



## **Statistical Press Notice: National Diet and Nutrition Survey: Blood folate results for the UK as a whole, Scotland, Northern Ireland (years 1 to 4 combined) and Wales (years 2 to 5 combined)**

Today, Public Health England published revised blood folate results from the National Diet and Nutrition Survey Rolling Programme (NDNS RP). The revised report, originally published in 2015, covers results for the UK as a whole and separately for Scotland, Northern Ireland and Wales, based on analysis of blood samples collected over 4 years 2008/09 to 2011/12 (2009/10 to 2012/13 for Wales).

Two measures of blood folate are reported: serum folate, which reflects recent dietary intake, and red blood cell (RBC) folate, which reflects longer term body stores and is generally considered the better measure of long term status.

Changes have been made to the criteria used in the report to assess folate status. Clinical thresholds for folate deficiency (based on haematological changes indicating the early stages of anaemia) are used as the main criteria<sup>1,2</sup>. In addition, a threshold for women of childbearing age to indicate increased risk of pregnancies affected by neural tube defects (NTD) is used<sup>3</sup>.

The thresholds used in the original report to define biochemical folate insufficiency are no longer used as the assay on which they were based was found to be incompatible with the assay used in NDNS. Measurements of blood folate are specific to the assay method and the laboratory used. New assay-adjusted thresholds have since been published<sup>4</sup> but they have not been used in the report as there is uncertainty about their applicability to the UK population. Instead, estimated threshold ranges are used, derived from statistical modelling of the NDNS data, to give an indication of the proportion of population age and sex groups which might be at risk of biochemical folate insufficiency.

The original published results have also been updated to correct for a calibration issue that led to a bias in the assay for unmetabolised (free) folic acid which was identified by the laboratory after publication of the original report. This correction reduced median unmetabolised folic acid

<sup>1</sup> Institute of Medicine (1998) Dietary Reference Intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin and choline. Washington, DC: The National Academies Press. <https://doi.org/10.17226/6015>

<sup>2</sup> WHO. Serum and red blood cell folate concentrations for assessing folate in populations. Vitamins and Mineral Nutrition Information System. 2015; 01.1-7

<sup>3</sup> Tinker SC, Hamner H, Qi YP, Crider KS. U.S. Women of Childbearing Age Who Are at Possible Increased Risk of a Neural Tube Defect-Affected Pregnancy Due to Suboptimal Red Blood Cell Folate Concentrations, National Health and Nutrition Examination Survey, 2007–2010. National Health and Nutrition Examination Survey 2007 to 2012. Birth Defects Research (Part A) 103:517–526, 2015

<sup>4</sup> Pfeiffer CM, Sternberg MR, Hamner HC, Crider KS, Lacher DA, Rogers IM, Bailey RL, Yetley EA (2016) Applying inappropriate cutoffs leading to misinterpretation of folate status in the US population. Am. J Clin Nutr. Doi: 10.3945/ajcn.116.138529

concentrations by 25 to 30%, median serum folate concentrations by around 0.5% and had a negligible impact on RBC folate. Overall, the impact of this error on published results is very small.

## **Key findings - UK**

### **Women of childbearing age (16 to 49 years)**

- Seven percent of women of childbearing age (16 to 49 years) and 12% of those aged 16 to 24 years had a red blood cell (RBC) folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L).
- Thirty-three percent of women of childbearing age had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13nmol/L); this includes 3% below the lower clinical threshold for folate deficiency (7nmol/L).
- Seventy-five percent of women of childbearing age had a RBC folate concentration below the threshold for increased risk of NTD-affected pregnancies (748nmol/L).

### **Girls aged 11 to 18 years**

- Thirteen percent of girls aged 11 to 18 years had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L).
- Thirty-eight percent of girls aged 11 to 18 years had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13 nmol/L); this includes 3% below the lower clinical threshold for folate deficiency (7nmol/L).

### **Other age groups**

- No more than 5% of adult men, older adults, boys aged 11 to 18 years or younger children (4 to 10 years) had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L). A third of adult men and older adult men, over 40% of boys aged 11 to 18 years, over a fifth of older adult women (22%) and 6% of younger children (4 to 10 years) had serum folate concentrations which fell below the clinical threshold for possible folate deficiency (13nmol/L); no more than 5% of these groups had a serum folate concentration below the lower clinical threshold indicating folate deficiency.

## **Key findings - Scotland**

### **Women of childbearing age (16 to 49 years)**

- Eleven percent of women of childbearing age in Scotland (16 to 49 years) had a red blood cell (RBC) folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L).

- Forty-six percent of women of childbearing age in Scotland had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13 nmol/L) this includes 7% below the lower clinical threshold for folate deficiency (7nmol/L).
- Eighty-one percent of women of childbearing age in Scotland had a RBC folate concentration below the threshold for increased risk of NTD-affected pregnancies (748nmol/L).

