

**Strategies for improving the folate-status of
the population in Germany –
benefits and risks**

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**Positionspapier der
Deutschen Gesellschaft für Ernährung e.V.
Strategien zur Verbesserung der
Folatversorgung in Deutschland
– Nutzen und Risiken**

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www.dge.de - Positionspapiere -

Folate intake through
- native food
- fortified food
- supplements

Nutrition Circle Of the German Society of Nutrition (DGE)



Folate intake from native food

- Main sources : vegetables, bread, milk and dairy products
- Nutrition survey 1998:
16% of men and 10% of women meet the RDA without fortified food
- Groups at main risk :
men > 50 years of age
young women <19 years of age
elder women > 65 years of age

Example diet plan for meeting the RDA for through native food

Bezeichnung	Menge [g]	Energie [kcal]	Folataquivalent [µg]
Aus dem Verzehr:	3615	2322	393
Frühstück	715	618	104
Vollkornbrot	150	282	54
Butter	15	111	1
Sauerkirsche Konfitüre	20	55	
Käse 20-40% Fett i.Tr.	30	73	16
Kaffee	300	7	3
Orange Fruchtsaft	200	90	30
Zwischenmahlzeit	600	198	39
Joghurt 1,5 % Fett	150	69	15
Obstmischung frisch	150	129	24
Mineralwasser	300		
Mittagessen	930	763	81
Kartoffeln geschält frisch gekocht	250	171	38
Gemüsemischung frisch gegart	200	67	32
Rind Fleisch mittelfett (mf) gebraten	150	292	6
Rapsöl	15	131	
Trinkmilch 1,5 %	100	49	5
Stärke	15	53	
Mineralwasser	200		
Zwischenmahlzeit	670	257	44
Obstmischung frisch	150	129	24
Vollkornbrötchen	50	111	12
Magerquark	20	15	6
Kräutertee (Getränk)	150	2	2
Mineralwasser	300		
Abendessen	700	486	126



Cochrane-Analysis:

4 Studies with folate **supplements**

Reduction of the frequency of neural tube defects by 72% (OR 0,28; 95%-CI 0,13-0,58)

Based on the observed association between folate supply and prevention of NTD it is recommended that women who want to become pregnant may ingest supplements containing 400 µg folate per day in addition to the recommended daily intake in Germany since 1995.



Two years after this public recommendation a survey in Munich found 4,3% of mothers reporting that they consumed folate supplements around the time of conception.

Two surveys in Saxonia-Anhalt revealed only 6% of all mothers in 1998 and 4% in 2000 supplementing folate.

In 2000 65% of the women had planned their pregnancy; these women interrupted contraceptive measures with the aim of getting pregnant. In this group only 7% took folate supplements although 72% knew about the recommendation.

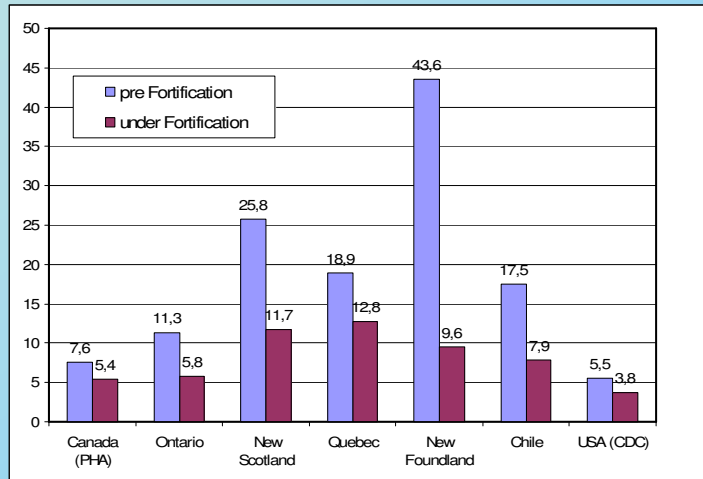
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Folate Fortification and incidence of neural tube defects in countries with mandatory folate fortification

