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ORIGINAL ARTICLE

EURRECA: development of tools to improve the alignment of micronutrient recommendations

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Approaches through which reference values for micronutrients are derived, as well as the reference values themselves, vary considerably across countries. Harmonisation is needed to improve nutrition policy and public health strategies. The EURRECA (*EURopean micronutrient RECommendations Aligned*, http://www.eurreca.org) Network of Excellence is developing generic tools for systematically establishing and updating micronutrient reference values or recommendations. Different types of instruments (including best practice guidelines, interlinked web pages, online databases and decision trees) have been identified. The first set of instruments is for training purposes and includes mainly interactive digital learning materials. The second set of instruments comprises collection and interlinkage of diverse information sources that have widely varying contents and purposes. In general, these sources are collections of existing information. The purpose of the majority of these information sources is to provide guidance on best practice for use in a wider scientific community or for users and stakeholders of reference values. The third set of instruments includes decision trees and frameworks. The purpose of these tools is to guide non-scientists in decision making based on scientific evidence. This platform of instruments will, in particular in Central and Eastern European countries, contribute to future capacity-building development in nutrition. The use of these tools by the scientific community, the European Food Safety Authority, bodies responsible for setting national nutrient requirements and others should ultimately help to align nutrient-based recommendations across Europe. Therefore, EURRECA can contribute towards nutrition policy development and public health strategies.
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Introduction

In Europe, most countries have established their own national nutrient requirements. Dietary recommendations serve as a basis for nutritional educational programmes, national and/or regional nutrition policies and food regulations such as nutrition labelling (King *et al.*, 2007; Ashwell *et al.*, 2008; Doets *et al.*, 2008; Pijls *et al.*, 2009). Dietary recommendations for micronutrients reflect intakes that prevent deficiency disorders, as well as toxic effects. Nutrient recommendations are also taken into account when planning dietary intakes for optimal health. However, currently, there is no standard approach for deriving micronutrient recommendations, and large differences exist across Europe and also worldwide (Doets *et al.*, 2008), causing confusion among consumers, food producers and nutrition policy makers.

The *EURopean micronutrients RECommendations Aligned* (EURRECA) Network of Excellence (funded by the European Commission) was established to identify and address differences between countries in micronutrient recommendations. It is expected to provide Europe with generic science-based instruments and evidence to be used in establishing micronutrient requirements and their translation into recommendations for dietary intake.

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Before the development of instruments for addressing differences across Europe, EURRECA initially reviewed methods currently used in European countries to (i) estimate dietary intake (Serra-Majem, 2009) and (ii) develop a methodology for use in the measurement of micronutrient status (Hooper *et al.*, 2009). Current research carried out by EURRECA involves collating and reviewing data to estimate micronutrient requirements systematically and transparently and to calculate interindividual variation in different population groups where feasible (Hall Moran *et al.*, 2010; Hermoso *et al.*, 2010; Iglesia-Altaba *et al.*, 2010). In addition, research using nutrigenomics and metabolomics is also addressed in EURRECA (van Ommen *et al.*, 2008), which brings an individual approach to micronutrient recommendations and aims to establish a basis for considering the effect of the interaction of multiple micronutrients on health outcomes (which, in the longer term, could be a new paradigm for setting micronutrient requirements). To place this Network into an institutional framework, core aspects of policy making were defined, including a framework that comprehensively structures the process of setting micronutrient recommendations (Dhonukshe-Rutten *et al.*, 2010). In addition, research is being undertaken to identify policy options available to use micronutrient recommendations in order to improve the diets of population groups (Timotijevic *et al.*, 2010). A further aim of EURRECA is to identify and create opportunities for small and medium-sized enterprises for developing innovative foods.

Across this variety of activities, generic instruments are being developed to be used for the establishment of micronutrient requirements and their translation into recommendations for dietary intake. This paper focuses on describing the various EURRECA instruments, both existing and under development. Three major types of instruments will be presented: (i) training tools, which are important for the acquisition of knowledge, skills and competencies; (ii) a range of information sources, which disclose relevant data and knowledge; (iii) decision trees and/or frameworks. The purpose of these instruments is to guide non-scientists in decision making based on scientific evidence. The integrated platform of instruments will, in particular in Central and Eastern European countries, contribute to future capacity-building development in nutrition (Pavlovic *et al.*, 2009).

