STOCHASTIC MODELLING TO ESTIMATE THE POTENTIAL IMPACT OF FORTIFICATION OF FLOUR WITH FOLIC ACID IN THE UK

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FINAL REPORT

31 July 2017

This project was commissioned by Food Standards Scotland and funded by Food Standards Scotland, Scottish Government, Welsh Government and the Food Standards Agency in Northern Ireland.

Acknowledgements

Professor Paul Haggarty, University of Aberdeen, who provided advice and expertise on the methodology for assessing NTD risk reduction.

Rufina Acheampong, Food Standards Agency, who provided pre-publication access to their database on flour contents of food.

Gillian Swan, Public Health England, who provided pre- publication access to the NDNS data and the UK Nutrient databank.

Mamta Singh and Rachel Stratton, Public Health England, who provided advice to Food Standards Scotland on the methodology.

Anne Milne and Evie Nikokavoura, Food Standards Scotland, who provided key literature sources, support and guidance throughout the preparation of this report.

Altea Lorenzo-Arribas, who helped with the analysis of the folate status data.

Contents

1 Summary

Background

Folate and folic acid intake during pregnancy has been known for some time to have a protective effect against the development of neural tube defects (NTDs). In the UK, the Scientific Advisory Committee on Nutrition (SACN) published a comprehensive report on Folate and Disease Prevention in 2006 which summarised the scientific evidence relating to mandatory folic acid fortification and discussed the wider potential impact of such a scheme. An important part of that report was a modelling exercise that used data available at the time on dietary intakes from the National Diet and Nutrition Survey (NDNS) and estimates of the wheat flour content of food items to calculate folic acid intakes for different subgroups of the population under a number of different mandatory fortification scenarios. In 2007/8 the Food Standards Agency (FSA) undertook an update of this modelling, using additional levels of folic acid, and considering the fortification of bread flour as well as wheat flour.

In 2016, Food Standards Scotland (FSS) commissioned the current update of the modelling using the latest available data and modelling techniques to inform the possibility of introducing mandatory fortification of wheat flour. The updated modelling in principle followed a similar strategy as the modelling in the 2006 SACN report and an update to the modelling by FSA in 2007/8 to look at the effect of different fortification scenarios on folate and folic acid intakes and the reduction in risk of neural tube defects for pregnant women.

Methods

Three main data sources were used in the modelling of intakes: 1) intake data from years 1 to 6 (2008/9-2013/14) of the NDNS rolling programme (NDNS RP), 2) up to date information about the folate content of food items in the NDNS nutrient databank (from years 7 and 8 (2014/15 & 2015/16)), 3) data provided by the Food Standards Agency[1] (FSA) on wheat flour content of foods in the NDNS dataset. Integrating these three data sources allowed assessment of current folate (natural folate and folic acid) intake of the population and modelling of the effect of different mandatory fortification scenarios.

We estimated the effect of these fortification scenarios on risk of neural tube defects in pregnant women. We did this by first studying NDNS data on blood folate status and its association with individual intake. This enabled us to predict the blood folate response to the different scenarios for each individual. We then used an established association between blood folate status and neural tube defect risk to predict the effect of these changes on the average risk among women of childbearing age.

As with the previous 2006 and 2007/8 modelling, the effect of fortifying flour (all non-wholemeal wheat flour or bread flour only) with different doses of folic acid (0µg, 100µg, 200µg, 250µg, 300µg, 350µg, 450µg per 100g of flour) was modelled focussing on:

- Intakes of total folate (natural and folic acid)
- Proportion of the population with total folate intakes below the Reference Nutrient Intake (RNI)
- Proportion of the population who might be exposed to intakes of folic acid above the tolerable upper intake level (UL) (SACN, 2006)

[1] available within the UK Data Service Archive at URL: https://discover.ukdataservice.ac.uk/catalogue?sn=8159

- Number of people aged 65 years and over with low vitamin B_{12} status who might be exposed to intakes of folic acid above the recommended upper limit
- Risk of NTD-affected pregnancies

The impact of placing a limit on the levels of folic acid in voluntarily fortified foods and supplements was also assessed by considering the following capping options:

- Capping breakfast cereals at 15% of adult RNI per 100g (30µg/100g)
- Capping, spreads at 15% of adult RNI per 100g (30µg/100g)
- Capping supplements at 200µg/day (600µg/day for women aged 14-49 years)

Following the analysis, it was noted that the capping level for spreads used in the modelling (30µg/100g) may not allow a 'source of' nutrient claim to be made. The basis for expressing 'source of' nutrient content claims for products consumed in small quantities is per-portion which could be 10-20g for spreads, rather than 100g. A capping at 15% of adult RNI per portion (e.g. 200µg/100g) may therefore be more realistic. We did run the analysis for this setting too but due to the relatively small contribution spreads make to folic acid intake (see Table 2) the changes are marginal and we will not present results for this scenario in this report.

In order to consider the impact of various fortification scenarios on intakes in different groups of the population, the modelling was conducted for various age and sex subgroups, with a more detailed analysis for women of childbearing age.

The strengths of the current study are that more comprehensive data were available to us than was the case in previous studies. We had access to: a larger set of intake data; to more detailed information on the flour content of different foods; and to blood folate status data in the same sample as the intake data that were modelled.

Results

Detailed results for different fortification levels and scenarios are presented. Three different fortification strategies were considered: fortification through wheat flour in bread in two different bread definitions and fortification of all wheat flour. Each of these can be combined with a scenario of capping folic acid in breakfast cereals, spreads or supplements. Fortifying all wheat flour (excluding wholemeal) rather than bread only would lead to a considerably larger effect on both intake and NTD risk. Capping folic acid in supplements would eliminate much of the adverse effect of greater numbers of people being above the tolerable upper intake level. Very few individuals over 65 who appear deficient in B_{12} would have excess intakes. Reductions in NTD risk of 20-25% can be obtained with the highest fortification levels, and these are only slightly reduced by capping scenarios.

2 Background

Folate and folic acid intake during pregnancy has been known for some time to have a protective effect against the development of neural tube defects (NTDs) in the offspring (SACN, 2006). Some countries like the USA and Canada have introduced mandatory fortification of wheat flour with folic acid for this reason (Crider et al, 2011; Food Fortification Initiative, 2016). Though evidence shows that this has benefitted pregnant mothers and led to a reduction of neural tube birth defects, there are also concerns that an increased folic acid intake might have a negative impact on others in the population; for example there is a concern that vitamin B_{12} deficiency in older people might be masked by high folic acid levels (SACN, 2006). Though many European countries have looked into the possibility of mandatory folic acid fortification, up until now none of them have implemented it (Food Fortification Initiative, 2016).

In the UK, the Scientific Advisory Committee on Nutrition (SACN) published a comprehensive report on Folate and Disease Prevention in 2006 which summarised the scientific evidence relating to mandatory folic acid fortification and discussed the wider potential impact of such a scheme. An important part of that report was a distributional modelling exercise that used data available at the time on dietary intakes from the National Diet and Nutrition Survey (NDNS) and estimates of the wheat flour content of food items to calculate folic acid intakes for different subgroups of the population under a number of different mandatory fortification scenarios. The modelling included a range of fortification scenarios with different levels of folic acid and included scenarios where folic acid from voluntarily fortified foods (breakfast cereal, spreads) and supplements were excluded. In 2007/8 the Food Standards Agency (FSA) undertook an update of this modelling, using additional levels of folic acid, and considering the fortification of bread flour as well as wheat flour. The more recent modelling included scenarios where folic acid from voluntarily fortified foods and supplements were capped rather than excluded.

In 2016, Food Standards Scotland (FSS) commissioned stochastic modelling using the latest available data and modelling techniques to inform the possibility of introducing mandatory fortification of wheat flour. The updated modelling in principle followed a similar strategy as the modelling in the 2006 SACN report and an update to the modelling by FSA in 2007/8 and was carried out on a UK basis.

Folate(s) is the generic term used to refer to various chemical forms of a family of water-soluble B-group vitamins. Total folate in the diet includes both naturally occurring folates found within foods and folic acid (pteroyl-monoglutamic acid) a synthetic form used in supplements and food fortification. Rich sources of natural folates include liver, yeast extract and green leafy vegetables (Department of Health, 1991; SACN, 2006).

Synthetic folic acid is more stable in foods and is more readily absorbed than naturally occurring food folate. When folic acid is consumed as a supplement without food, it is nearly 100% bioavailable. In contrast, naturally occurring folate is approximately 50% bioavailable. When folic acid is consumed with food, as is the case with fortified food products, its absorption is reduced and it is estimated to be approximately 85% bioavailable. Thus, folic acid taken with food (which includes folic acid added to food during fortification) is considered to be 1.7 times more bioavailable than natural folate and this factor is used in some countries such as the USA to calculate dietary folate equivalents (DFEs) (Suitor & Bailey, 2000).

SACN recommends that all women planning pregnancy should take 400 μg folic acid daily as a supplement before conception and until the 12th week of pregnancy to reduce the risk of a neural-tube defect (NTD) affected pregnancy. Although this has been shown to prevent NTDs, most women do not take the recommended supplement. Thus, mandatory fortification was recommended for implementation in the UK in 2006.

Currently, the average total prevalence of NTDs for the whole UK (2010- 2014) as provided in the European Surveillance of Congenital Anomalies (EUROCAT) is 1110 or 1043 NTD affected pregnancies per year depending on whether genetic cases are included. This equates to a rate per 1,000 births of around 1.3 or 1.2 NTD affected pregnancies[2] .

Not all NTDs can be prevented by increasing the intake of folic acid. Genetic factors prevent normal metabolism of folic acid in the body and increase risk of an NTD affected pregnancy in some people. Other maternal conditions, including diabetes (type 1 and type 2), obesity and epilepsy and some drugs used to treat epilepsy, increase the risk through their effect on folate metabolism. Based on a blood folate status of 1180 nmol/L, the World Health Organisation (WHO) report refers to a lowest level of risk of 0.6 cases per 1,000 births (Crider, 2014). Daly et al (1995) says that there is no further reduction in risk beyond a red cell folate value of 1292 nmol/L, which is equivalent to 0.83 per 1,000 births.

The size of the reduction in rates of NTDs with fortification will be lower in countries with a lower baseline prevalence of NTDs (Heseker et al, 2008). Prevalence rates will also depend on the ability to capture information on NTD cases using prenatal information including elective terminations. In the USA, there was a 28% reduction in NTD rates from 10.6 to 7.6 NTD per 10 000 births (including NTD-affected live births and stillbirths) between the pre-fortification period (1995–1996) and post-fortification period (1999–2000) (Williams et al, 2005). Canada, South Africa, Costa Rica, Chile, Argentina, and Brazil also have reported declines in NTDs (19%–55%) since the initiation of folic acid food fortification (Crider et al, 2011).

The dietary modelling estimates intakes of folate and folic acid following different scenarios of wheat flour fortification. It is then necessary to consider how this will change the risk of an NTD affected pregnancy for women of childbearing age.

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[2] In EUROCAT, total prevalence of NTDs includes live births, stillbirths and fetal deaths from 20 weeks gestation with a NTD, and termination of pregnancy for fetal anomaly following prenatal diagnosis of a NTD.

3 Methods

In this study we looked at two effects of fortification. The first was on the distribution of natural folate and folic acid intakes following different fortification scenarios. We report the mean and median intake in the population, and in age and gender subgroups, and the proportion below the recommended intake for total folate and above an upper limit (UL) for folic acid intake. This was done using intake data from the NDNS, and information on the flour content of different foods by recalculating the folic acid intake for each subject in the NDNS population assuming a mandatory fortification scheme had been in place (Note that this recalculation also applies for current intakes without fortification, where we used the latest available information on folic acid levels in food items, which in some cases differ from the levels at time of consumption). In this part of the project intakes were not modelled stochastically but the estimated intakes were used for the stochastic modelling of blood folate status later. All data manipulation and calculation was performed using Version 3.1.1 of the statistical programming environment R.

We also estimated the effect of these fortification scenarios on risk of neural tube defects in pregnant women. We did this by first studying NDNS data on blood folate status and its association with individual intake. This enabled us to predict the blood folate response to the different scenarios for each individual. We then used an established association between blood folate status and neural tube defect risk (Daly et al, 1995) to predict the effect of these changes on the average risk among women of childbearing age. Although there is much uncertainty in the predictions at an individual level, the average risk estimates are aggregated across a large sample. We note that there is a delay, averaging about 8 weeks, between the blood sampling and the dietary record, and so fluctuations in either will add to the prediction uncertainty. However, we assume that the fluctuations are random, and both blood folate status and diet recorded are typical for the individual, and so average risk estimates will still be valid.

Three main data sources were used in the modelling of intakes: 1) intake data from years 1 to 6 (2008/9-2013/14) of the NDNS RP, 2) up to date information about the folate content of food items in the NDNS nutrient databank (from years 7 and 8 (2014/15 & 2015/16)), 3) data provided by FSA on wheat flour content of foods in the NDNS dataset. Integrating these three data sources allowed assessment of current folate (natural folate and folic acid) intake of the population and modelling of the effect of different mandatory fortification scenarios.

As with the previous 2006 and 2007/8 modelling, the effect of fortifying flour (all non-wholemeal wheat flour or bread flour only) with different doses of folic acid (0µg, 100µg, 200µg, 250µg, 300µg, 350µg, 450µg per 100g of flour) was modelled focussing on:

- Intakes of total folate (natural and folic acid)
- Proportion of the population with total folate intakes below the Reference Nutrient Intake (RNI)[3]
- Proportion of the population who might be exposed to intakes of folic acid above the recommended upper limit[4]

[3] RNI 70µg/d 1-3y; 100µg/d 4-6y; 150µg/d 7-10y; 200µg/d 11y and above (Department of Health, 1991)

[4] UL 200µg/d 1-3y; 300µg/d 4-6y; 400µg/d 7-10y; 600µg/d 11-14y; 800µg/d 15-17y; 1mg/d 18y and above (Guidance Level of 1mg/d for adults in the UK set by the Expert Group on Vitamins and Minerals (2003). Tolerable upper intake levels for children and adults in Europe set by Scientific Committee for Food (2000)).

- Number of people aged 65 years and over with low vitamin B_{12} status[5] who might be exposed to intakes of folic acid above the recommended upper limit
- Risk of NTD-affected pregnancies

The impact of placing a limit on the levels of folic acid in voluntarily fortified foods and supplements was also assessed.

The NDNS dataset includes sampling weights for each subject to correct for subgroups being underrepresented (weight >1) or overrepresented (weight <1) in the survey population. These weightings were used in the modelling.

In order to consider the impact of various fortification scenarios on intakes in different groups of the population, the modelling was conducted for 15 age and sex subgroups (see Table 1). A more detailed analysis was performed for women of childbearing age, additionally focussing on income levels (using quintiles of equivalised income) and quintiles of current folate intakes.

The modelling did not include scenarios where folic acid from voluntarily fortified foods (breakfast cereal, spreads and supplements) were completely excluded as in the 2006 report, but used the more recent FSA 2007/8 modelling scenarios where a limit was placed on the amount of folic acid added to voluntarily fortified foods and supplements. The limits set for the modelling were 15% of RNI (30µg) of folic acid per 100g for foods and 200µg (600µg for women of childbearing age), for supplements.

Table 1: Population subgroups for modelling

Age-Gender Group
1.5-3 years old males and females
4-6 years old males and females
7-10 years old males and females
11-13 years old males and females
14-18 years old males
14-18 years old females
19-34 years old females
35-49 years old females
14-49 years old females
19-34 years old males
35-49 years old males
50 years and over males and females
50-64 years old males and females
65-74 years old males and females
75 years and over males and females

[5] Defined as serum B_{12}≤150pmol/L

3.1 Current intake data

The most recent consumption data for the UK (Scotland, England, Wales and Northern Ireland) population aged 1.5 years and above was obtained from the NDNS RP (rolling programme years 1-6, 2008/9 to 2013/14). It was assumed that children aged less than 1.5 years consumed minimal amounts of flour and therefore did not need to be included in the modelling.

Data on the folate content of food, including natural folate and foods voluntarily fortified with folic acid, were taken from the most recently available NDNS nutrient databank (year 7 (2014/15) for most foods and supplements which included the most recent updates for the majority of products but year 8 (2015/16) for breakfast cereals which had been more recently updated from product label information from retailer/ manufacturer websites).

For the purpose of the modelling, a number of assumptions were made in relation to voluntarily fortified foods and supplements and factors which affect fortification of flour (detailed in Appendix 1).

As noted in the 2006 report, overage of folic acid added to food products is a common practice for manufacturers to account for losses during manufacturing and storage. In line with the 2006 modelling, the following overages for voluntarily fortified products were assumed: 32% for breakfast cereals, 20% for spreads and 30% for supplements. As the current modelling also included voluntarily fortified food products outwith these food groups, an overage of 25% was assumed for all other products in line with recent Food Safety Authority of Ireland (FSAI) modelling levels (FSAI, 2016). For calculations including voluntarily fortified products, mean values of overages included and overages excluded were used (i.e. 16% for breakfast cereals, 10% for spreads, 15% for supplements and 12.5% for all other products) and the folic acid values in the database adjusted by inclusion of these additional percentages.

Under-reporting is an issue inherent to food intake studies and is important in this context as it could result in under estimation of folic acid intake. The standard methods of accounting for under-reporting involve adjustments based on energy intakes. The previous 2006 SACN modelling assumed no under-reporting and it is difficult to extrapolate estimates of under-reporting based on energy to individual foods and nutrients because they may be affected differently. For comparison purposes, in line with the 2006 SACN modelling, and following recommendations from Public Health England (PHE) (personal communication) the current modelling assumed no under-reporting. However, Appendix 2 shows the effect of adjustment based on estimates of under-reporting for subgroups in the NDNS RP through the use of doubly labelled water to measure total energy expenditure.

The NDNS RP is based on intakes of (mostly) 4 days for each individual. Assuming these are a random sample of typical daily intakes, this will lead to unbiased estimates of the mean daily intake in the population or subgroup being considered. However, these 4-day means will vary more than the unobservable long term individual means, and so the between individual variability will be overestimated. A consequence of this is that the proportion of individuals estimated to be in the extremes (e.g. the proportion of people with an intake higher than the UL or below the RNI) will tend to be overestimated, leading to more cautious conclusions. Although this issue was similarly noted in the 2006 SACN report, the previous modelling made no correction for this, and had the advantage of longer 7 day intakes. Therefore, as it is not straightforward to correct for this overestimation, since the true form of the distribution of between individual variability is unknown, for comparability with previous modelling the tables show uncorrected estimates. However, Appendix 3 explains this issue further and indicates the effect of adjustment.

3.2 Potential intake post-fortification

The potential impact of mandatory flour fortification was estimated in 3 ways by modelling:

- All wheat flour (excluding wholemeal)
- All bread flour (based on the NDNS definition) excluding wholemeal (Table A17)
- Bread flour as defined in the bread and flour regulation 1998 which excludes wholemeal bread (Table A17)

Detailed assessment of the wheat flour content of NDNS food codes from years 1-4 of the rolling programme was obtained from FSA. Additional foods from years 5 & 6 were identified and wheat flour content values assigned based on manufacturer information or the FSA database. In order to allow for consumer choice and in line with the 2007/8 FSA modelling, the modelling was done excluding wholemeal flour / breads. Non-wheat flour products (e.g. gluten free) were also excluded.

Appendix 1 contains more detail regarding the assumptions utilised in the modelling.

In line with the 2006 modelling, a processing loss of 25% folic acid in all flour containing foods was assumed (SACN, 2006; FSAI, 2008).

It was also assumed that wheat flour or wheat flour products imported into UK would not be subject to mandatory fortification and therefore following advice from the National Association of British and Irish Flour Millers (NABIM), the assumption that 11.3% of wheat flour or wheat flour products were imported was applied. The value of 11.3% was applied across all products, as although it is recognised that import levels are likely to vary across products, insufficient information was available to allow this variation to be accounted for.

Total folate intake was assessed for 7 different levels of fortification: 0µg, 100µg, 200µg, 250µg, 300µg, 350µg, 450µg folic acid per 100g flour. The impact of placing a limit on the levels of folic acid in voluntarily fortified foods and supplements was also assessed, with folic acid levels of supplements capped at adult RNI of 200µg (600µg for women of childbearing age) and voluntarily fortified foods capped at 15% of adult RNI (30µg) per 100g.

The effect of the different fortification scenarios on the number of people below the RNI and above the UL was estimated, as was the effect on the number of people aged 65 years and over with low vitamin B_{12} status who might be exposed to intakes of folic acid above the recommended upper limit.

3.3 Calculating folate and folic acid intakes

The NDNS databases provide information on the current total folate content of each food item recorded. It was assumed that folic acid is not present naturally, but only as a result of voluntary fortification. Food subgroups with potentially fortified foods were identified by calculating the maximum amount of total folate per g in each subgroup and ranking subgroups with respect to this. Based on the range of folate values observed within the database, subgroups with at least one food item with more than 100µg/100g folate were explored in more detail to capture those most likely to contain foods with added folic acid.

For foods that might contain both natural folate and folic acid, it was assumed that folic acid would dominate and the total folate content was used as the value for folic acid. For some of the identified food groups all non-zero folate content was assumed to be folic acid (breakfast cereals; infant formula; fat spreads; nutrition powders and drinks; supplements) whereas for other food groups, (biscuits; manufactured buns, cakes and pastries; chocolate confectionery; fruit juice; beverages dry weight; savoury sauces, pickles, gravies and condiments; commercial toddlers foods; soft drinks; brown, Granary and wheatgerm bread), only some non-zero folate content foods were considered as containing folic acid, identified by checking the ingredients of the item (e.g. savoury sauces, pickles, gravies and condiments) or by looking at the distribution of folate content in the food group and selecting a food group specific threshold, where every item exceeding that threshold was considered to be fortified (e.g. biscuits; commercial toddler foods).

With natural folate and folic acid separated, and with information on the flour content of the products being considered for mandatory fortification, it was possible to calculate the natural folate (which was unaffected by the various fortification scenarios and remained constant throughout) and folic acid content of the diet for each person in the NDNS datasets, for different amounts of fortification and different options for capping of the folic acid content of spreads, cereals or supplements. These intakes were summarised by the mean and median, as well as the proportion below the RNI[6] for total folate or above the UL[7] for folic acid intake.

3.4 *B_{12} and folic acid intake*

There is concern that high folic acid intakes may mask vitamin B_{12} deficiency in the elderly (SACN, 2006). In order to assess the risk of this occurring, the proportion of the population over 65 with blood B_{12} < 150pmol/L was estimated, using the blood results reported in the NDNS data. This is the recommended cut-off for defining vitamin B_{12} deficiency from a WHO Technical Consultation and is based on the B_{12} concentration below which methylmalonic acid (MMA) becomes elevated (WHO, 2008). Six percent (or 30 individuals, unweighted 7% of the sample) were recorded as vitamin B_{12} deficient. It is these who are at risk if their folic acid intake is high (above the UL). None of the 30 individuals was currently above the UL for folic acid or had a high total folate intake (the highest folic acid intake (from all sources, including supplements) in this group was 153µg/day, the highest total folate intake 452µg/day). The proportion at risk can be estimated by assuming independence of the vitamin B_{12} status and folic acid intake after supplementation. However, there are indications that folate intake and vitamin B_{12} status are positively correlated (correlation coefficient 0.15, p=0.002) (see Fig 1) implying that proportions low in one (B_{12}) and high in the other (folic acid intake) are likely to be fewer than will be estimated assuming independence.

