

Article

Prevalence and correlates of folic acid supplement use in Canada

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Abstract

Dietary supplements are an important source of folic acid, a nutrient that is vital in reducing the risk of neural tube defects. As part of the 2007 to 2009 Canadian Health Measures Survey, data were collected on supplement use, and biomarkers were directly measured. Use of supplements that contain folic acid was reported by 25% of Canadians aged 6 to 79. Females were more likely than males to report taking folic acid supplements. People who ate fruit and vegetables less than once a day had significantly lower odds of taking folic acid-containing supplements than did those who ate fruit and vegetables at least three times a day. Of those who consumed a folic acid supplement, 91% reported also taking a supplement that contained vitamin B₁₂. Red blood cell folate concentrations below the median (less than 1,248 nmol/L), low-to-marginal serum vitamin B₁₂ concentrations (221 pmol/L or less), and high concentrations of plasma homocysteine were negatively correlated with folic acid-containing supplement use.

Keywords

Biological markers, dietary supplements, folate, nutrition, vitamins

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Folate, one of the B-vitamins, is a key nutrient in reducing the risk of neural tube defects.¹ It plays an important role in metabolic pathways that involve vitamin B₁₂ and homocysteine.¹ While folate occurs naturally in many foods, such as dark green vegetables and legumes, the most common synthetic form in fortified foods and supplements is folic acid. Members of the general population do not commonly need supplemental folic acid unless it is recommended by a health care professional for certain medical conditions. In fact, high levels of supplemental folic acid may mask and exacerbate vitamin B₁₂ deficiency, particularly in the elderly, which could result in neurological damage.²⁻⁴

According to the Institute of Medicine's Dietary Reference Intakes, the Recommended Dietary Allowance for the population older than age 13 is 0.4 mg of folate a day.⁵ For women of childbearing age, an additional 0.4 mg per day from supplements or fortified foods is recommended.⁵ Because up to 50% of pregnancies are unplanned, and many women of childbearing age report irregular or no consumption of folic acid before pregnancy, in 1998, Canada approved folic acid fortification of white wheat and other selected grains,

in addition to previously implemented supplementation recommendations.⁶

This analysis uses data from the 2007 to 2009 Canadian Health Measures Survey (CHMS) to investigate self-reported intake of folic acid-containing supplements (see *The data*). Associations with socio-demographic, behavioural and clinical factors were studied, including, for the first time in a nationally representative sample, red blood cell folate concentrations.

The data

This study is based on results of cycle 1 of the Canadian Health Measures Survey (CHMS), which collected data from a nationally representative sample of the household population aged 6 to 79. Residents of Indian Reserves, Crown lands, institutions and certain remote regions, and full-time members of the Canadian Forces, were excluded. Data were collected at 15 sites across the country from March 2007 through February 2009.

A Statistics Canada interviewer administered a detailed in-home health questionnaire, which covered medication and natural health product use. One day to six weeks later, respondents visited a mobile examination centre for a series of physical measurements, including blood samples taken by a certified phlebotomist to measure a variety of analytes.⁷

Of the 8,772 households selected for the CHMS, 69.6% agreed to participate; 88.3% of them responded to the in-home survey, and of those, 84.9% visited the mobile examination centre. The overall response rate was 51.7%. A comprehensive consent process was employed; participation was voluntary and respondents could opt out of any part of the survey at any time.⁸ The final sample consisted of 5,604 respondents aged 6 to 79 and is representative of approximately 96.3% of the Canadian population. Details about the CHMS are available elsewhere.^{7,9}

Drug identification and natural health product numbers were collected from respondents during the in-home interview. This information was verified at the mobile examination centre visit, and changes in drug and supplement use were recorded.¹⁰ Consumption of folic acid supplements—alone or in a multi-vitamin—in the 30 days before the mobile examination centre visit was determined by matching drug identification and natural health product numbers to product information extracted from the Health Canada Drug Product and Licensed Natural Health Product databases.^{10,11,12} This approach was also used to quantify vitamin B₁₂ supplement use.

