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UNDER DISCUSSION

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Vitamins and minerals: A model for safe addition to foods

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Summary *Background* Significant subgroups in most European populations have intakes below nationally recommended levels for several vitamins, minerals and trace elements, placing individuals at risk of suboptimal intake of important vitamins and minerals. The voluntary addition of micronutrients to the appropriate foods may help address the risks associated with low micronutrient intakes. However, concerns need to be addressed regarding the potential for unacceptably high intakes, particularly for those people consuming very large amounts of food. *Aim of the study* To develop a model to estimate the level of each micronutrient that can be added safely to foods. *Methods* A theoretical model was developed based on the critical factors which determine the risk of unacceptably high intake for each micronutrient at high levels of food/energy intakes. These included 1) Tolerable Upper Intake Levels (UL), 2) high micronutrient intakes in Europe at the 95th percentile intake for each nutrient, 3) the proportion of fortified foods in the diets of individuals at the 95th percentile for energy intakes, 4) the proportion of foods to which micronutrients could practically be added, and 5) a range of estimates for the fractions of foods which might be actually fortified for each nutrient. A maximum level was set up for each micronutrient per typical serving or 100 kcal portion. The outputs of the model were then compared against a recent model developed by AFSSA, based on the food intake data in France. *Results* Three categories of micronutrients were identified, in which micronutrients could be added safely to foods at levels (per serving, e. g., 100 kcal) 1) greater than 1 European Commission Recommended Daily Intake (EC RDA): vitamin B12, vitamin C, vitamin E, riboflavin, panthothenic acid, niacin and thiamine; 2) between 50 and 100 % of the EC RDA: vitamin B6, vitamin D, folic acid, biotin, copper, iodine and selenium; 3) between 10 and 40 % of the EC RDA: iron, zinc, calcium, phosphorus and magnesium. A fourth category consisting of retinol, for which high end intake levels are close to UL for some population subgroups in Europe and thus requires further consideration. *Conclusions* A wide range of vitamins and minerals can be added safely to foods at nutritionally important levels in the current diets of Europeans.

Key words vitamins – minerals – fortification – tolerable upper intake levels – recommended daily intake

Introduction

The European Commission has recently published a draft proposal [65] for a harmonized regulatory framework on the voluntary addition of vitamins and minerals to foods in the EU. The proposal is based primarily on the need to ensure consumer safety and for a sound science base for any subsequent regulations governing nutrient addition levels elaborated within the proposed framework. The objective of this paper is to develop a model, which could assist in the development and implementation of such a framework, i. e., to determine the safe maximum levels of voluntary micronutrient addition to foods.

Data on micronutrient intakes are available in most European countries. Based on population means, it would appear that for most nutrients, the majority of individuals in Europe have adequate intakes. However, the realistic assessment of dietary adequacy is notoriously difficult due to lack good data on nutritional status [70], and on intakes of below the population mean by certain sub-groups. As such, there is a body of evidence suggesting that significant population subgroups have suboptimal nutritional status, as well as intakes below nationally recommended levels for many vitamins, minerals and trace elements, notably for iron, calcium, zinc, vitamins B1, B2, B6, D and folate [6, 12, 26, 27, 30, 45, 61, 70, 80, 81]. A number of studies show clear evidence that both mandatory and voluntary addition of nutrients to foods can help to address this problem in at-risk populations [10, 11, 13, 23, 51, 62].

At the other end of the consumption distribution, data on excessive intakes in Europe are rare. Moreover, interpretation of existing analyses on this question is difficult, and conclusions are strongly influenced by the choice of criteria to define "high" intakes [70]. Even so, it is also necessary to ensure that population groups that are not directly at risk of nutrient inadequacy, and also individuals consuming relatively high amounts of food, are not placed at risk due to unacceptably high nutrient intakes.

A further complicating factor is that some micronutrients have a relatively low margin of safety between adequate levels of intake and measures of maximum safe intake. Therefore, many nutrients with potentially the greatest risk of high intakes in some individuals are also those for which there is a clear risk of deficiency within the same population; good examples are iron, calcium and vitamin D.

The SCOOP task 7.1.1. Working Group report [70] suggested that, in establishing regulations, the margin of safety must be taken into account. The model proposed here is based on this principle.

The draft EC proposal is for a harmonized regulatory framework on the voluntary addition of vitamins and minerals to foods. In many European countries, specific foods are required by regulation to be restored to "natural" levels, because they replace similar foods of major importance in the diet (e. g., margarine replacing butter), or to restore processing losses. For the purposes of the present model, the fortification defined voluntary addition, either at restoration levels or above.

In the development of this model for addition of nutrients to foods, intakes from dietary supplements were not specifically considered. Supplement users represent a significant minority of the population [43], and it is recognized that consumers of fortified foods who also use supplements regularly may have a reduced margin of safety between intake (from all sources) and the UL for some nutrients. The European Commission has recently published a draft proposal for a harmonized regulatory framework on the addition of vitamins and minerals to food supplements in the EU [7]. It is proposed that supplement users will be protected by a number of measures, including the setting of maximum safe limits of nutrient content, together with provision of information through labelling.