[6] RNI 70µg/d 1-3y; 100µg/d 4-6y; 150µg/d 7-10y; 200µg/d 11y and above

[7] UL 200µg/d 1-3y; 300µg/d 4-6y; 400µg/d 7-10y; 600µg/d 11-14y; 800µg/d 15-17y; 1mg/d 18y and above

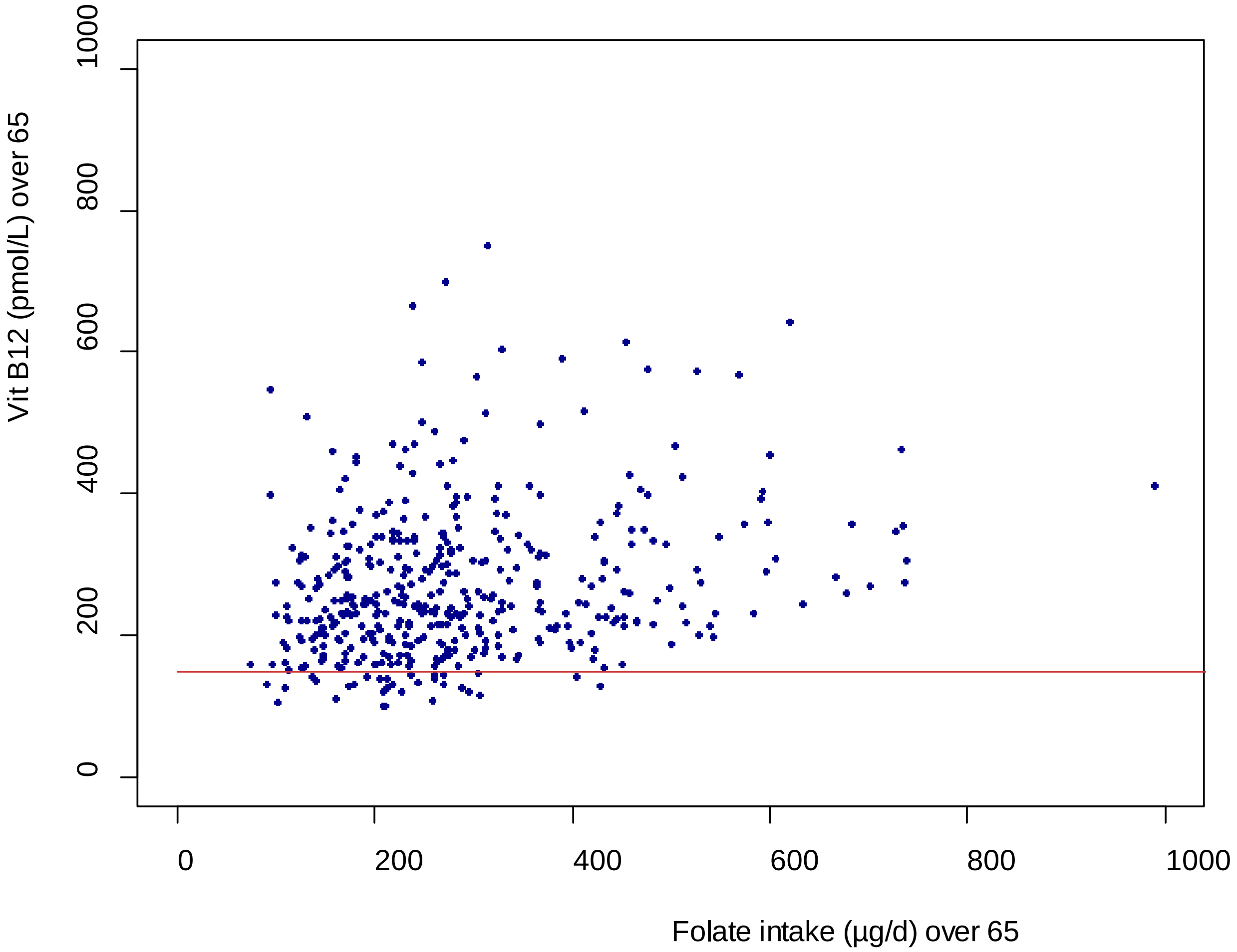

Fig 1. Folate intake and B_{12} status in those over 65 yrs.

3.5 Effect of fortification on NTD risk

The effect of folic acid fortification on NTD risk were estimated by first predicting its effect on blood folate status, and then using this to predict NTD risk. There are a number of ways of obtaining a prediction equation for this association.

The equations from Daly (1995) and Daly (1997) were used in the previous assessment of NTD risk by SACN in 2006 and also recently in the Update Report on Folic Acid and the prevention of birth defects in Ireland Report (FSAI, 2016). It was highlighted in the SACN report in 2006 that there were uncertainties in the data used by Daly (1995) and Daly (1997) and that the resulting equations if used, may either over or underestimate the impact of fortification on NTD risk. With new data on status from the NDNS RP and new evidence from the literature on the relationship between intake and status and status and NTD risk, there was a need to reconsider the relationship between intake and status and status and risk.

A review had been undertaken in September 2013 for the WHO Guideline on optimal serum and red blood cell (RBC) folate concentrations in women of reproductive age for prevention of neural tube defects (WHO, 2015). This was used as a source of systematic reviews to inform the assessment of NTD risk. Additional systematic reviews published more recently on the relationship between intake and status by Duffy et al (2014) and Marchetta et al (2015) were also considered. Duffy et al quantified the typical response of RBC folate to a change in folic acid intake and included the largest number of trials with a range of folic acid doses relevant to our purpose (50 to 400μg/d).

Studies identified by WHO (2015) that have examined the relationship between red blood cell folate status and NTD risk included only Daly (1995) and Crider (2014). It was highlighted in the WHO guideline that the dose–response relationship found by Daly had been confirmed in other populations including the US and Chinese populations by a Bayesian model developed by Crider et al (2014) which incorporates uncertainty intervals. Crider et al (2014) also found that the associations between risk of NTD and RBC folate concentrations were remarkably similar between the Irish, Chinese, and overall US populations. Tinker et al (2015) defined RBC folate concentrations associated with risk of NTDs (from Crider 2014, and Daly 1995), for different RBC folate assay methods and provided a conversion formula.

3.6 Folate intake and blood folate status in the NDNS dataset

Red cell folate status has been recorded for a subset (about 35%) of the participants in the NDNS rolling programme. Full details are published in National Diet and Nutrition Survey Rolling Programme (NDNS RP) Supplementary report: blood folate results for the UK as a whole, Scotland, Northern Ireland (Years 1 to 4 combined) and Wales (Years 2 to 5 combined), published by PHE. This can be used to estimate a prediction equation. This approach has some advantages compared to the alternative of using results from research and meta-analyses published elsewhere. One is that it is based on the same population and the same dietary assessment methodology as that used for estimating the effect of fortification on folate intake. Another is that it is possible to approximately split the folate intake into natural folate and folic acid, and so estimate separate effects, which can then be used in the prediction equation.

First, two linear regression models were fitted, one with total folate intake as a single predictor and one with two predictors, natural folate and folic acid intake. The link between total folate intake and blood folate is not particularly strong, and this can be seen in Fig 2, which shows the link between total folate intake and red cell folate status in adults.

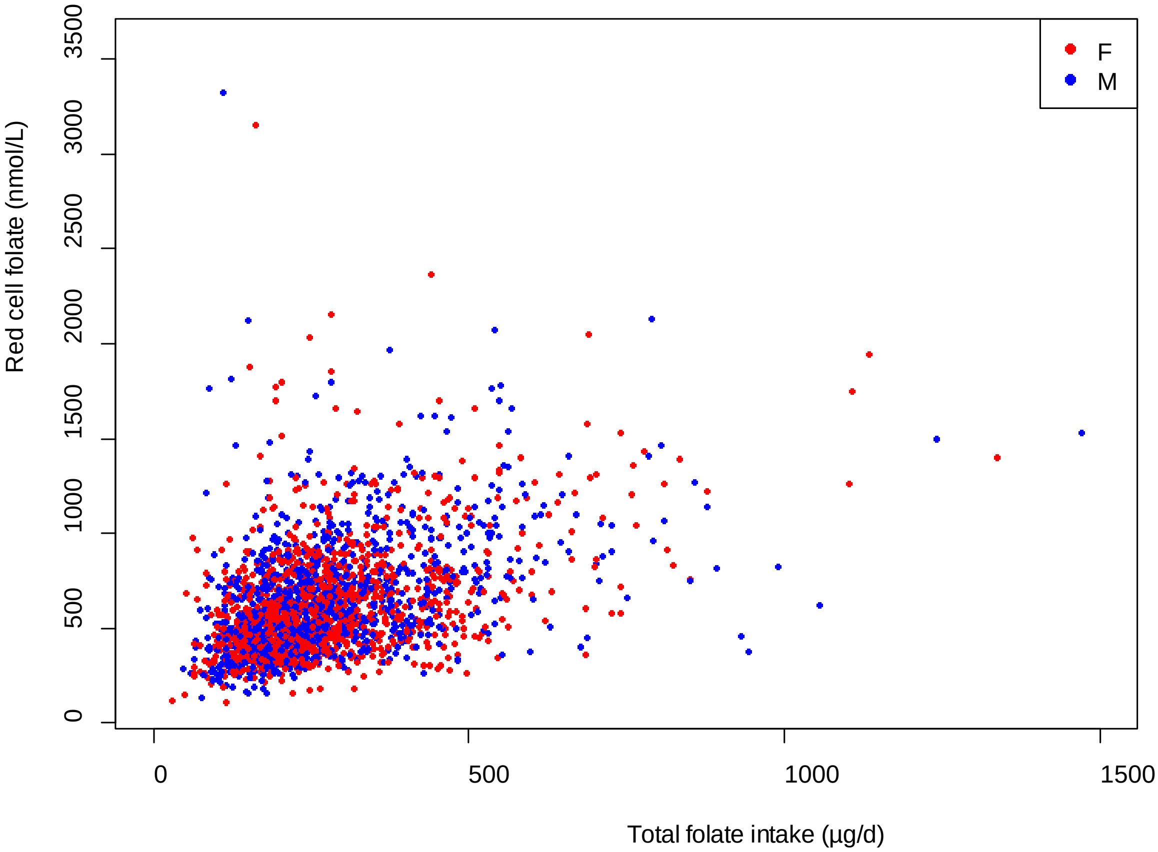

Fig2. Association between folate intake and red cell folate status in adults. R=0.39

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Total folate regression model
Coefficients:
              Estimate Std. Error  p-value
(Intercept) 459.21503   19.45152 < 0.0001
tot.fol       0.90042    0.04212 < 0.0001
gen         -48.21463   11.91079 < 0.0001
---
Residual standard error: 272.5 on 2240 degrees of freedom
Multiple R-squared:  0.1695,     Adjusted R-squared:  0.1687


Multiple regression with natural folate and folic acid
Coefficients:
              Estimate Std. Error  p-value
(Intercept) 487.30055   20.13958  < 0.0001
nat.fol       0.60356    0.07246  < 0.0001
folic.acid    1.07305    0.05419  < 0.0001
gen         -33.14727   12.22107   0.007
---
Residual standard error: 271.1 on 2239 degrees of freedom
Multiple R-squared:  0.1787,     Adjusted R-squared:  0.1776
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Gender was included as a term in the analysis, and was found to be significant, with women having a folate status 35-50nmol/L lower than men (p<0.001) at the same intakes of natural folate and folic acid. The coefficients are the important part of the regression, indicating how much blood folate changes on average in response to a change in natural folate or folic acid. The coefficient for natural folate is 0.60 (nmol/L)/(µg/day) and for folic acid is 1.07 (nmol/L)/(µg/day). This appears to indicate a greater bioavailability for folic acid than for natural folate.

However, if interaction terms for gender are included in the model, the one for natural folate x gender is significant (p=0.03), suggesting a different association between natural folate intake and red cell folate status in men and women.

Since the primary interest is in women of childbearing age (age 14-49 yrs), this suggests that the model should be developed for this subgroup only, accepting the trade-off of a smaller sample size to obtain more representative data. For this subgroup, the coefficients for natural folate and folic acid are almost the same.

```
Coefficients:
             Estimate Std. Error p-value
(Intercept) 339.17621   22.61133  < 0.0001
nat.fol       0.97401    0.12459  < 0.0001
folic.acid    0.92965    0.08827  < 0.0001

Residual standard error: 238.3 on 926 degrees of freedom
Multiple R-squared:  0.1693,    Adjusted R-squared:  0.1675
```

If a model is fitted for total folate (i.e. assuming the same effect for both natural folate and folic acid), the coefficient is estimated to be 0.95 (SE 0.07).

Although a linear model appears reasonable over the range of data, and is more easily extended to separate effects for different folate types, an association which is linear on the log scale gave a better fit, and is also what is used in the meta-analyses discussed below.

```
Coefficients:
             Estimate Std. Error  p-value
(Intercept)   4.03577    0.14190  < 0.0001
log(tot.fol)  0.41316    0.02652  < 0.0001

Residual standard error: 0.3758 on 927 degrees of freedom
Multiple R-squared:  0.2074,    Adjusted R-squared:  0.2066
```

The log scale coefficient estimate 0.413 implies that red cell folate increases as the power 0.4 of folate intake. As this closely matches what was estimated by Duffy et al (2014), who estimated that the exponent (power to which folate intake is raised) for red cell folate is 0.4, this regression model is used to estimate red cell folate responses to changes in intake. Fig 3 shows the data scatter and fitted association for women of childbearing age.

Misreporting has not been accounted for in these calculations, and this would not be appropriate as we will be using the prediction equation with unadjusted intake data.

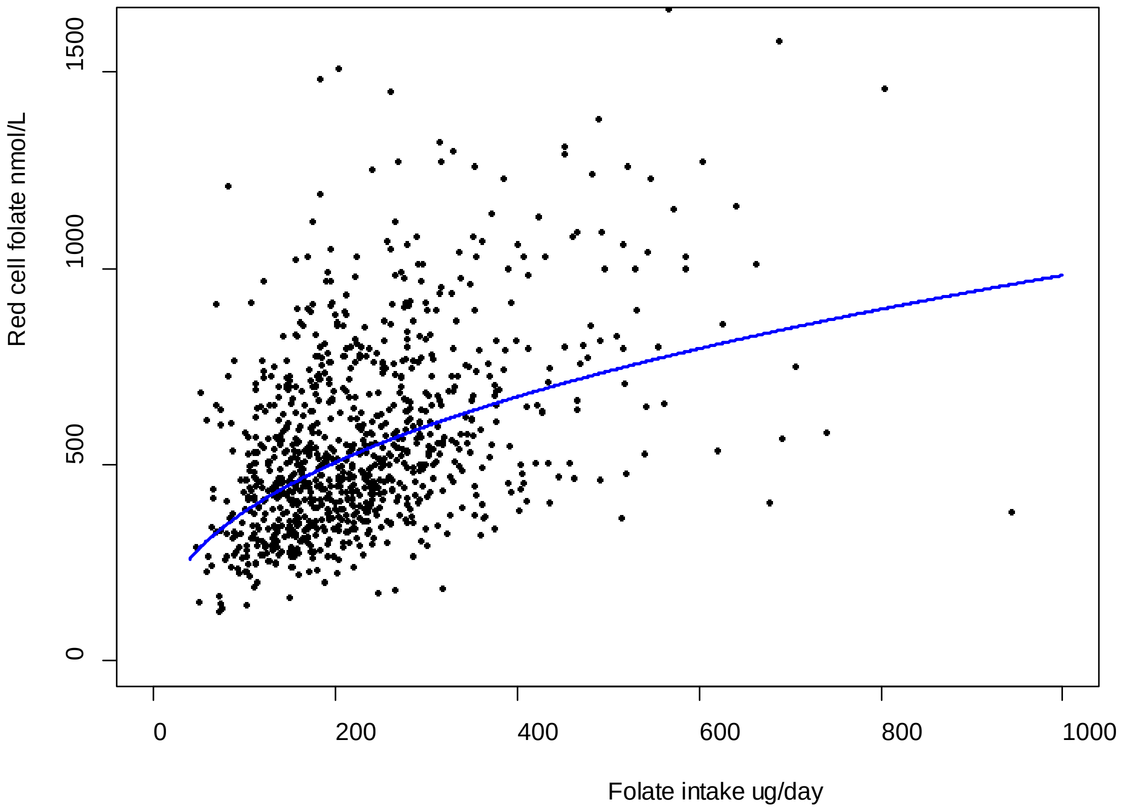

Fig 3. Fitted curve for predicting red cell folate from total folate intake for women of childbearing age

3.7 Other published research on the association between folate intake and blood status

Estimates of the association between folate intake and red cell folate from the published literature were also considered. Below are three systematic reviews which have looked at the relationship between folic acid intake and change in blood folate status.

Duffy et al (2014) have conducted a meta-analysis of studies which have looked at the change in blood folate status in response to folic acid supplementation. They present results in two ways. One assumes a linear association between the log red cell folate response and the log of the amount of folic acid supplementation, i.e. that red cell folate increases as a power of folic acid intake. For this, they estimate that the exponent for red cell folate is 0.4. In the context of the mean folate intake and mean red cell folate, this corresponds to a linear coefficient of about 0.9, which matches what we found in a linear model for women of childbearing age (Fig 3). In a meta-regression of factors affecting the response, they report a linear coefficient of β= 1.05, again similar to what we have found.

Marchetta et al (2015) have also carried out a meta-analysis, although in this case it is based on natural folate in food, and so complements the studies reported by Duffy et al (2014). They fit a similar form for the association (red cell folate increases as some power of folate intake), and estimate the exponent to be 0.64. This is larger than what was found by Duffy et al (2014) and by our data analysis. However, they also noted that models excluding data from two potential outlier studies influenced the results dramatically and lowered the estimated slope of the line.

Berti et al (2012) also have carried out a meta-analysis of associations between total folate intake and folate status, and have assumed the same form for the association. Their combined estimate for the exponent for red cell folate is 0.30. They note considerable heterogeneity between studies, and that in a subset of studies which administered L-Methylfolate (5-MTHF) the estimated exponent is 0.49.

3.8 Predicting red cell folate response to fortification

Our interest is in how red cell folate might increase, in women of childbearing age, in response to the different fortification scenarios. The simplest approach is to look at movement along the fitted curve in Fig 3. In this case we predict the current position on the curve (Fig 3), and the new position after a change in predicted folic acid intake following fortification. Risk of NTD is calculated for each woman in the sample, and a weighted mean of these is calculated to give the overall risk among women of childbearing age.

A disadvantage of this approach is that it doesn't account for variation in folate status among women reporting similar folate intakes. As the variation of risk with folate status is non-linear, this can have important effects on risk estimates. To account for this, we also used another approach, in which random samples are taken from the distribution of folate status for a specific folate intake. This was approximately normally distributed on the log scale, and the sampled distributions of red cell folate at a specific folate intake matched well those which were observed. In particular, very low folate status rarely occurred in the random samples. For these sampled values, mean red cell folate was then calculated, and NTD risk predicted as described above. This is referred to as Model A. The nonlinear nature of the association of folate status with NTD risk, in which it increases more sharply with folate status reduction than it falls with folate status increases, means that this approach gives higher risk estimates than the simpler approach (Model B). However, we found that estimates of the change in risk in response to fortification scenarios are quite similar.

A third model is also fitted (Model C), in which it is assumed that 30% of women who are planning to become pregnant will take folic acid supplements of 400µg/d (Haggarty et al, 2009).

3.9 Predicting NTD risk from red cell folate status

NTD risk is predicted as a function of red cell folate. Only two studies which provided the information to make this prediction were available. These are Daly et al (1995) and Crider et al (2014). Of these two, each has some features which make it more appealing as a choice for our prediction.

Daly et al (1995) was carried out in an Irish population which is likely to be more similar in diet and genetics to the Scottish/UK population for which we wish to estimate NTD risk, whereas Crider et al (2014) was carried out in a Chinese population.

Crider et al (2014) is more recent and so methodology may be more refined and developed in the two decades since Daly et al (1995). The sample size was also larger, and more detailed information is provided. They compare their results with those of Daly et al (1995) and conclude that they are compatible, even though the coefficients (below) in the prediction equations are not so similar. This means that although predicted risk over the main range of blood folate values is similar, changes in risk associated with changes in blood folate show greater difference. Fig 4 shows a plot of the risk predicted by each equation.

We chose the Daly et al (1995) prediction as preferable because of the population similarity. It predicts smaller reductions in risk than does the Crider et al (2014) prediction, so our estimates of the effects of fortification on NTD risk will therefore be more conservative. Predictions from both equations are presented in the tables.

Both predictions are of the same form, based on the logistic regression model. The log odds of risk are linearly related to the natural log of red cell folate. If p is the probability of NTD, then

$$\log \frac{p}{1-p} = A - B \log RCF$$

For Daly et al (1995), the estimates are A = 1.6463; B = 1.2193

For Crider et al (2014), the estimates are A = 4.57; B = 1.7

Fig 4 shows how both of these estimated equations predict NTD risk in the range of common red cell folate values. A conversion of units, as explained by Tinker et al (2015) was required to obtain a match between those used in the NDNS study (the NHANES method) and those used by both Daly et al (1995) and Crider et al (2014).

If these equations are used to estimate current NTD risk among women aged 14-49, we find for both of them that the predicted rate of NTD is 2.4 per 1,000 pregnancies. This is greater than any published information on observed current rates, such as 1.3 or 1.2 NTD affected pregnancies per 1,000 births reported by EUROCAT for the UK, and 1.02 per 1,000 births for 2007-2011, reported by Information Services Division Scotland (Scottish Perinatal and Infant Mortality and Morbidity Report, 2012).

There are reasons which may explain much of this:

1. Many women take folic acid supplements in early pregnancy or while intending to become pregnant, thus their blood folate status is higher during this period.

2. Blood from non-pregnant women was used in this analysis from the NDNS RP.

3. Genetics and other factors will differently affect the levels of NTD risk for different populations.

4. NTD pregnancies are often under-reported. Morris and Wald (2007) estimate that 44% of NTD terminations and 32% of births were not reported as such. Other research such as Boyd et al (2004) also refers to under-reporting of NTD occurrence.

5. It was noted by SACN in 2006 that in areas where ascertainment rates were more complete the rates were higher than average for England e.g. in Wales between 1998 and 2004 the average rate for an NTD affected pregnancy was 1.8 per 1,000 births.