Dietary reference intake *age groups* were used for this study. These age groups were collapsed into three categories to achieve adequate sample size in the analyses examining doses of folic acid-containing supplements. Socio-economic status was measured by per person *household income* equivalents (which grouped respondent household income into quartiles after adjusting for household size and composition) and highest level of *household education* (less than postsecondary graduation and postsecondary graduation).¹³ *Immigrant status* was defined as born in Canada or not born in Canada.

A brief, non-quantitative questionnaire was used to examine usual frequency of consumption from the *grains* and *fruit and vegetables* food groups. Cereal, white bread, brown bread and pasta were combined to formulate the derived variable for grains. Self-reported *smoking* status and history were used to categorize respondents as daily, former or never smokers. A *physical activity* index of active, moderately active or inactive was derived based on average daily energy expenditure values during self-reported leisure time activities in the three months before the in-home interview.¹⁴

Measured height and weight were used to calculate *body mass index* (wt(kg)/ht(m)²). The body mass index of adults, excluding pregnant women, was classified using Health Canada's guidelines.¹⁵ Children aged 6 to 17 were classified as being normal weight, overweight or obese based on definitions proposed by the International Obesity Task Force, which account for both the age and sex of the child.¹⁶

A clinical risk factor variable was created to combine self-reported diabetes mellitus, use of folic acid antagonist medication, and overweight/obesity. Folic acid antagonist medication was determined by matching drug identification numbers—from medications used in the 30 days before the mobile examination centre visit—to information in the Drug Product Database.^{11,17} The variable identified three parameters: no risk factors, one risk factor, and more than one risk factor.

Blood was taken from 5,373 CHMS respondents. Red blood cell folate was analyzed using the Immulite 2000 immunoassay (Siemens Canada Ltd., Mississauga).¹⁸ *Red blood cell folate concentration* was calculated from the measured whole-blood folate concentration adjusting for red blood cell volume, without correction for plasma folate concentration. *Serum vitamin B₁₂* was also assessed using the Immulite 2000 immunoassay, a solid phase, competitive chemiluminescent enzyme immunoassay involving an automated alkaline denaturation procedure. The cut-off for marginal Vitamin B₁₂ status was 221 pmol/L or less.^{2,19} The Vitros 5, 1FS (Ortho Clinical Diagnostics, Markham) was used to assess *plasma homocysteine concentrations*. The quantitative measurement of plasma homocysteine was performed using the VITROS Chemistry Products Homocysteine Reagent, a spectrophotometric method involving three coupled enzymatic reactions (cystathionine synthase, cystathionine lyase and lactate dehydrogenase). Normal plasma homocysteine status was as 8 µmol/L or less for respondents aged 10 or younger, and 15 µmol/L or less for older respondents.^{20,22}

Descriptive statistics (frequencies, percentiles) were used to characterize the population. Missing values for predictor variables were removed for individual analyses. T-tests were used to study differences between estimates. With separate logistic regression analyses that controlled for age and household income, each co-variate was examined as a correlate of folic acid-containing supplement use. All estimates were based on data weighted to represent the Canadian population. Variance estimation (95% confidence intervals) and significance testing were based on the bootstrap technique to account for the complex CHMS sampling design.²³ Analyses were conducted in SAS 9.1.3 (SAS Institute Inc., Cary, NC) and SUDAAN v.10.0 (RTI International, Research Triangle Park, NC), using DDF=11 in the SUDAAN procedure statements. Given the 11 degrees of freedom available for variance estimation, Satterthwaite-adjusted statistics were used to test the significance of each regression model's coefficients.²⁴ Significance was defined as a p-value of <0.05.

The overall response rate to the CHMS was slightly above 50%. Although the survey weights ensured that the sample was representative of the target population, bias might exist if the use of folic acid-containing supplements by non-respondents and respondents differed systematically. The number of independent variables in the regression model was limited by 11 degrees of freedom; future research that combines subsequent CHMS cycles will increase the number of degrees of freedom and permit more complex modelling. The cross-sectional nature of the survey precludes inferences about the temporal ordering of events or causality. As well, the CHMS was not designed to collect information on usual supplement dosage, so precisely how often supplements were consumed could not be determined.

One in four

Results from the CHMS show that one in four Canadians aged 6 to 79 (an estimated 25%) reported taking a supplement containing folic acid in the previous 30 days (Table 1). This figure

is consistent with data from the 2004 Canadian Community Health Survey, cycle 2.2 (Nutrition).²⁵ Females were significantly more likely than males to report taking a supplement that contained folic acid (28% versus 21%).