Principles of the model

The proposed model estimates the level of each nutrient that can be added safely to foods, to minimize the risks of excessive intakes in individuals with high food intakes. It is based on the following factors:

- UL: The Tolerable Upper Intake Level, i. e., the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans [68].
- CI_{95}: An estimate of current intakes of micronutrients from non-fortified foods (i. e., excluding voluntary addition) in Europe at the 95th percentile.
- E_{95}: An estimate of current energy intakes in Europe at the 95th percentile.
- MA_n: The maximum amount of each nutrient, which may be added to the diet as a whole, with little risk of adverse health effects in the population.
- FA_n: The amount of each nutrient which may be added safely to each 100 kcal portion.
- PFF_n: The fraction of foods in the market which is available for fortification, for each individual nutrient.

The following shows how these factors are used to derive the present model. The details of their derivation are discussed later.

a) The maximum amount of each nutrient, which may be added to the diet as a whole with little risk of adverse health effects in the population (MA_n), can be estimated as the difference between the UL and the current mean intake of individuals at the 95th percentile (CI_{95}) for each nutrient, i. e., $MA_n = UL\text{-}CI_{95}$.

b) In Europe the mean daily energy intake of adults is approximately 2000 kcal and the 95th percentile of daily energy intake by adult males (the highest energy consuming population group) is estimated to be in the region of 3600 kcal. If this is expressed in terms of food portions containing 100 kcal, then the average adult consumer eats the equivalent of 20 portions of food containing 100 kcal and the highest consumers of foods eat the equivalent of 36 portions per day.
c) The amount of each nutrient, which may be added safely to each 100 kcal portion of food (FA_n), is MA_n divided by the number of food portions fortified with that nutrient in the diet.
d) If all foods were fortified, then the amount of each nutrient, which may be added to each 100 kcal portion, FA_n, would be $MA_n/36$. More realistically, the addition of micronutrients to foods is significantly restricted by a large number of factors. Depending on the specific nutrient, these include technological, organoleptic, shelf-life, marketing and economic factors. For the purpose of this paper, as a conservative estimate, no more than half of all foods (or food energy) are amenable to fortification due to technological, cost or other constraints [1].

The remaining factors are accounted for in the model by assuming alternative, hypothetical fractions of potentially fortifiable foods in the market are fortified for each individual nutrient (PFF_n).

Therefore the final estimate for FA_n, taking into account the proportion of fortifiable foods and the proportion of fortifiable foods which is fortified, is:

$$FA_n = \frac{(UL\text{-}CI_{95})}{(0.5 \times 36 \times PFF_n)}$$

Table 3 gives values for FA_n expressed as percent EC RDA, for a range of vitamins and minerals, for proportions of 5, 10, 25, 50 and 100 % of all foods for which addition of nutrients is feasible. (The same data expressed as mg and μg is given in Appendix 1.)

Thus, the model is intended to allow significant safety margins for the majority of people consuming micronutrients and energy at levels closer to the mean, with the intention to protect high consumers of both micronutrients and food energy.

Elements of the model

Tolerable upper intake level

The UL of a micronutrient is the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans [68]. As there is a considerable amount of literature on the establishment of ULs, this paper will not review this field in depth. However, in general their derivation involves evaluation of all known data on potential adverse effects over extended periods and the use of safety factors to take account of uncertainties in the base data. Their values are set at levels which are unlikely to pose risk to the most sensitive members of the general population [34, 68].

The EC Scientific Committee on Food (SCF) has established a Task Force to review the ULs for vitamins and minerals and recently published reports on ULs for thirteen nutrients [69]. ULs were established for folic acid, vitamin B_6, niacin (nicotinic acid and nicotinamide), selenium, magnesium and molybdenum; ULs were not set for vitamins B_1, B_2, B_{12}, biotin or pantothenic acid, due to lack of evidence of adverse effects in humans, and manganese and β-carotene due to insufficient data on adverse effects on which to make a dose response assessment.

The US Institute of Medicine is currently establishing ULs as part of its revision of the RDAs. Four reports have been published to date, dealing with the B vitamins, vitamins A, D, C, E, K and the carotenoids and the minerals Ca, P, Mg, F, Se, As, B, Cr, Cu, I, Fe, Mn, Mo, Ni, Si, V and Zn [34, 36–38]. ULs were not set for vitamins B_1, B_2, B_{12}, pantothenic acid, biotin, vitamin K, Cr or Si due to lack of evidence on adverse effects in humans, or for β-carotene due to insufficient data on which to make a dose response assessment.

A report commissioned by the European Federation of Health Product Manufacturers has established upper safe levels of intake for a range of vitamins and minerals [73].

Upper safe levels have also been dealt with previously in several reviews. The Nordic Council of Ministers [59] published a report on "Risk Evaluation of Essential Trace Elements" and the WHO/FAO/IAEA [84] addressed the question of safe upper levels as part of a review of trace elements in human nutrition and health. Other national and EU expert groups reporting values for maximum daily intakes include Conseil Supérieure d'Hygiène Publique de France [3], the EU Scientific Committee on Food [67], the Dutch National Food and Nutrition Council [31], and UK COMA [14]. The German-speaking societies of Germany, Austria and Switzerland consider ULs for single nutrients in their new reference values for nutrient intake [16].