Country / Source	Type of fortification	Quantity of fortification	Number of pregnancies with NTD (per 10.000 live births)		Reduction of the no. of pregnancies affected (in %)
			Pre fortification	Under fortification	
Canada (Public Health Agency of Canada, unpubl.)	Mandatory since 1998	Mandatory: 150 µg/100 g flour; 200 µg/100 g fortified flour-based food; voluntary: 150 – 220 µg/100 g maize flour	7,6	5,4	29
Ontario			11,3	5,8	51
New Scotland			25,8	11,7	54
Quebec			18,9	12,8	32
New Foundland			43,6	9,6	78
Chile (Lopez-Camelo et al. 2005)	Mandatory since 2000	220 µg/100 g Flour	17,5*	7,9*	55
USA (Centers for Disease Control and Prevention 2004)	Mandatory since 1998	140 µg/100 g cereal in ready-to-eat foods	5,5	3,8	27

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Effect of folate fortification on the incidence of NTD



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Vitamins don't slow development of cardiovascular disease in high-risk women

*American Heart Association Scientific Sessions
Late-Breaking News:*

CHICAGO, Nov. 13, 2006 -- Antioxidant vitamins and folic acid didn't slow the development of cardiovascular disease among high-risk women in two long-running, randomized trials, researchers reported today at the American Heart Association's Scientific Sessions 2006. (Ref. WAFACS/WACS)

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WAFACS is a randomized, placebo-controlled study of folic acid and other B vitamins in a subset of 5,442 women participating in a larger trial called Women's Antioxidant Cardiovascular Study (WACS). WACS is a randomized, placebo-controlled trial of antioxidant vitamins with 8,171 females.

Participants were health professionals

- ***over age 40 who either had***
- ***a history of CVD or***
- ***were considered at high risk***
 - due to three or more CVD risk factors***
 - ***high blood pressure,***
 - ***high cholesterol levels***
 - ***diabetes and***
 - ***smoking.***

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- ***effects of folic acid (2.5 mg/d) plus***
- ***vitamin B6 (50 mg/d) plus***
- ***vitamin B12 (1 mg/d)***
- ***versus placebo***
- ***follow-up for heart attacks, strokes, coronary revascularization procedures and cardiovascular-related deaths***
 - for 7.3 years***

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WAFACS is a randomized, placebo-controlled study of folic acid and other B vitamins in a subset of **5,442** women participating in a larger trial called Women's Antioxidant Cardiovascular Study (WACS). WACS is a randomized, placebo-controlled trial of antioxidant vitamins with **8,171** females.

Researchers found *no adverse effects from the vitamins* but said there are other important non-cardiac reasons to take them including during pregnancy, when a woman's nutritional needs are higher.

Folic acid supplementation has been associated with reducing birth defects of the brain and spinal cord.

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Actual Recommendation of the German Society of Nutrition:

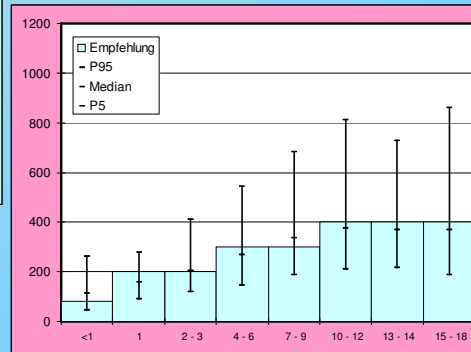
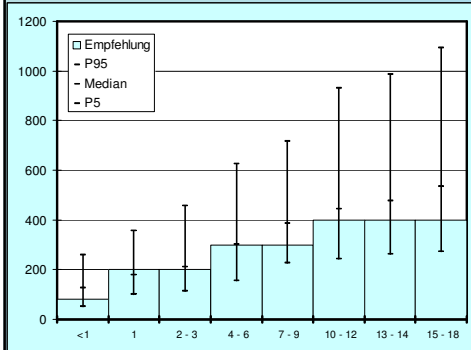
Fortification of flour with 150 µg folic acid per 100 g

In case of exclusive consumption of fortified bread and baking products men would get an average of 225 µg and women 176 µg folic acid per day in addition to their intake from native food. (Weißenborn et al. 2005).