The use of folic acid-containing supplements was highest in the youngest and oldest age groups, and lowest among teenagers and young adults. The greater likelihood of folic acid supplement use among females than males prevailed

Table 1
Prevalence and adjusted odds of folic acid-containing supplement use, by selected characteristics, household population aged 6 to 79, Canada, 2007 to 2009

Characteristics	Population distribution (%)	Supplement use					
		Prevalence			Adjusted odds ratio		
		%	95% confidence interval		(Controlling for age and household income)	95% confidence interval	
	from	to	from	to			
Total	100.0	25.0
Socio-demographic factors							
Sex							
Female	50.2	28.2*	25.9	30.5	1.53*	1.22	1.92
Male†	49.8	21.4	17.7	25.6	1.00
Age group							
6 to 8	3.5	28.5	23.3	34.4
9 to 13	6.8	19.5* ^E	15.1	24.8
14 to 18	7.1	12.5* [†]	6.9	12.4
19 to 30	18.1	16.5*	12.8	21.0
31 to 50	35.1	28.2	24.8	31.9
51 to 70	24.2	29.6	24.6	35.2
71 to 79	5.3	29.1	22.6	36.5
Household income quartile							
Q1 - lowest	23.2	17.0*	13.4	21.2
Q2	23.2	24.4*	21.1	28.1
Q3	23.4	25.7*	21.4	30.6
Q4 - highest†	23.4	32.5	26.1	39.5
Missing	6.7	22.9	17.5	29.3
Highest level of household education							
Less than postsecondary graduation	24.1	21.1	17.6	25.0	0.82	0.61	1.11
Postsecondary graduation†	75.9	26.2	23.0	29.7	1.00
Canadian-born							
Yes†	79.1	24.2	21.8	26.7	1.00
No	20.9	27.1	19.7	36.0	1.22	0.77	1.94
Behavioural factors							
Daily frequency of fruit and vegetable intake							
Less than once	6.4	12.9*	10.1	16.4	0.43*	0.33	0.57
1 to 2 times	45.2	22.6*	18.6	27.0	0.79	0.60	1.03
3 or more times†	48.4	28.4	25.9	31.0	1.00
Daily frequency of grain intake							
Less than once	14.6	22.7	16.2	30.8	0.93	0.44	1.96
1 to 2 times	76.7	25.5	22.9	28.3	1.08	0.65	1.80
3 or more times†	8.7	21.9 ^E	14.3	21.1	1.00
Leisure-time physical activity (aged 12 or older)							
Active†	26.6	28.4	23.7	33.7	1.00
Moderately active	25.1	26.3	20.7	32.8	0.88	0.59	1.31
Inactive	48.3	21.8*	19.0	24.8	0.68*	0.51	0.91
Smoking (aged 12 or older)							
Daily	20.3	18.9*	15.0	23.6	0.71*	0.52	0.98
Former	27.0	29.1*	25.0	33.6	1.02	0.78	1.33
Never smoked†	52.7	24.5	21.6	27.7	1.00
Clinical factors							
Body mass index (BMI)							
Underweight/Normal weight†	45.0	24.9	21.9	28.2	1.00
Overweight/Obese	55.0	24.0	21.1	27.1	0.80*	0.66	0.97
Red blood cell folate concentration							
Below median (less than 1,248 nmol/L)	50.1	14.2*	11.9	16.8	0.33*	0.25	0.43
At or above median (1,248 nmol/L or more)†	49.9	35.0	30.9	39.3	1.00
Serum vitamin B₁₂ concentration							
Low to marginal (≤221 pmol/L or less)	22.8	12.2*	9.1	16.1	0.33*	0.24	0.47
Replete (more than 221 pmol/L)†	77.2	28.3	25.4	31.3	1.00
Plasma homocysteine concentration							
Normal††	98.2	25.3	22.7	28.1	1.00
High	2.8	11.5*	8.0	16.2	0.33*	0.22	0.52

N = 5,604

† reference group

‡ 8 µmol/L or less at age 10 or younger, and 15 µmol/L or less for older than age 10

* significantly different from reference group (p<0.05)

^E use with caution

Note: Missing values were removed for individual analyses.

