Public health aspects of food fortification: a question of balance

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Micronutrient malnutrition is widespread throughout the world, with important health and economic consequences. Tools to address this situation include food fortification, supplementation and dietary diversification, each having different and complementary roles. Fortification (mandatory and voluntary) has been practised over several decades in Western countries as well as in developing countries. Iodised salt was introduced in the USA in 1924 to reduce severe I deficiency. In 1938 voluntary enrichment of flours and breads with niacin and Fe was initiated to reduce the incidence of pellagra and Fe-deficiency anaemia respectively. Micronutrient intakes in European countries appear to be generally adequate for most nutrients. However, a number of population subgroups are at higher risk of suboptimal intakes (below the lower reference nutrient intake) for some micronutrients, e.g. folate, Fe, Zn and Ca in children, adolescents and young women. Dietary surveys indicate that fortified foods play a role in mitigating such risks for several important nutrients. The number of foods suited to fortification are considerably limited by several factors, including technological properties (notably moisture, pH and O_2 permeability), leading to unacceptable taste and appearance, as well as cost and consumer expectations. In countries in which voluntary fortification is widely practised micronutrient intakes are considerably below tolerable upper intake levels. Concerns about safety are addressed in relation to the potentially increased level or proportion of fortified foods (e.g. following potential EU legislation), for nutrients with relatively low tolerable upper intake levels and where the potential benefit and risks are in different subpopulations (e.g. folic acid). Recent models for assessing these issues are discussed.

Food fortification: Micronutrient intakes

Micronutrient malnutrition is a widespread problem throughout the world in both developing and industrialised countries, with serious health and economic implications. Approximately two billion of the world population are at risk of Fe deficiency alone, together with its associated gamut of adverse functional consequences throughout the life cycle (ACC/SCN, 2000). Fortification continues to be one of the main strategies employed to tackle these serious global issues, and recommendations for food fortification programmes have been published (Food and Agriculture Organization, 1996).

One of the major public health achievements of the last century in developed countries has been the virtual elimination of nutritional deficiency diseases such as goitre, rickets and pellagra. Factors fundamental to this success were: first, the increased understanding of essential nutrients in disease prevention during the 20th century; second,

the ability to synthesise specific vitamins; finally, their large-scale production, enabling fortification of foods with the appropriate micronutrients.

The considerable literature on intervention strategies for developing countries has been well reviewed relatively recently (Darnton-Hill & Nalubola, 2002; Allen, 2003). Thus, the present paper will discuss nutritional aspects of fortification in the current context of developed countries only, with particular reference to Europe.

There is little good data on nutritional status (SCOOP Task 7.1.1 Working Group, 1997). Based on population means from national dietary surveys, it would appear that the majority of Europeans have adequate intakes for most nutrients. However, analysis of several national dietary surveys indicates the existence of important population groups with either suboptimal nutritional status or intakes below recommended levels for many vitamins, minerals and

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trace elements, notably for Fe, Ca, Zn, thiamin, riboflavin, vitamins B_6 and D and folate (De Groot *et al.* 1992; Bernier, 1995; Hallberg, 1995; Schneider *et al.* 1995; Van der Wielen *et al.* 1995; Hercberg *et al.* 1996; Brussaard *et al.* 1997; SCOOP Task 7.1.1 Working Group, 1997; Essama-Tjani *et al.* 2000; Gregory & Lowe, 2000; O'Brien *et al.* 2001). Several studies show evidence that mandatory and voluntary fortification can help to address the problem of at-risk populations (Department of Health, 1991; Gibson & O'Sullivan, 1995; Cuskelly *et al.* 1996; McNulty *et al.* 1996; Preziosi *et al.* 1999; Galvin *et al.* 2003; Gibson, 2003).

There is little evidence of over-consumption of micronutrients in European countries. Nevertheless, it is necessary to ensure that high food consumers are not placed at risk of over-consumption, whilst addressing the problem of micronutrient inadequacy. This concern is particularly relevant in the case of micronutrients with a relatively low margin between the recommended intake and measures of safe intake. For nutrients such as Fe, Ca and vitamin D there is risk of marked deficiency in several subgroups, and simultaneously the potential for high intakes in some individuals within the same population.

This apparent dichotomy is the main theme of the present paper.

Some milestones in food fortification

In 400 BC the Persian physician Melanpus suggested that Fe filings added to wine would increase the 'potency' of soldiers (Mejia, 1994).

In 1831 the French physician Boussingault recommended the addition of I to salt to prevent goitre. Fortification of salt with I was introduced in Switzerland in 1923 to prevent goitre and cretinism (Blum, 1997) and later introduced in Michigan, USA in 1924 (Sebrell, 1974). The dramatic fall in the prevalence of goitre that followed led to voluntary iodisation of salt throughout the USA (Lee *et al.* 1999).

