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Coláiste na hOllscoile Corcaigh

Title: ***Modelling the impact of mandatory folic acid fortification of bread or flour in Ireland on the risk of occurrence of NTD-affected pregnancies in women of childbearing age and on risk of masking vitamin B12 deficiency in older adults.***

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Abstract

Purpose: The rate of neural tube defects (NTDs) in Europe has remained similar since the 1990's despite folic acid supplement recommendations (400µg/d) for women of childbearing age (WBCA). Mandatory folic acid fortification of staple foods has proved effective for reducing the prevalence of NTDs in over 80 countries. This study estimated the impact of addition of folic acid to bread or flour in the Republic of Ireland on reducing the risk of occurrence of NTD-affected pregnancies and the possible risk of masking (undiagnosed) vitamin B12 deficiency in older adults.

Methods: Analyses were based on the Irish National Adult Nutrition Survey (NANS) (2008-2010). Folic acid fortification was modelled using DaDiet© software. Estimates were made of the increase in average daily folic acid intake in women (18-50 years) and the risk of exceeding the Tolerable Upper Intake Level (UL) of 1,000µg for folic acid in adults over 50 years of age.

Results: The fortification scenarios examined would reduce the risk of NTD-affected pregnancies by 8–32%, corresponding to an increase of 39–152µg in the mean daily folic acid intake of WCBA. The risk of masking anaemia associated with vitamin B12 deficiency in older adults would be negligible as the probability of exceeding the UL for folic acid, even by a small amount, is very low (≤0·2%).

Conclusions: These levels of addition of folic acid to bread or flour would effectively reduce the risk of NTDs while allowing safe consumption of folic acid at current levels from other fortified foods and supplements.

Introduction

Neural tube defects (NTDs) including spina bifida and anencephaly result from failure of the neural tube to close during embryogenesis giving rise to serious congenital malformations of the central nervous system[1]. Ireland has long been recognised as having one of the highest rates of NTD-affected pregnancies worldwide[2]. It is well established that folic acid (the synthetic form of the B-vitamin folate) when taken prior to conception and for the first few weeks of pregnancy can prevent up to 70% of NTD-affected pregnancies[3]. Since the mid 1990's, Ireland along with many other developed countries has advised all women of childbearing age (WBCA) who are capable of becoming pregnant to consume 400µg of folic acid daily as a supplement[4-7]. However, this advice has had limited effectiveness on reducing the incidence of NTDs due to the high rate of unintended pregnancies worldwide[8] and also due to low compliance with periconceptual folic acid supplementation guidelines in WCBA[9-13].

Mandatory fortification of staple foods with folic acid is a feasible public health policy option for reducing the prevalence of NTDs. It can provide an advantage over supplementation and/or voluntary fortification as it is not dependent on individual choices but rather ensures a more even distribution of intake in the general population. To date, over 80 countries worldwide have legislated for the mandatory fortification of staple foods (e.g. flour or cereals) with folic acid reducing the prevalence of NTD-affected pregnancies by 16 - 78%[14-19]. In recent years, mandatory fortification of food staples with folic acid has been under consideration in some European countries (including Ireland and the UK) but to date has not been implemented in any despite a recent study highlighting that even with long standing supplementation recommendations and the existence of voluntary folic acid fortification the prevalence of NTDs has not decreased in Europe over a twenty-year period[20,5,13,21].

Some potential risks of long-term exposure to high dose folic acid in the population have been proposed[22-27]. However, based on the available evidence, the only adverse effect for which a causal relationship with folic acid intake has been established is the possible masking of (undiagnosed) vitamin B12 deficiency anaemia in older adults, allowing the associated irreversible neurological symptoms to progress[25,28-31,24,32,33].