The Program in Food Safety at the Department of Nutritional Sciences, University of Toronto, reviewed the literature and proposed a risk classification [15]. However, this does not attempt to establish upper safe levels, but does quote values from a number of earlier published reports.

This paper uses the most recent estimates of ULs for adults established by the SCF, where available or, alternatively, the ULs set by the US Institute of Medicine in

Apendix 1 Maximum levels of addition of vitamins and minerals to foods (assuming 50 % of all foods can be fortified)

Micronutrient	EC RDA	Units mg or µg			% Foods fortified (of total available)				
					100 %	50 %	25 %	10 %	5 %
		Upper Level	95th percentile Intakes	Max available for Adding to Foods[5]	Max amount per 100 kcal portion[4] Units mg or µg				
				MA (UL-CI)			FA_n		
Vitamin B12 µg	1	3,000[2]	20	2,980	**166**	331	662	1656	3311
Riboflavin mg	1.6	200[2]	3.2	197	**11**	22	44	109	219
Vitamin E mg	10	1,000[2]	21	979	**54**	109	218	544	1088
Pantothenic acid mg	6	500[2]	10	490	**27**	54	109	272	544
Niacin mg (nicotinamide)	18	900[1]	41	859	**48**	95	191	477	954
Thiamin mg	1.4	50[2]	2.8	47.2	**3**	5	10	26	52
Vitamin C mg	60	2,000[2]	186	1814	**101**	202	403	1008	2016
Biotin µg	150	2,500[2]	68	2432	135	270	**540**	1351	2702
Vitamin B6 mg	2	25[1]	3.4	21.6	1	2	5	12	24
Vitamin D µg	5	50[2]	9.9	40	2	4	9	22	45
Copper mg	1.15[3]	10[2]	3	7	0	1	2	4	8
Iodine µg	130	1,100[2]	357	743	41	83	**165**	413	826
Selenium µg	55[3]	300[1]	90	210	12	23	**47**	117	233
Folic acid µg	200	1,000[1]	450	550	31	61	**122**	306	611
Phosphorus mg	800	4,000[2]	2598	1402	78	156	312	779	1558
Iron mg	14	45[2]	24	21	1	2	5	12	23
Zinc mg	15	40[2]	18	22	1	2	5	12	24
Magnesium mg	300	250[1]*	–	240	15	28	54	138	276
Calcium mg	800	2,500[2]	1918	136	8	15	30	76	151
Vitamin A µg	800	3,000[2]	3195	0	0	0	0	**0**	0

[1] EC SCF Tolerable Upper Intake Level
[2] US FNB Tolerable Upper Intake Levels
[3] EU PRI
[4] Maximum which can be added per 100 kcal food without exceeding UL at the 95th percentile intake
[5] Apparent errors in subtraction are due to rounding of presented figure, i. e., after not before calculation
* EU UL for magnesium excludes magnesium present in normal foods and beverages. It is intended for added magnesium and that present in water only; current intakes of magnesium from water are assumed to be generally very low compared to the UL

order to illustrate the model. β-carotene was not included since an UL has not been set for β-carotene due to insufficient data on adverse effects on which to make a dose response assessment [37, 69].

The estimates of ULs established by the SCF can subsequently be applied, as and when they become available.

The UL for niacin used here is that for nicotinamide, which is the main form used for food fortification.

The SCF UL for magnesium excludes magnesium present in normal foods or beverages, and is intended to apply to added magnesium and that present in water only. Current intakes of magnesium from water are assumed to be generally very low compared to the UL [69]. The calculation for FA of this nutrient is therefore based on the UL, rather than UL-CI_{95}.

Current intakes of micronutrients from non-fortified foods (CI_{95})

To ensure safe intakes from added nutrients, it is necessary to take account of individuals who already consume high levels of nutrients from non-fortified foods (i. e., excluding voluntary addition, but including statutory addition for restoration of food equivalence). This section derives an estimate of micronutrient intakes at the 95th–97.5th percentiles across Europe, representing individuals who have intakes considerably above the population mean, i. e., those in the top 5 % of consumption for each nutrient.

Table 1 shows available estimates of 90 to 97.5th percentiles of micronutrients in European countries where relatively recent data are available for individual intakes from large-scale representative surveys. Intakes are for either total population, all adults or adult men. These

Table 1* Micronutrient intakes from all sources in selected European Countries at the 90–97.5th percentiles, expressed as multiples of EC RDA