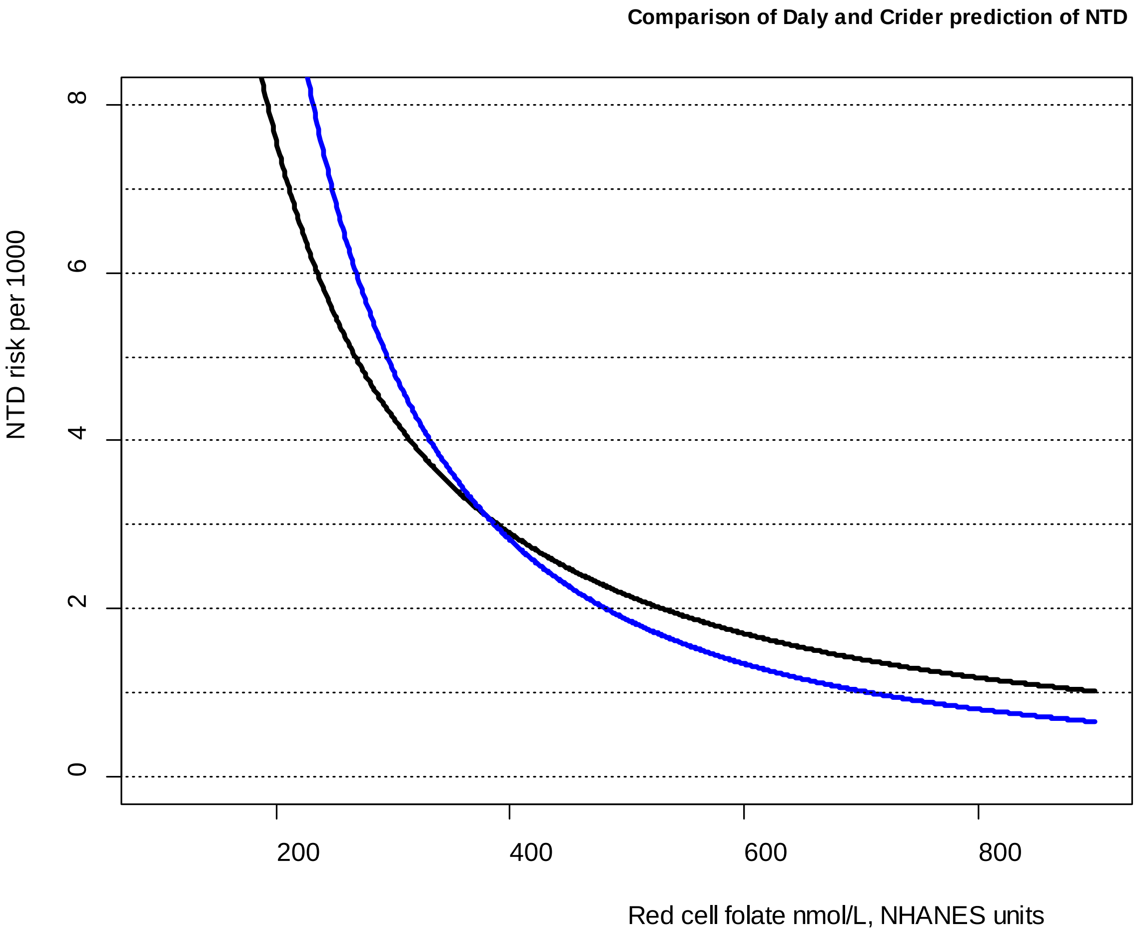

Fig 4. Prediction equations for NTD risk by Daly (black) and Crider (blue)

4 Results

We note that folate and folic acid intakes follow a skew distribution with some very high intakes that can have strong impact on the mean of the distribution. From a statistical point of view the median or geometric mean might be a better characterisation of the centre of this distribution, but these are quantities harder to interpret and in order to be able to compare our results to that of the previous modelling, we will mainly report means here. The Appendix (tables A11-A16) gives detailed results for all gender-age group combinations for some fortification scenarios that include medians too.

4.1 Current intakes of folate and folic acid

Current intakes of total folate and folic acid were assessed based on the latest available NDNS nutrient databank information. Fig 5 shows histograms of total folate and folic acid intake across the 9374 subjects recorded in the data from the NDNS RP. The x-axes here are scaled logarithmically and we can see that total folate intake is lognormally distributed. The same is true for folic acid intake with an added spike at 0 caused by 24% of subjects that recorded no folic acid intake at all.

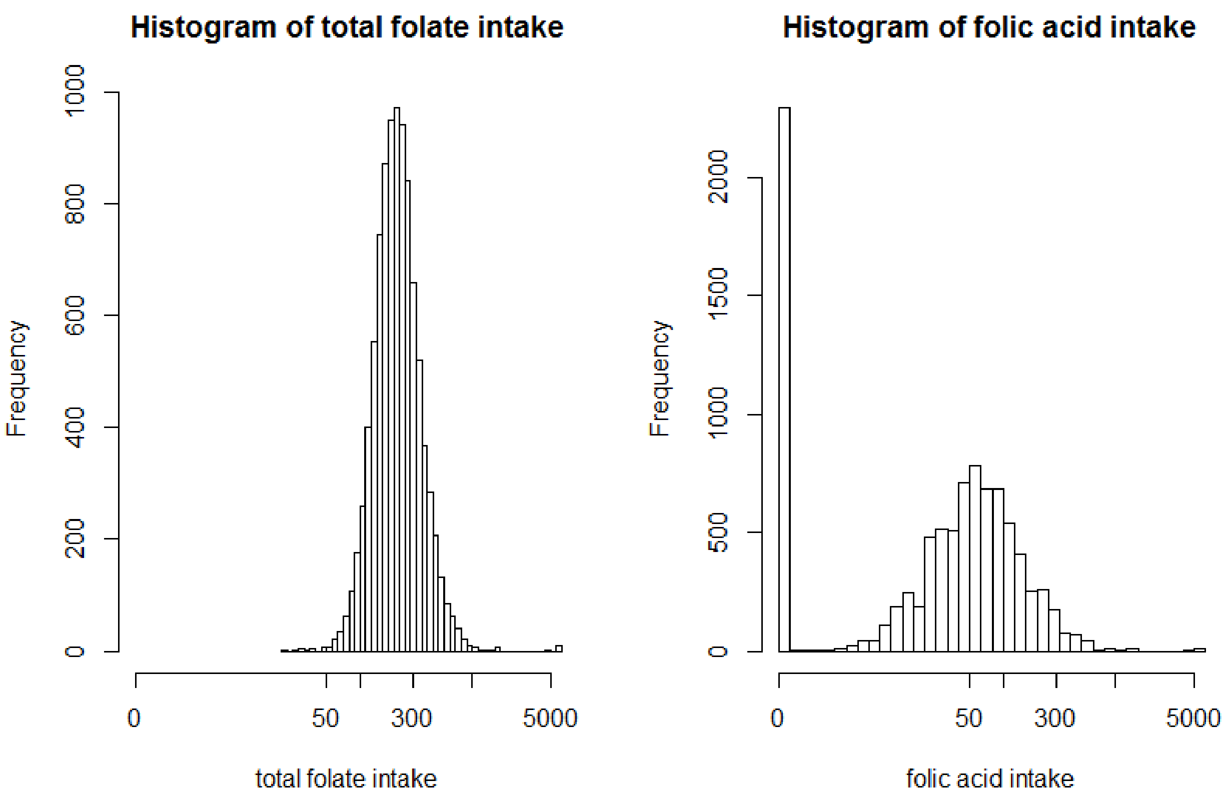

Fig 5. Distributions of daily total folate and folic acid intake (µg/d)

Table 2 gives folate and folic acid intakes from different sources for different age-gender groups. Note that we have additional columns in our table for fortified items other than spreads, breakfast cereals or supplements. A more detailed breakdown by different food groups is shown in Table A3 (Appendix 6).

Women of childbearing age were assessed in greater detail by grouping them into quintiles of total folate intake within each age group (see Table 3), where the first quintile has lowest intake and the 5th quintile highest intake. It is of note that those in the highest quintile of intakes obtain more than half of their folate from folic acid whereas that is only 7% in the lowest intake quintile.

Table 4 shows the same data split up into quintiles of equivalised household income, where the first quintile has lowest income and the 5th quintile highest income. The largest difference here is the very high intake for the second quintile of 19-34 year olds. This is caused by two individuals in this group who reported having taken a 5mg folic acid supplement. Other than that, there is indication that natural folate intake is higher in the highest income groups, and that both are lowest in the lowest quintile.

Table 2: Mean and % contributions of folic acid to total folate intake

Age-Gender Group	n	Natural folate (µg /d)	Natural folate % of total folate	Folic acid from breakfast cereals (µg /d)	Folic acid from breakfast cereals % of total folate	Folic acid from spreads (µg /d)	Folic acid from spreads % of total folate	Folic acid from supplements (µg /d)	Folic acid from supplements % of total folate	Folic acid from other sources (µg /d)	Folic acid from other sources % of total folate	Total folic acid (µg /d)	Total folic acid % of total folate	Total folate (µg /d)
1.5-3 males and females	819	112	71	27	17	7	5	2	2	8	5	45	29	157
4-6 males and females	804	137	71	35	18	8	4	9	5	4	2	57	29	195
7-10 males and females	968	147	69	43	20	9	4	6	3	7	3	66	31	213
11-13 males and females	717	151	71	42	20	9	4	4	2	7	3	62	29	213
14-18 males	636	185	75	40	16	10	4	8	3	5	2	63	25	248
14-18 females	692	144	72	30	15	9	4	10	5	6	3	55	28	199
19-34 females	659	174	67	24	9	9	3	49	19	3	1	85	33	259
35-49 females	841	184	71	23	9	10	4	35	14	5	2	74	29	258
19-34 males	408	223	75	32	11	12	4	21	7	8	3	74	25	296
35-49 males	580	235	76	29	10	13	4	28	9	4	1	74	24	309
50-64 males and females	1174	227	73	24	8	12	4	44	14	5	2	85	27	312
65 and over males and females	1076	206	66	27	9	13	4	58	19	6	2	105	34	311
overall population	9374	196	71	29	10	11	4	34	12	6	2	79	29	276

Table 3: Contribution of voluntary fortification to total folate intakes for women of childbearing age by quintile of current total folate intake

Female age group (yrs)	Quintile	Total folate (µg /d)	Natural folate (µg /d)	Natural folate % of total folate	Folic acid from breakfast cereals (µg /d)	Folic acid from breakfast cereals % of total folate	Folic acid from spreads (µg /d)	Folic acid from spreads % of total folate	Folic acid from supplements (µg /d)	Folic acid from supplements % of total folate	Folic acid from other sources (µg /d)	Folic acid from other sources % of total folate	Total folic acid (µg /d)	Total folic acid % of total folate
14-18	1st	98	88	90	6	6	2	2	0	0	1	1	10	10
	2nd	143	124	87	14	10	4	3	0	0	1	1	19	13
	3rd	178	144	81	24	13	6	4	1	1	3	2	34	19
	4th	221	165	75	41	19	9	4	1	0	5	2	56	25
	5th	344	194	56	61	18	21	6	48	14	21	6	150	44
19-34	1st	111	104	94	6	5	1	1	0	0	0	0	7	6
	2nd	162	142	88	14	9	4	3	0	0	1	1	20	12
	3rd	200	172	86	20	10	5	3	0	0	2	1	28	14
	4th	251	196	78	34	13	14	6	2	1	5	2	55	22
	5th	524	236	45	44	8	16	3	222	42	6	1	288	55
35-49	1st	119	109	91	6	5	3	3	0	0	1	1	10	9
	2nd	176	155	88	12	7	7	4	0	0	1	1	20	12
	3rd	228	184	81	28	12	7	3	3	1	5	2	43	19
	4th	286	229	80	32	11	12	4	9	3	5	2	57	20
	5th	487	241	50	38	8	20	4	172	35	17	3	246	50
14-49	1st	109	101	93	5	5	2	2	0	0	0	0	7	7
	2nd	159	140	88	13	8	4	3	0	0	2	1	19	12
	3rd	201	169	84	22	11	8	4	0	0	3	1	33	16
	4th	257	203	79	35	13	10	4	4	2	6	2	54	21
	5th	472	236	50	41	9	18	4	165	35	11	2	235	50

Table 4: Contribution of voluntary fortification to total folate for women of childbearing age, split into quintiles of household income

Female age group (yrs)	Quintile	Total folate (µg /d)	Natural folate (µg /d)	Natural folate % of total folate	Folic acid from breakfast cereals (µg /d)	Folic acid from breakfast cereals % of total folate	Folic acid from spreads (µg /d)	Folic acid from breakfast spreads % of total folate	Folic acid from supplements (µg /d)	Folic acid from supplements % of total folate	Folic acid from other sources (µg /d)	Folic acid from other sources % of total folate	Total folic acid (µg /d)	Total folic acid % of total folate
14-18	1st	181	129	71	29	16	13	7	5	2	6	3	52	29
	2nd	177	143	81	21	12	5	3	6	3	3	2	34	19
	3rd	200	150	75	26	13	11	5	8	4	6	3	50	25
	4th	241	153	64	46	19	8	3	21	9	14	6	88	36
	5th	212	151	71	30	14	6	3	20	9	6	3	61	29
19-34	1st	206	162	79	21	10	9	4	8	4	5	2	44	21
	2nd	347	159	46	29	8	6	2	152	44	1	0	188	54
	3rd	238	165	69	31	13	10	4	30	13	1	1	73	31
	4th	280	184	66	18	6	9	3	67	24	2	1	95	34
	5th	254	186	73	27	11	9	4	28	11	4	2	69	27
35-49	1st	253	182	72	23	9	9	3	38	15	2	1	72	28
	2nd	244	166	68	20	8	13	5	39	16	6	2	78	32
	3rd	270	181	67	25	9	11	4	48	18	6	2	90	33
	4th	239	184	77	23	10	7	3	20	8	5	2	55	23
	5th	300	206	69	23	8	8	3	54	18	9	3	94	31
14-49	1st	219	163	75	23	11	10	4	19	9	4	2	56	25
	2nd	280	159	57	24	9	9	3	85	30	3	1	121	43
	3rd	247	170	69	28	11	10	4	35	14	4	1	77	31
	4th	254	181	71	24	9	8	3	37	15	5	2	73	29
	5th	275	193	70	25	9	8	3	41	15	7	3	82	30

The current modelling has been conducted UK wide. The box-and-whisker plots (Fig 6 below) show the distributions of folate and folic acid intakes across the six regions: Central England (CE), Northern England (NE), Southern England (SE), Northern Ireland (NI), Scotland (SC) and Wales (WA). The y-axis shows daily intake in µg on a logarithmic scale. The black band in the middle here shows the median of the distribution, the box around it represents the 50% most central observations and the whiskers extend to a range that should cover most data points apart from outliers if the data are normally distributed. Observations outside the whisker-range are plotted individually. As we can see the centre of the distribution is not highly different across the regions but Northern England, Scotland and Wales have more people with very low folic acid intakes.

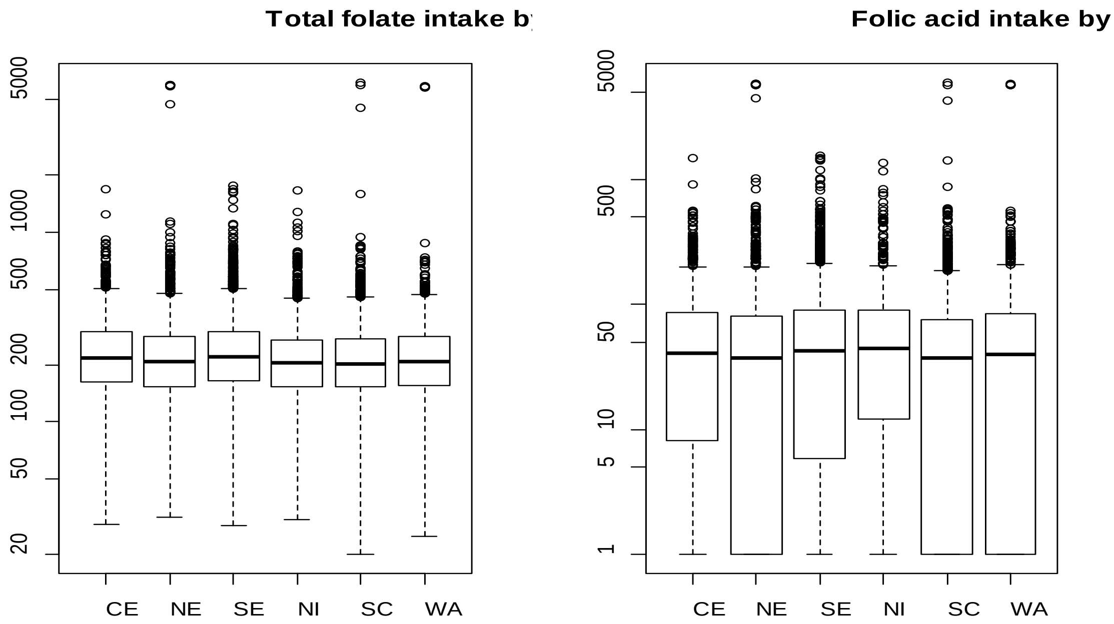

Fig 6. Box and whisker plots of total folate and folic acid intake by region

Based on the NDNS reported intakes, and most recent food composition tables, and with no misreporting adjustment, it is estimated that the proportion of the total population with intakes of folate below the RNI is 29.8%. If calculated separately for each region, the estimates are: CE 28.7%, NE 31.3%, SE 27.9%, NI 32.2%, SC 35.4% and WA 32.2%. The difference between these numbers is statististically significant (p<0.001 using a chi-square test), which illustrates that there are regional differences in the intake distribution, though it must be kept in mind that with a high sample size even small differences can become significant. In order to obtain a UK wide picture, and to use the maximal sample size, we will concentrate on analyses based on data from all regions in this report.

4.2 Current intakes of flour

The current flour and bread consumption (excluding wholemeal) in the NDNS data are presented in Table 5. Note that while our modelling of folic acid intakes after fortification assumes that 11.3% of flour is being imported, no adjustment has been made for imports in this table.

Table 5: Flour and bread consumption

Age-Gender Group	Flour consumption (g/d)	Flour from bread (NDNS) (g/d)	% Flour from bread (NDNS)	Flour from bread (1998) (g/d)	% Flour from bread (1998)
1.5-3 males and females	33	17	50	13	39
4-6 males and females	51	26	52	18	34
7-10 males and females	60	30	49	19	31
11-13 males and females	70	36	52	19	28
14-18 males	82	41	51	22	27
14-18 females	58	29	51	15	26
19-34 females	56	30	54	16	29
35-49 females	48	26	55	15	31
19-34 males	78	43	54	23	29
35-49 males	70	40	57	21	30
50-64 males and females	53	29	55	17	33
65 and over males and females	53	27	51	20	37
overall population	59	31	54	18	31

4.3 *Effects of mandatory fortification*

A FSA board paper from 2008 that updates the 2006 SACN report states the aims of a fortification scenario should be to:

- reduce the incidence of NTDs;
- increase folic acid intakes by an average of 60-100 micrograms/day (a range of values that were considered to be necessary to reduce NTD risk);
- ensure numbers not achieving the RNI for folate do not exceed the current level;
- ensure that numbers exceeding the UL for folic acid do not increase above current levels;
- ensure folic acid reaches those with intakes within the lowest quintile of consumers.

The first point will be discussed later in the NTD modelling section of this report. The other four points help to discuss the output of the current modelling of different fortification scenarios. In all scenarios presented a production loss of 25% (i.e. a fortification of 200 µg/100g would end up as 150 µg/100g at the point of consumption) and 11.3% of imported and thus not-fortified flour were assumed. As there was no available data on how these import levels differ for different food items, it was assumed that the 11.3% holds for all flour containing items. Our definition of bread (in particular the 1998 bread and flour regulation one) in this modelling is tighter than the one used in previous modelling and excludes most types of imported breads. For this reason the figure of 11.3% is likely to overestimate the percentage of imported flour when fortifying bread only. This needs to be taken into account when interpreting tables of the effect of fortification. We can obtain an upper bound for the corresponding intakes by reversing the 11.3% reduction, i.e. by multiplying flour/folic acid intakes by 1/(1-0.113) = 1.13, that is by adding 13%.

Changes in distribution of folic acid intake after fortification

Our report mainly focuses on changes in the mean of the distribution of averaged daily folic acid and folate intakes after a potential mandatory fortification but this would impact other features of that distribution too. Below we show a histogram of the current intake distribution of folic acid and total folate and what it would be under 3 fortification scenarios:

1) capping of breakfast cereals, spreads and supplements and fortification of all wheat flour with 450 µg/100g
2) capping of breakfast cereals and spreads only and fortification of all wheat flour with 200 µg/100g
3) capping of supplements only and fortification of all wheat flour with 300 µg/100g

Note that we have cut off the peak in 0 in the current distribution here, so we could display all histograms with the same y-Axis without making them very flat for the three fortification scenarios).

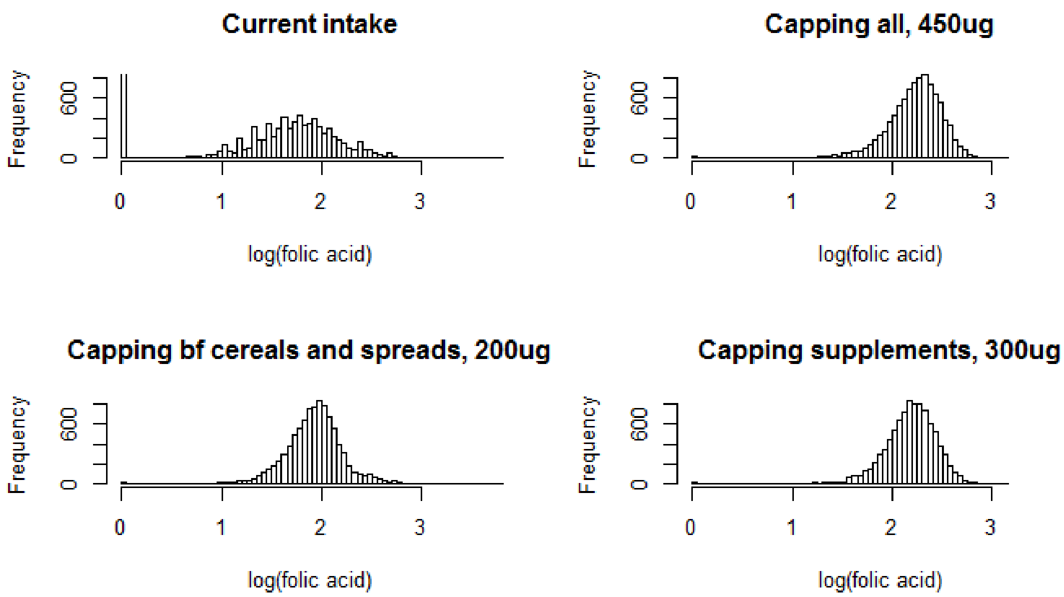

Fig 7. Histograms of folic acid intake on a logarithmic scale for different scenarios

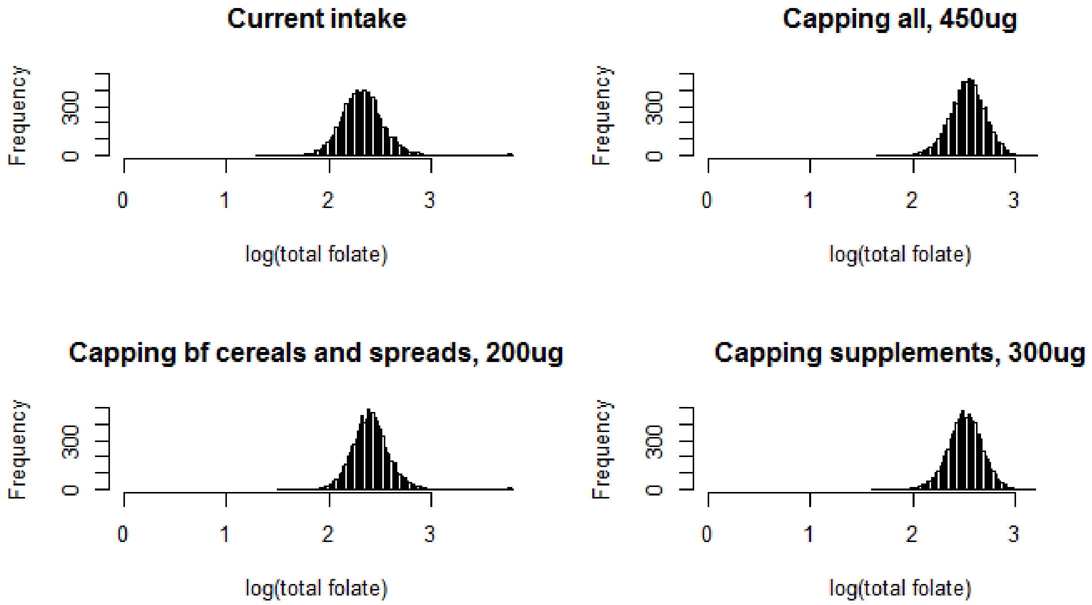

Fig 8. Histograms of total folate intake on a logarithmic scale for different scenarios

Unfortunately the histograms are not very good at showing the biggest changes in the distribution which happen in the tails (very small and very large intakes). In this situation comparing the (weighted) standard deviations (SDs) are more informative, and shown in the table 6 below.