The potential impact of mandatory folic acid fortification of food staples has been examined through dietary modelling studies in many countries[30,34,35,28]. In Ireland, the Food Safety Authority of Ireland (FSAI) recommended the implementation of mandatory fortification of bread with folic acid (120µg/100g) in 2006[20]. However, this was subsequently postponed due to a number of factors, including a reduction in the incidence of NTDs and improved folate status of Irish population groups, likely to be due to an increased voluntary fortification of foods with folic acid[36]. In 2011, data from the nationally representative Irish National Adult Nutrition Survey (NANS) (2008-2010) showed that foods that are voluntarily fortified with folic acid made important contributions to intakes of folate in WCBA[37], yet over two-thirds of WCBA did not have optimal folate status for NTD protection (≥907nmol/L) (median red blood cell (RBC) folate 799nmol/L)[38]. More recently there has been a significant reduction in the number of breads and fat-spreads that are voluntarily fortified with folic acid in Ireland and recent studies have suggested that the incidence of NTD-affected pregnancies may have increased from 2005-2006 to 2012-2015[20,39,40]. This has prompted renewed interest in the possibility of mandatory fortification of staple foods with folic acid to help reduce the incidence of NTD-affected pregnancies. Therefore, the aims of the current study were to estimate the impact of mandatory fortification of bread or flour with folic acid in the Republic of Ireland on first, reducing the risk of occurrence of NTD-affected pregnancies, and second, the possible risk of masking (undiagnosed) vitamin B12 deficiency in older adults.

Experimental methods

Sample recruitment and food intake data collection

Analyses for this study were based on data from the Irish National Adult Nutrition Survey (NANS), which was a cross-sectional survey conducted in the Republic of Ireland in 2008 – 2010 by the Irish Universities Nutrition Alliance (IUNA) units at University College Cork and University College Dublin to establish a database of habitual food and beverage consumption in a representative sample of 1500 adults aged between 18 and 90 years (men: *n*=760; women: *n*=740). A detailed overview on sampling and recruitment, food intake data collection and food quantification methods are outlined elsewhere[41,42,38,43]. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and ethical approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals, University College Cork [ECM 3 (p) 4 September 2008] and informed consent was obtained from all participants. Food and beverage intake data were collected using a 4-day semi-weighed food record as described in detail elsewhere[41,42,38,43]. For all participants, the study period included at least one weekend day. The final response rate for the survey was 60% (response rate calculated as: number of participants / (total contacted – ineligible) X100). Demographic analysis of the sample has shown it to be nationally representative of Irish adults with respect to age, gender, social class and geographical location when compared to Irish Census 2006 data[44].

Estimation of folate and folic acid intake at baseline

Total folate intake was estimated using data from McCance and Widdowson's The Composition of Foods, fifth and sixth editions plus all nine supplemental volumes as described elsewhere[41]. This dataset was updated to include recipes of composite dishes, nutritional supplements, fortified foods and generic Irish foods that were commonly consumed and new foods on the market[45]. To estimate folic acid intake, fortified foods and nutritional supplements containing folic acid were identified using the ingredients list on the label at the time of the survey. The folic acid composition of fortified foods and nutritional supplements was established from the food packaging labels or obtained directly from the manufacturer. The majority of manufacturers reported that the folate value on the nutrition label corresponded to the amount of total folate in the product (i.e. natural folate and added folic acid combined). The added folic acid content of fortified foods was therefore estimated as the difference between total folate content as declared on the label (where appropriate) and the natural folate content obtained from manufacturers or published food composition data for an unfortified equivalent. Due to the significant reduction in the number of breads and fat spreads voluntarily fortified with folic acid since the time of the survey (2008-2010), the food composition database was further updated in 2015 for these food categories. Dietary folate equivalents (DFE) were estimated using the following equation: 1µg DFE = 1µg food folate + (1.7*Folic Acid)[46]. As it is usual for manufacturers to include additional amounts of nutrients as 'overage' in fortified foods and supplements to allow for losses during processing and shelf life, all estimates of folic acid intakes factored in an overage of 25% compared to that declared on the label for voluntarily fortified foods and nutritional supplements. Seven individuals consuming supplements which contained levels of folic acid deemed to be medicinal (5000µg) were removed from the analysis.