	Multiples of EC RDA								
Micronutrient	EC RDA 1990	Belgium BIRNH 1985 P90 Adults	Denmark NFA 1985 P95 Adults	France ASPCC 1994 P95 Adults	Ireland IUNA 2001 P95 Men	Germany VERA 1988 P97.5 Men	Holland DNFCS-3 1998 P97.5 Adults	UK NDNS 1990 P97.5 Men	Representative Value (means)
Vitamin A (retinol) µg	800	1.8	3.2	3.7	1.5	5.6	4.0	8.2	4.0
Thiamin mg	1.4	1.5	1.9	N/A	2.5	1.9	2.2	2.1	2.0
Riboflavin mg	1.6	1.4	3.2	1.6	2.0	2.0	1.8	2.3	2.0
Niacin mg	18	N/A	2.0	N/A	2.3	1.6	2.0	3.5	2.3
Vitamin B6 mg	2	1.3	1.4	1.2	2.7	1.7	1.5	2.2	1.7
Total folate µg	200	N/A	N/A	2.1	2.6	1.7	2.1	2.8	2.3
Vitamin B12 µg	1	N/A	18.1	N/A	19.8	19.3	N/A	22.9	20.0
Pantothenic acid mg	6	N/A	N/A	N/A	1.6	N/A	N/A	1.8	1.7
Vitamin C mg	60	3.0	2.4	2.7	2.9	4.5	3.4	2.8	3.1
Vitamin D µg	5	N/A	1.8	1.3	1.7	3.4	1.8	2.0	2.0
Vitamin E mg	10	N/A	1.9	1.7	1.2	3.3	2.8	2.0	2.1
Biotin µg	150	N/A	N/A	N/A	0.4	N/A	N/A	0.5	0.5
Calcium mg	800	1.9	4.6	1.7	2.0	2.2	2.5	2.0	2.4
Copper mg	1.15**	N/A	N/A	N/A	2.3	3.5	1.7	3.0	2.6
Iodine µg	130	N/A	1.9	N/A	N/A	3.2	N/A	3.2	2.7
Iron mg	14	1.6	2.3	1.5	1.6	1.9	1.4	1.8	1.7
Magnesium mg	300	1.9	2.2	1.5	1.8	2.1	1.9	1.8	1.9
Phosphorus mg	800	N/A	3.8	N/A	3.1	3.1	3.3	2.9	3.2
Zinc mg	15	N/A	N/A	1.2	1.1	1.4	1.1	1.3	1.2
Selenium µg	55**	N/A	N/A	N/A	N/A	N/A	1.6	N/A	1.6

* See ref. [24, 29, 32, 39, 70]
** EU P. R. I. [20]

values are expressed as percentages of the EC RDA, to facilitate comparisons between nutrients. A similar approach was taken by the AFSSA diet-based simulation of fortification in the French diet [1].

Nutrient intakes are not directly comparable between National surveys for a variety of reasons. Surveys provide data on different population groups and micronutrients; food composition tables vary considerably by country, both in the variety of foods covered, and the range of nutrients analyzed; the methodology for measuring intakes also varies greatly by country and by survey. Differences in intake methodology in particular may exacerbate disparities at the higher consumption levels. For some countries, voluntary addition of nutrients may influence the estimates for some nutrients; however, it is not possible to exclude this component of intake because it is not specifically quantified in the published data.

Therefore, it is not possible to derive fully valid pan-European estimates of 95th percentile intakes from non-fortified foods based on the data currently available. The present model may be most appropriately applied to data for individual intakes from National surveys.

Notwithstanding this, an approximation of typical European upper intakes (CI_{95}) is given in Table 2, based on values from each national survey, in order to allow a pan-European overview. In general, similar patterns of intakes can be seen between countries for most nutrients, and this approximation is considered adequate within the context of the present analysis. Intakes of niacin are for pre-formed niacin in most cases as this should be distinguished from potential niacin as tryptophan, which is not relevant to this analysis; the published data do not distinguish between nicotinic acid

Table 2 Upper energy intakes in some European populations, in men at the 95th percentile

Country	Age range Years	MJ	Kcal
Netherlands [31]	22–50	16.4	3908
Netherlands [32]	22–50	16.4	3916
Sweden*		12.8	3050
UK [24]	25–34	15.5	3700
UK [24]	35–49	15.2	3620
Ireland [39]	18–64	16.3	3890

* Personal communication

and nicotinamide but it is likely that most is present as nicotinamide. Intakes of folate are expressed as total folate. Although it is not possible to quantify separately the intakes of natural food folates and folic acid, it is likely that only a small proportion of the folate from dietary sources is in the form of folic acid.

Because the estimates of CI_{95} include voluntary addition to foods and food supplements in the data for some of the countries, they may overestimate intakes in the actual base diet, therefore, providing an additional degree of conservatism into the model. On the other hand, some of the surveys have not taken into account the possible effect of underreporting of food intake on estimates of micronutrient intake.

Maximum amounts for safe addition to foods (MA)

The UL is an estimate of the highest level of intake of a nutrient, which carries no appreciable risk of adverse health effects [68]. The 95th percentile intake may be used as a basis of determining whether a population is at risk, i. e., a population is considered at little risk if the 95th percentile intake does not exceed the UL [35].

The maximum amount of a nutrient, which may be added to the diet (MA), with little risk of adverse effects, can therefore be estimated as the difference between the UL and the current intake at the 95th percentile (CI_{95}).

Energy intake at the mean and 95th percentile (E_{95})

It cannot be assumed that there is a relationship between energy intake and positive selection of fortified foods. However, some individuals, in addition to having a high baseline intake for one or more micronutrients, also consume high amounts of food per se and therefore may consume proportionally higher amounts of fortified foods.

Hence, in order to ensure the safe addition of nutrients at the extremes of both nutrient and food intake, the present model distributes the estimate of MA equally between all fortified foods eaten by the highest consumers of food energy, thus, ensuring that excessive nutrient intakes are unlikely, even at extreme food intakes. This provides a further safety margin for the majority of people who are closer to mean intakes of micronutrients and foods.