Training instruments

The first set of training tools that has been developed are interactive digital learning materials. These can be used within courses that are taught by one or several lecturers from partner institutions through online or blended (including both online and face-to-face activities) learning. The level and nature of collaboration between tutors and students may differ depending on the choices made by the tutors. The level of digitisation of the course may differ as well, meaning some courses will be more 'blended' than others (E-Leru, 2009). Potential audiences for these e-modules include university students, scientists, policy makers and members of industry. The aim of the first EURRECA interactive digital learning module is to gain insight into the principles of evaluation studies within nutritional research. The interactive digital learning material contains a sequence of interactive exercises, relevant information and associated theory modules, which guide the student through the design and analysis of evaluation studies. Most information in this module is presented in the form of animations, schemes or short texts to obtain an optimal balance between theoretical information and practical application. A large variety of exercises are used within the module (including drag and drop exercises, multiple choice questions, completion of schemes, essay questions and data analysis assignments; see Figure 1). The exercises are formulated in such a way that they point out frequently made mistakes and common misconceptions. Therefore, all exercises are accompanied by a detailed feedback on both incorrect and correct answers (Busstra *et al.*, 2010). The interactive digital learning materials are used by the EURRECA partners and in the Nutrition and Lifestyle Epidemiology course run by 'Voeding, Levensmiddelentechnologie, Agrobiotechnologie en Gezondheid' Graduate School in the Netherlands. From a technical point of view, it is possible to run the interactive materials on the EURRECA website, as well as on other learning management systems such as WebCT and Blackboard.

The Network is identifying learning objectives and topics for a second e-module consisting of two parts: 'Introduction to recommendations and requirements' and 'Evidence for requirements'.

Information resources

The second set of EURRECA instruments comprises the development of a system for collecting different information resources. These information resources are collections of existing data and/or knowledge; no new data are generated, although new analyses are undertaken on the collated data. The purpose of the majority of these information resources is to provide guidance on best practice for use in a wider scientific community and for users of and stakeholders for reference values.

EURRECAWIKI

The first information resource created, the EURRECA nutrition software WIKI (http://www.eurrecawiki.org), is a collation of key software programmes used for dietary assessment in Europe and in the United States of America. Nutrition software combines a data entry module (for example, entering the amount of foods consumed) with one or more food composition databases to assess the nutrient intake of an individual or a population group.

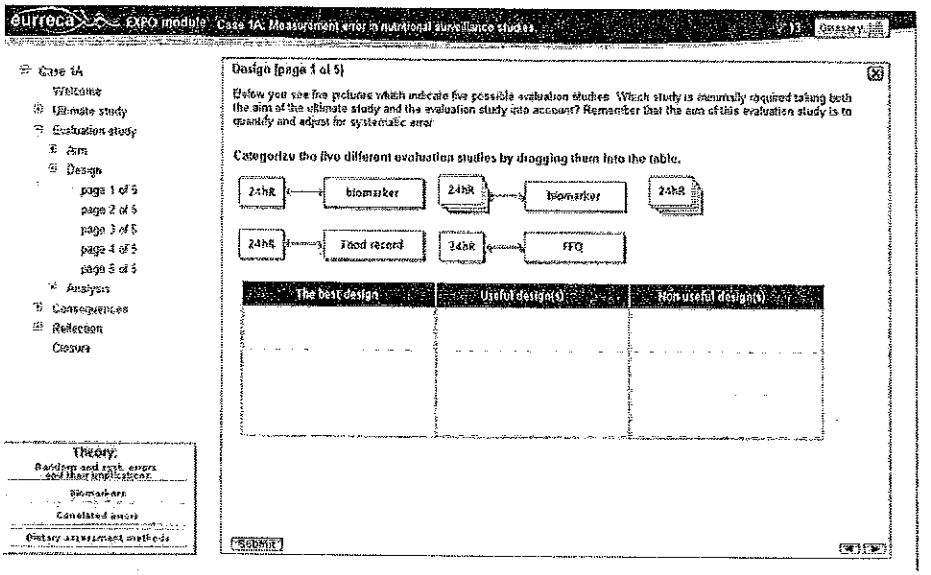

Figure 1 Example of a 'drag-and-drop' exercise that aims to give the student insight into the relationship between aim and design of evaluation studies.

The purpose of EURRECAWIKI is to create an open directory of nutrition software products, including necessary information to help individuals and/or organisations make an informed choice about which software will best fit their specific needs.

EURRECAWIKI provides the following information: background information about the technical aspects of each software product; the food composition database(s) used; specifications of the data entry systems; selected nutrient recommendations included in the software; possibilities to create food package labels; contact information; targeted end users of the software.

Currently, 123 software programmes from 12 countries have been identified. Software producers and users can update the information on each software package; updates are monitored by the EURRECAWIKI team. This mechanism reduces the burden of maintaining the database and allows comparison of different software packages.

Nutri-RecQuest

The second information resource developed within the EURRECA network is *Nutri-RecQuest*, a web-based search tool. It is a collation of the micronutrient recommendations of 37 European countries/organisations and eight key non-European countries/regions, and comprises 29 micronutrients (Cavelaars *et al.*, 2010b). General information on the source of recommendations, as well as on the scientific background, is available. *Nutri-RecQuest* provides easy access to micronutrient recommendations and efficient search, comparison, display, print and export functions through a user-friendly interface. It is a valuable resource for bodies responsible for setting recommendations, as well as for users of recommendations, including scientists, policy makers, health professionals and the food industry.