Table 6: Standard deviations of folic acid (total folate) intake for different scenarios

Fortification/Capping Scenario	**Fortification level (µg) for all wheat flour**	**Increase in average daily folic acid intake (µg/d)**	**Standard Deviation of Folic Acid (Total Folate) intake (µg/d) across population**
Current Status	0	0	270 (283)
Capping breakfast cereals, spreads and supplements	450	124	120 (160)
Capping breakfast cereals and spreads only	200	43	266 (282)
Capping supplements only	300	101	108 (148)

The scenarios alter the SD in two ways:

1) Fortification itself increases variability as every subject in the population will have a different intake in fortified folic acid. The only situation where this would not be true is if intake of wheat flour was strongly negatively correlated to current folic acid intake, i.e. if the subjects with current low (high) folic acid intake had a high (low) wheat flour

intake. This is not the case though: current folic acid intake does not seem to be correlated with wheat flour intake at all ($r < 0.01$).

2) Capping on the other hand reduces variability as it moves high intakes from the right tail of the distribution towards the centre. This is particularly true for very high supplement intakes, if supplement capping is used.

The results for the SDs in the table illustrate these two competing mechanisms. In the scenario where breakfast cereals and spreads only are capped there is only a small decrease in standard deviation. Here the increase by fortification and decrease by capping largely cancel each other out. If supplements are capped however, there is a considerable reduction in SD even at high levels of fortification.

Subjects above the UL of folic acid intake

A particular concern of a potential fortification scheme is that it might drive people over the upper limit of folic acid intake. Currently 0.42% of the NDNS population is above their age-specific UL of folic acid intake (note that this percentage is calculated using the sample weights given to subjects). This corresponds to 38 individuals, 15 of which are children aged 10 and below, 23 of which are adults above 21. We checked that in all 38 cases eliminating the main source of folic acid (i.e., setting the corresponding food group intake level to 0) would mean the individual is no longer above the UL. We considered a food group to be the main source of folic acid for a subject if it had the largest contribution to intake among the 4 categories (supplements, breakfast cereals, spreads, other). We also checked that in no case removing another food group would have achieved this reduction to below the UL. For this reason, the main source of folic acid can in all 38 cases also be regarded as the reason for pushing the person above his/her UL.

Table 7 below gives a breakdown of the 38 subjects above the UL by age group and their main sources of folic acid. For all adults, supplements are the main reason for exceeding the UL, while it is a slightly more mixed picture in children. Here supplements are the main source of folic acid in 10 out of 15 cases, breakfast cereals in 3 and folic acid from other sources in 2 cases. These other sources are a multivitamin fruit juice for one subject and the PKU LOPHLEX LQ liquid, which the NDNS nutrient database lists under “Nutrition powder and drinks”, for the other.

Table 7: Main sources of folic acid for people currently above UL. Table shows numbers in NDNS data.

	Main source of folic acid				
Age range (years)	**Supplements**	**Breakfast Cereals**	**Spreads**	**Other**	**Sum**
0-3	4	1		1	6
4-6	4	1			5
7-10	2	1		1	4
11-13					
14-18					
19-34	3				3
35-49	6				6
50-64	8				8
65-74	2				2
75-	4				4

Because supplement use has this big impact on the percentage of people above the UL, capping supplements turns out to be an efficient mechanism of ensuring that despite fortification the percentage above the UL will not increase.

Effects on the population mean of average daily folic acid intake

For any scenario and any subgroup the average folic acid intake will rise by the same amount for every 100µg (per 100g) of additional fortification. Also capping folic acid will reduce the average intake for a subgroup by a constant that can be separately calculated for capping of breakfast cereals, spreads and supplements. In Table 8 we give these values for the whole population, women of childbearing age (split up into 3 age subgroups) and subjects in the lowest quintile of folate intake in the whole population and also in the group of women of childbearing age.

The table shows with the narrowest definition of bread the highest achievable increase of folic acid at a level of 450µg/100g = 4.5µg/g would be 4.5 × 12.23 = 55µg/day and thus be below the 60µg/day increase desired. The wider NDNS definition of bread can achieve a maximum increase of 4.5 × 20.86 = 93µg/day, but would also struggle to fulfil the requirements if supplements and breakfast cereals were capped. It can also be seen that the lowest folate consumers both in the overall population and particularly among women of childbearing age would benefit less from fortification than the population average.

It is worth noting that a capping of supplements would not reduce the folic acid and total folate status of those individuals with low folate intake as they do not seem to take any of the supplements.

Table 8: Increase per 100µg fortification for 3 scenarios and reductions caused by capping

Group	folic acid (µg/d) increase for every 100µg of fortification per 100g bread flour (1998 definition)	folic acid (µg/d) increase for every 100µg of fortification per 100 g bread flour (NDNS definition)	folic acid (µg/d) increase per 100µg of fortification per 100g of flour (all flour)	folic acid (µg/d) reduction from breakfast cereal capping	folic acid (µg/d) reduction from spread capping	folic acid (µg/d) reduction from supplement capping
whole population	12	21	39	25	10	16
14-49 females	10	19	35	21	8	13
14-18 females	10	19	38	25	8	0
19-34 females	11	20	37	21	8	26
35-49 females	10	18	32	20	9	5
lowest quintile of folate intake	10	16	32	7	2	0
lowest quintile of folate intake among 14-49 females	10	16	30	4	2	0

Table 8 allows us to assess the increase in average folic acid intake under different scenarios but has no information on the percentage of subjects above the UL or below the RNI. Tables 9-13[8] show these numbers along with the averages of folate and folic acid intakes for all 3 fortification scenarios and the following 5 capping options:

- Table 9: No capping
- Table 10: Capping breakfast cereals (at 15% of RNI), spreads (at 15% of RNI) and supplements (at 200µg/day (600µg/day for women aged 14-49 years))
- Table 11: Capping supplements at 200µg/day (600µg/day for women aged 14-49 years)) only
- Table 12: Capping breakfast cereals (at 15% of RNI) only
- Table 13: Capping breakfast cereals and spreads (both at 15% of RNI), but no capping of supplements

[8] As in all tables we give percentages above UL and below RNI with one decimal place, as more precision would give a misleading sense of certainty in these numbers.

Table 9 shows no capping, and without capping the percentage of people above the UL will inevitably rise.[9] Tables 12 and 13 show that only scenarios that include capping supplements manage to keep the percentage above the UL below current levels and raise the average daily folic acid by at least 60µg at the same time, which suggests that capping of supplements is inevitable if this objective remains. From Table 11 it can be seen that bread fortification using the NDNS definition of bread can only achieve the 60µg/d increase at the highest level of 450µg per 100g if supplements only are capped. Note that in these tables we assume a fortification with 0µg to present the current baseline status and we assume there to be no capping either. As a result, a low fortification level with additional capping can lead to a reduction of folic acid intakes in these tables.

In Appendix 6, Tables A11-A16 we give more detailed results for different age-gender combinations for a scenario of no capping and one with capping breakfast cereals, spreads and supplements. In contrast to the tables in the main text Tables A14-A16 show the effect of capping also at 0µg fortification level.

Table 9: Effects of fortification on the whole population assuming no capping

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
Bread (1998 regulation)	0	276	79	29.8	0.4
	100	288	91	25.7	0.4
	200	300	104	21.2	0.4
	250	306	110	19.5	0.4
	300	312	116	18.1	0.5
	350	318	122	17.0	0.5
	450	331	134	15.4	0.6
Bread (NDNS definition)	0	276	79	29.8	0.4
	100	296	100	22.4	0.4
	200	317	121	16.6	0.5
	250	328	131	14.3	0.5
	300	338	142	13.0	0.5
	350	349	152	11.7	0.6
	450	369	173	9.7	0.8
All wheat flour	0	276	79	29.8	0.4
	100	314	118	17.0	0.5
	200	353	157	9.5	0.5
	250	373	176	7.4	0.6
	300	392	196	6.0	0.8
	350	412	215	5.2	1.1
	450	451	254	3.6	1.8

[9] For assessing whether the percentage above UL is larger than its baseline value, more decimal places are needed in some cases. These can be found in Table A18 in the Appendix. Note that some of the statements regarding tables 9-13 are based on these values with 3 decimal places.

Table 10: Effects of fortification on whole population assuming capping of breakfast cereals, spreads and supplements

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
Bread (1998 regulation)	0	276	79	29.8	0.4
	100	237	40	37.9	0.0
	200	249	52	32.2	0.0
	250	255	58	29.4	0.0
	300	261	65	27.5	0.0
	350	267	71	25.7	0.0
	450	279	83	23.2	0.1
Bread (NDNS definition)	0	276	79	29.8	0.4
	100	245	49	33.6	0.0
	200	266	70	25.5	0.0
	250	276	80	22.0	0.0
	300	287	90	19.9	0.0
	350	297	101	17.8	0.0
	450	318	122	14.9	0.1
All wheat flour	0	276	79	29.8	0.4
	100	263	67	25.5	0.0
	200	302	106	14.4	0.1
	250	322	125	11.1	0.1
	300	341	145	9.1	0.1
	350	361	164	7.5	0.2
	450	400	203	5.4	0.5

Table 11: Effects of fortification on the whole population assuming capping of supplements only

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
Bread (1998 regulation)	0	276	79	29.8	0.4
	100	271	75	25.7	0.0
	200	284	87	21.3	0.1
	250	290	93	19.5	0.1
	300	296	100	18.1	0.1
	350	302	106	17.0	0.1
	450	314	118	15.4	0.2
Bread (NDNS definition)	0	276	79	29.8	0.4
	100	280	84	22.4	0.0
	200	301	105	16.6	0.1
	250	311	115	14.3	0.1
	300	322	125	13.0	0.1
	350	332	136	11.7	0.2
	450	353	157	9.7	0.4
All wheat flour	0	276	79	29.8	0.4
	100	298	102	17.0	0.1
	200	337	141	9.5	0.2
	250	357	160	7.4	0.2
	300	376	180	6.0	0.4
	350	396	199	5.2	0.7
	450	434	238	3.6	1.4

Table 12: Effects of fortification on whole population assuming capping of breakfast cereals only

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
Bread (1998 regulation)	0	276	79	29.8	0.4
	100	263	67	34.8	0.3
	200	275	79	29.4	0.4
	250	282	85	27.2	0.4
	300	288	91	25.5	0.4
	350	294	97	23.9	0.4
	450	306	110	21.6	0.4
Bread (NDNS definition)	0	276	79	29.8	0.4
	100	272	75	30.6	0.3
	200	293	96	23.4	0.4
	250	303	107	20.3	0.4
	300	314	117	18.3	0.4
	350	324	128	16.7	0.5
	450	345	148	13.9	0.6
All wheat flour	0	276	79	29.8	0.4
	100	290	93	23.2	0.4
	200	329	132	13.1	0.4
	250	348	152	10.2	0.5
	300	368	171	8.4	0.6
	350	387	191	7.1	0.7
	450	426	230	5.1	1.2

Table 13: Effects of fortification on whole population assuming capping of breakfast cereals and spreads only

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
Bread (1998 regulation)	0	276	79	29.8	0.4
	100	253	56	37.9	0.3
	200	265	69	32.2	0.3
	250	271	75	29.4	0.3
	300	277	81	27.5	0.3
	350	283	87	25.7	0.3
	450	296	99	23.2	0.4
Bread (NDNS definition)	0	276	79	29.8	0.4
	100	261	65	33.5	0.3
	200	282	86	25.5	0.3
	250	293	96	22.0	0.3
	300	303	107	19.9	0.4
	350	314	117	17.8	0.4
	450	334	138	14.9	0.4
All wheat flour	0	276	79	29.8	0.4
	100	280	83	25.5	0.3
	200	318	122	14.4	0.4
	250	338	142	11.1	0.4
	300	357	161	9.1	0.5
	350	377	180	7.5	0.6
	450	416	219	5.4	1.0

Women of childbearing age

As Tables 9-13 suggest that fortification with all wheat flour while capping supplements might be the most flexible approach, the effect of this scenario on women of childbearing age was considered in Table 14 and the subgroup of 20% women of lowest current folate intake in Table 15. Comparing these results with Table 11 it can be seen that the impact of the fortification is smaller on women aged 14-49 due their lower flour intake and higher intake from supplements. Women in the lowest quintile of intake however benefit relatively more from the fortification mainly because they have no intake from supplements. However, even at the highest level of fortification more than 30% would stay below the RNI.

Table 14: Effects of fortification on women of childbearing age assuming capping of supplements only

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
All wheat flour	0	251	76	45.3	0.3
	100	273	98	28.7	0.1
	200	307	133	16.3	0.1
	250	325	150	12.6	0.2
	300	342	168	10.4	0.2
	350	360	185	9.5	0.2
	450	395	220	6.5	0.2

Table 15: Effects of fortification on women of childbearing in the lowest quintile of folate intake assuming capping of supplements only

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
All wheat flour	0	109	7	100.0	0
	100	138	37	99.4	0
	200	168	67	72.1	0
	250	183	82	59.5	0
	300	198	97	51.2	0
	350	213	112	47.0	0
	450	243	141	32.5	0

Masking of vitamin B_{12} deficiency in over 65's

As one potential negative impact of mandatory fortification could be masking vitamin B_{12} deficiency in the elderly, the effect of fortification on people 65 years and older was assessed in more detail. As far as supplements are concerned the intake of folic acid is strongly correlated to that of vitamin B_{12}. Of the 646 NDNS participants who took supplements containing folic acid, only 44 participants took folic acid supplements that did not also contain B_{12}. Among those aged 65 and over, 98 took supplements containing folic acid, but only 10 of those did not take supplements that also contain B_{12}.

Table 16 shows the effect of the most extreme fortification scenario (fortifying all wheat flour without capping). At moderate fortification levels (200-350µg/100g) the percent above the UL rises from 0.5% to 0.7%, which implies that even without any capping there would not be a drastic impact on this age group.

The NDNS data includes blood measurements of B_{12} status for a subset of participants which suggests that 6% of those aged 65 years or older were vitamin B_{12} deficient (blood B_{12} < 150pmol/L). Assuming that vitamin B_{12} deficiency is not associated with folic acid intake and taking into account that there are 11.4 million people in this age group in the UK (Office of National Statistics, mid 2014 estimate), we can derive an estimate of $11.4 \times 10^6 \times 0.06 \times 0.005 = 3420$ older people in the UK who may currently be vitamin B_{12} deficient and also above the upper limit of folic acid intake. With the most extreme fortification scenario this number would rise to $11.4 \times 10^6 \times 0.06 \times 0.008 = 5470$ cases.

If supplements are capped however, Table 17 shows that the percentage above UL drops to 0 in all but the most extreme fortification scenario (450µg/100g) and even in that case it is estimated that there would be a reduction to $11.4 \times 10^6 \times 0.06 \times 0.001 = 680$ older people who are over the UL and also vitamin B_{12} deficient.

Within the NDNS data 30 participants in this age group were identified as being vitamin B_{12} deficient (blood B_{12} < 150pmol/L). Table 18 shows how they would be affected by wheat flour fortification without capping. It can be seen that their baseline folic acid is far lower than the average for their age group, which suggests that the numbers indicated by the calculations given above probably overestimate the true number of people in the population who are both vitamin B_{12} deficient and above the UL of folic acid intake.

Table 16: Effects of fortification on males and females aged 65 years or older assuming no capping

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
All wheat flour	0	311	105	27.4	0.5
	100	346	140	16.3	0.7
	200	381	175	10.0	0.7
	250	399	192	8.3	0.7
	300	416	210	6.5	0.7
	350	434	228	5.2	0.7
	450	469	263	2.8	0.8

Table 17: Effects of fortification on males and females aged 65 years or older assuming capping of supplements

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
All wheat flour	0	311	105	27.4	0.5
	100	309	103	16.3	0.0
	200	344	138	10.0	0.0
	250	362	156	8.3	0.0
	300	379	173	6.5	0.0
	350	397	191	5.2	0.0
	450	432	226	2.8	0.1

Table 18: Effects of fortification on 30 males and females aged 65 years or older in the NDNS with low vitamin B_{12} blood status, assuming no capping

Fortification Scenario	Fortification level (µg /100g)	mean total folate (µg/d)	mean folic acid (µg/d)	% below RNI (total folate)	% above UL (folic acid)
All wheat flour	0	239	39	32.4	0
	100	278	78	11.9	0
	200	317	118	9.5	0
	250	337	137	9.5	0
	300	357	157	9.3	0
	350	376	176	8.3	0
	450	415	215	8.3	0

4.4 NTD risk

Tables 20 to 22 show the estimates of the mean red cell folate, and the reduction in NTD risk for the different choices of flour to be fortified, for different capping scenarios and for a range of fortification levels. Although in most cases the change in NTD risk is modest, for some scenarios the NTD risk increases slightly. This can happen even if mean folate intake increases slightly, as the overall distribution will change and the association between risk and folate status is non-linear. Likewise, small reductions in risk can be seen even in scenarios where there are small reductions in mean folate intake. This will occur when very large intakes, which inflate the mean but bring negligible reduction in NTD risk, are prevented by capping supplements.

There is uncertainty in the NTD reduction associated with any scenario. Model C is the most realistic, but the Daly and Crider prediction equations lead to different estimates. There is also uncertainty in the prediction of both equations. Information provided by Crider et al (2014, supplementary material) indicate that this is about ±20%. This is not available in Daly et al (1995), but is unlikely to be less, as it is based on a smaller sample. The difference between the two predictions (and it is unclear which is more relevant) and the additional ±20% uncertainty should be recognized when considering the estimates of NTD reduction.

It should also be noted that changes in mean risk refer to the whole population of women of childbearing age. In any fortification scenario, the risk change will vary widely between women, according to their current folate status. The biggest reductions in risk will occur in those who currently have low status, and any capping scenario will lead to an increase in risk for some women. Table 19 illustrates this for fortification of all flour at 350µg/100g with capping of supplements. It shows that among women with current folate intakes less than 100µg/d there will be a reduction in risk from 4.22 per 1,000 to 2.83 per 1,000, while for women with current intakes above 1000µg/d, there will be a small increase in risk, as these women take supplements which would be capped. However, there are few women whose intakes are currently this high.

Table 19: Variation in change in NTD risk (per 1,000 pregnancies) using Daly prediction equation, Model A, by baseline folate status

Folate intake range (µg/d)	Percent of sample	Current risk	Risk after fortification
0-100	5.7	4.22	2.83
100-200	44.2	2.86	2.09
200-300	31.7	2.19	1.77
300-400	11.5	1.84	1.58
400-500	3.5	1.60	1.42
500-600	1.3	1.45	1.34
600-700	1.0	1.33	1.25
700-800	0.4	1.26	1.19
800-900	0.1	1.21	1.17
900-1000	0.0	1.14	1.06
> 1000	0.4	0.95	1.13

Table 20: Effect of fortification scenarios for bread (1998 regulations) on red cell folate, and reduction in NTD risk according to model A (accounting for variation in folate status) and model B (predicting mean response only) and model C (as A, but assuming 30% of women take 400µg/d folic acid) using prediction equations of Daly (1995) and Crider (2014).

Capping	Fortification µg/100g	Mean folate intake µg/day	Mean red cell folate nmol/L	Model A, (Daly)	Model B (Daly)	Model C (Daly)	Model A (Crider)	Model B (Crider)	Model C (Crider)
No capping	0	251	570	0	0	0	0	0	0
	100	261	581	2.92	2.87	2.5	4.26	4.11	3.8
	200	271	591	5.37	5.3	4.61	7.74	7.48	6.93
	250	277	596	6.47	6.39	5.56	9.27	8.97	8.31
	300	282	601	7.49	7.41	6.45	10.7	10.4	9.6
	350	287	606	8.46	8.37	7.29	12	11.6	10.8
	450	297	615	10.2	10.1	8.83	14.4	14	13
Capping breakfast cereals	0	251	570	0	0	0	0	0	0
	100	240	559	-2.26	-2.25	-1.96	-3.12	-3.04	-2.83
	200	250	570	0.52	0.49	0.43	0.89	0.84	0.76
	250	255	575	1.76	1.72	1.49	2.65	2.54	2.34
	300	260	580	2.91	2.86	2.49	4.26	4.11	3.8
	350	265	585	3.99	3.93	3.42	5.77	5.57	5.16
	450	276	595	5.96	5.89	5.14	8.48	8.22	7.63
Capping breakfast cereals and spreads	0	251	570	0	0	0	0	0	0
	100	232	550	-4.32	-4.29	-3.73	-6.05	-5.88	-5.46
	200	242	561	-1.31	-1.33	-1.16	-1.69	-1.67	-1.57
	250	247	567	0.01	-0.02	-0.02	0.21	0.17	0.14
	300	252	572	1.24	1.2	1.04	1.95	1.85	1.7
	350	257	577	2.39	2.33	2.03	3.56	3.42	3.16
	450	267	587	4.48	4.41	3.85	6.46	6.24	5.78
Capping supplem ents	0	251	570	0	0	0	0	0	0
	100	240	572	2.41	2.34	2.02	3.6	3.44	3.15
	200	250	583	4.87	4.78	4.15	7.09	6.84	6.3
	250	255	588	5.97	5.88	5.1	8.64	8.34	7.69
	300	260	593	7	6.9	6	10.1	9.73	8.98
	350	265	597	7.97	7.87	6.84	11.4	11	10.2
	450	276	607	9.74	9.64	8.39	13.8	13.4	12.4
Capping all	0	251	570	0	0	0	0	0	0
	100	210	542	-4.91	-4.9	-4.28	-6.82	-6.65	-6.21
	200	220	553	-1.9	-1.93	-1.7	-2.43	-2.41	-2.29
	250	226	558	-0.56	-0.61	-0.55	-0.52	-0.57	-0.58
	300	231	563	0.67	0.61	0.51	1.22	1.13	0.99
	350	236	569	1.83	1.76	1.52	2.85	2.7	2.46
	450	246	579	3.94	3.85	3.34	5.76	5.54	5.1

Table 21: Effect of fortification scenarios for bread (NDNS definition) on red cell folate, and reduction in NTD risk according to model A (accounting for variation in folate status) and model B (predicting mean response only) and model C (as A, but assuming 30% of women take 400µg/d folic acid) using prediction equations of Daly (1995) and Crider (2014).