Modelling scenarios

The modelling scenarios were conducted using DaDiet© (Version 15.05; Dazult Ltd, Co. Kildare, Republic of Ireland). The models included addition of folic acid to:

1) Selected breads at a level of 120μg/100g bread, as consumed, as recommended by the Irish National Committee on Folic Acid Food Fortification[20].
2) Selected breads at a level of 225μg/100g bread, as consumed, equivalent to the level of addition to flour recommended by the UK Scientific Advisory Committee on Nutrition[5].
3) All wheat flour at a level of 225μg/100g, as consumed as recommended by the UK Scientific Advisory Committee on Nutrition[5].

Further details on these scenarios are provided below:

Addition of folic acid to bread

For both bread models, all food codes relating to white, wholemeal and brown pan-breads and rolls and recipes containing white or brown bread in which the weight of bread contributed >10% of the total recipe weight were identified for inclusion. *(Breads excluded from the models were: white and brown soda breads, gluten free breads, pitta breads, scones, bagels, croissants, paninis, tortillas, bracks, currant breads, muffins, malt and rye breads and naan breads).* The amount of folic acid from mandatory fortification was calculated as follows:

Folic acid intake (μg) = 120μg folic acid / 100g x weight of bread consumed (g)

Folic acid intake (μg) = 225μg folic acid / 100g x weight of bread consumed (g)

For recipes, the proportion of the total weight made up by bread was estimated and the folic acid content for that proportion was calculated as *per* the above formula. Folic acid in breads that are currently fortified with folic acid voluntarily was removed (changed to 0μg) for the bread models.

Addition of folic acid to flour

For flour, food groups which were contributors to wheat flour in the diet were identified and included breads, biscuits, savouries, cakes, pastries, buns, sponge and other cereal-based puddings. The amount of wheat flour per 100g of each food was estimated from the starch content of the food based on the assumption that all the starch content came from flour and that 1g of flour contains 0.762g of starch[47]. The amount of flour was calculated for each food as follows:

Flour content (g) = starch content (g) / 0.762

The amount of folic acid from mandatory fortification was calculated for each food as follows:

Folic acid intake (μg) = 225μg / 100g x weight of flour consumed (g)

Folic acid in flour-containing foods that are currently fortified with folic acid voluntarily was removed (changed to 0μg) for the flour model.

Four scenarios were created and assessed for all bread and flour models **(Table 1)**

A) Intakes of folic acid were examined from mandatory fortification of bread or flour including folic acid intake at current levels from voluntarily fortified foods and nutritional supplements.
B) Intakes of folic acid were examined from mandatory fortification of bread or flour and included folic acid intake at current levels from nutritional supplements but excluding folic acid from voluntarily fortified foods.
C) Intakes of folic acid were examined from mandatory fortification of bread or flour and included folic acid intake at current levels from voluntarily fortified foods but excluding folic acid from nutritional supplement use.
D) Intakes of folic acid were examined from mandatory fortification of bread or flour only excluding all other sources of folic acid.

Estimation of usual intakes

Usual intake distributions of folic acid were estimated using the validated National Cancer Institute (NCI)-Method[48] using SAS Enterprise Guide© Version 6.1 (SAS Institute Inc., Cary, NC, USA). The NCI-method has been implemented in SAS macros (version 2.1) which were downloaded from the website www.riskfactor.gov/diet/usualintakes/macro.html (date of download: July 2015). The NCI-method calculates usual intake based on non-linear mixed regression models. The model separates usual intake into two parts: the probability to consume a food or nutrient on a particular day, and given that the food/nutrient was consumed, the amount eaten on the consumption day. In addition to the correction for within-person errors in the dietary data, the statistical model includes a random effect to account for person-specific errors. This method results in a better estimate of the true distribution of usual intakes of nutrients with shorter tails at the upper and lower ends therefore improving the estimates of the proportions of the population with intakes above or below a particular reference value (e.g. EAR or UL) which would otherwise be overestimated.