The mean additional folic acid intake is expected to amount to 135 µg per day for men and 106 µg per day for women.

It is recommended to restrict the fortification to the flour types 550 und 630 (**„Bäckermehle“, flour used by bakeries**), and to exempt whole grain flour and the common household wheat flour (,type 405') and barley flour. Thereby, the consumer will have the choice to eat fortified food or to cover their folate needs on their own.

Folatzufuhr bei Kindern und Jugendlichen
Mehl mit 150 µg Folsäure pro 100 g angereichert
 (Berechnungen auf Basis der DONALD-Studie, Weißenborn et al. 2005)
 (µg Folat-Äquivalente/Tag)

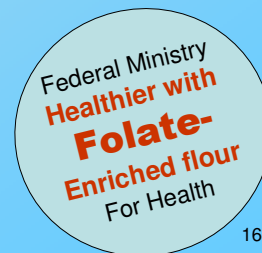


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The success of the proposed intervention depends on information campaigns in order to achieve a high acceptance by bakers, producers of bakery products as well as by consumers of cereal products.

As part of these campaign a 'folate-stamp' for fortified flour-based food could be designed underlining the health claim of the fortification.



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Risks of the consumption of food fortified with folic acid and f a - supplements

- Vitamin B12-deficiency could be masked
- Induction of twin pregnancies
- cancer
- Interaction with medicines
- Immune response

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Risks of the consumption of food fortified with folic acid and f.a.- supplements

Vitamin B12-deficiency could be masked

The identical hematologic findings in vitamin B12- & folate deficiency (macrocytic hyperchromatic anemia) improve under folic acid medication (≥ 5 mg); neurological symptoms of vitamin B12-deficiency may persist under f.a. – and get eventually aggravated (IOM 2000, SCF 2000).

There are no informations of the occurrence of masked vitamin B12-deficiency after the introduction of mandatory folic acid-fortification in the US and Canada .

„ ... The PH solution to any vitamin B-12 deficiency problem is to directly address the problem and not to use it to stop the remedy of another public health problem (NTD) that can be substantially prevented through folic acid fortification.“
(Wald & Law, 2004)

Risks of the consumption of food fortified with folic acid and f a - supplements

Induction of twin pregnancies

A number of studies found an association between a higher risk of twin-pregnancies and folate intake by women around the time of conception.

Women with induced pregnancies and in-vitro-fertilisation have not been separately evaluated; they have a high number of twins and get special advice to take folic acid supplements.

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Risks of the consumption of food fortified with folic acid and f.a. - supplements

Cancer

Experiments with rats and mice resulted in the induction and progression of cancers after high doses of folic acid in case of pre-existing microscopic colorectal carcinomas.

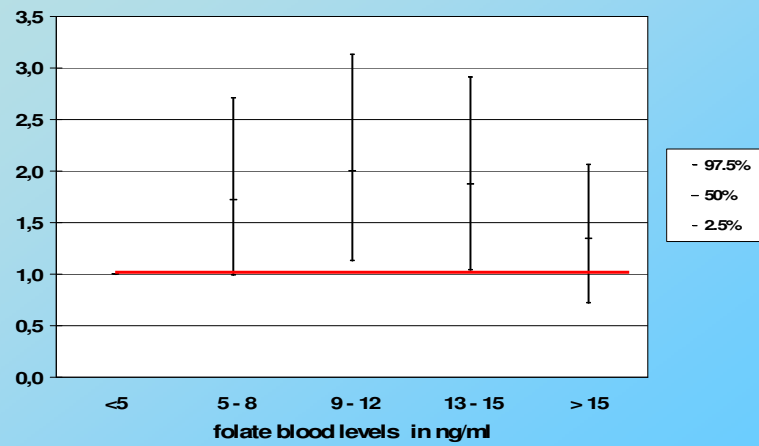
Folate in nmol/l	Men	Women
Risiko ↓	≤ 5,1	≤ 5,7
Risiko ↑	6,8 - 11,3	7,5 - 13,0
Risiko ↓	> 11,3	> 13,0