In the UK vitamin A was first added to margarine voluntarily in 1927. This practice became mandatory, along with vitamin D, during the Second World War in order to achieve nutritional equivalence to butter. Currently in the UK all fat spreads have added vitamins A and D, and many also include vitamin E.

Between 1907 and the 1940s it is estimated that three million cases and 100 000 deaths resulted from an epidemic of pellagra in the USA, initially thought to be caused by infection. The Nobel Prize for medicine was awarded in 1929 for work in chickens demonstrating a nutritional aetiology. Voluntary enrichment of bread and other grain products with niacin was implemented in 1938. Mandatory fortification with niacin, thiamin, riboflavin and Fe followed in 1940. As a result pellagra had become almost non-existent by 1950 (Bollet, 1992; Lanska, 1996).

In 1998 the US Food and Drug Administration introduced mandatory addition of folic acid to enriched grain products (including bread, rolls, crackers, tortillas, pasta and rice), at a level of 1400 µg/kg product (Food and Drug Administration, 1996). The stated aim of adding folic acid was to reduce the occurrence of neural-tube defects in the newborn, with a secondary objective of reducing CVD and certain cancers (Choi & Mason, 2002). Initial results indicate that folate deficiency is currently declining and there has been a 19 % decrease in the number of births with neural-tube defects since the introduction of mandatory folic acid fortification (Honein *et al.* 2001). The incidence of elevated plasma total homocysteine, a biochemical marker of folate deficiency and a probable risk factor for CVD, has also declined. Preliminary evidence indicates that there has been no elevation of undetected vitamin B_{12} deficiency and its associated neuropathy, which is a hypothetical risk of widespread folic acid fortification (Mills *et al.* 2003).

Addition of nutrients to food

Food fortification is an important tool in helping populations meet their dietary requirements; however, it is by no means a panacea. Three approaches are currently employed to address micronutrient deficiencies: dietary diversification; supplementation; food fortification. Each of these approaches has different advantages and limitations.

Consumer education programmes to encourage changes in dietary patterns are possibly the best long-term solution. However, factors affecting food choice are complex, and therefore programmes to effect changes in dietary patterns may take a relatively long time.

Dietary supplements, on the other hand, have the potential to target specific risk groups very quickly. However, this approach relies on the ability to identify at-risk individuals and then motivate them to comply with the prescribed treatment. In addition, there are concerns about the relatively high micronutrient content of some food supplements, which can increase the risk of deliberate or accidental over-consumption.

Food fortification can provide relatively rapid solutions to address low micronutrient intakes at a population level, whilst maintaining traditional dietary patterns (American Dietetic Association, 2001; Serra-Majem *et al.* 2001). However, concerns need to be addressed in relation to the hypothetical risk of over-consumption in individuals outside the at-risk groups or those who choose to eat high amounts of fortified foods (Serra-Majem, 2001).

The addition of micronutrients to foods has been classified according to the purpose of the addition and the amounts added. The precise definitions and terms vary, but generally they are similar to those of the (UK) Expert Group on Vitamins and Minerals (2003), which used the following:

restoration: the replacement, either fully or partially, of nutrients lost during some stage of food production and distribution. Examples are the fortification of white flour with thiamin or Fe, or the addition of vitamin A to skimmed milk powder;

nutritional equivalence of substitute foods: the addition of one or more nutrients to a food that is intended as a substitute for another food in the diet. Examples are the addition of vitamins A and D to margarine and other spreads that replace butter;

fortification or enrichment: the addition of nutrients to levels above those normally present in that food. In some cases nutrients that are not normally present in that particular food may be added to that food;

mandatory fortification: the addition of specified nutrients to certain foods required by national legislation in most countries. In the UK this legislation includes the addition of vitamins A and D to spreads;

voluntary fortification: the addition of nutrients to foods, practised by food producers. Examples are the fortification of breakfast cereals and the addition of Ca to orange juice.

The regulatory status in Europe

The free movement of goods is a fundamental principle of the European Treaty (Articles 28 and 30; European Community, 2002). This regulation specifies that goods that are legally marketed in one country cannot be prohibited in another. However, national regulations governing the fortification of foods intended for general consumption still vary widely throughout the EU. Voluntary fortification has enjoyed a long and safe history in several member states (UK, Republic of Ireland, Spain, Portugal and Austria). In other member states (notably Denmark, Finland and Sweden) voluntary fortification is either severely restricted or disallowed. A recent review of regulations covering vitamin D fortification and supplements throughout Europe (Ovesen et al. 2003) illustrates the present national regulatory differences in this respect.

