EUthyroid: making Europe smarter with iodine
EUthyroid: a new pan-European initiative to ensure adequate iodine intakes

Programs set up to prevent iodine deficiency disorders (IDD) may not remain effective as a result of changing government policies, commercial factors, and human behavior that may affect them in unpredictable ways. To ensure that IDD prevention is effective, we need standardized monitoring and a better understanding of health outcomes and economic benefits. A new pan-European research initiative called EUthyroid has been launched to address these gaps.

The case for monitoring is compelling. So why is Europe lagging behind?

The West and Central Europe region has a total population of about 600 million in over 40 countries and territories, with populations ranging from 0.3 to 82 million (1). For a number of years, the World Health Organization has drawn attention to the fact that many Europeans are affected by iodine deficiency. As recently as in 2007, a quarter of the countries in the region were classified as iodine deficient (2), and there has been little progress in the intervening years.

The European continent represents a complex patchwork of iodine prophylaxis: there is no harmonized approach to ensure that iodine intake of its population is sufficient to prevent health problems. Due to regional differences in eating habits, the natural iodine intake is heterogeneous. Despite the major global expansion of salt iodization over the past five decades, up to 400 million people from 20 countries across Europe have no or limited access to iodized salt (3). Only a small number of countries carry out regular monitoring of iodine intake, and the amount of comparable data is very limited: a recent review found that at least 14 countries have not performed a national survey of iodine status in the previous two years, and at least 17 are thought to have no monitoring at all (Figure 1) (3).

This article is based on information provided on the EUthyroid project website (http://euthyroid.eu) and Henry Völzke et al. Ensuring Effective Prevention of Iodine Deficiency Disorders. Thyroid 2016, 26(2).

![FIGURE 1](image_url) In Europe, IDD prevention programs (PP) and monitoring are heterogeneous.
While goiter as a result of iodine deficiency is widely known, it is less acknowledged that thyroid hormones regulate normal growth and development. Many governments may still be unaware of the adverse effects of ID on reproduction and fetal brain development. There is irrefutable evidence that improved iodine status in regions with severe iodine deficiency will reduce the rates of cretinism and adverse effects on neurocognitive function in children. And there is a growing number of studies showing that exposure to even mild iodine deficiency during pregnancy may have a negative impact on cognition and educability (3). And even small changes in the mean population IQ may affect the economy and well-being of societies (4). To overcome iodine deficiency and its consequences in Europe, the World Health Organization has called for a review of the situation in Europe through uniform monitoring as a basis for improved prevention.

But how good are the assessment methods of iodine status?

Studies that measure urinary iodine concentration (UIC) directly face a challenge: gold standard methods such as inductively coupled plasma-mass spectroscopy are costly and, therefore, not feasible for most field studies. Some alternative methods show good correlation with the best, but results from different methods and laboratories may still vary considerably. In general, UIC analysis is demanding, and it requires well-trained and experienced laboratory personnel. Participation in an external quality assessment program is helpful (such as the EQUIP program of the U.S. Centers for Disease Control and Prevention). In UIC analyses it is important to consider within-person variability that is caused by day-to-day variation in intake and hydration status. UIC measurements from spot samples can be relied upon for sufficiently large study populations (at least 100 study participants) and can use urinary creatinine to correct for hydration status. Alternatively, day-to-day variation can be addressed by repeating the measurements in a sub-group of study participants.

How valid are international maps of iodine status?

WHO and IGN publications have provided maps illustrating the current status of iodine supply across the world. Epidemiological researchers usually strive to achieve good internal validity of single surveys or trend studies performed by single centers. However, external validity may be hampered by applying different UIC measurement methods (or in the case of thyroid examination, different ultrasound devices, probes, or observers). This may limit the comparability of studies, which is essential for accurate mapping. A multinational iodine survey with centralized standardization and quality assurance would help map the regional disparities in iodine supply. In Europe, population studies such as the proposed European Health Examination Survey (5) would offer a good opportunity for routine monitoring of UIC levels.