In Europe the mean daily energy intake of adults is approximately 2000 kcal and the 95th percentile energy intakes by adult men (the highest energy consuming population group) is estimated from five national dietary surveys to be approximately 3600 kcal (15 MJ) per day (Table 2). Expressed in terms of food portions containing 100 kcal, this is the equivalent of 20 portions of food containing 100 kcal for the average adult consumer and the equivalent of 36 portions for the highest consumers.

Proportion of the diet from fortified foods (PFF_n)

There are few estimates of the proportion of the diet which is potentially amenable to voluntary fortification with vitamins and minerals. A recent analysis estimated that, taking into account all relevant factors, up to 47 % of foods in the French diet (278 out of 590 foods recorded in a nationally representative survey of food consumption) could hypothetically be fortified with vitamins and minerals [1]. This analysis excluded foods such as non-processed and non-packaged and non-labeled foods, as well as traditional and other foods, which are considered unlikely to be fortified. A similar analysis of the North/South Ireland Food Consumption Survey indicates that, on average, approximately 50 % of food energy consumed by adults is potentially fortifiable (A. Flynn, unpublished). This model takes these as the most reasonable estimates presently available, and assumes a value of approximately 50 % of food energy is potentially fortifiable.

However, what proportion of potentially fortifiable foods is likely to be fortified in European countries in the context of the proposed regulatory framework? The most useful indication may be derived from those countries where voluntary addition of nutrients is currently permitted.

Few good data exist on the proportion of foods fortified in Europe or in North America. In Ireland, a recent representative survey of 18–64 year old adults (n = 1379) [39] indicates that Irish men consume 71 kcal and women 69 kcal per day as foods voluntarily fortified with one or more micronutrients, which is 3.1 % of the mean total food energy (A. Flynn, unpublished). The 95th percentile for energy intake from fortified foods in Irish men is 230 kcal (equivalent to 2.3 portions of 100 kcal).

A similar value of 3 % energy from voluntarily fortified foods has been estimated in the UK (personal communication R. Fletcher) based on household intake data from the NFCS 1999 [50] and the CIAA survey of fortified foods in Europe [8].

An analysis of ten-year trends in micronutrient intakes by German children and adolescents [74] suggests that total energy intake from foods fortified with one or more nutrients was approximately 9 % in 1996.

The AFFSA diet-based mathematical model suggests that the most reasonable estimate of the proportion of the diet from fortified foods in France would be 5 % [1].

Since the proportion of foods which are likely to be fortified will vary by nutrient, the calculation of the maximum safe amount for addition to foods must be done individually for each nutrient. Therefore in this context, the proportion of foods fortified must be ex-

pressed for single nutrients, because the proportion of food energy fortified with one particular nutrient will be significantly smaller than the cumulative values from two or more nutrients. The present model is based on intakes from individual nutrients.

Cost, technological and other constraints on the addition of nutrients (see below) restrict both the number and quantity of micronutrients added to any particular food, and hence limit the proportion of potentially fortifiable foods to a greater or lesser extent for each nutrient. The relatively low prevalence of food fortification in European countries where voluntary addition of nutrients is currently permitted may be partly due to such practical and economic constraints.

Factors limiting the addition of nutrients to foods

The proportion of foods which is likely to be fortified is limited by a number of factors. Many foods are not amenable to fortification, e. g., foods such as non-processed and non-packaged and non-labeled foods. These include fresh products like fruits and vegetables, meat or fish. Indirect "fortification" of meat and fish is theoretically possible by supplementation of animal food, as it has been done in former Eastern Germany with iodine. However, we do not take this into consideration, as the practice is very limited. In addition, traditional foods and certain foods with a 'quality image' are considered unlikely to be fortified [1].

For those foods, which are potentially fortifiable, many factors influence the feasibility of adding nutrients to particular foods. This may limit the proportion of such foods which are fortified and the maximum levels at which particular micronutrients are added. These factors include costs associated with ingredients, processing, quality control and routine analysis; adverse effects on sensory properties, taste, odor and appearance; reduced product shelf-life; and nutrient stability, either in processing or during storage. For any added nutrient the technological problems increase as a higher proportion of the RDA is included in the food [63, 64].

Technical barriers may exist due to chemical incompatibility between foods, and nutrients, e. g., lipophilic substances in water-based foods, or hydrophilic substances in fatty foods. The stability of most vitamins is particularly susceptible to a large number of factors found in most foods and food processes, including temperature, moisture, oxygen, light, pro-oxidants, reducing agents, high/low pH, and metallic ions [60]. Transition metal ions, such as iron are highly pro-oxidant, leading to severe problems of rancidity and off flavors in host foods.

Calculation of the amount which can be safely added to foods (FA_n)

The calculation of the model is worked through below, using vitamin C as the example, initially assuming that 50 % of all potentially fortifiable foods are actually fortified.

Vitamin C

- Parameters: UL = 2000 mg; CI_{95} = 186 mg; EC RDA = 60 mg; Added to 50 % of potentially fortifiable foods. The maximum amount of each nutrient which may be added to the diet as a whole with little risk of adverse health effects (MA_n) can be estimated as the difference between the UL and the current mean intake of individuals in the 95th percentile (CI_{95}) for each nutrient.