The European Court of Justice recently ruled that a prohibition on the grounds of public health may be justified on the basis of public health concerns, but Member States proposing the disallowance of voluntarily fortification must first provide a detailed assessment of the risks to human health based on sound science. The lack of nutritional need alone or other hypothetical considerations cannot be the main justifications for such a ban. The EC has recently proposed a draft regulation to harmonise fortification based on similar principles, i.e. safety rather than demonstrated nutritional need (Commission of the European Communities, 2003).

Prevalence of inadequate micronutrient intakes

Micronutrient intakes in European countries appear to be generally adequate for most nutrients. However, several population groups exhibit evidence of suboptimal intakes (De Groot et al. 1992; Bernier, 1995; Hallberg, 1995; Schneider et al. 1995; Van der Wielen et al. 1995; Hercberg et al. 1996; Brussaard et al. 1997; SCOOP Task 7.1.1 Working Group, 1997; Essama-Tjani et al. 2000; Gregory & Lowe, 2000; O'Brien et al. 2001). Examples that have particular public health importance include low intakes of folate, Fe, Zn and Ca in children, adolescents and young women (Hallberg, 1995; Brussaard et al. 1997; Gregory & Lowe, 2000).

Table 1 shows the percentage of the females who have intakes below the lower reference nutrient intake (LRNI), as reported in the UK National Diet and Nutrition Surveys (Gregory et al. 1995; Finch et al. 1998; Gregory & Lowe, 2000; Henderson et al. 2003). The LRNI is defined as the lowest amount of a nutrient estimated to be sufficient to meet the needs of the few individuals in the population (<2·5 %) who have very low requirements. Intakes below this amount will be insufficient for the majority of the population. Substantial proportions of teenage girls and adult women in the UK have intakes below the LRNI for several important micronutrients, notably vitamin A, riboflavin, Fe, Ca, Mg, K, Zn and I. The percentages of those aged 11–14 years who consume less than the LRNI for these micronutrients are: vitamin A 20, riboflavin 22, Ca 24, Zn 24, Fe 44, Mg 53. Similar percentages of 15–18-year-old girls have intakes below the LRNI. There are also low Fe intakes in the <4 year olds and women of child-bearing age, low Zn intakes in 4–6 year olds and low K intakes in adult men and women.

As a measure of inadequate intake the LRNI needs to be used with caution, because the intake of an individual may be associated with his/her requirement for each

Table 1. Percentage of British females below lower reference nutrient intake (data from UK National Diet and Nutrition Surveys; Gregory et al. 1995; Finch et al. 1998; Gregory & Lowe, 2000; Henderson et al. 2003)

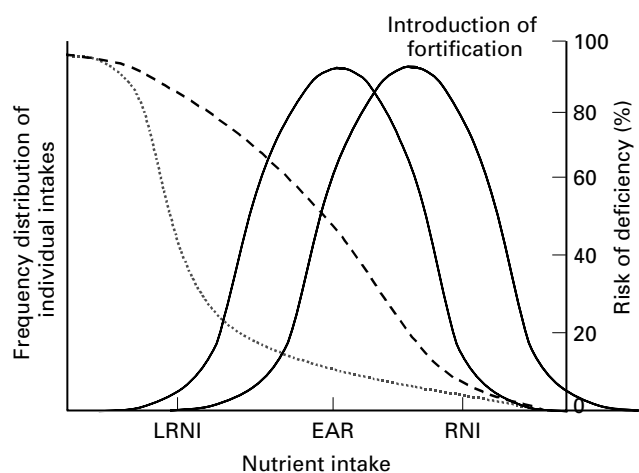| Age (years)	< 4	4–4·5	4–6	7–10	11–14	15–18	16–18	19–34	35–64	65+
Vitamin A	8	7	6	9	20	12	7	13	5	3
Thiamin	0	1	0	0	1	2		<1	<1	0
Riboflavin	0	0	0	1	22	21	9	12	5	9
Niacin	0	0	0	0	0	1				0
Vitamin B_6	1	5	0	0	1	5		7	1	2
Vitamin B_{12}	0	0	0	1	1	2	4	1	1	1
Folate	0	1	0	2	3	4	4	3	2	5
Vitamin C	1	1	0	0	1	0	0	0	0	1
Fe	16	4	1	3	44	48	33	40	23	5
Ca	1	2	2	5	24	19	27	7	5	9
P			0	0	0	1				0
Mg	0	2	1	5	51	53	39	21	9	23
K	0	1	0	1	19	38	30	30	13	39
Zn	14	37	26	10	37	10	6	5	3	5
I	3	5		3	13	10	4	9	3	6

Fig. 1. Dietary intakes and risk of deficiency. (—), Assuming the distribution of intakes is identical to the distribution of requirements; (- - -), risk with no adjustment; (····), estimated risk with adjustment. LRNI, lower reference nutrient intake; EAR, estimated average requirement; RNI, reference nutrient intake. (From Department of Health, 1991.)