### **Girls aged 11 to 18 years**

- Thirteen percent of girls aged 11 to 18 years in Scotland had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L).
- Forty-eight percent of girls aged 11 to 18 years in Scotland had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13nmol/L); this includes less than 0.5% below the lower clinical threshold for folate deficiency (7nmol/L).

### **Other age groups**

- Mean RBC folate level was significantly lower in Scotland than in the UK for people aged 65 years and over.
- Eight percent of boys aged 11 to 18 years and less than 5% of other age groups in Scotland had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L). Between 30 and 40% of any age group had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13nmol/L); this includes less than 5% with a level below the lower clinical threshold for folate deficiency (7nmol/L).

## **Key findings – Northern Ireland**

### **Women of childbearing age (16 to 49 years)**

- Mean red blood cell (RBC) folate and serum folate levels for women of childbearing age (16 to 49 years) were significantly lower in Northern Ireland than in the UK as a whole.
- Fifteen percent of women of childbearing age in Northern Ireland had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L).
- Fifty-eight percent of women of childbearing age in Northern Ireland had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13 nmol/L); this includes 8% below the lower clinical threshold for folate deficiency (7nmol/L).

- Eighty-three percent of women of childbearing age in Northern Ireland had a RBC folate concentration below the threshold for increased risk of NTD-affected pregnancies (748nmol/L).

### **Girls aged 11 to 18 years**

- Eleven percent of girls aged 11 to 18 years in Northern Ireland had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L).
- Fifty-two percent of girls aged 11 to 18 years in Northern Ireland had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13nmol/L); this includes 5% below the lower clinical threshold for folate deficiency (7nmol/L).

### **Other age groups**

- Three percent of men aged 19 to 64 years in Northern Ireland had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L). Forty-four percent of the same age group had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13nmol/L); this includes 3% below the lower clinical threshold for folate deficiency (7nmol/L).

## **Key findings - Wales**

### **Women of childbearing age**

- Six percent of women of childbearing age in Wales (16 to 49 years) had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L).
- Forty-five percent of women of childbearing age in Wales had a serum folate concentration below the clinical threshold indicating possible folate deficiency (13nmol/L); this includes 3% below the lower clinical threshold for folate deficiency (7nmol/L).
- Seventy-nine percent of women of childbearing age in Wales had a RBC folate concentration below the threshold for increased risk of NTD-affected pregnancies (748nmol/L).

### **Other age groups<sup>5</sup>**

Four percent of children aged 11 to 18 years and less than 0.5% of men aged 19 to 64 years had a RBC folate concentration below the clinical threshold indicating risk of anaemia (305nmol/L). Thirty-seven percent of children aged 11 to 18 years and 36% of men aged 19 to 64 years had a serum folate concentration below the clinical threshold indicating possible folate deficiency

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<sup>5</sup> Cell size for girls 11-18 years in Wales too small to report results separately.

(13nmol/L); this includes 5% and 2% of these groups respectively below the lower clinical threshold for folate deficiency (7nmol/L).

## Biochemical folate insufficiency

Substantial proportions of all age/sex groups had blood folate levels indicating risk of biochemical insufficiency based on raised homocysteine concentration. In the UK population between a fifth and a half of most age/sex groups (excluding children aged 4 to 10 years) had red blood cell folate levels below the estimated threshold range indicating biochemical folate insufficiency (450 to 550nmol/L). These proportions tended to be higher in older girls and women. A similar pattern was seen for serum folate although the proportions below the estimated threshold range tended to be slightly lower than for red blood cell folate. Findings for Scotland, Northern Ireland and Wales were similar to those for the UK as a whole.

### Background notes

- 1) The NDNS rolling programme is a continuous cross-sectional survey, designed to assess the diet, nutrient intake and nutritional status of a representative sample of around 1000 people per year (500 adults and 500 children) from the general population aged 18 months upwards living in private households in the UK. Devolved government bodies in Scotland, Northern Ireland and Wales have funded additional recruitment in their countries in order to provide a large enough sample size in each country to enable results to be compared with the UK as a whole. The NDNS comprises an interview, a 4-day diet diary and collection and analysis of blood and urine samples. Results are used by government to monitor the diet and nutritional status of the population, to provide the evidence base for policy development and to track progress towards public health objectives such as reducing saturated fat and salt intakes.
- 2) The NDNS rolling programme was originally commissioned to collect data over a 4-year period from 2008/09 to 2011/12 with an extension to a fifth year covering 2012/13. The current contract covers 2013/14 to 2017/18 (years 6 to 10) and a new contract for years 11 to 14 is under negotiation following a retendering process earlier this year.
- 3) The NDNS is jointly funded by Public Health England and the UK Food Standards Agency. Work for years 1 to 4 was carried out by a consortium of three organisations: National Centre for Social Research (NatCen Social Research), MRC Human Nutrition Research<sup>6</sup> (HNR) and the University College London Medical School (UCL).
- 4) Responsibility for nutrition policy in England and Wales transferred from FSA to Health Departments in 2010. Management of NDNS also transferred to the Department of Health in England at that time. From 1 April 2013, responsibility for NDNS transferred to Public Health England, an operationally autonomous executive agency of DH.
- 5) The blood folate analyses carried out for this survey used the best available analytical methods based on the recommendations of an international expert workshop in 2008. The analyses were carried out by the Center for Disease Control laboratory in Atlanta US, who are the leading international experts in folate analysis. Blood samples collected in NDNS

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<sup>6</sup> Now known as MRC Elsie Widdowson Laboratory.

since July 2014 have been analysed for serum folate at the MRC Elsie Widdowson Laboratory in Cambridge using a state of the art analytical method.