Estimation of reduction in risk of occurrence of NTD-affected pregnancies in women aged 18 – 50 years

Estimates were made of the reduction in risk of occurrence of NTD-affected pregnancies based on the increase in average daily folic acid intake from fortified bread or flour in women aged 18 – 50 years (*n* 485). The studies of Daly *et al*[49] and Daly *et al*[50] were used to relate the additional intake of folic acid to the reduction in risk of NTDs (established through a continuous relationship with maternal RBC folate levels). Based on the observations provided by Daly *et al* for 100µg and 200µg supplements of folic acid, an additional intake of 100µg folic acid corresponds to a reduction in risk of NTDs of 22% and an additional intake of 101 - 200µg folic acid corresponds to a further reduction in risk of NTDs of 19%.

Assessing the possible risk of masking anaemia associated with (undiagnosed) vitamin B12 deficiency in older adults

The possible risk of masking of megalobalstic anaemia associated with (undiagnosed) vitamin B12 deficiency in older adults was assessed from the probability of exceeding the Tolerable Upper Intake Level (UL) of 1000µg for folic acid[51] based on the total intake of folic acid in men and women aged over 50 years (*n* 527), together with the magnitude of any possible excess above the UL. For each fortification scenario the increase in the % > UL and the 95th and 99th percentile of folic acid intake were calculated for adults aged >50 years. In addition, intakes of folic acid in the highest consumers were examined to estimate the magnitude of any possible excess above the UL.

Results

Usual distribution of folate intakes at baseline

The distribution of usual intakes of total folate, natural folate, folic acid and dietary folate equivalents (DFE) in women of child bearing age (WCBA) (18 – 50 years) and older adults (>50 years) at baseline is presented in **Table 2.** Mean dietary intakes of total folate, natural folate, folic acid and DFE were 308, 195, 114 and 385µg/d, respectively, in WBCA and 347, 237, 111 and 421µg/d, respectively, in older adults. Overall 74% of WCBA consumed folic acid from voluntarily fortified foods (70%) or nutritional supplements (16%) with a mean intake of 63 and 51µg/d, respectively. Foods voluntarily fortified with folic acid consumed in the NANS are presented in **Supplementary Table 1**. For older adults, 66% consumed folic acid from voluntarily fortified foods (61%; mean 72µg/d) or nutritional supplements (13%;

mean 40μg/d). The 95th percentile intake of total folic acid was 427 and 409μg/d for WCBA and older adults, respectively.

Impact of mandatory folic acid fortification of bread or flour on usual folic acid intakes in women of childbearing age (WCBA)

The impact of mandatory fortification of bread or flour on folic acid intakes and reduction in NTD risk in WCBA is presented in **Table 3.** At baseline, 74% of WCBA consumed folic acid from voluntarily fortified foods and/or nutritional supplements (mean intake; 114μg/d). All scenarios involving the mandatory folic acid fortification of bread or flour would increase the proportion of WCBA consuming folic acid to 90 - 99% with the greatest increase observed for the bread models 120A and 120C (96%), 225A and 225C (96%) and all flour models (99%). For the bread 120A-D models, the greatest effect on mean intake of folic acid in WCBA would be observed for bread120A resulting in an increase of 77μg/d, equivalent to a reduction in risk of NTD-affected pregnancies by 17%. The exclusion of folic acid from voluntarily fortified foods or nutritional supplements (Bread120B-C models) would result in smaller reduction in risk of NTD-affected pregnancies (3 to 6%) while exclusion of folic acid from both voluntarily fortified foods and nutritional supplements (Bread120D) would result in increased risk of NTD-affected pregnancies (7%) highlighting the important contribution of currently voluntarily fortified foods and supplements to folic acid intake in this population group. For the bread225 and flour225 models examined, bread225A and flour225A would reduce the risk of NTD-affected pregnancies by 31 and 32%, respectively, equivalent to an increase of 148 and 152μg folic acid/d in WCBA. For both bread225 and flour225 models, exclusion of folic acid from voluntarily fortified foods, nutritional supplements or both would result in smaller reductions in risk of NTD-affected pregnancies (19, 21 and 8%, respectively for Bread225B-D) and (20, 22 and 9%, respectively for Flour225B-D).

