to be used in baseline and follow-up data collection and measuring urinary iodine concentrations in a centralised laboratory. In addition, WP4 will be responsible for data management and statistical analyses.

In close collaboration with WP2 and WP3, WP5 will produce communication materials, such as leaflets, booklets, factsheets, and educational videos, as part of the intervention methods. Furthermore, all findings from WP2-4 will be disseminated by WP5. Apart from the scientific community, the general public, healthcare professionals, and the political sphere will be targeted. Compliance with ethical requirements will be monitored within WP1. EUthyroid2 will be managed as outlined in WP5. The integration of 15 partners will be achieved by establishing professional management structures and measures.

Future perspectives

This project, by identifying the most effective intervention tools, will establish a solid foundation for paving the way for future national awareness campaigns. The comprehensive knowledge gained will be instrumental in the crucial political work for not only raising awareness among the general population but equally important among political decision-makers and other gatekeepers in relation to promoting a euthyroid world.

Declaration of interest

HV has received travel grant and speaker honoraria from Sanofi Aventis. All other authors do not declare any conflicts of interest.

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