Capping	Fortification µg/100g	Mean folate intake µg/day	Mean red cell folate nmol/L	Model A, (Daly)	Model B (Daly)	Model C (Daly)	Model A (Crider)	Model B (Crider)	Model C (Crider)
No capping	0	251	570	0	0	0	0	0	0
	100	270	589	5.12	5.04	4.39	7.41	7.15	6.63
	200	289	608	9.16	9.06	7.89	13.1	12.7	11.7
	250	298	617	10.9	10.8	9.41	15.5	15	13.9
	300	308	625	12.5	12.4	10.8	17.7	17.1	15.9
	350	317	634	14	13.9	12.1	19.7	19.1	17.8
	450	336	649	16.7	16.6	14.5	23.2	22.6	21
Capping breakfast cereals	0	251	570	0	0	0	0	0	0
	100	249	568	0.22	0.19	0.16	0.49	0.43	0.39
	200	268	587	4.78	4.7	4.09	6.96	6.71	6.22
	250	277	597	6.74	6.65	5.79	9.69	9.37	8.68
	300	286	605	8.52	8.44	7.34	12.2	11.8	10.9
	350	296	614	10.2	10.1	8.79	14.4	14	13
	450	315	631	13.1	13.1	11.4	18.4	17.9	16.6
Capping breakfast cereals and spreads	0	251	570	0	0	0	0	0	0
	100	240	560	-1.72	-1.74	-1.51	-2.26	-2.23	-2.08
	200	259	579	3.13	3.05	2.65	4.67	4.48	4.14
	250	268	589	5.19	5.11	4.44	7.57	7.3	6.75
	300	278	598	7.08	6.99	6.08	10.2	9.85	9.11
	350	287	607	8.82	8.72	7.6	12.6	12.2	11.3
	450	306	623	11.9	11.8	10.3	16.7	16.3	15.1
Capping supplements	0	251	570	0	0	0	0	0	0
	100	249	581	4.61	4.52	3.92	6.77	6.5	5.99
	200	267	600	8.68	8.57	7.45	12.5	12.1	11.1
	250	277	609	10.4	10.3	8.98	14.9	14.4	13.3
	300	286	617	12.1	12	10.4	17.1	16.6	15.3
	350	296	626	13.6	13.5	11.7	19.1	18.5	17.2
	450	315	642	16.2	16.2	14.1	22.6	22	20.5
Capping all	0	251	570	0	0	0	0	0	0
	100	219	551	-2.3	-2.33	-2.05	-3	-2.97	-2.8
	200	238	571	2.58	2.49	2.15	3.97	3.78	3.45
	250	247	580	4.66	4.56	3.95	6.88	6.62	6.08
	300	257	589	6.56	6.45	5.6	9.51	9.18	8.46
	350	266	598	8.31	8.2	7.12	11.9	11.5	10.6
	450	285	615	11.4	11.3	9.85	16.1	15.6	14.5

Table 22: Effect of fortification scenarios for all wheat flour on red cell folate, and reduction in NTD risk according to model A (accounting for variation in folate status) and model B (predicting mean response only) and model C (as A, but assuming 30% of women take 400µg/d folic acid) using prediction equations of Daly (1995) and Crider (2014).

Capping	Fortification µg/100g	Mean folate intake µg/day	Mean red cell folate nmol/L	Model A, (Daly)	Model B (Daly)	Model C (Daly)	Model A (Crider)	Model B (Crider)	Model C (Crider)
No capping	0	251	570	0	0	0	0	0	0
	100	286	606	8.81	8.71	7.58	12.6	12.2	11.3
	200	321	638	15.2	15.1	13.1	21.3	20.7	19.2
	250	338	653	17.8	17.7	15.4	24.8	24.1	22.4
	300	356	668	20.1	20.1	17.5	27.9	27.2	25.3
	350	373	682	22.2	22.2	19.3	30.6	29.8	27.8
	450	408	708	25.8	25.9	22.6	35.3	34.5	32.2
Capping breakfast cereals	0	251	570	0	0	0	0	0	0
	100	265	585	4.42	4.34	3.77	6.5	6.27	5.79
	200	300	619	11.5	11.4	9.94	16.4	15.9	14.7
	250	317	634	14.4	14.3	12.5	20.3	19.7	18.3
	300	335	649	17	16.9	14.7	23.7	23.1	21.5
	350	352	664	19.3	19.3	16.8	26.8	26.1	24.3
	450	387	691	23.3	23.3	20.3	31.9	31.2	29.1
Capping breakfast cereals and spreads	0	251	570	0	0	0	0	0	0
	100	256	577	2.69	2.62	2.27	4.1	3.93	3.61
	200	291	611	10.2	10.1	8.76	14.6	14.1	13.1
	250	309	627	13.2	13.1	11.4	18.7	18.1	16.8
	300	326	642	15.9	15.8	13.8	22.3	21.6	20.1
	350	344	657	18.3	18.2	15.9	25.4	24.8	23
	450	378	685	22.4	22.4	19.5	30.8	30.1	28.1
Capping supplem ents	0	251	570	0	0	0	0	0	0
	100	265	597	8.33	8.21	7.13	12	11.6	10.7
	200	300	630	14.7	14.6	12.7	20.8	20.2	18.7
	250	317	645	17.3	17.3	15	24.3	23.6	21.9
	300	334	660	19.7	19.6	17.1	27.4	26.6	24.8
	350	352	674	21.8	21.8	19	30.1	29.3	27.3
	450	387	700	25.4	25.5	22.2	34.8	34	31.8
Capping all	0	251	570	0	0	0	0	0	0
	100	235	568	2.14	2.05	1.76	3.39	3.22	2.92
	200	270	603	9.67	9.54	8.29	13.9	13.4	12.4
	250	287	619	12.7	12.6	11	18	17.5	16.2
	300	305	634	15.4	15.3	13.3	21.7	21	19.5
	350	322	649	17.8	17.8	15.5	24.9	24.2	22.5
	450	357	677	22	22	19.2	30.3	29.6	27.5

5 Discussion

This report is based on intake data from years 1-6 of the NDNS rolling program. We present data on current intake levels of folic acid and total folate and recalculate how these intakes would change under various fortification scenarios. Based on these potential intakes we use stochastic models to predict blood folate status and reduction in NTD risk following a mandatory fortification scenario. As our work updates the similar modelling exercise presented in the SACN (2006) report, we will compare our results on current intake with the findings with the previous report in the first section of the discussion. In the second part we will discuss the potential impact of the various fortification scenarios on folic acid and folate intake across the population before discussing the possible changes in NTD risk in the last section.

5.1 Comparison with previous modelling

The current results can be compared with those in the SACN (2006) report. This comparison needs to be interpreted with caution as there are some differences between the data sources available then and now. The current modelling was based on data from 6 years of the NDNS rolling programme where data is collected concurrently across age groups and consistent methods have been used throughout and across age groups. In contrast, the previous modelling was based on data from 3 separate surveys conducted at different timepoints in children, adults and older individuals with differing methodologies and with some of the data being quite old (survey in older adults conducted in 1994/1995, children 1997/1998 and adults 2000/1). Also, the previous modelling was based surveys which utilised 7 day weighed records whereas the current modelling was based on non-weighed 4 day records. Another change is that where previously wheat flour content was only available on a food group level, we could use updated food item specific information. For folic acid content too, we looked into individual food items and identified a number of additional items that do not belong to the food groups for breakfast cereals, spreads or supplements. The additional information should make our modelling more accurate and realistic, but it also means that comparisons with previous results are difficult to interpret.

When comparing Table 2 with Table 13 from the SACN report 2006, the average population baseline intakes of both natural folate and folic acid are lower than estimated from the previous modelling for most age and sex groups. Average population total folate intake was 317µg/d and is now 276µg/d with a standard error (SE) of 4.7µg/d and natural folate was 228µg/d and is now 196µg/d (SE = 1.4µg/d). Folic acid intakes are slightly lower (79ug/d (SE = 4.5µg/d) vs 89µg/d) and this is despite the current analysis including additional sources of folic acid such as fortified drink powders, infant formula or cereal bars which were not included in the 2006 modelling (on average 8µg/d came from these sources), and a much higher average population intake of folic acid from supplements than previously (34 vs 16µg/d). Note that the SEs reported here assume a Normal distribution. However, as we have seen our intake data are quite skew, i.e. definitely do not follow a bell-shaped normal distribution, so these standard errors should only be seen as very rough quantifiers of the uncertainty. For this reason and to simplify the results we do not report SEs in the tables, but the uncertainty is discussed further in Appendix 4.

The lower intake of folic acid in the current report may be related to the reduced intake of folic acid from fat spreads (11 vs 30µg/d), and this fits with the knowledge that most fat spread manufacturers have stopped adding folic acid. The average population intake of folic acid from breakfast cereals is also lower compared to the previous modelling (29 vs 43µg/d).

It should be noted that lower intakes of breakfast cereals and spreads per se would also contribute to lower intakes of folic acid in addition to lower levels of voluntary fortification.

The lower levels of average folate and folic acid intakes compared to previously is also reflected in the results for women of childbearing age (see Table 3). However, the findings are consistent with the previous modelling in that the group with the highest intakes of total folate obtain more than half of their total folate from folic acid whereas the lowest intake group only obtain 7% of their total folate from folic acid.

The current analyses suggest that the population average intake of flour which has the potential to be fortified is much lower than previously suggested in the SACN report (59 vs 80g/day), see Table 5, which corresponds to Table 12 in the SACN 2006 report. There are a number of factors which may contribute to this difference:

a) The previous estimate of 80g/day includes wholemeal flour, which is excluded in our calculation.

b) The recent FSA values used for the flour content of bread and other products are generally lower than the values described in Table 19 of the SACN report e.g. white bread (52% vs 63%), brown bread (40% vs 63%) and biscuits (35% vs 50%), see Table A4 in Appendix 6.

c) As mentioned above we used flour content information at food item level, whereas the previous modelling did so at food group level. As a result our modelling will have excluded some items from food groups, where the SACN report assumed all food items within the included food groups to contain wheat flour. This is particularly the case for breads where we excluded items like (for example) rye or soya breads. On the other hand, a broader range of food categories containing flour was considered in the current analysis. Both mechanisms work in different directions as far as flour intake is concerned and it is unclear whether they will balance each other out or one of them will dominate.

Despite these different overall levels, the relative differences in flour intakes between age/sex groups generally show a similar pattern in both the current and 2006 analyses.

As a result of the lower estimated intakes of flour eligible for fortification, the increases in folic acid levels after fortification are lower than they were in the previous modelling. As Table 6 shows for 100µg/100g of flour fortification the current modelling estimates a 39µg increase in folic acid levels across the population, whereas the SACN report from 2006 provides an estimate of 51µg increase in their Table 17.

5.2 Effects of mandatory fortification

Due to the lower intake of flour and bread, fortification levels will have to be higher compared to the previous modelling exercise to obtain the same overall rise in folic acid levels. In the presence of capping of voluntarily fortified foods and/or supplements the fortification scenarios using the narrow 1998 regulation definition of bread is unlikely to have sufficient impact on folic acid levels. Capping seems inevitable if any rise in the percentage of individuals above the upper limit of folic acid is to be avoided. As Table 8 shows, capping supplements would have the biggest impact on reducing the percentage of people above the upper limit and as Tables 10 and 11 show it would help to keep this percentage below current levels in most fortification scenarios.

If we allow for a small increase in people exceeding the UL, and also consider scenarios that might raise population levels of folic acid intake by less than 60µg/d, but show a good reduction of NTD risk (see Tables 21 and 22) there is a wider range of possibilities. We highlight 6 potential scenarios here for which Tables A5-A10 in Appendix 6 give details of their impact on folic acid and folate intakes in different age-gender groups:

- Fortification of non-wholemeal bread (NDNS definition) at 250µg folic acid per 100g of bread flour without capping. This would achieve a 52µg/d increase in folic acid levels across the population with a small rise of the percentage above the upper limit from 0.4% to 0.5%.
- Fortification of all non-wholemeal wheat flour at 200µg folic acid per 100g of flour without capping. This would achieve a 78µg/d increase in folic acid levels across the population with a small rise of the percentage above the upper limit from 0.4% to 0.6%.
- Fortification of non-wholemeal bread (NDNS definition) at 450µg folic acid per 100g of bread flour with capping of breakfast cereals, spreads and supplements. This would achieve a modest 43 µg/d increase in folic acid levels across the population with a reduction of the percentage above the upper limit from 0.4% to 0.1%.
- Fortification of all non-wholemeal wheat flour at 350µg folic acid per 100g of flour with capping of breakfast cereals, spreads and supplements.This would achieve an 85µg/d increase in folic acid levels across the population while keeping the percentage above upper limit below 0.4%.
- Fortification of non-wholemeal bread (NDNS definition) at 450µg folic acid per 100g of bread flour with capping of supplements only. This would achieve a modest 60µg/d increase in folic acid levels across the population with a reduction of the percentage above the upper limit from 0.4% to 0.3%.
- Fortification of all non-wholemeal wheat flour at 300µg folic acid per 100g of flour with capping of supplements only. This would achieve an 83µg/d increase in folic acid levels across the population while reducing the percentage above the upper limit from 0.4% to 0.3%.

As women of childbearing age consume less flour than the population average, their folic acid levels would rise less than that of the overall population but Table 14 shows that a substantial reduction in the percentage of women who are below the RNI, is still achievable in this group, for example in a scenario with 300µg wheat flour fortification with capping of supplements this percentage would drop from 45.3% to 10.4%. Table 15 shows that this effect would also reach the 20% of consumers with the lowest folate intakes among women of childbearing age, where the same scenario would see a drop from 100% below the RNI to 51.2%.

Table 17 shows that in the case of supplement capping there would be no increase in the numbers of people aged 65 years and older who are above the upper limit of folic acid intake and Table 18 indicates that this would be even less of an issue among the vitamin B_{12} deficient subjects in this age group, as folic acid levels appear far lower in this vitamin B_{12} deficient subgroup. As our results show, the risk of being above the upper limit might indeed be more of an issue in children than in the elderly. Twenty of 38 subjects identified as being above the upper limit in the NDNS data were children aged 10 and younger. This is also the only age group exceeding 1% above the upper limit in the scenarios highlighted above. The reason for this are lower UL for children combined with high intakes of supplements, savoury sauces, gravies and condiments (including Marmite and related products), breakfast cereals and nutrition powders and drinks. Also, the previous modelling excluded 1.5-3 year olds as they were assumed not to consume flour, as a result of no data being available at the time. However, based on current data, Table 5 shows moderate flour consumption for this age group.

5.3 Reduction in NTD risk

As might be expected, there is a clear dose response in the risk reduction estimates. Our results are generally similar to what was found in the SACN 2006 study. Higher levels of fortification for all non-wholemeal wheat flour and not just bread is required to achieve risk reductions of 20-25% or more. Capping of supplements enables this to be done while avoiding increasing the proportion of people above the recommended UL. Fortification of bread flour only, particularly if a narrow definition is used and wide ranging capping is imposed, could lead to reduced folate intakes overall, and a corresponding increase in risk.

Mandatory fortification has been implemented elsewhere, and reductions in NTD rates have been reported. Crider et al (2011) reviewed this, and found that for example, in the USA estimates of rate of reduction have been 19-33% with 140µg/100g fortification of enriched cereal grain products. An updated estimate (CDC, 2011) indicates a 28% reduction. De Wals et al (2007) estimated a 46% reduction following fortification in Canada. Santos et al (2016) report a 30% reduction in Brazil and Nazar & Cifuentes (2013) a 44% reduction in Chile. Castillo-Lancellotti et al (2013) systematically review results reported elsewhere, citing a wide range of reduction estimates, from 16% to 58%.

While a reduction in rates is universally reported following implementation of fortification, there appears to be either substantial variation in these reductions, or uncertainty in their reported estimates. We have acknowledged this by reporting the risk reduction estimates obtained following two independent studies (Daly et al, 1995 and Crider et al, 2014), and also considered the possible effects of women taking folic acid supplements periconceptually. Considering the range of these estimates, and their comparability with observed effects of fortification programmes elsewhere, should give the best estimate of the possible effects on NTD rates of mandatory folic acid fortification in the UK.

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Appendix 1: Assumptions

Subject	Assumption BioSS/UoA 2016	Basis	Source
Intake data	Dietary intake data from 2008/9 to 2013/14 of the NDNS rolling programme represents current usual folate, flour and bread intakes in the UK population.	Preliminary analysis of the data from the rolling programme showed no substantial or systematic changes across the 6 years of the rolling programme. The NDNS programme was based on 4 day weighted intake data. This approach may overestimate extremes in folate intake. Overestimation will lead to more cautious conclusions (See Appendix 3 for further details). Estimates of extremes were based directly on the 4 day intakes as well as providing a table in Appendix 3 to indicate how these can be adjusted, based on the observed variability within and between individuals.	NDNS rolling programme years 1-6.
Underreporting	No adjustment should be made for underreporting.	The previous 2006 SACN modelling assumed no underreporting and it is difficult to extrapolate estimates of underreporting based on energy to individual foods and nutrients because they may be affected differentially. In line with the 2006 SACN modelling and based on advice from SACN, the current modelling assumed no underreporting. However, Appendix 2 shows the effect of adjustment based on estimates of underreporting for subgroups in the NDNS RP through the use of doubly labelled water to measure total energy expenditure (NDNS doubly labelled water study, NDNS years 1-4 report Appendix X).	SACN report 2006; FSS personal communicati on with SACN, 2016; NDNS years 1-4 report Appendix X
Flour intake from all products and from bread only	Assessment of wheat flour content of all products excluding wholemeal. Detailed assessment of the wheat flour content of NDNS food codes from years 1-4 of the rolling programme was obtained from FSA. Any additional foods from years 5 & 6 were identified and wheat flour content values assigned based on manufacturer information or the FSA database.	When considering fortifying all wheat flour with the exception of wholemeal, the total flour consumption for each participant excluding wholemeal flour was assessed to allow the assessment of folic acid intake from fortified flour. Those products identified as containing wholemeal flour were either excluded completely if they did not contain any other type of wheat flour or for those containing a mixture of wholemeal and other wheat flour, the wholemeal fraction was excluded. When considering fortifying bread, the total flour consumption excluding wholemeal from bread for each participant was assessed.	FSA database of wheat flour containing products
Folic acid content of	The most up to date data from the NDNS nutrient databank (Year 7 for the majority of foods and	Food subgroups with potentially fortified foods, were identified by calculating the maximum amount of folate per g in each subgroup and ranking subgroups with respect to this. Subgroups with least one food item with more than 100µg/100g	NDNS nutrient databank

voluntarily fortified foods	supplements and year 8 for breakfast cereals) reflect current levels of folic acid in voluntarily fortified foods and supplements.	folate were explored in more detail to capture those most likely to contain foods with added folic acid. For foods that might contain both natural folate and folic acid, it was assumed that folic acid would dominate and the total folate content was used as the value for folic acid. For some of the identified food groups all non-zero folate content was assumed to be folic acid (breakfast cereals; infant formula; fat spreads; nutrition powders and drinks; supplements) whereas for others, only some non-zero folate content foods were considered as containing folic acid (biscuits; manufactured buns cakes and pastries; chocolate confectionery; fruit juice; beverages dry weight; savoury sauces, pickles, gravies and condiments; commercial toddlers foods; soft drinks; brown, granary and wheatgerm bread), which were identified by checking the ingredients of the item (e.g. savoury sauces, pickles, gravies and condiments) or by looking at the distribution of folate content in the food group and selecting a threshold, where every item exceeding that threshold was considered to be fortified (e.g. biscuits; commercial toddler foods). This combination of data analysis and expert opinion guarantees that all major contributors to folic acid intake are covered in the modelling.	(Years 7 and 8 –breakfast cereals)
Overage	Overage applies to folic acid values for voluntarily fortified products: 32% for breakfast cereals, 20% for spreads, 30% for supplements and 25% for all other food groups.	Previous SACN modelling used 32% for breakfast cereals, 20% for spreads, 30% for supplements and no evidence to suggest these values not still relevant. FSAI 2016 used 25% overage value for all foods and supplements. SACN values not substantially different to FSAI but more specific for main food group sources, therefore this value was applied to those foods not covered by SACN.	SACN report 2006; FSAI 2016
Capping	Intake of supplements capped at adult RNI of 200µg (600µg for women of childbearing age). Folic acid levels of voluntarily fortified breakfast cereals and spreads capped at 15% of adult RNI (30µg).	RNI for adults 200µg; additional 400µg supplement recommended for women of childbearing age. 15% of adult RNI minimum level needed for industry to be able to label a food as a source of folic acid. These values are in line with those applied in the FSA 2007/8 modelling and are in line with previous recommendations to restrict voluntary fortification if mandatory fortification is introduced, to prevent increases in the number of people exceeding the GL/UL. No capping was placed on other miscellaneous voluntarily fortified foods, other than breakfast cereals and spreads, as this may be difficult to implement, and these foods were also not major contributors to folic acid intakes.	Dietary Reference Values 1991; SACN 2006; Regulation (EU) No 1169/2011; FSA 2008
Definitions of bread	Two ways of defining bread were used: a) NDNS food group definition excluding wholemeal (77 items) and b) 1998 Bread and Flour regulation definition excluding wholemeal (32 items).	When considering possible future legislation it is more practical to have a category which has meaning for the millers and bakers. Therefore, the definition described in the 1998 Bread and Flour Regulations was used. In addition to broaden this narrow definition to include a wider range of bread products we used the NDNS food category definition.	NDNS; 1998 Bread and Flour regulations; FSA database of

		We also considered a definition of bread products using items from the FSA database on wheat flour containing products which were identified as containing strong flour. However, this excludes some breads which are made with brown flour and white flour, and also includes some non-bread products, so it was not considered useful to use the strong flour containing foods to define a bread category to be modelled. Wholemeal breads were excluded based on the name/description of the product or food grouping within the NDNS database.	wheat flour containing products.
Bread	All breads assumed to have no added folic acid prior to mandatory fortification.	Two products identified within NDNS database as being fortified assumed to be zero for modelling of fortification scenarios. One of these products was an older product not currently available and not in the NDNS database beyond year 3. The other product was only available in Northern Ireland and therefore only appeared within the data from that country.	NDNS year 7 nutrient databank
Imported Flour	Wheat flour or wheat flour products imported into UK would not be subject to mandatory fortification. 11.3% of flour is imported into the UK and that this level is uniform across all products.	UK flour production is approximately 3.9 million tonnes a year, imports as flour and flour in products is 0.44 million tonnes and exports of flour and flour in products is 0.41 million tonnes. Therefore, the % of flour equivalents which would be for sale would be 11.3% of the UK market.	FSS personal communication with the National Association of British and Irish Flour Millers (NABIM) 2017.
Fortification applies to all non-imported wheat flour (not wholemeal)	All non-imported wheat flour (not wholemeal) used in manufactured products and non-imported food products in all the categories included in the modelling is fortified.	In line with 2006 modelling, it is assumed flour fortification will take place at the milling process and therefore all products made with wheat flour milled in the UK will be subject to fortification. Following a review of the FSA flour content database, it was decided that all products with a wheat flour (not wholemeal) content of 4% or over would be included, as those with less than 4% were considered to contain minimal amounts. Main food groups included were non-wholemeal breads; pizza; biscuits; buns, cakes, pastries and fruit pies; puddings; meat based products and dishes; fish based products and dishes; egg dishes; meat alternatives; vegetable based products and dishes. Following discussion with FSA, wheat containing food categories excluded completely from the modelling were breakfast cereals, pasta and pasta products which normally do not contain a substantial amount of non-wholemeal UK milled flour.	FSA database of wheat flour containing products; Personal communication with FSA.