Fig. 2. Distribution of total iron intakes for British girls aged 15–18 years compared with UK dietary reference values (lower reference nutrient intake (LRNI), estimated average requirement (EAR) and reference nutrient intake (RNI)). Mean 9 (sᴅ 3·75), *n* 207. Further analysis of data from the National Diet and Nutrition Survey of Young People Aged 4 to 18 Years (SA Gibson, unpublished results).

micronutrient (Department of Health, 1991). For example, individuals with low body weight are likely to have lower requirements as well as lower intakes (Fig. 1). However, such relatively high percentages indicate that a substantial proportion of individuals may be at risk of deficiency for one or more nutrients.

The consequences of inadequate Fe and Ca intakes in young people are of particular concern. Fe deficiency ultimately results in anaemia, but serious functional consequences may occur before anaemia is present (Hallberg, 1995). These consequences include adverse effects on work capacity, resistance to infection, intellectual performance and behaviour. As a further illustration of the magnitude of the inadequate intakes for some micronutrients, the distribution of intakes relative to reference values for Fe is shown in Fig. 2 for British girls aged 15–18 years.

The role of voluntary fortification

It has been estimated from household intake data (Ministry of Agriculture, Fisheries and Food, 2000) and the Confederation of the Food and Drink Industries of the European Union (1999) survey of fortified foods in Europe that in the UK diet mandatorily-fortified foods represent approximately 19% of the total energy intake (Table 2). These foods are mainly those made from white or brown flour, to which the following nutrients must be added by law (Act of Parliament, 1998; mg/kg): $CaCO_3$ 2350–3900, Fe minimum 16·5, thiamine 2·4, nicotinic acid 16. Margarines and spreads must, by law (Act of Parliament, 1995), also contain (μg/kg) between 8000 and 10 000 vitamin A and between 70·5 and 88·2 vitamin D.

Products that are voluntarily fortified provide a further 3% of the energy intake, predominantly breakfast cereals, but also some milk products and fruit juices. This value is in close agreement with those estimated for the Irish diet (3% of the energy intake; Flynn *et al.* 2003) and
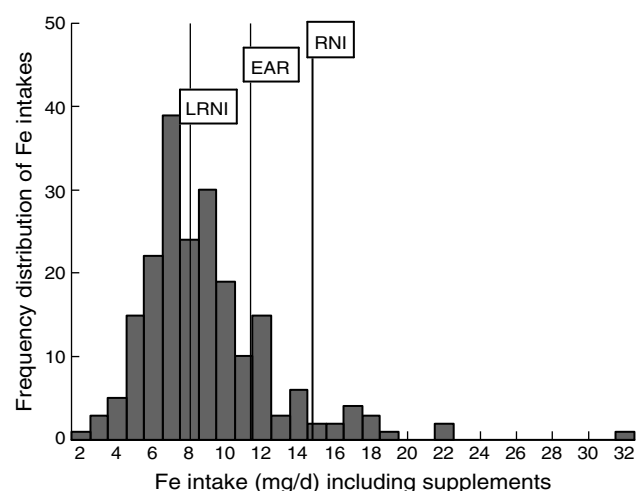
the French diet (5% of the energy intake; D Rigaud, I Giachetti, M Deheeger, J-M Borys, JL Volatier, A Lemoine and D Cassuto for l'Agence Française de Sécurité Sanitaire des Aliments, unpublished results). The low percentage of fortified foods in the diet is not surprising, considering the number of technological factors and other factors that place a constraint on foods appropriate to the purpose. Non-packaged foods such as fruits, vegetables, meat and fish bought fresh normally have no added ingredients. For processed foods, the constraining factors include: higher cost of ingredients, processing, quality control and routine analysis; adverse effects on sensory properties, taste, odour and appearance; reduced product shelf-life; nutrient stability, either in processing or during storage. For any added nutrient the technological problems increase as the proportion of the RDA included in the food is increased (Richardson, 1990, 1997). The stability of vitamins is susceptible to temperature, moisture, O_2, light, pro-oxidants, reducing agents, high and low pH, and metallic ions (Ottaway, 1995). These factors are found in most foods and food processes.