  Expressed as EC RDA
  UL = 2000/60 = **33.3 EC RDAs;**
  $CI_{95 Vitamin\ C}$ = 186/60 = **3.1 EC RDAs**
  $MA_{Vitamin\ C}$ = UL-CI_{95} or 33.3–3.1 = **30.2 EC RDAs**

- The 95th percentile of daily energy intake by adult males is 3600 kcal per day or 36 portions of 100 kcal. Only 50 % of these can potentially be fortified, i. e., $PFF_{Vitamin\ C} = 36 \times 0.5 = 18$ portions 100 kcal.

  Assuming that only half of these are *actually* fortified, then the number of 100 kcal food portions which are fortified with vitamin C in the diets of the highest energy consumers are:

  $18 \times 0.5 = 9$ food portions of 100 kcal

- The amount of each nutrient that may be added safely to each 100 kcal portion is $MA_{Vitamin\ C}$ divided by the number of fortified food portions in the diet. Therefore, expressed as percent EC RDA:

  At 50 % of potential foods fortified (multiplying by 100 to express as %),
  $FA_{Vitamin\ C}$ = 30.2/9 = 3.36 RDA/100 kcal portion (336 % per 100 kcal portion).

For other hypothetical proportions of potentially fortifiable foods, the values of $FA_{Vitamin\ C}$ are as follows.

% Potentially Fortifiable Food Energy Actually Fortified with Vitamin C	Maximum amount of Vitamin C which may be added per 100 kcal food portion	
	%EC RDA	mg
100	168 %	101
50	336 %	201
25	671 %	403
10	1678 %	1,007
5	3336 %	2,002

N. B. 100 % of potentially fortifiable foods equates to 18 portions of 100 kcal (i. e., 50 % of 95th percentile total energy intake).

The estimates of the maximum levels of other vitamins and minerals, which can be added per 100 kcal food without exceeding UL at the 95th percentile intake, are presented in Table 3. This shows that, even with fortification of 25 % of all potentially fortifiable foods for each individual nutrient, nutritionally important levels (>/= 16 % RDA per 100 kcal portion) of all nutrients, except retinol, could be added safely to foods.

In the application of this model, account is not taken of low energy foods for which the maximum levels of added micronutrient per serving would be low using 100 kcal as the reference base. A practical approach for low calorie foods might be to set a maximum level for each nutrient per portion, i. e., per typical portion/serving or per 100 kcal portion if the typical portion/serving contains more than 100 kcal. This would overcome the possibility of very high addition levels for low calorie foods.

Application to the diets of children

While the present model was derived using adult intake data and ULs established for adults, it is also applicable for children, since i) their intakes of food and nutrients are lower than those of adults and ii) on a body weight basis, children are not considered to have greater sensitivity to adverse effects of micronutrients compared to adults. Indeed some nutrients are considered to present a lower hazard to children versus adults, on a body weight or energy intake basis; examples being calcium and vitamin D for which the ULs are the same for children aged 1–18 years as for adults [34].

Table 3 Maximum levels of addition of vitamins and minerals to foods (assuming 50 % of all foods can be fortified)

							% Foods fortified (of total available)				
	Units mg or µg			Expressed as EC RDAs			100 %	50 %	25 %	10 %	5 %
Micronutrient	EC RDA	Upper level	95th percentile intakes	Upper level	95th percentile intakes	Max available for adding to foods[5]	% EC RDA per 100 kcal portion[4]				
				UL_n	CI	MA (UL-CI)			FA_n		
Vitamin B12 µg	1	3,000[2]	20	3000	20.0	2,980	**16556**	33111	66222	165556	331111
Riboflavin mg	1.6	200[2]	3.2	125	2.0	123	**683**	1367	2733	6833	13667
Vitamin E mg	10	1,000[2]	21	100	2.1	98	**544**	1088	2176	5439	10878
Pantothenic acid mg	6	500[2]	10	83	1.7	82	**454**	907	1815	4537	9074
Niacin mg (nicotinamide)	18	900[1]	41	50	2.3	48	**267**	533	1067	2667	5333
Thiamin mg	1.4	50[2]	2.8	36	2.0	34	**187**	375	749	1873	3746
Vitamin C mg	60	2,000[2]	186	33	3.1	30	**168**	336	672	1680	3359
Biotin µg	150	2,500[2]	68	17	0.5	16	90	180	360	901	1801
Vitamin B6 mg	2	25[1]	3.4	13	1.7	11	60	120	240	600	1200
Vitamin D µg	5	50[2]	9.9	10	2.0	8.0	45	89	178	446	891
Copper mg	1.15[3]	10[2]	3	8.7	2.6	6.1	34	68	135	338	676
Iodine µg	130	1,100[2]	357	8.5	2.7	5.7	32	64	127	318	635
Selenium µg	55[3]	300[1]	90	5.5	1.6	3.8	21	42	85	212	424
Folic Acid µg	200	1,000[1]	450	5.0	2.3	2.8	15	31	61	153	306
Phosphorus mg	800	4,000[2]	2598	5.0	3.2	1.8	10	19	39	97	195
Iron mg	14	45[2]	24	3.2	1.7	1.5	8	17	33	83	167
Zinc mg	15	40[2]	18	2.7	1.2	1.5	8	16	33	81	163
Magnesium mg	300	250[1]*	–	0.8	–	0.8	5	9	18	46	92
Calcium mg	800	2,500[2]	1918	3.1	2.4	0.7	4	8	16	40	81
Vitamin A (retinol) µg	800	3,000[2]	3195	3.8	4.0	0	0	0	0	0	0