		For miscellaneous foods which are currently voluntarily fortified and contain flour (e.g. cereal bars, beverages dry weight), it was assumed that folic acid from mandatory fortification of flour was additional to current voluntary fortification levels, as this was considered to be the most easily implemented approach.	
Wholemeal flour	Wholemeal flour will not be subject to fortification.	Products containing wholemeal flour (or the wholemeal flour content of those containing a mix) were excluded when modelling potential fortification of bread and wheat flour. Wholemeal flour was excluded at the request of FSS who wished to exclude wholemeal flour to allow consumer choice and this was also in line with the FSA 2007/8 modelling. The 2006 modelling had been done with and without wholemeal. Wholemeal flour is also not subject to fortification of other nutrients, so this would place folic acid fortification in line with that of other nutrients.	FSA provided detailed assessment of the flour content of products; FSA 2008; SACN 2006; 1998 Bread and Flour regulations
Processing losses for flour/bread	Processing losses of 25%	No evidence to suggest using a different value to that utilised in 2006 modelling. FSAI 2008 reported values of between 20-28% for white and brown breads. Assumed that fortification of bread will be through the fortification of flour. Advised by NABIM that processing losses are very variable depending on the product and could be up to 50% for some products but that 25% was a reasonable assumption.	SACN report 2006; FSAI 2008; FSS personal communication with NABIM 2016.
Children aged 0-3 years	Children aged 1.5-3 years consume wheat flour containing products and therefore should be included in the modelling. Children aged <1.5 years consume a minimal amount of wheat flour containing products and will not be considered in the modelling.	The previous 2006 SACN modelling assumed children aged 0-3 years did not consume food products containing flour, partly due to the lack of data in this age group which wasn't included in previous NDNS samples. However, the NDNS rolling programme includes children aged 1.5-3 years and as these children are consuming wheat flour containing products they should be included in the modelling. Children aged 0-1.5 years are not included in NDNS rolling programme. There is a lack of up to date intake data for children aged 0-1.5 years, however data from DNSIYC 2011 suggested intake of wheat flour containing foods to be minimal in children aged <1.5 years. Therefore, children aged 0-1.5 years were not included in the current modelling.	NDNS rolling programme data; DNSIYC 2011.

Current blood folate distribution	Blood folate data from 2008/9 to 2013/14 of the NDNS rolling programme represents current usual blood folate levels in the UK population	Study was on a nationally representative sample	NDNS rolling programme supplementary report: blood folate results for the UK, Scotland, Northern Ireland and Wales
Blood folate response to fortification	Blood folate can be predicted from natural folate and folic acid intakes using NDNS data and data reported in published literature.	Blood folate distributions for different fortification scenarios were estimated in different ways: (i) using the observed association in the NDNS folate data between red cell folate and observed total folate intake (ii) using a version of (i) in which natural folate and folic acid are treated as separate predictors. Fortification will only affect folic acid (iii) using estimated effects (regression coefficients) from published meta-analysis: Duffy et al (2014) and Marchetta et al (2015), though the latter is less relevant as it considers natural folate only.	NDNS rolling programme years 1-6; Duffy et al 2014; Marchetta et al 2015.
Predicting NTD risk	The prediction equations of Daly (1995) and Crider (2014) are the most suitable available.	Used by WHO in their investigations. Equations give similar predictions over most of the distribution of typical blood folate values.	Crider (2014) compares both equations
Estimating NTD risk reduction	NTD risk reduction rather than overall risk will be predicted	Prediction of NTD rates from current blood folate distribution overestimates rates compared with any recently published statistics, such as those reported by ISD Scotland. Some of this is likely to be due to underreporting of NTD pregnancies, as indicated by authors such as Morris & Wald, 2007. Assumed that under-reporting is unrelated to folate intake and blood status, and so the predicted percent reduction in risk will be applicable to the reported NTD rates.	Scottish Perinatal and Infant Mortality and Morbidity Report, 2012

Appendix 2: Adjustment for Underreporting

The results of the analysis of the NDNS doubly labelled water sub-study indicated variation in underreporting by age group (Appendix X NDNS year 1-4 rolling programme report). Overall, the mean energy intake to total energy expenditure ratio was 0.73, however, agreement was better in children than adults ranging from 0.64 in females aged 16-49 years to 0.89 in females aged 4-10 years. There were not large differences between the sexes within age groups.

Table A1: Ratio of reported EI to measured TEE (kcal) in the NDNS RP doubly labelled water sub-study (years 1 and 3).

Age group	**Sex**	**N**	**EI:TEE**
4-10 years	Males	41	0.87
	Females	41	0.89
11-15 years	Males	34	0.76
	Females	38	0.72
16-49 years	Males	38	0.66
	Females	40	0.64
50-64 years	Males	41	0.69
	Females	37	0.66
65+ years	Males	29	0.71
	Females	32	0.72

To illustrate the possible effects of misreporting adjustment, we consider two scenarios for the whole population: fortification of flour for all bread (based on the NDNS definition) excluding wholemeal by 350 µg per 100g with no capping and with capping of cereals, spreads and supplements.

Capping	Misreporting adjustment	Mean total folate (µg/d)	Percent below RNI	Percent above upper limit
No	No	348.55	11.7%	0.57%
No	Yes	499.76	2.8%	1.43%
Yes	No	301.03	17.2%	0.04%
Yes	Yes	438.7	4.4%	0.35%

Appendix 3. List of Abbreviations, Tables and Figures.

Abbreviations

FSAI	Food Safety Authority of Ireland
FSA	Food Standards Agency
FSS	Food Standards Scotland
GL	Guidance Level
NABIM	National Association of British and Irish Flour Millers
NDNS	National Diet and Nutrition Survey
NDNS RP	National Diet and Nutrition Survey Rolling Programme
NTD	Neural Tube Defects
PHE	Public Health England
RNI	Reference Nutrient Intake
SACN	Scientific Advisory Committee on Nutrition
UL	Tolerable Upper Intake Level
WHO	World Health Organisation

Tables.

Figures

Fig 1. Folate intake and B_{12} status in those over 65 yrs

Fig 2. Association between folate intake and red cell folate status in adults. R=0.39

Fig 3. Fitted curve for predicting red cell folate from total folate intake for women of childbearing age

Fig 4. Prediction equations for NTD risk by Daly (black) and Crider (blue)

Fig 5. Distributions of daily total folate and folic acid intake

Fig 6. Box and whisker plots of total folate and folic acid intake by region

Fig 7. Histograms of folic acid intake on a logarithmic scale for different scenarios

Fig 8. Histograms of total folate intake on a logarithmic scale for different scenarios

Fig A1.Variability in sample weights.

Fig A2: Overestimation of proportions in extremes of the between individual distribution. The blue line is the correct proportion. The black line shows the overestimation.

Appendix 4. Uncertainties and limitations

We have presented the results and estimates based on our current understanding of the issues and the best information to which we had access. However, we are aware that there are many uncertainties which can affect these results, and these are listed here as matters that should be kept in mind when examining the tables and other results presented.

Sampling variation.

The sample size of 9374 individuals across all 6 years is a good sample size for estimating means and medians, and for proportions below or above limits, as long as those proportions are not small. However, the proportions above upper limits are estimated to be small in most scenarios, and so the sampling uncertainty becomes substantial. The table below shows standard errors for the unweighted estimated proportion for a range of true proportions and sample sizes.

	Sample size				
True proportion	100	500	1000	2000	9000
0.1%	0.32%	0.14%	0.10%	0.07%	0.03%
0.2%	0.45%	0.20%	0.14%	0.10%	0.05%
0.5%	0.71%	0.32%	0.22%	0.16%	0.07%
1.0%	0.99%	0.44%	0.31%	0.22%	0.10%
2.0%	1.40%	0.63%	0.44%	0.31%	0.15%
5.0%	2.18%	0.97%	0.69%	0.49%	0.23%

Note that 2000 is approximately the number of women of child-bearing age in the sample. Weighted proportion estimates will have even higher standard errors, depending on the variability of the weights within the subgroup. It can be seen that for small estimated proportions these standard errors can be substantial. Another way to consider this is to note that estimated proportions of 0.1% and 0.2% will correspond to 10 or 20 individuals respectively, possibly fewer because of the weighting, and random fluctuation can easily vary this by a substantial amount.

The above assumes only sampling variation. If there is any non-response bias, i.e. any pattern of those who refuse to participate in the survey having different dietary characteristics from those who do participate, but are otherwise demographically similar, then this will add further uncertainty to the results.

Misreporting

This is a hazard in all dietary assessments. We have chosen not to report results with any adjustment for this. This will tend to lead to underestimation of folate and folic acid intakes, with or without mandatory fortification. Any attempt to adjust for misreporting introduces additional uncertainty, since it is not uniform across individuals. It is also expected to vary between food groups. The adjustment factors presented in Appendix 2 are based on various assumptions which are themselves uncertain.

4-day vs long term intakes

We are interested in long terms intakes, but have data only on intakes over 4 consecutive days. The implications of this are discussed in detail in Appendix 5.

Adjustments in calculations

Adjustment factors were used in the calculations for overage, production loss and proportion of imported products. Although the values used were based on the best information we had available, as with the previous modelling, some uncertainty is likely to remain.

Voluntary sources of folic acid

We did not place a capping on products other than breakfast cereals, spreads and supplements in the modelling and therefore intakes from other sources of voluntary fortification were not capped in any of the scenarios.

Many of those above the upper limit for folic acid in our tables reported consuming Marmite. This was particularly so for children, whose upper limit is lower than adults. Marmite has a high folate content, which we understand to be mostly folic acid. We made the more cautious assumption that it is all folic acid.

Weighting

NDNS data contain sample weights, which were used for the results presented in this report. The full details of the weighting are presented in the NDNS reports produced by Public Health England. It adjusts for the intentional oversampling (children, and the boost samples in Scotland, Wales and Northern Ireland) as well as non-response, which differs according to age, gender and other factors. Using the weights ensures that estimates are unbiased if any of these factors affects the variables being summarised, but increases variability of the estimates. This depends on how variable the weights are, and is illustrated in Fig A1. It shows that some individuals can effectively be counted as two or more, and up to 10 in one case, when proportions above or below limits are calculated.

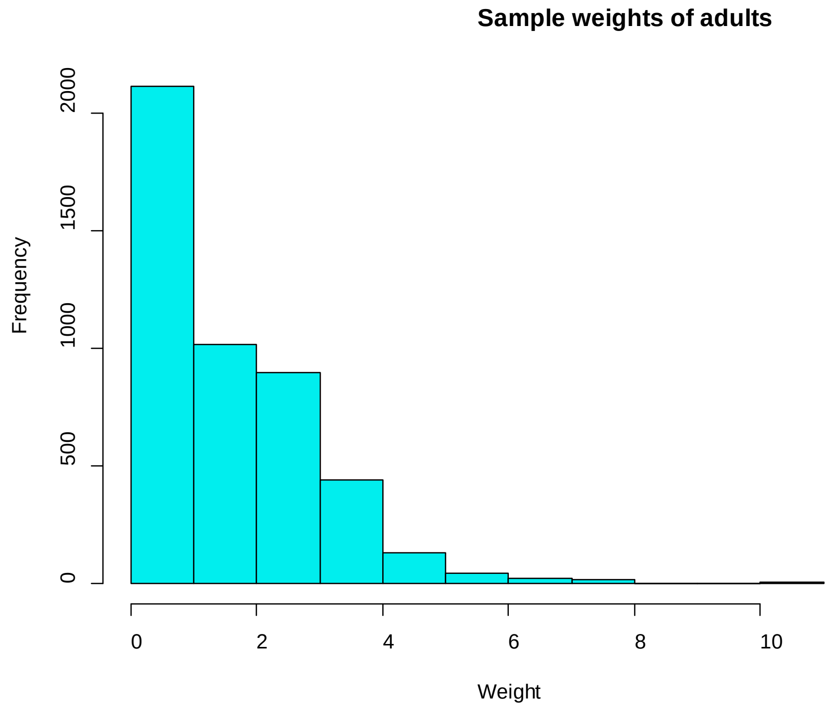

Fig A1. Variability in sample weights.

Prediction equations.

The blood folate prediction and NTD risk prediction are based on equations whose parameters (the constant and the multiplier of log red cell folate) are uncertain. We have estimates of the standard error of the blood folate prediction equation (plotted in Fig 3), which shows that these are 5-10%. They are also based on blood folate determined from a single blood sample, and so if blood folate fluctuates over time, this will weaken the link between intake and long term blood folate average.

The NTD risk equations are based on information in the literature. In the case of Crider et al (2014), the uncertainty information is presented in the supplemental material, and this produced uncertainty intervals (rather than confidence intervals, as it used a Bayesian analysis) of 2.45 to 6.64 for the intercept of 4.57, and -2.01 to -1.38 for the red cell folate coefficient of -1.70. In the case of the Daly et al (1995) prediction, confidence intervals were not presented, though as the sample size was smaller than Crider et al (2014), we can expect that they would be at least as wide.

Appendix 5: Overestimation of extreme intakes

Our interest is to estimate the distribution across individuals of their mean daily intake of folate (natural or folic acid). However, the NDNS rolling programme only supplies data on intakes for (mostly) 4 days for each individual. If these are a random sample of their typical daily intakes, which we assume, then this will lead to unbiased estimates of the mean daily intake in the population or subgroup being considered. We obtain this from the individual 4-day means we have for each individual. However, these 4-day means will vary by more than the unobservable long term individual means do, and so the between individual variability will be overestimated. A consequence of this is that the proportion of individuals estimated to be in the extremes will tend to be overestimated.

It is not straightforward to correct for this overestimation, since the true form of the distribution of between individual variability isn't known. The technique of kernel based deconvolution[10] in theory offers a solution, but our experimentation with it indicates that for the sample sizes we have, and the regions in the extremes of the distribution we will be studying, that it is quite variable in the extent of the correction it applies, and will lead to substantially more uncertain estimates, even if unbiased. Because of this, our tables show uncorrected estimates, for simplicity and to be comparable with previous work.

We can use Monte-Carlo simulation to estimate the extent of the overestimation. This requires information on the relative magnitudes of within and between individual variability. This will vary a little depending on the scenario, but we found that generally they are about the same (i.e. ratio of the variances is approximately 1.0). If we assume Normal distributions for both sources of variability, then Table A2 shows the extent of overestimation. This table can be used to approximately correct any estimates of the proportions above or below any limit. For example, the proportion is estimated to be about 5%, then the table below shows that this can have resulted from a true proportion of 3% to 3.5%. The same information is also shown in Fig A2.

The biased estimates of proportions can only overestimate, leading to more cautious conclusions. Underestimation cannot result from this issue.

[10] Wang, X.F. and Wang, B. (2011). Deconvolution estimation in measurement error models: The R package decon. Journal of Statistical Software, 39 (10), 1-24.

Table A2. Overestimation of proportions in extremes

True proportion	Estimated proportion		True proportion	Estimated proportion
0.001	0.003		0.030	0.046
0.002	0.005		0.040	0.059
0.003	0.007		0.050	0.071
0.004	0.009		0.060	0.082
0.005	0.011		0.070	0.093
0.006	0.012		0.080	0.104
0.007	0.014		0.090	0.115
0.008	0.016		0.100	0.126
0.009	0.017		0.200	0.226
0.010	0.019		0.250	0.273
0.020	0.033		0.300	0.320

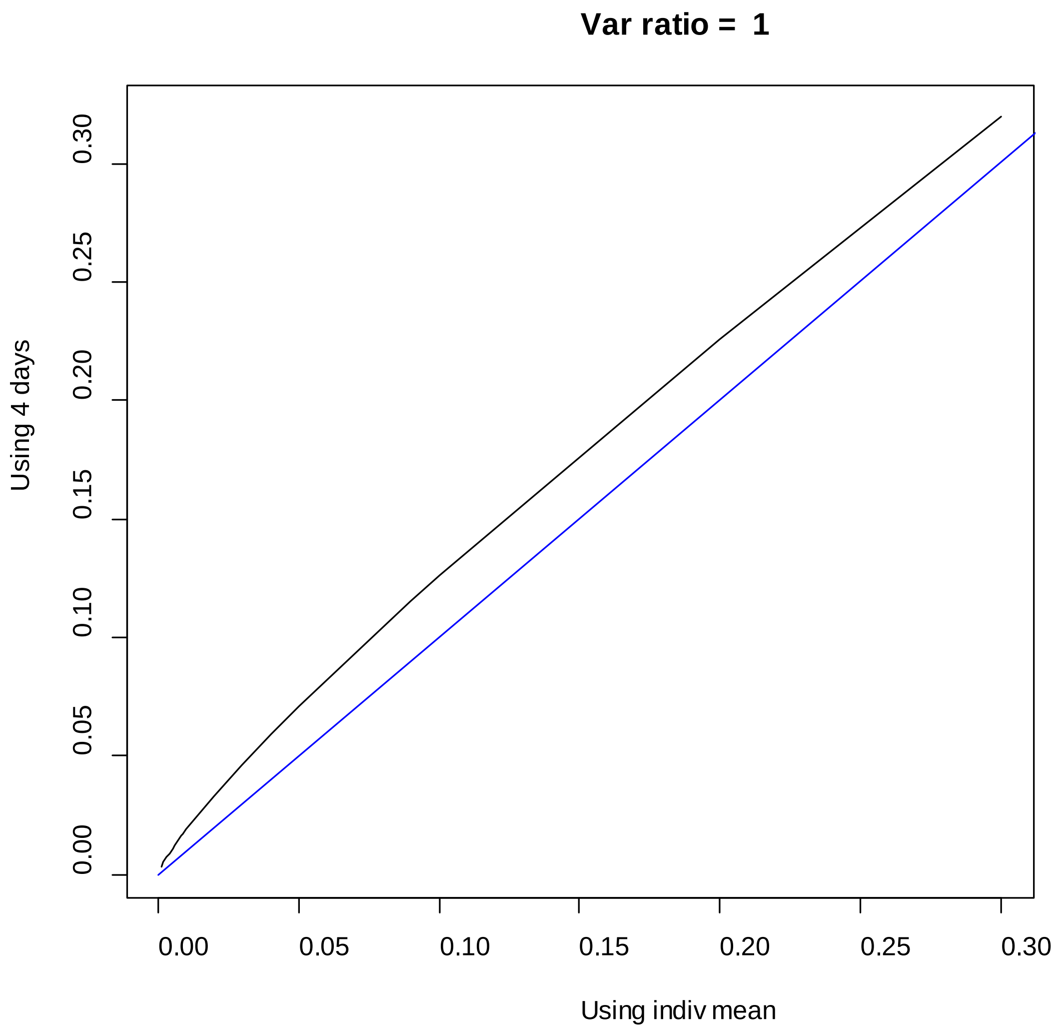

Fig A2: Overestimation of proportions in extremes of the between individual distribution. The blue line is the correct proportion. The black line shows the overestimation.

Appendix 6. Additional Tables

Table A3: Main contributors to folate and folic acid intake in NDNS year 1-6 rolling programme

Folic acid			Natural folate			Total folate		
Food subgroup	Description	% Contribution	Food subgroup	Description	% Contribution	Food subgroup	Description	% Contribution
06R	OTHER BREAKFAST CEREALS (NOT HIGH FIBRE)	22.07	02R	WHITE BREAD (NOT HIGH FIBRE; NOT MULTISEED BREAD)	6.81	06R	OTHER BREAKFAST CEREALS (NOT HIGH FIBRE)	6.25
05R	WHOLEGRAIN & HIGH FIBRE BR'FAST CEREALS	20.15	45R	FRUIT JUICE	6.20	05R	WHOLEGRAIN & HIGH FIBRE BR'FAST CEREALS	6.15
54I	VITAMINS AND MINERALS (INCL MULTIVITS & MINERALS)	14.30	39B	OTHER POTATOES INCLUDING Â HOMEMADE DISHES	5.83	02R	WHITE BREAD (NOT HIGH FIBRE; NOT MULTISEED BREAD)	4.96
54D	FOLIC ACID	12.30	37M	OTHER VEGETABLES INCLUDING HOMEMADE DISHES	4.75	45R	FRUIT JUICE	4.57
21A	REDUCED FAT SPREAD (POLYUNSATURATED)	8.10	11R	SEMI SKIMMED MILK	4.62	39B	OTHER POTATOES INCLUDING Â HOMEMADE DISHES	4.24
19A	POLYUNSATURATED LOW FAT SPREAD	6.85	49A	BEERS AND LAGERS	4.57	54I	VITAMINS AND MINERALS (INCL MULTIVITS & MINERALS)	3.90
54G	VITAMINS (TWO OR MORE INCL MULTIVITS) Â NO MINERALS	5.29	59R	BROWN GRANARY AND WHEATGERM BREAD	3.78	37M	OTHER VEGETABLES INCLUDING HOMEMADE DISHES	3.46
50R	SAVOURY SAUCES PICKLES GRAVIES & CONDIMENTS	4.89	36B	SALAD AND OTHER RAW VEGETABLES	3.65	11R	SEMI SKIMMED MILK	3.36
50A	BEVERAGES DRY WEIGHT	1.08	37D	LEAFY GREEN VEGETABLES NOT RAW	3.06	54D	FOLIC ACID	3.35
50E	NUTRITION POWDERS AND DRINKS	0.93	40R	OTHER FRUIT NOT CANNED	3.03	49A	BEERS AND LAGERS	3.32

Table A4: Flour content of main contributors to non-wholemeal flour intake in NDNS year 1-6 rolling programme

Food subgroup	Description	% Contribution to flour intake	Flour content %
2R	WHITE BREAD (NOT HIGH FIBRE; NOT MULTISEED BREAD)	44.24	52
7A	BISCUITS MANUFACTURED / RETAIL	8.31	35
1C	PIZZA	7.76	33
59R	BROWN GRANARY AND WHEATGERM BREAD	7.50	40
8D	BUNS CAKES & PASTRIES MANUFACTURED	6.70	27
1R	OTHER CEREALS	4.20	44
31A	MANUFACTURED MEAT PIES AND PASTRIES	3.28	21
26A	MANUFACTURED COATED CHICKEN / TURKEY PRODUCTS	2.82	15
33R	WHITE FISH COATED OR FRIED	2.37	14
30B	OTHER SAUSAGES INCLUDING HOMEMADE DISHES	2.25	11
29R	BURGERS AND KEBABS PURCHASED	1.46	16
50R	SAVOURY SAUCES PICKLES GRAVIES & CONDIMENTS	1.40	12
8E	BUNS CAKES & PASTRIES HOMEMADE	1.26	27
4R	OTHER BREAD	0.93	37
44R	CHOCOLATE CONFECTIONERY	0.48	13
8B	FRUIT PIES MANUFACTURED	0.48	21
31B	HOMEMADE MEAT PIES AND PASTRIES	0.43	20
9H	OTHER CEREAL BASED PUDDINGS - HOMEMADE	0.42	15
38C	OTHER MANUFACTURED POTATO PRODUCTS FRIED/BAKED	0.40	34
3R*	WHOLEMEAL BREAD	0.37	19

* Non-wholemeal fraction of products containing a mix of wholemeal and non-wholemeal flour

Table A5: Effects of fortification of bread (NDNS definition) with 250µg per 100g bread flour assuming no capping

Age-Gender Group	mean folic acid (µg/d)	mean(total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	75	189	0.6	1.5
4-6 males and females	101	238	0.3	1.0
7-10 males and females	115	263	5.7	0.4
11-13 males and females	122	273	22.1	0.0
14-49 females	123	298	24.1	0.3
14-18 females	103	247	36.0	0.0
14-18 males	132	317	16.6	0.0
19-34 females	136	309	22.9	0.5
19-34 males	144	367	12.8	0.0
35-49 females	118	302	21.8	0.3
35-49 males	140	376	9.2	0.5
50 and over males and females	141	358	12.2	0.7
50-64 males and females	133	360	10.5	0.7
65-74 males and females	141	361	11.5	0.5
75 and over males and females	163	348	18.2	1.0
overall population	131	328	14.3	0.5