Source: 2007 to 2009 Canadian Health Measures Survey.

in age groups older than 30 (data not shown). Use peaked among women older than age 70 (36%) and was lowest among boys aged 14 to 18 (11%) (data not shown).

A positive gradient by household income emerged, with those in the lower income quartiles being significantly less likely than those in the highest quartile to have taken a supplement containing folic acid.

Even when the potential influence of age and household income was taken into account, females were significantly more likely than males to have consumed a folic acid-containing supplement (OR: 1.53; CI: 1.22, 1.92). Household education and country of birth were not significant correlates of folic acid supplement use.

Diet, exercise and smoking

Together, grains and fruit and vegetables are responsible for 62% to 78% of Canadians' dietary folate intake.^{10,26,27} However, people who ate fruit and vegetables relatively infrequently (less than once a day), had significantly low odds (OR: 0.43; CI: 0.33, 0.57) of taking a supplement that contained folic acid, compared with people who ate fruit and vegetables three or more times a day. Grain intake was not significantly related to folic acid supplement use (Table 1).

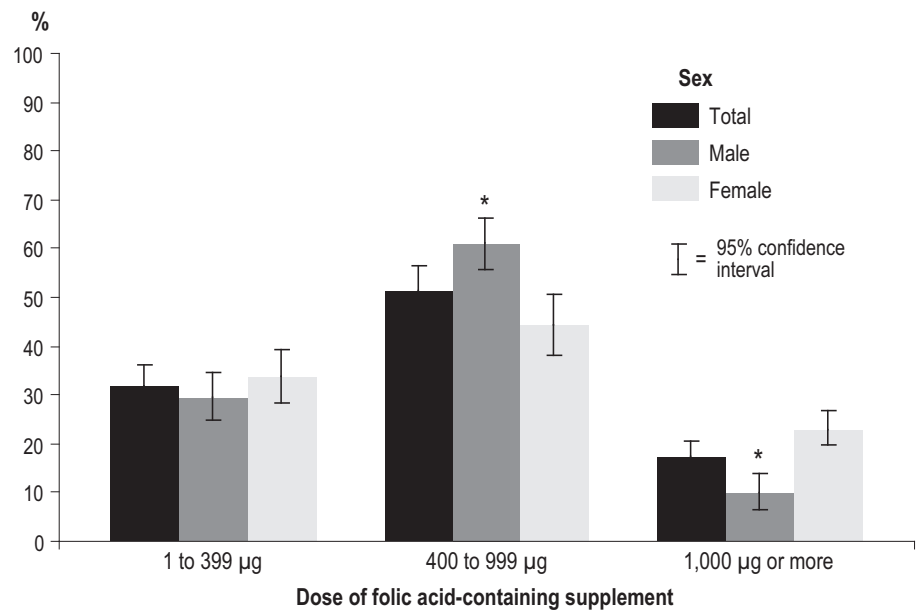
People who reported inactive leisure time had significantly low odds of taking folic acid supplements, compared with those whose leisure time was active. As well, the odds of folic acid supplement use were significantly low for daily smokers, compared with people who had never smoked. Having a family physician and the frequency of alcohol consumption were not related to the use of folic acid-containing supplements (data not shown).

The odds of taking a supplement that contained folic acid were significantly low for people whose BMI put them in the overweight/obese category.

Biomarkers

Red blood cell folate is the best indicator of tissue folate stores.²⁸ People whose

Figure 1
Reported dose of folic acid-containing supplement, by sex, household population aged 6 to 79, Canada, 2007 to 2009