Do not ignore the costs

Prevention programs have to be beneficial for individuals and societies. To allocate limited resources efficiently in healthcare systems is one of the major aims of prevention. For example, in Germany the estimated annual economic impact of endemic goitre was €1 billion before the national IDD prevention program was established. Studies of projected healthcare costs have estimated that IDD prevention programs can be highly cost-effective (6). But there is currently no comprehensive analysis evaluating the cost-effectiveness of established IDD programs. Such analyses will be essential for meaningful discussion with health authorities in countries that have remained mildly or moderately iodine deficient or that are considering switching from voluntary to mandatory prevention programs.

Keeping our eyes on the goal

In light of the overwhelming evidence that IDD prevention is effective in regions with severe iodine deficiency, it is easy to forget that data are also needed from mildly-to-moderately iodine deficient regions. Indeed, little research has been published on outcomes following the implementation of iodine fortification programs in mildly iodine-deficient regions (7,8). What’s more, only few studies compare the rates of hyper- and hypothyroidism in populations that have IDD prevention programs. The benchmark for this approach is the Danish longitudinal study DanThyr, which combines repeated cross-sectional and cohort studies with analyses of registry data. More projects like DanThyr and disease-registry data are urgently needed to determine what outcomes can be tolerated safely under IDD prevention programs.
EUTHYROID: an initiative to make Europe smarter

EUTHYROID is the first pan-European initiative to investigate the iodine status of the European population, and in parallel to address the above-mentioned systemic gaps in data collection, outcome research, and cost-analysis identified as barriers to achieving effective IDD prevention. Launched in June 2015 and supported by the European Union’s Horizon 2020 research & innovation programme, the project will receive almost €3.5 million in funding over three years (see Box).

Dr. Henry Völzke, Professor of Clinical-Epidemiological Research at the Institute of Community Medicine, University of Greifswald, Germany, is the principal coordinator of EUTHYROID and has been instrumental in pushing the project forward. “Currently in Europe there is no uniform dataset for iodine intake. Therefore, we can only speculate about the magnitude of health problems resulting from a deficient iodine intake. The fact is that even in Germany many children are born with intellectual disabilities. In this respect, I am very pleased as an epidemiologist and physician to see that, with EUTHYROID, the EU has now opened a new opportunity to change this unsatisfactory situation. I am convinced that an improved iodine intake can make Europe more intelligent,” he enthused.

Within EUTHYROID, 30 partners from 27 countries pool the expertise of renowned epidemiologists, endocrinologists, nutritionists, and health economists, many of whom are also representatives of the Iodine Global Network for West and Central Europe Region.

Focus on iodine deficiency during pregnancy

The EUTHYROID network will perform research into the current situation regarding iodine intake and the health consequences of iodine deficiency in the countries involved. The main task will be to standardize data collection and perform a cost-to-benefit analysis of existing programs. The overarching goal will be to provide the basis for harmonizing and improving the iodine intake across Europe in cooperation with national authorities. A particular focus will be placed on pregnant women and the potential impact of iodine deficiency on the intellectual development of the child. EUTHYROID will examine this issue using three separate mother-child studies taken from regions of differing iodine intake. For example, it is estimated that as many as 50% of all newborns in Germany have been exposed to iodine deficiency during pregnancy, which could lead to adverse affects. However, reliable data is not available in Europe.

With the establishment of central databases and structures for inter-laboratory comparison as well as the introduction of quality assurance measures for data collection, the conditions are already being created that, over the three-year duration of the project, will lead to improvements in the iodine intake of the European population.

References


EUTHYROID project

Start date: 1 June 2015
Duration: 36 months
Total budget: €3,375,330

Participants

22 Member States of the EU (exceptions being Cyprus, Lithuania, Luxembourg, Malta, and Romania) and 5 countries from the IGN West & Central Europe (Iceland, Israel, Macedonia, Norway, and Switzerland) corresponding to 95% of the Union’s population.

EUTHYROID objectives:

• Build capacity of national studies to enable collection of standardized data on the iodine intake of the population (general population and pregnant women) to create a map of iodine status across Europe
• Compare national IDD programs and dietary habits to identify sources of dietary iodine
• Harmonize and standardize data collection of future studies
• Analyze the effectiveness and the cost-to-benefit ratio of existing prevention programs
• Develop appropriate measures toward an improved and unified iodine intake
• Analyze three mother-child studies from regions with different iodine intake
• Establish thyroglobulin as a biomarker for individual iodine status.

Prof. Dr. Henry Völzke from the University of Greifswald is the principal coordinator of the EUTHYROID project.