[1] EC SCF Tolerable Upper Intake Level
[2] US FNB Tolerable Upper Intake Levels
[3] EU PRI
[4] Maximum which can be added per 100 kcal food without exceeding UL at the 95th percentile intake
[5] Apparent errors in subtraction are due to rounding of presented figure, i. e., after not before calculation
* EU UL for magnesium excludes magnesium present in normal foods and beverages. It is intended for added magnesium and that present in water only; current intakes of magnesium from water are assumed to be generally very low compared to the UL

Similarly for magnesium and phosphorus, the ULs are the same for children over four years (magnesium) [69] or over eight years (phosphorus) [34] of age as for adults. In the case of iron, the upper level for children is equal, or close, to the adult value (1–13 yr: 40 mg; 14–18 yr: 45 mg; adults 45 mg) [38].

For these nutrients, children are more protected than adults by the estimates of maximum addition of nutrients to foods in the present model. For other nutrients, where little data are available for the different life stages, including children, ULs are usually derived by adjusting the adult values on the basis of body weight.

For vitamin B_6 ULs for children have been estimated by adjusting the adult values on a body weight basis. The maximum amount that may be added safely to foods for children would be correspondingly lower than the adult value. Using estimates of the intakes for children who are high consumers of vitamin B_6 (at 97.5th percentiles) [26], it can be estimated that this nutrient could be added safely at levels above 50 % of the EC RDA per 100 kcal portion, assuming 25 % of all potentially fortifiable foods are fortified with Vitamin B_6.

Application to the diets of older people

This model is also applicable for older people. Their intakes of food and nutrients are lower, on average, than those of younger adults, and on a body weight basis, older people are not considered to have greater sensitivity to adverse effects of micronutrients compared to younger adults. ULs for vitamins and minerals, which have been established for older people, are not different from those of younger adults [34, 36–38, 69]. One exception is phosphorus for which the UL is set lower for those aged > 70 yr because of increased prevalence of impaired renal insufficiency in this group [34]. Thus, older people are protected as well as younger adults by the estimates of maximum addition of nutrients to foods in the present model.

Comparison with the AFFSA model

The present model was evaluated by comparison with a recent report modeling the effect of nutrient addition to the diets of French adults [1]. This modeling study was based on food consumption of a representative sample of French male and female adults (n = 890), aged 18–75 years, assuming different percentages of the potentially fortifiable fraction of the diet are fortified to various levels with selected micronutrients. The potentially fortifiable fraction was estimated to be 47 % of foods consumed (278 out of 590 foods recorded in a nationally representative survey of food consumption) and excludes foods such as non-processed and non-packaged and non-labeled foods, as well as traditional foods and foods with a quality image which are considered unlikely to be fortified. Adjustment for possible underreporting of food intake was made by excluding subjects with implausibly low energy intakes.

The data in Table 4 confirm that for most of the nutrients examined, the proposed model predicts with a high degree of agreement the maximum amount of in-

Table 4 Comparison of the maximum percentage of the EC RDA per 100 kcal which could be safely added to foods using the proposed model with that obtained using AFSSA data, assuming different proportions of the potentially fortifiable fraction of the diet are fortified

Nutrient	UL	Max % EC RDA per 100 kcal[1]					
		100 % fortified		50 % fortified		10 % fortified	
		Model[2]	AFSSA[3]	Model[2]	AFSSA[3]	Model[2]	AFSSA[3]
Riboflavin	200 mg	683	651	1367	1238	6833	5070
Vitamin E	1000 mg	544	526	1088	1010	5439	4457
Vitamin C	2000 mg	168	172	336	337	1680	1721
Vitamin B6	25 mg	60	61	120	113	600	492
Vitamin D	50 µg	45	49	89	92	446	396
Folic acid	1000 µg	15	20	31	35	153	140
Iron	45 mg	8	13	17	20	83	75
Calcium	2500 mg	4	15	8	20	40	65
Magnesium	350 mg	5	9	9	13	46	41
Retinol	3000 µg	0	7	0	11	0	22

[1] Maximum that can be added per 100 kcal food without exceeding UL at the 95th percentile intake

[2] assuming 100, 50 or 10 % of the potentially fortifiable fraction of the diet (50 % of food energy or half of food intake) is fortified

[3] assuming 100, 50 or 10 % of the potentially fortifiable fraction of the diet (47 % of foods consumed) is fortified [1]

Values were obtained by interpolating estimates of 95th percentile intakes at different simulated levels of nutrient addition (10, 20, 40, and 100 % EC RDA per 100 kcal) for each proportion of the potentially fortifiable fraction of the diet, which is fortified

dividual micronutrients, which may be added safely to foods. For those nutrients (retinol, magnesium and calcium) for which there is limited scope for addition to foods due to the low margin between the dietary intake of high consumers and the UL, the present model is conservative.