NutPlan

A new software programme, *NutPlan*, is being developed following the creation of EURRECAWIKI. This innovative software supports nutrition planning for individuals and groups, recipe calculation, diet planning, creation of food labels and nutrient intake assessment (Gurinovic *et al.*, 2010). It is particularly aimed at Central and Eastern European countries and at some other European countries where the need for innovative software has been identified (for example, Portugal). This software programme could also be used by a wide range of professionals and organisations, including food-producing small and medium enterprises, dietitians, nutritionists, caterers, health professionals and policy makers. An added value of *NutPlan* is the link with *Nutri-RecQuest*, which enables the comparison of dietary nutrient intake with a wide spectrum of reference values. Similar to most advanced software packages, *NutPlan* is flexible for editing and can incorporate existing harmonised food composition databases, ensuring more complex applications that can respond to the evolving demands for nutritional information and regulation.

'Quality of measurements' fact sheet

When assessing nutrient intake, it is important to know the micronutrient content of the different foods consumed. The fact sheet on 'Quality of measurements' is aimed at

evaluating the quality of the laboratory methods used to measure nutrient contents. An inventory was made of the various methods used to measure basic micronutrients in food and water. The inventory of the different methods included (i) the effectiveness; (ii) associated difficulties; and (iii) costs (Eleftheriou and Papastefanou, 2009). The take-home messages of the fact sheet are based on this inventory. The target audience for this fact sheet includes food analysis laboratories, food producing companies and policy makers.

Best practice guidelines for biomarkers

Best practice guidelines describing biomarkers for micronutrient status have been developed on the basis of (i) expert-based assessment of the usefulness and application of key biomarkers (Fairweather-Tait, 2009) and (ii) evidence-based systematic reviews of the responsiveness of biomarkers to changes in exposure (Hooper *et al.*, 2009). These guidelines contain measures of status and exposure for 20 key micronutrients, including cutoff values for key biomarkers of EURRECA priority micronutrients. The guidelines also describe the advantages and limitations of each measure. This information may be used by international expert committees with responsibilities for setting and/or evaluating dietary recommendations. Both the European Food Safety Authority and the United States of America Dietary Reference Intake Committee have expressed interest in including the outputs from this activity in their discussions when setting and reviewing dietary guidelines. A lack of good biomarkers for many micronutrients and the need to develop better biomarkers have become apparent while working on the guidelines. The Best Practice Guidelines cover the following micronutrients: calcium, chromium, copper, iodine, iron, magnesium, phosphorus, potassium, selenium, zinc, vitamin A, vitamin B6, vitamin B12, folate (vitamin B9), niacin (vitamin B3), riboflavin (vitamin B2), thiamin (vitamin B1), vitamin C (ascorbic acid), vitamin D and vitamin E.

Information resources for micronutrients (Micronutrient WIKI)

The systematic reviews that are the basis for the best practice guidelines are closely related to the development of another initiative that aims to chart, quantify and model micronutrient status and health parameters, leading to 'individual' quantification of micronutrient requirements through the use of modern systems biology (systems biology is the study of multiple processes that together determine molecular/cellular and whole-body physiology) approaches. The *Micronutrient WIKI* pages (http://wiki.nugo.org/index.php/Category:Micronutrients) provide information about several micronutrients, including their biological function, catabolism, biomarkers and related diseases.

The relationship between micronutrient intake and/or status and a range of biomarkers, including inflammatory, oxidative stress and metabolic stress processes, has been reviewed. The selected biomarkers are metabolites that are known to respond to dietary interventions and are associated with (or are predictive of) certain chronic metabolic diseases. A summary of the relationships between micronutrient status or intake and these markers, along with the accompanying references, has been made available in a series of *Micronutrient WIKI* pages. The overview presented on these pages is not a comprehensive review of available data but an expert-based opinion backed by scientific references. Currently, information about the relationship between micronutrient status and biomarkers of health is far from complete; however, external experts are explicitly invited to check the information and, if available, add relevant data on micronutrient–biomarker associations. The collected data, combined with additional data from metabolite databases, will be used to build biological networks that will allow more insight into the role and interactions of the various micronutrients. This ongoing work is carried out in collaboration with the European Nutrigenomics Organisation (http://www.nugo.org).