Impact of mandatory folic acid fortification of bread or flour on usual folic acid intakes in older adults (>50 years)

The impact of mandatory fortification of bread or flour on folic acid intakes and the proportion of older adults with intakes greater than the UL is presented in **Table 4.** At baseline, 66% of older adults consumed folic acid from voluntarily fortified foods and/or nutritional supplements (mean intake; 111μg/d) with 0.1% having intakes above the UL. All modelling scenarios would increase the number older adults consuming folic acid to 92 -100%. However, for all scenarios the probability of exceeding the UL for folic acid, even by a small amount is very low (≤0.2%). The magnitude of any possible excess intake of folic acid above the UL would be small, given the patterns of folic acid intake observed in the highest consumers. P95 and P99 intakes of folic acid did not exceed 623 or 822µg/d, respectively, for any fortification scenario examined. The highest consumption of folic acid in these fortification scenarios was mainly associated with use of multiple supplements and supplements containing 400µg folic acid per daily amount. Thus, the risk of masking anaemia associated with (undiagnosed) vitamin B12 deficiency would be negligible.

Discussion

This study examines the potential impact of mandatory folic acid fortification of bread or flour in the Republic of Ireland on reducing the risk of occurrence of NTD-affected pregnancies in WCBA and also on the possible risk of masking (undiagnosed) vitamin B12 deficiency anaemia in older adults. The main finding was that the levels of addition of folic acid to bread or flour examined in this study would significantly reduce the risk of NTD-affected pregnancies while allowing safe consumption of folic acid for older adults at current levels of intake from other foods voluntarily fortified with folic acid and from nutritional supplements.

Of the scenarios examined in this study the mandatory fortification of bread or flour with 225µg folic acid/100g while maintaining current voluntary fortification and nutritional supplement practices would provide the greatest benefit (increased intake of 148 and 152µg of folic acid daily for WCBA), reducing the risk of occurrence of NTD-affected pregnancies by 32 and 33%, respectively. For all scenarios examined, exclusion of folic acid from voluntarily fortified foods, nutritional supplements or both would result in smaller reductions in risk of NTD-affected pregnancies highlighting the importance of voluntarily fortified foods and nutritional supplements. It is estimated that current folic acid intake from voluntarily fortified foods and nutritional supplements reduce the risk of NTD-affected pregnancies by about 14% and 11%, respectively. The potential benefit for NTD reduction of mandatory folic acid fortification of food staples has been shown using similar modelling studies in Ireland and other countries[20,25,28,30,34,35].

The risk of masking anaemia associated with (undiagnosed) vitamin B12 deficiency in older adults would be negligible for all scenarios examined as the probability of exceeding the UL for folic acid, even by a small amount, is very low (≤0.2%). This conclusion is supported with data from the US where there is no evidence of a higher prevalence of vitamin B12 deficiency in the absence of anaemia or macrocytosis among a nationally representative sample of US adults >50 years from exposure to higher levels of folic acid in fortified foods after mandatory folic acid fortification[52]. Other possible adverse effects of folic acid fortification of foods have been proposed, including cognitive decline in older adults, cognitive development in children, increased risk of some cancers (e.g. prostate, breast, colorectal), diabetes-related disorders and potential adverse effect of increased circulating unmetabolised folic acid. However, available evidence for these effects is weak and inconsistent and insufficient to establish causal relationships at intakes of folic acid associated with mandatory fortification of foods[25,28-31,24,32,33]. Nevertheless, further research has been recommended to address remaining uncertainties.