The AFSSA data also show that even with the fortification of 50 % of all fortifiable foods all nutrients examined could be added at nutritionally relevant levels, e. g., calcium and magnesium at 20 and 13 % RDA per 100 kcal portion, respectively.

Discussion

The model described estimates the maximum safe levels of addition of vitamins and minerals to foods, based on intakes and ULs for individual nutrients. An important aspect of the model is that it treats each nutrient individually, since *inter alia* the proportion of foods likely to be fortified will be different for each nutrient. Also, the margin between the UL and the RDA varies considerably by nutrient.

The mean proportion of dietary energy from foods technically suitable for the addition of one or more nutrients is estimated to be about 50 %. However, the actual proportion of food energy likely to be fortified in the context of a harmonized regulatory framework in the EU can be anticipated to be significantly less than this. This is evident from markets in European countries where voluntary addition of nutrients is currently permitted, which show that 25 % would be a conservative estimate of the proportion of all potentially fortifiable foods likely to be fortified. Furthermore, not all fortified foods contain all nutrients. Therefore it is a reasonable assumption that considerably less that 25 % of amenable foods are likely to be fortified with a particular nutrient.

Overall, the present model shows that, even with fortification of 25 % of all potentially fortifiable foods (i. e., half of total food intake) for each individual nutrient, nutritionally relevant levels (= 0.16 × RDA per 100 kcal portion) of all micronutrients examined, except retinol, could be added safely to foods. This includes zinc, calcium, phosphorus, and magnesium for which the margin between the intakes of high consumers and the UL is comparatively low. This is also supported by the French data referred to above [1], which show that with fortification of 50 % of all fortifiable foods, all nutrients examined, including calcium and magnesium, could be added safely at nutritionally significant amounts.

It is proposed that nutrients can be grouped into 4 bands, based on estimates for the maximum safe level of addition.

Band 1 Nutrients, which can be added safely to food at levels greater than 1 EC RDA per 100 kcal portion/serving, regardless of assumptions made for proportion of amenable foods fortified (Table 3). This is mainly due to the large difference between the respective UL and current intake. These include vitamins B_{12}, C, E, riboflavin, pantothenic acid, niacin (as nicotinamide), and thiamin. Estimates of maximum safe addition levels in this group range from 1.7 times the RDA for vitamin C upwards (see Table 3).

Band 2 Nutrients which may be added at greater than 0.5 times EC RDA per 100 kcal portion/serving, assuming the high estimate of 25 % amenable foods are fortified as discussed above. In order to maintain a distinction between this and the first band, this can be expressed as 50 to 100 % EC RDA. This band comprises vitamin B6, D, folic acid, biotin, copper, iodine and selenium.

Band 3 The minerals calcium, magnesium, zinc, iron and phosphorus, which can be added at levels between 0.16 (calcium) to 0.4 (phosphorus) x EC RDA.

Band 4 Retinol, for which the current intake from food sources approaches the UL for some population groups in the EU, at the 95th centile of intake. Present levels of retinol addition to foods (e. g., restoration and substitute foods such as margarines; and voluntary fortification) appear to pose no problems in the diets of Europeans. Indeed there is evidence that they play an important role in the diets of some people. However, regulation of further voluntary addition of retinol to foods merits careful consideration, both of the level of addition and the range of foods fortified, bearing in mind that the risk group is women in childbearing years.

Although the present model is intended for the protection of consumers against the risk of excessive intakes of micronutrients, the prevalence in Europe of inadequate dietary intakes and suboptimal nutritional status for many vitamins, minerals and trace elements, notably for iron, calcium, zinc, vitamins B_1, B_2, B_6, D and folate [6, 12, 26, 27, 29, 45, 61, 70, 80, 81] should be taken into consideration in drafting regulations. There is clear evidence that both mandatory and voluntary addition of nutrients to foods can help to address the problem of nutritional inadequacy in at-risk populations [10, 11, 13, 23, 51, 62].

It has been suggested that wider voluntary fortification should be accompanied by more effective monitoring of micronutrient intakes in the EU. The design and analysis of such surveys would need to allow distinction between the different sources of nutrients, e. g., indigenous nutrients in foods versus added nutrients (including voluntary addition, restoration and substitute foods); different chemical forms of nutrients (such as folic acid versus natural food folates; pre-formed niacin versus potential niacin from tryptophan; nicotinamide versus nicotinic acid) and possibly differences in bioavailability in the prevailing diet. In addition, such surveys would need to record supplement use using reliable methods.

Conclusions

This proposed model to determine the safe maximum levels of micronutrient addition to foods is designed to protect high consumers of fortified foods against possible adverse effects of excessive intakes of vitamins and minerals. Although derived on the basis of adult data, it is also applicable to children and older people. The model uses conservative estimates of the proportion of foods likely to be voluntarily fortified in the context of a change in the regulatory environment to permit voluntary addition of vitamins and minerals to foods. It is applicable to all foods, including low energy foods. The validity of the model was confirmed using modeling data for fortification of foods based on a survey of food consumption in a representative sample of adults in France. From this analysis it is concluded that a wide range of vitamins and minerals can be added safely to foods, at nutritionally relevant levels (>/= 15 % RDA per portion) in the current diets of Europeans.

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