Most of the studies on the contribution of fortified foods to dietary adequacy have investigated breakfast cereals, probably because they comprise the major food group with voluntary fortification. Studies in several countries have reported a consistent positive association between micronutrient intakes and the level of breakfast cereal consumption (Gibson & O'Sullivan, 1995; McNulty *et al.* 1996; Ortega *et al.* 1996; Bertrais *et al.* 2000; Galvin *et al.* 2003; Gibson, 2003). Gibson (2003) has examined the UK National Diet and Nutrition Survey of Young People Aged 4 to 18 Years (Gregory & Lowe, 2000) for associations between breakfast cereal consumption and micronutrient intake. Girls and boys who eat an average of one portion of cereal daily (30 and 40 g respectively) have 20–60%

Table 2. The relative contribution to dietary energy intake of foods mandatorily restored or voluntarily fortified in the UK (from Ministry of Agriculture, Fisheries and Food, 2000 and Confederation of the Food and Drink Industries of the European Union, 1999)

			Energy contribution of foods			
	Contribution to dietary energy		Mandatorily restored		Voluntarily fortified	
Food group	kJ	kcal	kJ	kcal	kJ	kcal
Milk and milk products	780	187	–	–	15	3·7
Cheese	246	59	–	–	–	–
Meat and meat products	1096	263	–	–	–	–
Fish	117	28	–	–	–	–
Eggs	83	20	–	–	–	–
Fats	930	223	–	–	–	–
Of which: Butter	171	41	–	–	–	–
Margarine	159	38	159	38	–	–
Low-fat spreads	254	61	254	61	–	–
Vegetable oils	271	65	–	–	–	–
Sugar and preserves	405	97	–	–	–	–
Vegetables	826	198	–	–	–	–
Fruit	329	79	–	–	–	–
Of which: Fruit	171	41	–	–	–	–
Fruit juices	58	14	–	–	0·58	0·14
Cereals	2677	642	–	–	–	–
White bread	434	104	392	94	–	–
Brown and wholemeal bread	221	53	–	–	–	–
Cakes, pastries and biscuits	701	168	630	151	–	–
Breakfast cereals	279	67	–	–	209	50
Other foods	233	56	–	–	–	–
Soft drinks	188	45	Negligible	Negligible	Negligible	Negligible
Alcoholic drinks	117	28	–	–	–	–
Confectionery	154	37	–	–	6·3	1·5
Total food and drink	7723	1852	1435	344	234	56
Percentage of the total energy	100		18·6		3	

higher intakes of Fe, B-vitamins and vitamin D. Although fewer in number, studies investigating the micronutrient status also show a positive association between micronutrient status and intakes of fortified breakfast cereal, especially for B-vitamins (Preziosi *et al.* 1999). More recent analyses of national surveys in the UK (Gibson, 2003) and in Ireland (North/South Ireland Food Consumption Survey; Galvin *et al.* 2003) have shown similar associations between breakfast cereal consumption and micronutrient intake or status.

Given their relatively small contribution to the energy content of the UK diet, can voluntarily-fortified foods help to address the nutritional inadequacies discussed earlier? McNulty *et al.* (1996) were the first to show a reduced risk of micronutrient inadequacy in 12–15-year-old children who regularly consume breakfast cereals. Of the 12-year-old girls who consume one portion of breakfast cereals daily 13 % consume less than the LRNI for Fe (compared with 35 % for the non-consumers). Gibson (2003) has also found that children who consume the highest amount of breakfast cereals have a lower prevalence of intakes below the LRNI for Fe, K, Ca, riboflavin, folate and vitamin B_{12}, and have a better folate, vitamin B_{12} and riboflavin status than children who consume little or no cereal. However, Fe status shows no difference, probably because of the complexities of the inter-relationships between the form of Fe in cereals, meat and vitamin C intakes, and Fe absorption

(Gibson, 2003). In the North/South Ireland Food Consumption Survey (Hannon *et al.* 2001; O'Brien *et al.* 2001) fortified breakfast cereal consumption is associated with a higher nutrient density of the diet for Ca, Fe, thiamin, riboflavin and folate (Galvin *et al.* 2003). A number of intervention studies indicate that changes in intakes of fortified foods are reflected in changed status and functional effects for some micronutrients. A recent example is a randomised intervention trial by Tucker *et al.* (2004), which used breakfast cereal fortified with folic acid, vitamin B_6 and vitamin B_{12}, that shows not only increased serum concentrations, but also reduced homocysteine concentrations.

There is, therefore, a large body of evidence to indicate that voluntary fortification does play a valuable role in helping to reduce the prevalence of inadequate intakes (and possibly status) for several important nutrients.

The risk of over-consumption

Whilst there is evidence that food fortification can help address nutritional deficiency in some population groups, is there a risk of overnutrition in other population groups (e.g. potentially Fe in some groups of men)?