Table A6: Effects of fortification of all non-wholemeal wheat flour with 200 µg per 100g assuming no capping

Age-Gender Group	mean folic acid (µg/d)	mean(total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	93	207	0.5	2.8
4-6 males and females	125	263	0.0	1.1
7-10 males and females	146	293	2.2	0.7
11-13 males and females	155	306	11.1	0.0
14-49 females	146	321	16.3	0.4
14-18 females	131	275	22.8	0.0
14-18 males	171	356	10.5	0.0
19-34 females	159	333	15.1	0.5
19-34 males	178	400	8.1	0.0
35-49 females	138	322	15.7	0.3
35-49 males	167	402	5.6	0.5
50 and over males and females	165	382	8.7	0.7
50-64 males and females	155	382	7.5	0.7
65-74 males and females	165	386	7.7	0.5
75 and over males and females	189	374	13.4	1.0
overall population	157	353	9.4	0.6

Table A7: Effects of fortification of bread (NDNS definition) with 450µg per 100g bread flour assuming capping of breakfast cereals, spreads and supplements

Age-Gender Group	mean folic acid (µg/d)	mean(total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	68	182	2.2	1.8
4-6 males and females	96	233	1.8	0.6
7-10 males and females	109	256	9.7	0.2
11-13 males and females	125	277	22.8	0.0
14-49 females	118	293	24.1	0.1
14-18 females	109	253	34.1	0.0
14-18 males	142	327	16.6	0.2
19-34 females	120	294	23.1	0.0
19-34 males	155	378	12.5	0.0
35-49 females	118	302	22.4	0.2
35-49 males	142	377	9.3	0.0
50 and over males and females	115	332	13.0	0.0
50-64 males and females	117	344	11.8	0.0
65-74 males and females	118	339	11.0	0.0
75 and over males and females	104	289	19.5	0.0
overall population	122	318	14.9	0.1

Table A8: Effects of fortification of all non-wholemeal wheat flour with 350µg per 100g assuming capping of breakfast cereals, spreads and supplements

Age-Gender Group	mean folic acid (µg/d)	mean(total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	97	212	0.8	3.6
4-6 males and females	136	273	0.2	0.8
7-10 males and females	160	307	1.3	0.8
11-13 males and females	180	332	7.0	0.0
14-49 females	155	330	13.3	0.1
14-18 females	155	300	16.7	0.0
14-18 males	208	393	5.2	0.2
19-34 females	160	333	11.9	0.0
19-34 males	210	433	6.7	0.0
35-49 females	152	336	13.7	0.2
35-49 males	185	421	4.0	0.0
50 and over males and females	154	371	7.3	0.0
50-64 males and females	153	380	7.1	0.0
65-74 males and females	159	380	5.4	0.0
75 and over males and females	148	333	10.6	0.0
overall population	164	361	7.5	0.2

Table A9: Effects of fortification of bread (NDNS definition) with 450µg per 100g assuming capping of supplements only

Age-Gender Group	mean folic acid (µg/d)	mean(total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	99	213	0.6	6.0
4-6 males and females	133	270	0.1	3.8
7-10 males and females	154	301	3.7	1.0
11-13 males and females	169	321	12.2	0.0
14-49 females	148	322	16.6	0.1
14-18 females	142	286	25.3	0.0
14-18 males	185	370	12.2	0.2
19-34 females	150	323	15.1	0.0
19-34 males	195	417	8.2	0.0
35-49 females	147	332	15.5	0.2
35-49 males	179	414	5.9	0.0
50 and over males and females	149	366	8.7	0.0
50-64 males and females	149	376	8.0	0.0
65-74 males and females	154	374	6.9	0.0
75 and over males and females	141	326	13.3	0.0
overall population	157	353	9.7	0.4

Table A10: Effects of fortification of all non-wholemeal wheat flour with 300µg per 100g assuming capping of supplements only

Age-Gender Group	mean folic acid (µg/d)	mean(total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	116	230	0.5	6.4
4-6 males and females	156	293	0.0	3.1
7-10 males and females	185	333	0.6	1.7
11-13 males and females	201	353	5.9	0.0
14-49 females	168	342	10.4	0.2
14-18 females	170	314	14.0	0.0
14-18 males	224	409	4.8	0.0
19-34 females	170	344	8.9	0.0
19-34 males	224	446	4.8	0.0
35-49 females	165	349	10.8	0.4
35-49 males	199	434	4.0	0.0
50 and over males and females	170	387	5.8	0.0
50-64 males and females	168	394	5.2	0.0
65-74 males and females	177	397	5.2	0.0
75 and over males and females	168	353	8.5	0.0
overall population	180	376	6.0	0.4

Table A11: Effects of fortification of bread (1998 regulation) assuming no capping

Age-Gender Group	Fortification (µg/100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	0	45	39	159	149	1.38	0.79
	100	54	48	169	160	0.80	0.96
	200	64	57	178	168	0.80	1.43
	250	68	61	182	173	0.76	1.47
	300	73	65	187	178	0.62	2.28
	350	77	69	192	181	0.62	2.31
	450	87	79	201	188	0.62	3.96
4-6 males and females	0	57	44	195	186	4.68	0.58
	100	69	56	206	198	1.94	0.58
	200	81	68	218	208	1.46	0.75
	250	87	75	224	213	1.30	0.75
	300	92	81	230	219	1.23	0.78
	350	98	85	236	225	1.09	1.01
	450	110	96	247	239	0.98	1.63
7-10 males and females	0	66	51	213	198	18.96	0.36
	100	78	63	226	212	13.09	0.36
	200	91	75	238	227	9.17	0.36
	250	97	82	244	232	8.00	0.36
	300	103	88	250	238	6.95	0.36
	350	109	94	257	245	6.62	0.66
	450	121	105	269	258	6.17	0.66
11-13 males and females	0	62	47	213	198	50.29	0.00
	100	75	62	226	211	43.89	0.00
	200	88	78	239	227	35.40	0.00
	250	94	85	246	235	32.59	0.00
	300	101	91	252	243	30.46	0.00
	350	107	99	259	248	27.54	0.00
	450	120	110	272	261	24.02	0.00
14-49 females	0	76	28	251	212	45.27	0.34
	100	87	39	261	219	41.08	0.34
	200	97	52	271	230	34.94	0.34
	250	102	58	277	236	32.38	0.34
	300	107	64	282	242	30.08	0.34
	350	112	69	287	248	28.31	0.34
	450	122	79	297	259	25.68	0.34
14-18 females	0	55	31	199	180	60.81	0.00
	100	65	43	209	193	56.07	0.00
	200	75	55	219	200	50.00	0.00
	250	80	61	224	206	46.26	0.00
	300	85	65	229	209	43.88	0.00
	350	90	69	234	215	40.92	0.00
	450	100	78	244	226	36.82	0.00
14-18 males	0	63	38	248	226	38.96	0.00
	100	77	55	262	245	32.88	0.00
	200	92	71	277	262	27.82	0.00
	250	99	79	284	272	26.33	0.00
	300	106	86	292	280	24.48	0.00
	350	114	95	299	288	23.37	0.00
	450	128	107	313	296	21.21	0.00
19-34 females	0	85	27	259	205	47.03	0.53
	100	96	37	270	214	42.24	0.53
	200	107	50	280	223	35.04	0.53
	250	112	56	286	231	31.98	0.53
	300	117	63	291	238	29.20	0.53
	350	123	67	296	243	27.64	0.53
	450	133	78	307	255	24.86	0.53

Age-Gender Group	Fortification (µg/100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
19-34 males	0	74	39	296	266	27.94	0.00
	100	89	55	311	280	25.69	0.00
	200	104	74	326	291	21.36	0.00
	250	111	84	334	299	19.65	0.00
	300	119	91	341	307	17.74	0.00
	350	126	97	349	315	16.43	0.00
	450	142	112	364	333	15.22	0.00
35-49 females	0	74	29	258	228	39.33	0.26
	100	84	40	268	240	35.86	0.26
	200	93	55	277	249	30.70	0.26
	250	98	60	282	254	28.93	0.26
	300	103	65	287	258	27.12	0.26
	350	108	71	292	263	25.49	0.26
	450	118	80	302	273	23.40	0.26
35-49 males	0	74	31	309	273	21.18	0.48
	100	88	50	323	287	16.38	0.48
	200	102	62	337	306	14.51	0.48
	250	109	70	344	312	13.75	0.48
	300	116	78	351	319	13.20	0.48
	350	123	87	358	325	12.93	0.48
	450	137	100	372	336	11.31	0.48
50 and over males and females	0	94	34	311	263	25.80	0.62
	100	107	46	324	275	21.48	0.62
	200	119	63	336	288	16.99	0.62
	250	125	70	342	294	15.32	0.62
	300	131	77	348	299	14.22	0.69
	350	138	84	354	304	13.19	0.69
	450	150	95	367	314	12.08	0.69
50-64 males and females	0	85	28	312	271	24.37	0.71
	100	96	42	323	285	20.00	0.71
	200	108	58	335	296	15.21	0.71
	250	114	66	341	299	13.36	0.71
	300	120	74	346	303	12.57	0.71
	350	125	79	352	309	12.06	0.71
	450	137	90	364	322	11.30	0.71
65-74 males and females	0	94	40	314	265	22.51	0.24
	100	107	54	327	277	18.79	0.24
	200	120	70	340	289	15.58	0.24
	250	126	79	347	294	14.38	0.24
	300	133	84	353	303	13.54	0.47
	350	139	87	360	307	12.14	0.47
	450	153	103	373	317	10.26	0.47
75 and over males and females	0	122	36	306	233	34.64	0.97
	100	135	50	320	250	29.58	0.97
	200	148	69	333	266	23.96	0.97
	250	154	76	339	272	22.09	0.97
	300	161	82	346	278	19.77	0.97
	350	168	87	352	283	17.86	0.97
	450	181	102	366	297	16.96	0.97
overall population	0	79	36	276	235	29.81	0.42
	100	91	49	288	247	25.67	0.42
	200	104	63	300	260	21.22	0.44
	250	110	69	306	266	19.52	0.45
	300	116	76	312	273	18.11	0.49
	350	122	82	318	278	16.97	0.52
	450	134	93	331	291	15.40	0.58

Table A12: Effects of fortification of bread (NDNS definition) assuming no capping

Age-Gender Group	Fortification (µg/100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	0	45	39	159	149	1.38	0.79
	100	57	51	171	163	0.80	0.96
	200	69	63	183	174	0.66	1.47
	250	75	69	189	179	0.62	1.49
	300	81	74	195	184	0.62	2.37
	350	87	80	201	190	0.62	3.49
	450	99	91	213	199	0.62	6.03
4-6 males and females	0	57	44	195	186	4.68	0.58
	100	75	61	212	204	0.98	0.60
	200	92	77	230	221	0.36	0.98
	250	101	88	238	228	0.32	0.98
	300	110	98	247	235	0.27	1.26
	350	119	106	256	244	0.15	1.49
	450	136	122	273	263	0.12	3.97
7-10 males and females	0	66	51	213	198	18.96	0.36
	100	86	70	233	219	10.58	0.36
	200	105	90	253	242	6.36	0.38
	250	115	100	263	253	5.73	0.38
	300	125	109	273	264	5.19	0.38
	350	135	120	282	273	4.26	0.75
	450	155	139	302	292	3.69	1.26
11-13 males and females	0	62	47	213	198	50.29	0.00
	100	86	74	237	225	37.33	0.00
	200	110	99	261	251	25.56	0.00
	250	122	113	273	263	22.15	0.00
	300	134	123	285	276	20.27	0.00
	350	146	133	297	287	16.57	0.00
	450	170	155	321	309	12.15	0.00
14-49 females	0	76	28	251	212	45.27	0.34
	100	95	49	270	232	36.03	0.34
	200	114	73	289	253	27.52	0.34
	250	123	83	298	262	24.05	0.34
	300	133	93	308	272	21.72	0.34
	350	142	104	317	282	19.48	0.34
	450	161	123	336	300	16.55	0.34
14-18 females	0	55	31	199	180	60.81	0.00
	100	74	54	218	199	50.74	0.00
	200	93	75	238	220	40.07	0.00
	250	103	85	247	234	35.97	0.00
	300	113	95	257	247	32.18	0.00
	350	122	105	267	255	28.56	0.00
	450	142	123	286	273	25.28	0.00
14-18 males	0	63	38	248	226	38.96	0.00
	100	90	64	275	256	28.21	0.03
	200	118	97	303	289	19.99	0.03
	250	132	114	317	302	16.61	0.03
	300	146	130	331	315	14.30	0.03
	350	159	144	344	329	13.43	0.03
	450	187	177	372	358	12.22	0.27
19-34 females	0	85	27	259	205	47.03	0.53
	100	106	50	279	227	36.02	0.53
	200	126	74	299	250	26.56	0.53
	250	136	85	309	260	22.92	0.53
	300	146	93	319	271	20.59	0.53
	350	156	103	329	279	18.02	0.53
	450	176	126	349	295	15.11	0.53

Age-Gender Group	Fortification (µg/100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
19-34 males	0	74	39	296	266	27.94	0.00
	100	102	65	324	294	21.39	0.00
	200	130	99	353	323	14.46	0.00
	250	144	117	367	339	12.75	0.00
	300	159	130	381	355	11.73	0.00
	350	173	149	395	368	10.37	0.00
	450	201	182	424	397	8.15	0.00
35-49 females	0	74	29	258	228	39.33	0.26
	100	91	48	275	244	32.01	0.26
	200	109	71	293	264	24.99	0.26
	250	118	82	302	275	21.84	0.26
	300	126	92	310	283	19.91	0.26
	350	135	104	319	291	18.37	0.26
	450	153	122	337	305	15.53	0.26
35-49 males	0	74	31	309	273	21.18	0.48
	100	100	65	336	300	14.53	0.48
	200	127	93	362	332	10.73	0.48
	250	140	107	376	346	9.16	0.48
	300	154	120	389	360	8.24	0.48
	350	167	132	402	376	7.99	0.48
	450	194	156	429	395	5.88	0.48
50 and over males and females	0	94	34	311	263	25.80	0.62
	100	113	52	330	281	19.22	0.62
	200	132	76	349	299	14.49	0.69
	250	141	86	358	308	12.24	0.69
	300	150	96	367	315	11.23	0.69
	350	160	106	377	323	10.19	0.69
	450	178	125	395	342	8.68	0.69
50-64 males and females	0	85	28	312	271	24.37	0.71
	100	104	47	331	292	17.40	0.71
	200	124	73	350	308	12.67	0.71
	250	133	84	360	315	10.49	0.71
	300	143	94	370	322	9.83	0.71
	350	153	105	379	331	8.98	0.71
	450	172	124	399	349	7.98	0.71
65-74 males and females	0	94	40	314	265	22.51	0.24
	100	113	59	333	283	16.99	0.24
	200	131	81	352	304	13.24	0.47
	250	141	92	361	316	11.47	0.47
	300	150	103	370	328	10.18	0.47
	350	159	115	380	340	8.92	0.47
	450	178	134	398	357	6.87	0.47
75 and over males and females	0	122	36	306	233	34.64	0.97
	100	138	56	323	251	27.53	0.97
	200	155	75	340	269	21.35	0.97
	250	163	84	348	277	18.16	0.97
	300	172	91	356	292	16.61	0.97
	350	180	95	365	299	15.41	0.97
	450	197	109	382	312	13.34	0.97
overall population	0	79	36	276	235	29.81	0.42
	100	100	58	296	257	22.42	0.42
	200	121	80	317	277	16.57	0.47
	250	131	92	328	286	14.29	0.48
	300	142	103	338	296	12.97	0.51
	350	152	114	349	306	11.67	0.57
	450	173	134	369	326	9.72	0.76

Table A13: Effects of fortification of all non-wholemeal wheat flour assuming no capping

Age-Gender Group	Fortification (µg /100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	0	45	39	159	149	1.38	0.79
	100	69	64	183	175	0.62	1.78
	200	93	86	207	196	0.51	2.85
	250	104	98	219	208	0.49	4.37
	300	116	110	230	219	0.49	6.40
	350	128	123	242	232	0.49	10.29
	450	152	145	266	253	0.49	19.87
4-6 males and females	0	57	44	195	186	4.68	0.58
	100	91	78	229	218	0.29	0.60
	200	125	112	263	253	0.03	1.14
	250	142	127	279	270	0.00	1.38
	300	159	145	296	288	0.00	3.49
	350	176	163	313	305	0.00	6.81
	450	210	200	347	339	0.00	13.39
7-10 males and females	0	66	51	213	198	18.96	0.36
	100	106	91	253	242	6.01	0.38
	200	146	134	293	284	2.21	0.70
	250	166	156	313	305	0.92	1.09
	300	186	176	333	323	0.65	1.93
	350	206	195	353	344	0.65	3.06
	450	246	238	393	387	0.64	6.55
11-13 males and females	0	62	47	213	198	50.29	0.00
	100	108	96	260	247	25.45	0.00
	200	155	148	306	297	11.14	0.00
	250	178	171	330	321	8.17	0.00
	300	201	194	353	344	5.90	0.00
	350	225	217	376	364	3.98	0.00
	450	271	260	423	409	2.16	0.15
14-49 females	0	76	28	251	212	45.27	0.34
	100	111	67	286	249	28.70	0.38
	200	146	107	321	285	16.30	0.38
	250	164	127	338	301	12.59	0.47
	300	181	145	356	316	10.37	0.47
	350	199	163	373	334	9.50	0.47
	450	233	199	408	369	6.46	0.47
14-18 females	0	55	31	199	180	60.81	0.00
	100	93	71	237	220	40.33	0.00
	200	131	113	275	260	22.75	0.00
	250	150	136	295	279	17.78	0.00
	300	170	157	314	299	14.04	0.00
	350	189	174	333	317	12.25	0.00
	450	227	216	371	357	8.95	0.00
14-18 males	0	63	38	248	226	38.96	0.00
	100	117	96	302	281	17.94	0.03
	200	171	153	356	336	10.52	0.03
	250	198	181	383	362	8.15	0.06
	300	225	211	410	395	4.83	0.06
	350	252	240	438	420	3.21	0.33
	450	307	296	492	475	2.30	0.96
19-34 females	0	85	27	259	205	47.03	0.53
	100	122	69	296	246	28.42	0.53
	200	159	109	333	282	15.08	0.53
	250	178	129	352	298	10.58	0.53
	300	196	150	370	313	8.88	0.53
	350	215	166	388	332	8.31	0.53
	450	252	202	425	369	4.79	0.53

Age-Gender Group	Fortification (µg /100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
19-34 males	0	74	39	296	266	27.94	0.00
	100	126	91	348	317	15.05	0.00
	200	178	156	400	379	8.06	0.00
	250	204	184	426	411	5.66	0.00
	300	230	214	452	436	4.77	0.00
	350	256	244	478	461	3.72	0.00
	450	308	297	531	516	3.14	0.00
35-49 females	0	74	29	258	228	39.33	0.26
	100	106	65	290	262	25.77	0.34
	200	138	102	322	292	15.69	0.34
	250	154	122	338	309	13.07	0.54
	300	170	141	354	325	10.77	0.54
	350	186	156	370	339	9.89	0.54
	450	218	190	402	373	7.37	0.54
35-49 males	0	74	31	309	273	21.18	0.48
	100	120	85	356	324	10.48	0.48
	200	167	139	402	372	5.58	0.48
	250	190	163	426	397	4.55	0.48
	300	214	187	449	424	3.95	0.48
	350	237	213	472	448	3.26	0.48
	450	283	262	519	499	2.30	0.48
50 and over males and females	0	94	34	311	263	25.80	0.62
	100	130	70	346	299	15.10	0.69
	200	165	110	382	337	8.69	0.69
	250	182	129	399	353	7.17	0.69
	300	200	148	417	370	5.82	0.76
	350	217	166	434	385	5.07	0.76
	450	253	203	469	420	3.38	0.81
50-64 males and females	0	85	28	312	271	24.37	0.71
	100	120	66	347	310	13.98	0.71
	200	155	107	382	345	7.51	0.71
	250	173	126	400	361	6.11	0.71
	300	191	145	417	380	5.22	0.84
	350	208	163	435	394	4.94	0.84
	450	243	203	470	430	3.87	0.84
65-74 males and females	0	94	40	314	265	22.51	0.24
	100	130	76	350	302	12.85	0.47
	200	165	116	386	343	7.68	0.47
	250	183	133	404	360	6.46	0.47
	300	201	155	421	375	5.15	0.47
	350	219	171	439	391	3.66	0.47
	450	255	212	475	426	1.44	0.47
75 and over males and females	0	122	36	306	233	34.64	0.97
	100	155	74	340	273	21.56	0.97
	200	189	111	374	306	13.41	0.97
	250	206	128	391	322	11.14	0.97
	300	223	148	408	343	8.48	0.97
	350	240	161	425	358	7.58	0.97
	450	274	202	459	387	4.97	1.25
overall population	0	79	36	276	235	29.81	0.42
	100	118	76	314	277	17.03	0.48
	200	157	119	353	315	9.45	0.55
	250	176	139	373	336	7.38	0.63
	300	196	159	392	354	5.99	0.83
	350	215	178	412	373	5.20	1.11
	450	254	219	451	412	3.59	1.80

Table A14: Effects of fortification of bread (1998 regulation) assuming capping of breakfast cereals, spreads and supplements

Age-Gender Group	Fortification (µg /100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	0	14	7	129	120	5.23	0.15
	100	24	16	138	129	3.42	0.29
	200	33	25	147	139	2.91	0.29
	250	37	29	152	142	2.91	0.29
	300	42	33	156	146	2.59	0.29
	350	47	37	161	149	2.24	0.29
	450	56	45	170	157	2.24	0.96
4-6 males and females	0	17	8	154	148	13.74	0.00
	100	29	20	166	158	9.68	0.00
	200	40	32	178	170	6.75	0.00
	250	46	37	183	177	5.40	0.00
	300	52	43	189	181	4.87	0.00
	350	58	47	195	186	4.58	0.00
	450	69	57	207	198	4.10	0.00
7-10 males and females	0	20	10	167	154	47.33	0.03
	100	32	23	180	166	36.89	0.03
	200	45	34	192	179	27.56	0.12
	250	51	40	198	186	24.70	0.12
	300	57	46	204	192	22.30	0.12
	350	63	51	211	198	20.97	0.21
	450	75	63	223	209	18.37	0.21
11-13 males and females	0	17	9	169	160	75.74	0.00
	100	30	22	182	173	69.85	0.00
	200	43	35	195	187	60.69	0.00
	250	50	40	201	192	55.40	0.00
	300	56	45	208	197	51.12	0.00
	350	63	50	214	203	47.83	0.00
	450	75	61	227	215	42.14	0.00
14-49 females	0	33	4	208	180	60.75	0.07
	100	44	15	218	189	56.35	0.07
	200	54	25	228	200	50.35	0.07
	250	59	30	233	204	47.31	0.07
	300	64	35	239	208	44.31	0.07
	350	69	40	244	214	41.74	0.07
	450	79	49	254	225	37.14	0.07
14-18 females	0	22	5	166	149	78.10	0.00
	100	32	16	176	161	75.28	0.00
	200	41	25	186	171	67.56	0.00
	250	46	30	191	178	63.45	0.00
	300	51	34	196	182	60.39	0.00
	350	56	38	201	186	58.37	0.00
	450	66	45	211	198	51.11	0.00
14-18 males	0	18	8	203	186	57.59	0.00
	100	33	23	218	203	48.63	0.00
	200	47	35	232	222	40.87	0.00
	250	54	41	239	228	39.12	0.00
	300	62	47	247	238	35.74	0.00
	350	69	53	254	244	33.24	0.00
	450	84	65	269	259	30.36	0.00
19-34 females	0	30	4	204	179	62.12	0.00
	100	41	15	214	188	57.60	0.00
	200	51	24	225	199	51.66	0.00
	250	57	29	230	203	47.52	0.00
	300	62	33	236	207	44.80	0.00
	350	67	39	241	211	42.25	0.00
	450	78	48	252	222	38.03	0.00