Van Guelpen et al 2006

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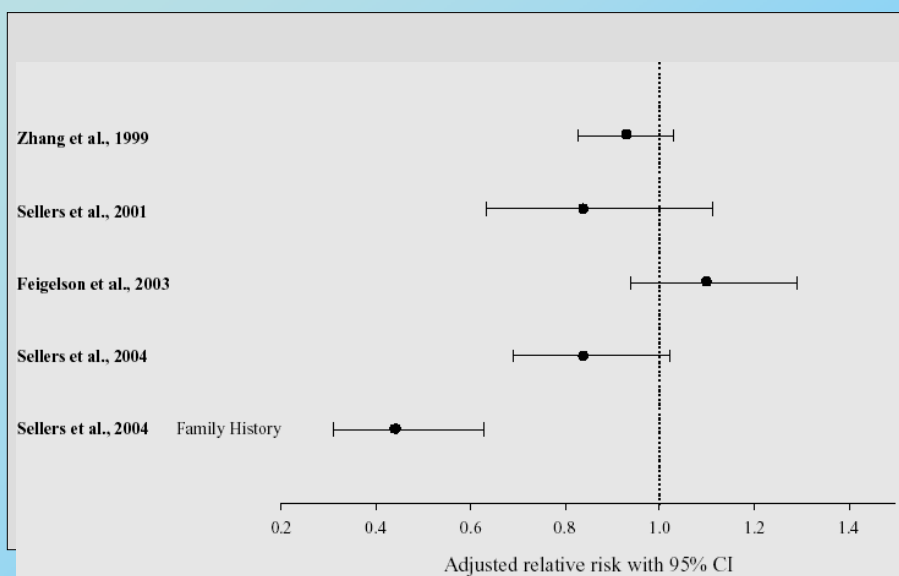
Risks of the consumption of food fortified with folic acid and folic acid - supplements

Median OR for colorectal cancer with 95% CI



Mod. After van Guelpen 2006

Cohort studies about the association between Folate intake and breast cancer risk (SACN 2005)



Risks of the consumption of food fortified with folic acid and f.a. - supplements

Immun response

Unmetabolised folic acid appears in the bloodstream after a single oral dose of 260 µg.

The presence of free folic acid in plasma of post-menopausal women was found to be associated with a reduced specific activity of natural killer cells, a subpopulation of lymphocytes.

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Deckung des Folatbedarfs durch natürliche Lebensmittel

Optimale Versorgung mit Nahrungsfolat:

- täglich mindestens 2-3 Portionen Gemüse und Salate zu verzehren und
- bei der Zubereitung darauf achten, Gemüse kurz zu waschen, zu dünsten statt zu kochen und nicht länger warm zu halten
- täglich Vollkorngetreideprodukte zu essen
- täglich fettarme Milch und Milchprodukte und hin und wieder Leber zu verzehren.

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Folic acid in salt should be avoided, if flour is fortified.



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General Public Health (Nutrition) Activities:

1. Implementation of a national registry for congenital malformations (prevalence and incidence of congenital malformations after the introduction of the folic acid fortification of flour – not as a specific co-intervention but as a necessary tool to provide a scientific basis for health and nutrition policies)
2. Performing regular representative surveys about consumption and nutrient status for Germany, in order to regularly update the information on folate status and vitamin B12-deficiency. (Regular re-evaluation of the need for fortification of foods)
3. Recognition of low folate intake as a risk factor for cardiovascular diseases and stroke
4. Observation of potential associations between a high folic acid intake and changes in the risk of diseases within the regular health reporting activities.

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