Tolerable upper intake levels (UL), also referred to as safe upper levels, are the reference standard for evaluating the risk of excessive intakes of individual micronutrients
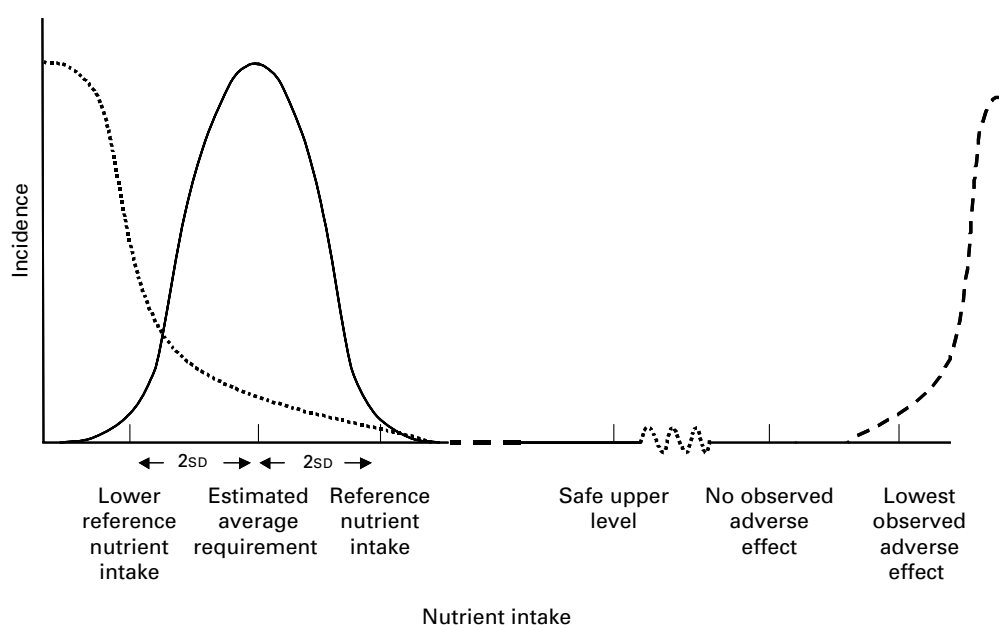
Fig. 3. Setting dietary reference values: the balance of the impact of risk at both ends of the intake scale. (···), Incidence of deficiency; (- - -), incidence of adverse effects.

(see Fig. 3). They are an estimate of the highest level of long-term intake that carries no risk to health in the general population. The (EU) Scientific Committee on Foods (2000) defines the UL as 'the maximum level of total chronic daily intake of a nutrient (from all sources, including foods, water, nutrient supplements and medicines) judged to be unlikely to pose a risk of adverse health effects to almost all individuals in the general population'. Comprehensive reviews and recommendations on UL have been undertaken recently in the USA (Institute of Medicine, 1997, 1998, 2000*a*,*b*, 2001), EU (since 2000 the Scientific Committee on Food have published a series of opinions on UL for individual vitamins and minerals; see http://europa.eu.int/comm/food/fs/sc/scf/out80_en.html) and the UK (Expert Group on Vitamins and Minerals, 2003).

For some nutrients the risk of excessive intakes is potentially high, whereas for others it is negligible, depending in each case on the margin between the daily requirement and the respective UL. Those nutrients that exhibit a narrow safety margin include vitamins A and D, Fe, P, Zn and Se. Individuals at greatest risk of exceeding the UL are those who consume large amounts of food, choose proportionally more fortified foods or take dietary supplements. The proportion of individuals at risk of excessive intakes can be estimated by comparing the 97·5 percentile intakes (i.e. the top 2·5 %) against the respective UL.

The UK National Diet and Nutrition Surveys report comprehensive data on percentiles of intakes for all micronutrients. Intake levels reported in each age and gender grouping are below the respective UL for virtually all nutrients, even at the 97·5th percentile level. The findings are the same for most nutrients with a narrow margin of safety. For retinol the US UL of 3000 µg/d (Institute of Medicine, 2001) is exceeded in some groups. However, this situation is mainly the result of high intakes of liver rather than fortified foods or dietary supplements.
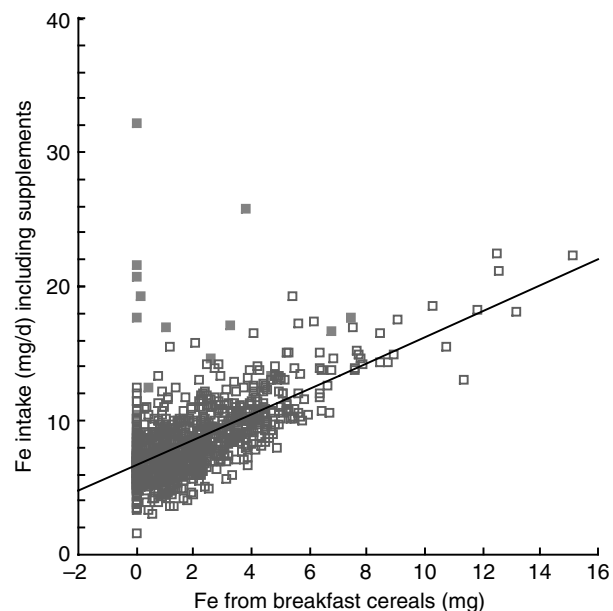