- 6) Folate analyses were carried out in previous NDNS in the 1990s but these surveys used clinical assays which are less accurate and are not comparable with the current methods. Therefore it is not possible to compare the current results with those obtained in previous surveys.
- 7) Clinical thresholds for folate deficiency:
  - a. Red blood cell (RBC) folate below 305nmol/L. Based on haematological changes indicating risk of development of anaemia.
  - b. Serum folate below 7nmol/L. Defined by WHO as indicating folate deficiency.
  - c. Serum folate below 13nmol/L. Defined by WHO as indicating possible folate deficiency.
- 8) WHO set a threshold for RBC folate of 748nmol/L in women of childbearing age as the lower limit of optimal for avoiding NTD-affected pregnancies.
- 9) The term folate deficiency refers to concentrations below the clinical thresholds. Individuals below these thresholds are at risk of developing clinical symptoms, in particular anaemia. The term biochemical folate insufficiency refers to concentrations below the indicative threshold ranges based on analysis of NDNS data to find the folate concentration below which metabolic changes including raised homocysteine levels start to occur. The indicative threshold ranges for biochemical folate insufficiency are higher than those for clinical deficiency.
- 10) Folate in the diet comes from naturally occurring folates in foods and folic acid from fortified foods such as some breakfast cereals and from dietary supplements. Low folate status of women of childbearing age (16 to 49 years) is a particular public health concern. Increased folic acid intake through supplementation has been shown to reduce the risk of neural tube defects such as spina bifida if taken in the periconceptional period. Women planning pregnancy are therefore advised to take a 400µg folic acid supplement daily until the 12th week of pregnancy.
- 11) Results for the UK as a whole are based on blood samples collected for 1,769 adults and 902 children, collected over 4 years: 2008/09 to 2011/12, and are presented for 5 standard age groups: 1½ to 3 years; 4 to 10 years; 11 to 18 years; 19 to 64 years; 65 years and over, split by sex in all except the youngest age group. Results are also presented for women of childbearing age (16 to 49 years), split into three groups: 16 to 24 years; 25 to 34 years and 35 to 49 years. These numbers include the additional recruitment in Scotland, Wales and Northern Ireland which have been weighted down in the final analysis to give a UK representative sample.
- 12) Results for Scotland are based on blood samples collected for 440 adults and 216 children, collected over 4 years: 2008/09 to 2011/12, and are presented for standard age groups: 4 to 10 years, 11 to 18 years, 19 to 64 years and 65 years and over, split by sex for 11 to 18 years and 19 to 64 years. Results are also presented for women of childbearing age (16 to 49 years). Insufficient blood samples were collected for children aged 1½ to 3 years to present reliable results for this age group.
- 13) Results for Northern Ireland are based on blood samples collected for 264 adults and 96 children, collected over 4 years: 2008/09 to 2011/12, and are presented for the standard age groups: 11 to 18 years, 19 to 64 years and 65 years and over, split by sex for the 11 to

18 and 19 to 64 year age groups. Results are also presented for women of childbearing age (16 to 49 years). Insufficient blood samples were collected for children aged 1½ to 3 years and 4 to 10 years to present reliable results for these age groups.

- 14) Results for Wales are based on blood samples collected for 228 adults and 60 children collected over 4 years: 2009/10 to 2012/13 and are presented for the standard age groups: 11 to 18 years, 19 to 64 years and 65 years and over, split by sex for the 19 to 64 years age group only. Results are also presented for women of child-bearing age (16 to 49 years). Insufficient blood samples were collected for children aged 1½ to 3 years or 4 to 10 years to present reliable results for these age groups.
- 15) Nutritional status means the level of nutrients available to the body (after absorption) for use in metabolic processes. Folate status is assessed by measuring the level of total folate in the serum, which reflects recent dietary intake, and the level of folate in red blood cells, which reflects body stores.
- 16) Data for 3 adults (one male and one female aged 19 to 64 years and one female aged 65 years and over) with unusually high blood folate concentrations have been excluded from the main results as they caused the estimates of mean and standard deviation to be inflated. Each individual had consumed a 5mg folic acid supplement each day during the four day dietary recording period, approximately 8 weeks before the blood sample was taken.
- 17) Significantly different refers to statistical significance at  $p < 0.05$  or  $p < 0.01$ .

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