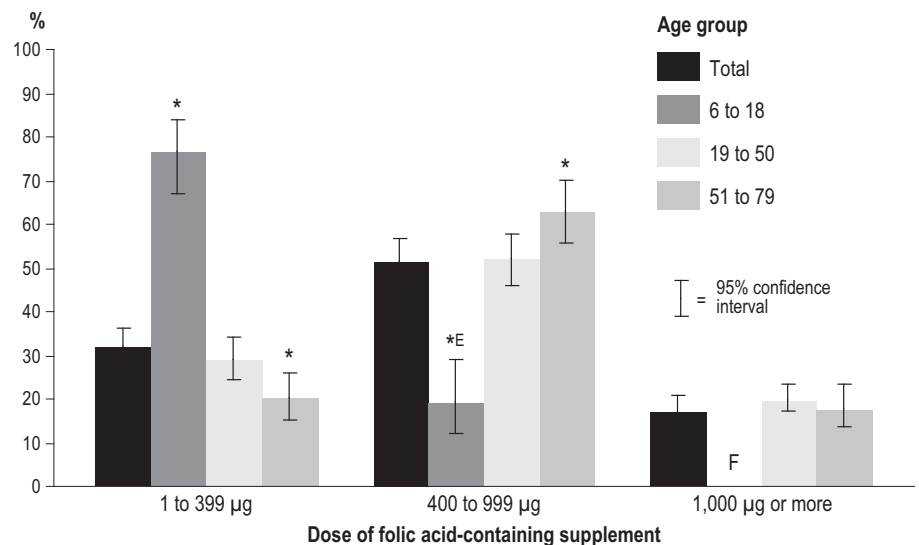
N = 1,357

* significantly different from females (p<0.05)

Note: Based on respondents who reported taking folic acid-containing supplement.

Source: 2007 to 2009 Canadian Health Measures Survey.

Figure 2
Reported dose of folic acid-containing supplement, by age group, household population aged 6 to 79, Canada, 2007 to 2009



N = 1,357

* significantly different from 19- to 50 age group (p<0.05)

E use with caution

F too unreliable to be published

Note: Based on respondents who reported taking folic acid-containing supplement.

Source: 2007 to 2009 Canadian Health Measures Survey.

red blood cell folate concentrations were below the median (less than 1,248 nmol/L) were significantly less likely to report taking a folic-acid containing supplement (OR: 0.33; CI: 0.25, 0.43) than were people whose concentrations were at or above the median.

The Tolerable Upper Limit for folate is 1,000 µg of the synthetic form a day. Higher amounts may mask a vitamin B₁₂ deficiency.⁵ Overall, 17.4% of folic acid supplement users consumed 1,000 µg or more (Figures 1 and 2). Canadian prenatal nutrition guidelines and federal natural health product regulations^{29,30} support the combined use of vitamin B₁₂ and folic acid supplements to reduce the risk of masking a vitamin B₁₂ deficiency. A large majority (91%) of CHMS respondents who took a folic acid-containing supplement also reported taking a supplement that contained vitamin B₁₂. Further, individuals with low serum vitamin B₁₂ concentrations were less likely to have consumed a folic acid-containing supplement (OR: 0.33; CI: 0.24, 0.47) than were people whose vitamin B₁₂ concentrations were higher.

High plasma homocysteine concentrations are a biomarker for low concentrations of both folate and vitamin B₁₂.²⁰ Individuals with high homocysteine concentrations were less

likely to consume folic acid-containing supplements (OR: 0.33; CI: 0.22, 0.52) than were those whose plasma homocysteine concentrations were in the normal range.

The clinical risk factor variable was not significantly correlated with folic acid-containing supplement use (data not shown).

Dosage

The amount of folic acid in the supplements used by about half (51%) of supplement takers ranged from 400 to 999 µg, and for another third (32%), the folic acid dose was 1 to 399 µg (Figure 1). The remaining 17% took supplements that contained 1,000 µg or more of folic acid: 22% of females and 10% of males.

The most common dose of folic acid for children and teenagers aged 6 to 18 was 1 to 399 µg (Figure 2). Folic acid-containing supplements designed for Canadian children contain 100 to 400 µg.⁷ At older ages, particularly 51 to 79, the dosage most frequently reported was 400 to 999 µg. Around 20% of people older than 19 reported taking supplements containing at least 1000 µg of folic acid. Such high intake was extremely rare at younger ages.

Conclusion

The use of folic acid-containing supplements is associated with a number of factors: socio-demographic (sex, age, household income), behavioural (frequency of consumption of fruit and vegetables, physical activity, smoking, overweight/obesity) and clinical (blood concentrations of RBC folate, serum vitamin B12 and plasma homocysteine). The results in this overview can inform fortification and supplementation policy in Canada. ■

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