Fig. 4. Iron intakes from breakfast cereals and food supplements for girls. (■), Iron supplement; (□), no iron supplement; (- - - -), reference value. For the total population R^2 0·4090. (From the National Diet and Nutrition Survey of young people aged 4–18 years; S Gibson, unpublished results.)

Mean intakes compare favourably with the reference nutrient intake (Department of Health, 1991).

Using Fe as a specific illustration, consumers at the 97·5th percentile do not exceed 30 mg/d in any age group, and are well within the US UL of 40–45 g/d (Institute of Medicine, 2001) and the Scientific Committee on Food (see http://europa.eu.int/comm/food/fs/sc/scf/out80_en.html) maximum level of 30–100 mg/d. Fig. 4 shows a good

correlation between Fe intakes from breakfast cereals and total Fe from food in the diets of girls from the UK National Diet and Nutrition Survey of young people aged 4–18 years. Fe supplements, taken by 3 % of the sample, increase intakes above the mean, but in no case is the intake above the UL. Thus, on balance, the evidence indicates that there is not a major problem of excessive intake of micronutrients, including those with a narrow margin between the reference nutrient intake and UL.

Some studies have examined the risk of excessive micro-nutrient intakes in regular consumers of fortified foods. The Irish population has one of the highest *per capita* consumptions of fortified breakfast cereals (Kellogg Europe, unpublished results), and is therefore an excellent population in which to study this risk. The analysis by Galvin *et al.* (2003) of the dietary survey of Irish adults has shown a reduced percentage of individuals with intakes below the average requirement for Ca, Cu, Zn, riboflavin and vitamin C for both men and women. However, the top tertile of breakfast cereal consumers does not exceed the UL for any fortified nutrient. Furthermore, an earlier report (Kiely *et al.* 2001) has shown that all individuals in this study population who exceeded the UL for Fe and vitamin B_6 were consumers of nutritional supplements. This finding suggests that food fortification, as currently practised in Ireland, does not result in excess intakes. Thus, it would be reasonable to conclude that responsible fortification of the appropriate foods poses little or no risk to health at levels currently consumed, even in countries with high intakes.

The earlier discussion considers current diets only. If the practice of fortification were to become more widespread, would this pose an increased risk of over-consumption for vitamins and minerals with a low safety tolerance? Two mathematical models have recently been developed in order to estimate the level of nutrients that might be safely added to foods in the event that voluntary fortification practices become more widely practised. Flynn *et al.* (2003) have proposed an empirical model, based on food intakes from several national dietary surveys across Europe, to calculate the level of each micronutrient that could be safely added to foods in Europe. A number of scenarios have been envisioned at considerably higher hypothetical proportions of foods fortified than those in current UK and Irish practice. Factors of the model include: micronutrient intakes at the 95th centile level; proportion of fortified foods in the diets of consumers at the 95th centile of food energy intakes; the proportion of foods in the diet to which micronutrients could in principle be added; the types of foods that might in practice be fortified. The results indicate that for all reasonably feasible scenarios all micronutrients could be safely added at nutritionally-relevant levels without exceeding the UL, with the exception of vitamin A.

L'Agence Française de Sécurité Sanitaire des Aliments have also used a mathematical model to examine hypo-thetical fortification levels and different market shares of foods with added nutrients, based on actual intakes in the French population (D Rigaud, I Giachetti, M Deheeger, J-M Borys, JL Volatier, A Lemoine and D Cassuto for l'Agence Française de Sécurité Sanitaire des Aliments,

unpublished results), to study the same question. Several categories of foods were assumed to be technically or culturally unsuited to fortification, including unprocessed non-prepacked non-labelled products, products with a specific or traditional quality image and products with no energy value. The remaining foods used in the model represent 47 % of the energy in the French diet. The results obtained from the two studies are highly consistent.