Worldwide, the mandatory fortification of food staples with folic acid has been a successful strategy for reducing the prevalence of NTD-affected pregnancies by 16-78%[14-19]. A recent systematic review and meta-analysis has reported that areas with mandatory folic acid fortification have 30-33% lower NTD-affected pregnancies than areas with voluntary fortification[53]. Despite this, mandatory legislation enforcing folic acid fortification of the food supply lags behind in some regions and it is estimated that just 15-25% of the possible folic acid preventable NTD cases are prevented by mandatory folic acid fortification worldwide[53,54]. Within Europe mandatory fortification of bread or flour with folic acid has not yet been implemented in any country but has been recommended in the UK, Ireland, Norway, the Netherlands, Germany and France but not in Italy [28,55,30,56-59]. A common conclusion for all countries was that a continued recommendation for WCBA to consume a daily supplement of 400μg folic acid prior to conception and until the twelfth week of pregnancy would be necessary.

The key strengths of this study are the nationally representative sample included in the NANS and the comprehensive dietary intake and food composition data (including brand level detail) which allowed for the estimation of natural and synthetic folate intakes from fortified foods and nutritional supplements. The food composition database was also updated in 2015 to account for changes in voluntary fortification practices since the time of the survey. Furthermore, this study factored in an overage of 25% compared to that on the label for voluntarily fortified foods and nutritional supplements to account for additional amounts added by manufacturers to allow for losses during processing and shelf life. Another important strength is the use of statistical modelling to estimate the ‘usual intakes’ of folate and its derivatives, resulting in a better estimate of the true distribution of usual intakes with shorter tails at the upper and lower ends therefore improving the estimates of the proportions of the population with intakes above or below a particular reference value (e.g. EAR or UL) which would otherwise be overestimated. Misreporting or under reporting of energy intake, is a known limitation with all dietary assessment; this issue was minimised by a high-level of researcher-participant interaction by trained nutritionists. Potential under reporters were not excluded from this analysis as we found that their exclusion did not increase the proportion of the population exceeding the UL (data not shown).

In conclusion, this study has shown that mandatory fortification of bread or flour with folic acid in Ireland would substantially reduce the risk of occurrence of NTD-affected pregnancies while allowing safe consumption of folic acid for older adults at current levels of intake from other foods voluntarily fortified with folic acid and from nutritional supplements. As with any public health programme, this policy would require careful monitoring of the food supply and dietary patterns within the population and should be reviewed on a regular basis for efficacy and safety as new evidence arises.

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Table 1. Folic acid modelling scenarios

Fortification scenarios	Mandatory fortification folic acid µg/100g bread/flour	Folic acid from voluntary fortification	Folic acid from supplement use
Bread120 A	120	Included[‡]	Included
Bread120 B	120	Excluded	Included
Bread120 C	120	Included[‡]	Excluded
Bread120 D	120	Excluded	Excluded
Bread225 A	225	Included[‡]	Included
Bread225 B	225	Excluded	Included
Bread225 C	225	Included[‡]	Excluded
Bread225 D	225	Excluded	Excluded
Flour225 A	225	Included[ȣ]	Included
Flour225 B	225	Excluded	Included
Flour225 C	225	Included[ȣ]	Excluded
Flour225 D	225	Excluded	Excluded

[‡] With the exception of voluntarily fortified breads.

0 [ȣ] With the exception of voluntarily fortified flour products.

Table 2. Distribution of usual dietary intakes of total folate, natural folate, folic acid and dietary folate equivalents in women of child bearing age (WCBA) (18-50y) and older adults (>50 years) from all sources, fortified foods and nutritional supplements at baseline*

Dietary intakes (µg/d)	WCBA‡ (18-50 years) (*n* 485)					Older adults (>50 years) (*n* 527)				
	% Consumers	Mean	5th	50th	95th	% Consumers	Mean	5th	50th	95th
Total folate	100	308	110	281	600	100	347	132	318	661
Natural folate	100	195	113	190	295	100	237	136	229	365
Total folic acid	74	114	0.5	53.8	427	66	111	0.0	51.1	409
Folic acid - fortified foods	70	63.0	0.7	36.7	211	61	71.9	0.0	31.2	268
Folic acid - supplements†	16	51.5	0.0	0.0	500	13	39.6	0.0	0.0	375
Dietary folate equivalents	100	385	110	331	843	100	421	128	366	905

*Baseline data includes 25% overage for fortified foods and nutritional supplements

‡WCBA: Women of child bearing age

†Usual intakes of folic acid from supplements could not be calculated via the NCI-method due to the limited number of dietary records with a positive value on more than one recording day; distribution presented from mean daily intakes over the 4 recording days

% consumers: proportion of the population consuming nutrient at least once in the recording period.