Literature review databases

At present, systematic reviews to estimate requirements of prioritised micronutrients (iron, zinc, vitamin B12, folate and iodine (Cavelaars *et al.*, 2010a)) are being undertaken using EURRECA's best practice guidelines on biomarkers and intake assessment (see above). Centralised searches are conducted to collate papers on associations between micronutrient intake and status, nutrient status and health, and nutrient intake and health. Health indicators relevant to the selected micronutrients have been identified and prioritised using public health reports and the scientific literature. Endnote (software for publishing and managing bibliographies) libraries, with bibliographic data and abstracts of relevant papers for all population groups by micronutrient, have been developed. Moreover, common Microsoft Access databases, with detailed information (including study characteristics, study results and study validity) from the relevant papers, are being finalised. These databases will be used in the next phase of EURRECA for meta-analyses.

Framework/decision trees

Frameworks (a basic conceptual structure used to solve or address complex issues) and decision trees are also being developed within EURRECA and form the third kind of instrument.

Quality scoring

A scoring system to rate the quality of data in surveys assessing nutrient intake has been developed. A step-by-step guidance diagram summarises the process used to select the highest-quality dietary surveys/studies in each country

Table 1 EURRECA instruments

Name	*Short description*
Interactive digital training module	Insight into principles of evaluation studies in nutritional research
EURRECAWIKI	Collation of key software programmes for dietary assessment
Nutri-RecQuest	Web-based search tool on micronutrient recommendations, collation of the micronutrient recommendations of 37 European countries/organisations and eight key non-European countries/regions, comprising 29 micronutrients
NutPlan	Nutritional software supporting nutrition planning for individuals and groups, recipe calculation, diet planning, creation food labels and nutrient intake assessment
'Measurements of quality' fact sheet	Fact sheet on micronutrient analysis methods for food labelling and micronutrient intake
Best Practice Guidelines for Biomarkers	Guidelines on biomarkers that provide useful information about the effect of dietary exposure and the levels of each marker, indicating optimal nutrient intake
Micronutrient WIKI	Information resource on micronutrients including the following topics: (1) Introduction, (2) Biological function, (3) Catabolism, (4) Diseases/conditions related to nutrition, (5) Other (monogenic) disorders, (6) Nutritional information, (7) Markers of homeostasis and/or health, (8) Determinants of status and (9) Other resources.
Literature review databases	Collation of scientific papers on micronutrient intake-status, status-health and intake-health associations
Nutritional survey scoring system	Scoring system to rate the quality of data obtained in surveys addressing adequacy of nutrient intake
Scientific triage of micronutrients	Prioritisation of micronutrients for the purpose of reviewing their requirements

(Blanquer *et al.*, 2009; Garcia-Alvarez *et al.*, 2009). The guidance diagram is based on an expert consultation that identified criteria to be included in the scoring system, as well as their ranking according to their relevance. The six main criteria included in the scoring system are scope and type of surveys; dietary assessment methods (for example, 24 h recall, food frequency questionnaire); food composition database used (including information on inclusion of fortified foods and supplements); misreporting; year of survey; other relevant information (for example, use of supplements and functional/fortified foods, physical activity levels and anthropometric measurements). In the case of the quality assessment of food composition databases, the recommendation is to follow the quality standards developed by the European Food Information Resource Network of Excellence (Westenbrink *et al.*, 2009).

Scientific triage of micronutrients

As micronutrient recommendations should be regularly updated to reflect new scientific evidence, a decision tree on how to prioritise micronutrients for the purpose of reviewing their requirements has been developed by EURRECA (Cavelaars *et al.*, 2010a). The strategy of priority setting will be a helpful procedure for policy makers and scientific advisory bodies who face the problem of making optimal use of limited resources. Three criteria are the basis for the prioritisation of each micronutrient:

(a) amount of relevant, new scientific evidence available for a particular micronutrient for different life-stage population groups;
(b) public health relevance of the micronutrient for the different population groups, including vulnerable groups such as low income and immigrant populations;
(c) heterogeneity defined as variations in current micronutrient recommendations in different European countries.

These three theoretical criteria have been translated into quantifiable indicators for the 28 selected micronutrients, which have then been combined into an assessment matrix. Highest priority is given to micronutrients for which (A) the amount of new evidence is substantial, (B) there is most relevance for public health and (C) for which variations in current recommendations are relatively large.

Conclusion

The EURRECA Network of Excellence is developing a number of instruments to support alignment of micronutrient requirements based on scientific evidence between European countries. Table 1 gives an overview of all current EURRECA instruments. Currently, these instruments stand alone, but it is the purpose of EURRECA to integrate the tools with the generated knowledge. Therefore, a generic decision tree will be developed, which will facilitate the process of weighing the evidence for deriving micronutrient reference values. This decision tree will use data on the relationships between intake, status and health outcomes, and instruments developed for the assessment of micronutrient intake and status in various population groups. The decision tree will thus be the culmination of all activities undertaken by the EURRECA Network of Excellence.

Conflict of interest

The authors declare no conflict of interest.

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