A question of balance

As discussed earlier, increasing the level of specific nutrients in the general food supply has the potential to decrease the risk of inadequate intakes in one population subgroup, but simultaneously to increase the hypothetical risk of over-consumption in different proportions of the population. Folic acid is a good example of a nutrient for which there are demonstrated benefits of increased intakes in subpopulations (reduced neural-tube defects and possibly CVD) that may be addressed by food fortification or dietary supplements. Yet other subpopulations may not benefit, and could be at risk from increased intakes (the hypothetical risk of undetected vitamin B_{12} deficiency in the elderly).

No objective methods are available at present to enable the balancing of nutritional risks for both under- and overnutrition in the same population, partly because the yardsticks used for dietary assessment (reference nutrient intakes and UL) are largely based on tentative data, with little (if any) information on human dose response.

A multidisciplinary team involving both toxicology and nutrition experts has developed, in conjunction with the
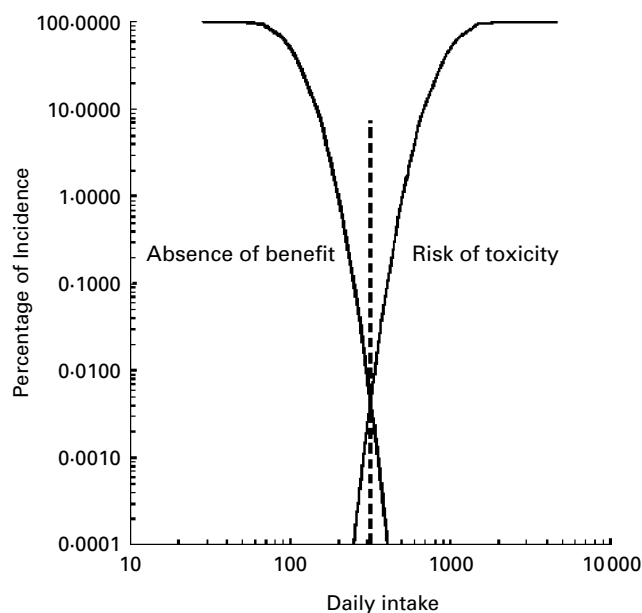

Fig. 5. International Life Sciences Institute risk–benefit analysis model. Dose–incidence relationships extrapolated to low incidences in order to define the optimum intake (---). The optimum nutritional intake would be the intake that maximises benefit and minimises toxicity when all variables have been taken into account. (From Renwick & Flynn, 2004; with permission from the International Life Sciences Institute Europe.)

International Life Sciences Institute, a methodology to assess and balance the impact of risk at both ends of the intake scale (Renwick & Flynn, 2004). The approach assumes that the range of acceptable intakes for a nutrient would be that which results in the lowest incidence of adverse health effects from either too low an intake (deficiency) or too high an intake (toxicity). Two dose–effect relationships therefore need to be considered (Fig. 5). Adverse effects as a result of nutritional deficiency are present at very low intakes, but decrease with increased intake. The adverse effects of excessive intake increase with an increase in dose. The curves for these two relationships (Fig. 5) represent the incidence of individuals 'at risk'. The minimal risk for the population as a whole is the mean nutrient intake at the point where both curves cross.

This continuous statistical approach to risk–benefit analysis has a number of advantages over current discrete methods. However scientific, societal and ethical judgements will always be important factors in risk management. Finally, such an approach suggests new approaches to the setting of dietary reference values, and has the exciting potential for application beyond classical nutrition.

Conclusions

During the last century voluntary fortification played a valuable role in reducing the occurrence of several nutrition-related health problems. Substantial proportions of the population, particularly susceptible groups such as young children, women of childbearing age and the elderly, continue to be at risk of low intakes or deficiency for one or more micronutrients, even in developed countries. Consumer education programmes to encourage changes in dietary patterns are a relatively long-term solution, as eating habits change slowly. Food fortification can be an immediate measure to help in addressing low micronutrient intakes at a population level, whilst maintaining traditional dietary patterns. A relatively small proportion of foods is currently fortified on a voluntary basis, because of technological constraints, commercial viability and consumer preferences. Hypothetically, an increase in the number of enriched foods for the general population has the potential to increase the risk of over-consumption in some subgroups. However, the evidence suggests that prevalence of excessive micronutrient intakes in current European diets is non-existent or extremely low, even for consumers choosing higher amounts of fortified foods. Diet-based models indicate that future increases in the proportion of foods fortified at levels between 10 and 50 % RDA/420 kJ (100 kcal) would not be expected to lead to excessive intakes for the majority of vitamins and minerals. A risk analysis based on sound scientific principles may be desirable under some circumstances, but, currently, tools to achieve this outcome in an objective manner are lacking. The application of statistical methods to risk–benefit (with considerable advantages over 'traditional' techniques) is being developed to help risk managers to identify optimal intakes that take into account the needs of subgroups at both ends of the consumption scale. Such statistical approaches also have potential for application.

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