Age-Gender Group	Fortification (µg /100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
19-34 males	0	28	5	250	225	40.60	0.00
	100	43	22	265	237	35.54	0.00
	200	58	35	280	251	29.47	0.00
	250	65	41	288	256	25.97	0.00
	300	73	48	296	264	24.91	0.00
	350	81	55	303	268	23.22	0.00
	450	96	71	318	285	21.33	0.00
35-49 females	0	40	4	224	190	54.68	0.15
	100	49	16	233	200	49.97	0.15
	200	59	27	243	209	44.38	0.15
	250	64	32	248	215	42.69	0.15
	300	69	36	253	225	39.43	0.15
	350	74	41	258	229	36.69	0.15
	450	84	50	268	238	32.45	0.15
35-49 males	0	22	6	258	234	34.11	0.00
	100	36	20	272	250	25.66	0.00
	200	50	33	286	264	20.75	0.00
	250	57	39	293	272	18.43	0.00
	300	64	46	300	279	17.85	0.00
	350	72	51	307	289	17.34	0.00
	450	86	64	321	303	15.13	0.00
50 and over males and females	0	31	5	248	225	37.13	0.00
	100	43	19	260	238	31.50	0.00
	200	56	32	273	249	26.08	0.00
	250	62	38	279	254	23.20	0.00
	300	68	43	285	262	21.63	0.00
	350	74	50	291	269	19.83	0.00
	450	86	60	303	282	18.31	0.00
50-64 males and females	0	30	4	257	235	34.37	0.00
	100	42	18	268	244	28.79	0.00
	200	53	29	280	255	23.59	0.00
	250	59	34	286	262	20.52	0.00
	300	65	40	292	271	19.08	0.00
	350	71	46	297	278	17.89	0.00
	450	82	56	309	290	17.00	0.00
65-74 males and females	0	34	7	254	227	34.42	0.00
	100	47	21	267	240	28.74	0.00
	200	60	36	280	254	24.15	0.00
	250	67	43	287	260	21.66	0.00
	300	73	49	294	266	20.98	0.00
	350	80	54	300	272	18.90	0.00
	450	93	64	313	283	16.27	0.00
75 and over males and females	0	29	6	214	203	48.75	0.00
	100	43	20	227	215	43.03	0.00
	200	56	34	241	224	35.77	0.00
	250	62	41	247	231	32.84	0.00
	300	69	47	254	234	29.56	0.00
	350	75	54	260	240	26.55	0.00
	450	89	67	273	253	24.93	0.00
overall population	0	28	6	224	199	43.68	0.02
	100	40	19	237	212	37.95	0.03
	200	52	30	249	224	32.23	0.03
	250	58	36	255	230	29.39	0.03
	300	65	41	261	237	27.52	0.03
	350	71	47	267	243	25.73	0.03
	450	83	57	279	254	23.17	0.05

Table A15: Effects of fortification of bread (NDNS definition) assuming capping of breakfast cereals, spreads and supplements

Age-Gender Group	Fortification (µg /100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	0	14	7	129	120	5.23	0.15
	100	26	19	140	132	3.38	0.29
	200	38	32	152	143	2.77	0.29
	250	44	37	158	149	2.77	0.29
	300	50	43	164	154	2.59	0.29
	350	56	49	170	158	2.24	0.29
	450	68	60	182	172	2.24	1.77
4-6 males and females	0	17	8	154	148	13.74	0.00
	100	34	26	172	164	6.84	0.00
	200	52	44	189	180	3.40	0.00
	250	61	52	198	190	2.59	0.00
	300	69	61	207	199	2.25	0.00
	350	78	69	215	208	1.90	0.02
	450	96	86	233	225	1.76	0.59
7-10 males and females	0	20	10	167	154	47.33	0.03
	100	40	30	187	174	29.47	0.03
	200	59	50	207	193	19.24	0.12
	250	69	60	217	205	16.20	0.12
	300	79	69	226	215	14.53	0.12
	350	89	80	236	225	12.42	0.21
	450	109	99	256	244	9.71	0.25
11-13 males and females	0	17	9	169	160	75.74	0.00
	100	41	34	193	183	61.65	0.00
	200	65	57	217	205	46.44	0.00
	250	77	68	229	216	39.27	0.00
	300	89	80	241	225	32.15	0.00
	350	101	91	253	237	29.17	0.00
	450	125	113	277	259	22.75	0.00
14-49 females	0	33	4	208	180	60.75	0.07
	100	52	25	227	198	50.91	0.07
	200	71	44	246	219	40.61	0.07
	250	80	54	255	229	36.13	0.07
	300	90	63	264	238	32.50	0.07
	350	99	73	274	247	28.48	0.07
	450	118	91	293	268	24.15	0.07
14-18 females	0	22	5	166	149	78.10	0.00
	100	41	25	185	173	66.77	0.00
	200	60	45	204	190	55.04	0.00
	250	70	54	214	198	51.27	0.00
	300	80	64	224	208	45.10	0.00
	350	89	74	233	218	39.62	0.00
	450	109	93	253	239	34.06	0.00
14-18 males	0	18	8	203	186	57.59	0.00
	100	46	37	231	214	42.20	0.00
	200	73	65	258	245	28.36	0.00
	250	87	77	272	259	23.92	0.00
	300	101	90	286	273	21.11	0.00
	350	114	103	300	289	19.08	0.00
	450	142	129	327	316	16.64	0.21
19-34 females	0	30	4	204	179	62.12	0.00
	100	50	25	224	198	51.64	0.00
	200	70	45	244	220	39.63	0.00
	250	80	56	254	230	34.62	0.00
	300	90	66	264	238	31.97	0.00
	350	100	76	274	246	27.45	0.00
	450	120	96	294	266	23.08	0.00

Age-Gender Group	Fortification (µg /100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
19-34 males	0	28	5	250	225	40.60	0.00
	100	56	36	279	258	30.18	0.00
	200	84	64	307	282	21.53	0.00
	250	99	79	321	294	19.05	0.00
	300	113	94	335	311	17.74	0.00
	350	127	109	350	326	16.27	0.00
	450	155	139	378	351	12.47	0.00
35-49 females	0	40	4	224	190	54.68	0.15
	100	57	25	241	210	45.87	0.15
	200	75	44	259	228	37.57	0.15
	250	83	52	267	239	33.41	0.15
	300	92	61	276	248	29.54	0.15
	350	101	70	285	257	26.40	0.15
	450	118	87	302	275	22.44	0.15
35-49 males	0	22	6	258	234	34.11	0.00
	100	49	33	284	263	22.83	0.00
	200	75	58	311	295	15.73	0.00
	250	89	70	324	306	12.88	0.00
	300	102	83	337	317	11.50	0.00
	350	115	95	351	329	10.85	0.00
	450	142	121	377	348	9.26	0.00
50 and over males and females	0	31	5	248	225	37.13	0.00
	100	50	26	267	241	28.06	0.00
	200	68	45	285	261	21.78	0.00
	250	78	55	295	272	18.34	0.00
	300	87	64	304	282	17.02	0.00
	350	96	73	313	294	15.38	0.00
	450	115	91	332	311	13.03	0.00
50-64 males and females	0	30	4	257	235	34.37	0.00
	100	49	26	276	252	24.74	0.00
	200	69	46	295	274	18.75	0.00
	250	78	55	305	283	15.64	0.00
	300	88	65	315	295	14.86	0.00
	350	98	74	324	303	13.57	0.00
	450	117	92	344	324	11.76	0.00
65-74 males and females	0	34	7	254	227	34.42	0.00
	100	53	29	273	250	25.86	0.00
	200	72	48	292	266	20.49	0.00
	250	81	56	301	276	16.88	0.00
	300	90	66	311	285	15.38	0.00
	350	100	75	320	295	13.48	0.00
	450	118	94	339	313	11.01	0.00
75 and over males and females	0	29	6	214	203	48.75	0.00
	100	46	23	231	218	40.44	0.00
	200	63	42	248	234	32.03	0.00
	250	71	50	256	243	27.90	0.00
	300	79	59	264	250	25.41	0.00
	350	88	67	273	258	23.17	0.00
	450	104	84	289	271	19.52	0.00
overall population	0	28	6	224	199	43.68	0.02
	100	49	28	245	221	33.56	0.03
	200	70	49	266	242	25.47	0.03
	250	80	59	276	252	22.00	0.03
	300	90	69	287	263	19.90	0.03
	350	101	79	297	273	17.80	0.03
	450	122	99	318	292	14.87	0.10

Table A16: Effects of fortification of all non-whoelmeal wheat flour assuming capping of breakfast cereals, spreads and supplements

Age-Gender Group	Fortification (µg /100g)	mean folic acid (µg/d)	median folic acid (µg/d)	mean total folate (µg/d)	median total folate (µg/d)	% below RNI (total folate)	% above UL (folic acid)
1.5-3 males and females	0	14	7	129	120	5.23	0.15
	100	38	32	152	144	1.92	0.45
	200	62	57	176	169	0.83	0.77
	250	74	69	188	182	0.81	0.77
	300	85	81	200	194	0.81	1.69
	350	97	92	212	205	0.81	3.65
	450	121	116	235	228	0.49	8.89
4-6 males and females	0	17	8	154	148	13.74	0.00
	100	51	43	188	181	3.11	0.00
	200	85	78	222	215	1.79	0.43
	250	102	95	239	233	0.56	0.46
	300	119	113	256	250	0.53	0.67
	350	136	130	273	267	0.15	0.80
	450	170	164	307	298	0.10	4.51
7-10 males and females	0	20	10	167	154	47.33	0.03
	100	60	52	207	194	17.09	0.12
	200	100	94	247	238	5.84	0.16
	250	120	115	267	257	3.33	0.41
	300	140	136	287	278	1.61	0.41
	350	160	157	307	296	1.27	0.84
	450	200	197	347	340	1.17	1.69
11-13 males and females	0	17	9	169	160	75.74	0.00
	100	64	56	215	207	44.90	0.00
	200	110	101	262	255	21.23	0.00
	250	134	123	285	278	14.82	0.00
	300	157	144	308	299	10.10	0.00
	350	180	167	332	322	6.97	0.00
	450	227	211	378	368	4.12	0.14
14-49 females	0	33	4	208	180	60.75	0.07
	100	68	43	243	215	41.40	0.07
	200	103	79	278	252	24.51	0.07
	250	121	97	295	270	18.88	0.07
	300	138	115	313	289	15.72	0.07
	350	155	133	330	307	13.29	0.10
	450	190	169	365	340	9.13	0.20
14-18 females	0	22	5	166	149	78.10	0.00
	100	60	46	204	193	55.32	0.00
	200	98	86	242	229	32.42	0.00
	250	117	105	261	250	25.67	0.00
	300	136	123	280	269	19.26	0.00
	350	155	141	300	291	16.70	0.00
	450	194	180	338	330	12.34	0.00
14-18 males	0	18	8	203	186	57.59	0.00
	100	72	64	257	242	29.13	0.00
	200	126	118	311	299	15.58	0.00
	250	153	144	339	326	11.24	0.00
	300	181	171	366	355	7.23	0.00
	350	208	198	393	382	5.25	0.21
	450	262	251	447	436	4.25	0.27
19-34 females	0	30	4	204	179	62.12	0.00
	100	67	44	241	215	41.11	0.00
	200	104	82	278	250	23.92	0.00
	250	123	101	296	270	17.08	0.00
	300	141	119	315	290	14.24	0.00
	350	160	138	333	307	11.89	0.00
	450	196	174	370	343	6.98	0.02

19-34 males	0	28	5	250	225	40.60	0.00
	100	80	64	302	282	22.02	0.00
	200	132	119	354	334	12.32	0.00
	250	158	147	381	360	9.88	0.00
	300	184	173	407	393	8.91	0.00
	350	210	200	433	421	6.68	0.00
	450	262	256	485	473	3.86	0.00
35-49 females	0	40	4	224	190	54.68	0.15
	100	72	40	256	225	37.85	0.15
	200	104	75	288	260	22.89	0.15
	250	120	92	304	277	18.72	0.15
	300	136	108	320	294	16.17	0.15
	350	152	125	336	312	13.69	0.22
	450	184	160	368	345	10.31	0.43
35-49 males	0	22	6	258	234	34.11	0.00
	100	69	55	304	283	16.13	0.00
	200	115	101	351	332	9.11	0.00
	250	139	125	374	357	6.11	0.00
	300	162	150	397	376	5.39	0.00
	350	185	173	421	399	3.97	0.00
	450	232	219	467	446	2.97	0.00
50 and over males and females	0	31	5	248	225	37.13	0.00
	100	66	45	283	259	21.40	0.00
	200	101	82	318	297	12.35	0.00
	250	119	100	336	314	10.05	0.00
	300	137	119	353	331	8.39	0.00
	350	154	136	371	348	7.30	0.00
	450	189	172	406	385	5.79	0.00
50-64 males and females	0	30	4	257	235	34.37	0.00
	100	65	44	292	270	19.13	0.00
	200	101	81	327	308	11.14	0.00
	250	118	99	345	324	9.15	0.00
	300	136	118	362	344	7.89	0.00
	350	153	135	380	365	7.12	0.00
	450	189	170	415	395	6.26	0.00
65-74 males and females	0	34	7	254	227	34.42	0.00
	100	70	47	290	264	18.86	0.00
	200	106	86	326	304	9.80	0.00
	250	124	104	344	320	8.38	0.00
	300	141	123	362	335	6.83	0.00
	350	159	141	380	350	5.41	0.00
	450	195	176	415	387	3.68	0.00
75 and over males and females	0	29	6	214	203	48.75	0.00
	100	63	44	248	237	31.40	0.00
	200	97	80	282	268	19.46	0.00
	250	114	98	299	286	15.01	0.00
	300	131	114	316	304	12.11	0.00
	350	148	132	333	323	10.62	0.00
	450	182	164	367	349	7.66	0.00
overall population	0	28	6	224	199	43.68	0.02
	100	67	48	263	240	25.47	0.03
	200	106	88	302	279	14.39	0.06
	250	125	108	322	299	11.06	0.07
	300	145	128	341	318	9.13	0.10
	350	164	147	361	337	7.54	0.20
	450	203	184	400	376	5.41	0.54

Table A17. List of breads containing wheat flour reported being consumed at the NDNS that fulfil either the 1998 or the NDNS Bread definition

Bread (1998 Regulation): 32 items

Food.Code	Name
102	BROWN BREAD NO ADDED BRAN
106	BROWN BREAD FRIED IN LARD
107	BROWN BREAD TOASTED
110	WHEATGERM BREAD EG HOVIS WHEATGERM BREAD
111	WHEATGERM BREAD, TOASTED
112	BREAD GRANARY
113	GRANARY BREAD, TOASTED
118	BREAD VIT-BE
120	BREAD, WHITE SLICED, NOT FORTIFIED
121	BREAD WHITE CRUSTY
122	BREAD WHITE ANY FRIED IN BLENDED VEG OIL
123	BREAD WHITE FRIED IN PUFA OIL
125	BREAD WHITE FRIED IN LARD
126	BREAD WHITE TOASTED
128	MILK BREAD WHITE
129	BREAD WHITE SLIMMERS
139	BREADCUMBS WHITE HOMEMADE DRIED
140	BREADCRUMBS SHOP-BOUGHT DRIED
162	BREAD VITBE FRIED BLENDED OIL
3863	BREAD WHITE FRIED IN BUTTER
3904	WHITE AND WHOLEMEAL BREAD WITH ADDED WHEATGERM
4168	HOVIS, BEST OF BOTH WHITE BREAD WITH ADDED WHEATGERM, TOASTED
7609	BREAD HIGH FIBRE WHITE
8020	MULTISEED BREAD WHITE ONLY
8073	MILK LOAF TOASTED
10203	MULTISEED BREAD WHITE ONLY TOASTED
10324	BREAD WHITE SLIMMERS TOASTED
10774	BREAD, WHITE WITH ADDED WHEATGERM
10775	BREAD, 50% WHITE AND 50% WHOLEMEAL FLOURS
10776	BREAD, WHITE WITH ADDED WHEATGERM TOASTED
10777	BREAD, 50% WHITE AND 50% WHOLEMEAL FLOURS TOASTED
10807	BROWN BREAD WITH ADDED WHEAT BRAN AND FOLIC ACID

NDNS Bread Definition: 77 items

Food.Code	Name
116	BREAD PITTA WHITE
127	BREAD WHITE FRENCH STICK
131	BREAD WHITE SODA
144	CHAPATIS WHITE IN BUTTER GHEE
145	CHAPATIS WHITE IN VEGETABLE GHEE
146	CHAPATI WHITE MADE WITHOUT FAT
147	CRUMPETS PIKELETS
148	CRUMPETS PIKELETS TOASTED
151	MUFFINS PLAIN ENGLISH NOT WHOLEMEAL
152	MUFFINS WHITE TOASTED
157	ROLLS HAMBURGER BUNS
158	ROLLS WHITE CRUSTY
159	ROLLS, WHITE SOFT, NOT FORTIFIED
170	HAMBURGER ROLLS TOASTED
171	ROLLS WHITE TOASTED
3148	PITTA BREAD, WHITE, TOASTED
6838	TORTILLA (WHEAT) SOFT
6839	GARLIC BREAD. LOWER FAT
6974	FOCACCIA, PLAIN, GARLIC OR HERBS
6976	CHEESE TOPPED ROLLS/BAPS, WHITE
6977	CIABATTA, PLAIN
7615	GARLIC (& HERB) BREAD
7622	NAAN BREAD PLAIN
8131	CIABATTA / PANINI TOASTED
8416	STONEBAKED GARLIC PIZZA BREADS
8670	WHITE CHAPATTI MADE WITH SUNFLOWER OIL
8744	CIABATTA WHITE BREAD MADE WITH OLIVE OIL
8964	PURI MADE WITH WHITE FLOUR ANCHOR BUTTER VEG GHEE
9054	PARATHA WITH BUTTER (WHITE FLOUR)
9129	BRIOCHE
9372	CONTINENTAL BREADS EG. CIABATTA FOCACCIA
9373	BAGELS PLAIN ONLY
10179	WEST INDIAN HARD DOUGH BREAD
10771	BAGELS PLAIN TOASTED
6135	PESHWARI NAAN SWEET NAAN WITH ALMONDS
7617	OATMEAL BREAD
7618	BREAD OATMEAL TOASTED

169	ROLL GRANARY BROWN WHEATGERM TOASTED
7616	GRANARY FRENCH STICK
7620	ROLLS BROWN GRANARY WHEATGERM CRUSTY
8142	WHITE AND WHOLEMEAL BREAD ROLLS
8143	SEEDED OR MULTISEED BAGELS
10772	SEEDED OR MULTISEED BAGELS TOASTED
10778	BREAD ROLLS, WHITE WITH ADDED WHEATGERM
10779	BREAD ROLLS, 50% WHITE AND 50% WHOLEMEAL FLOURS
120	BREAD, WHITE SLICED, NOT FORTIFIED
121	BREAD WHITE CRUSTY
122	BREAD WHITE ANY FRIED IN BLENDED VEG OIL
123	BREAD WHITE FRIED IN PUFA OIL
125	BREAD WHITE FRIED IN LARD
126	BREAD WHITE TOASTED
128	MILK BREAD WHITE
129	BREAD WHITE SLIMMERS
139	BREADCUMBS WHITE HOMEMADE DRIED
140	BREADCRUMBS SHOP-BOUGHT DRIED
3863	BREAD WHITE FRIED IN BUTTER
8073	MILK LOAF TOASTED
10324	BREAD WHITE SLIMMERS TOASTED
102	BROWN BREAD NO ADDED BRAN
106	BROWN BREAD FRIED IN LARD
107	BROWN BREAD TOASTED
110	WHEATGERM BREAD EG HOVIS WHEATGERM BREAD
111	WHEATGERM BREAD, TOASTED
112	BREAD GRANARY
113	GRANARY BREAD, TOASTED
118	BREAD VIT-BE
162	BREAD VITBE FRIED BLENDED OIL
3904	WHITE AND WHOLEMEAL BREAD WITH ADDED WHEATGERM
4168	HOVIS, BEST OF BOTH WHITE BREAD WITH ADDED WHEATGERM, TOASTED
7609	BREAD HIGH FIBRE WHITE
8020	MULTISEED BREAD WHITE ONLY
10203	MULTISEED BREAD WHITE ONLY TOASTED
10774	BREAD, WHITE WITH ADDED WHEATGERM
10775	BREAD, 50% WHITE AND 50% WHOLEMEAL FLOURS
10776	BREAD, WHITE WITH ADDED WHEATGERM TOASTED
10777	BREAD, 50% WHITE AND 50% WHOLEMEAL FLOURS TOASTED
10807	BROWN BREAD WITH ADDED WHEAT BRAN AND FOLIC ACID

Table A18: % above UL (folic acid) for Tables 9-13 with additional decimal places

Fortification Scenario	Fortification level (µg /100g)	Table 9	Table 10	Table 11	Table 12	Table 13
Bread (1998 regulation)	0	0.417	0.417	0.417	0.417	0.417
	100	0.421	0.025	0.049	0.342	0.338
	200	0.439	0.030	0.069	0.351	0.338
	250	0.448	0.030	0.078	0.355	0.343
	300	0.493	0.030	0.100	0.367	0.343
	350	0.517	0.033	0.119	0.393	0.346
	450	0.581	0.051	0.186	0.447	0.392
Bread (NDNS definition)	0	0.417	0.417	0.417	0.417	0.417
	100	0.422	0.026	0.049	0.350	0.343
	200	0.473	0.030	0.079	0.359	0.343
	250	0.482	0.030	0.088	0.367	0.343
	300	0.515	0.030	0.126	0.424	0.375
	350	0.571	0.034	0.182	0.450	0.379
	450	0.755	0.101	0.370	0.552	0.441
All wheat flour	0	0.417	0.417	0.417	0.417	0.417
	100	0.476	0.034	0.098	0.363	0.347
	200	0.545	0.059	0.155	0.422	0.384
	250	0.635	0.071	0.242	0.507	0.435
	300	0.831	0.102	0.416	0.594	0.511
	350	1.114	0.195	0.679	0.727	0.592
	450	1.802	0.539	1.392	1.165	0.954

Table 9: Effects of fortification on the whole population assuming no capping

Table 10: Effects of fortification on whole population assuming capping of breakfast cereals, spreads and supplements

Table 11: Effects of fortification on the whole population assuming capping of supplements only

Table 12: Effects of fortification on whole population assuming capping of breakfast cereals only

Table 13: Effects of fortification on whole population assuming capping of breakfast cereals and spreads only