Table 3. Impact of mandatory fortification of bread or flour on folic acid intakes (µg/d) and reduction (%) in NTD risk in women of child bearing age (WCBA) (*n* 485)

	Consumers	Mean	Increase	NTD Reduction
	%	µg/d	µg/d	%
Baseline*	74	114	-	-
Bread120 A	96	191	77	17
Bread120 B	92	127	13	3
Bread120 C	96	141	27	6
Bread120 D	90	80	-34	-7
Bread225 A	96	262	148	31
Bread225 B	92	200	86	19
Bread225 C	96	211	97	21
Bread225 D	90	149	35	8
Flour225 A	99	266	152	32
Flour225 B	99	204	90	20
Flour225 C	99	215	101	22
Flour225 D	99	153	39	9

* Baseline data includes 25% overage for fortified foods and nutritional supplements. A: Including folic acid intake from voluntarily fortified foods and nutritional supplements, B: Effect of exclusion of folic acid from voluntarily fortified foods, C: Effect of exclusion of folic acid from nutritional supplements, D: Effect of exclusion of folic acid from all voluntarily fortified foods and nutritional supplements.

% consumers: proportion of the population consuming nutrient at least once in the recording period.

Table 4. Impact of mandatory fortification of bread or flour on folic acid intakes (µg/d) and % with intakes > UL in older adults (*n* 527)

	Consumers	Mean	95th	99th	> UL
	%	µg/d			%
Baseline*	66	111	409	681	0.1
Bread120 A	97	210	489	695	0.1
Bread120 B	93	139	342	499	0.0
Bread120 C	95	171	369	505	0.0
Bread120 D	92	101	206	263	0.0
Bread225 A	97	300	623	822	0.2
Bread225 B	93	229	501	670	0.0
Bread225 C	95	260	517	667	0.0
Bread225 D	92	190	386	493	0.0
Flour225 A	100	289	592	774	0.1
Flour225 B	99	218	455	594	0.0
Flour225 C	100	249	477	604	0.0
Flour225 D	99	179	328	408	0.0

* Baseline data includes 25% overage for fortified foods and nutritional supplements. A: Including folic acid intake from voluntarily fortified foods and nutritional supplements, B: Effect of exclusion of folic acid from voluntarily fortified foods, C: Effect of exclusion of folic acid from nutritional supplements, D: Effect of exclusion of folic acid from all voluntarily fortified foods and nutritional supplements.

% consumers: proportion of the population consuming nutrient at least once in the recording period.

Supplementary Table 1. Folic acid fortified foods (*n*, %) consumed in the National Adult Nutrition Survey

Food group	Number of foods fortified per group	Total foods in food group	% of foods fortified with folic acid per food group
Cereals			
Ready-to-eat breakfast cereals	82	101	81
Hot oat, museli and granola type cereals	3	65	5
Cereal bars	28	65	43
Bread and rolls‡	6	326	2
Beverages			
Low fat & skimmed milks	11	67	16
Whole milk	3	46	7
Fruit juices	6	147	4
Other beverages*	11	31	35
Packet & tinned soups	21	95	22
Butter & fat spreads‡	5	111	5
Yoghurts	7	267	3

‡ Due to the significant reduction in voluntary folic acid fortification of breads and fat spreads with folic acid since the time of the survey (2008 – 2010) the 2015 composition is used for these food groups.

* Powdered beverages, beef & yeast extracts & food supplements.