Folic acid fortification above mandated levels results in a low prevalence of folate inadequacy among Canadians[1–3]

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ABSTRACT

Background: Understanding folate intakes after folic acid fortification of the food supply will help to establish dietary and supplement recommendations that balance health benefits and risks.

Objectives: The objectives were to estimate the prevalence of folate inadequacy (POFI) and intakes above the Tolerable Upper Intake Level (UL) among Canadians and to estimate the supplemental dose that, with diet, provides reproductive-aged women with 400 μg folic acid/d to prevent neural tube defects.

Design: Twenty-four-hour recall and supplement (prior 30 d) data from the 2004 Canadian Community Health Survey (n = 35,107) were used to calculate the POFI and intakes above the UL with and without adjustment for fortification overages. POFI was also estimated by risk factors thought to be related to low folate intake. The Software for Intake Distribution Evaluation (SIDE program; Department of Statistics and Center for Agricultural and Rural Development, Iowa State University) was used to estimate usual dietary intakes in all analyses.

Results: Except for women aged >70 y, POFI was <20% after adjustment for fortification overages. For children aged <14 y, POFI approached zero, even when supplement use was excluded. POFI among adults was unaffected by supplement use, except for women aged >70 y. Only 18% of reproductive-aged women consumed 400 μg folic acid/d from diet and supplements. Modeling showed that supplements containing 325–700 μg folic acid would provide adult women with 400 μg/d but not more than the UL. Diabetes was associated with POFI.

Conclusions: Innovative strategies are needed to ensure that the subgroups of Canadians who could still benefit from improved folate intake are targeted. Consideration should be given to removing folic acid from supplements designed for young children and men. *Am J Clin Nutr* 2010;92:818–25.

INTRODUCTION

To address inadequate folate intakes among women of childbearing age and to reduce the incidence of neural tube defects (NTDs), folic acid fortification of white wheat flour (150 μg/100 g) has been mandatory in Canada since 1998 (1, 2). Since the initiation of folic acid fortification, there has been a rise in blood folate concentrations and a 46% reduction in NTDs (3–6). Given data suggesting that up to 75% of NTDs may be prevented by providing folic acid during the periconceptional period, the Canadian Society for Obstetricians and Gynecologists suggests that doubling the level of folic acid fortification in Canada should be considered (7). Folic acid fortification and supplementation has also been associated with a reduction in other birth defects (oral clefts and congenital heart disease), cancer (colon and breast), stroke, and neuropsychiatric disorders (1, 8).

However, debate exists about the wisdom of exposing the entire population to higher levels of folic acid. Concerns range from masking and progression of vitamin B-12 deficiency to the reduced effectiveness of antifolate drugs and to the risk of promoting colorectal cancer in individuals with preexisting neoplasms (1, 9–13). Folic acid supplementation during pregnancy was recently associated with risk of asthma, obesity, and insulin resistance in offspring (14, 15).

To evaluate whether the current folic acid–fortification strategy in Canada strikes the right balance of known benefits and potential risks, an understanding of folate intakes is required at the national level. National dietary and supplement intake data, collected as part of the Canadian Community Health Survey cycle 2.2 (CCHS 2.2), are now available for the first time in Canada in >30 y (16). The objective of this study was to use these data to model the folate intakes (statistically adjusted to represent usual or long-term intakes) of Canadians by using the Software for Intake Distribution Evaluation (SIDE) to determine the prevalence of folate inadequacy (POFI). The percentage of individuals with folic acid intakes above the Tolerable Upper Intake Level (UL), defined as the highest intake of a nutrient thought to pose no adverse health effects, will also be determined (17). Importantly, determination of the POFI and folic acid intakes above the UL will be done with adjustment to reflect "predicted actual" and "mandated" levels of fortification. Second, these data will be used to estimate the dose of folic acid that should be in supplements designed for reproductive-aged women to prevent NTDs. Finally, the POFI by risk factors often

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associated with suboptimal folate status prefortification of the food supply (alcohol, diabetes, smoking, and obesity) will be examined.

In this article, the terms *food folate* and *folic acid* refer to the naturally occurring and synthetic forms of the vitamin, respectively; *dietary folate* refers to all folates found in food (food folate plus folic acid); *dietary folic acid* refers to folic acid found in food; and *total folate* refers to the sum all forms of folate consumed (dietary folate and supplemental folic acid).

SUBJECTS AND METHODS

Data source

Data were collected under the authority of the Statistics Act of Canada. The CCHS 2.2 was conducted in 2004 and contains data from 35,107 Canadians of all ages and is representative of >98% of the population from all 10 provinces. Food intake data were collected by the 24-h recall method by using a modified version of the US Department of Agriculture (USDA) Automated Multiple Pass Method (16, 18). All respondents completed one in-person 24-h recall with a trained interviewer, and a subsample of 10,786 respondents completed a second 24-h recall 3–10 d later by telephone interview. Dietary supplement use was collected as 30-d frequency data. All respondents ≥1 y were included in these analyses, which were stratified by Dietary Reference Intake (DRI) sex and age categories unless otherwise specified (1). Because of the small sample sizes for pregnant (n = 175) and lactating (n = 91) females, these 2 groups were not included in the analyses.

Model 1: dietary folate intake based on mandated fortification levels

For each respondent, dietary folate intake, which is the sum of naturally occurring folate and folic acid as a fortificant, was tabulated by using Health Canada's Canadian Nutrient File, version 2001b (19). Food composition values for the database were derived from the USDA Nutrient Database for Standard Reference 13 and modified to reflect current mandated fortification regulations in Canada (20). Thus, model 1 represents each respondent's dietary folate intake, assuming folic acid fortification at mandated levels.

Model 2: dietary folate intake adjusted for overages in fortified foods

It was previously estimated that there is ≈50% more folate in fortified foods in Canada than would be expected based on mandated fortification levels and food composition values (21, 22). Currently in Canada, there is no regulated allowable upper limit to folic acid fortification (2). Manufacturers are allowed and do fortify at higher levels than the mandated minimum to ensure that the amount of folic acid never falls below this level during the shelf-life of the product. To adjust for this overage, each respondent's food record from the CCHS 2.2 was accessed and, on the basis of Health Canada's Bureau of Nutritional Sciences food codes, foods eligible for folic acid fortification were assigned to 1 of 7 food categories. On the basis of a previously published direct laboratory analysis of 92 of the most commonly consumed foods across these 7 food categories, an adjustment was made to account for the "predicted" actual compared with the mandated level of fortification (22). The overage factors used in each of the food categories were as follows: *1*) bread, 1.34; *2*) buns and rolls, 1.17; *3*) cookies: 1.66; *4*) ready-to-eat cereals: 1.87; *5*) prepackaged desserts: 1.84; *6*) cooked pasta, 1.38; and *7*) crackers, 1.31. Because the 92 foods were analyzed for their dietary folate content (ie, naturally occurring folate and synthetic folic acid) and not only for folic acid, both the folic acid and naturally occurring folate values were multiplied by overage factors. Each respondent's predicted actual dietary folate intake was then computed from the adjusted food records.

Model 3: total folate intake from food and supplemental sources

Unlike the dietary folate intake data, supplement consumption in the CCHS 2.2 was collected as frequency data during the first 24-h recall and reflects how often multivitamins and/or minerals were consumed over the previous 30 d. For each supplement reportedly consumed, respondents stated how often they took the supplement during the past 30 d and the dose usually ingested each time. As recommended by Carriquiry (23), the average daily supplemental folic acid intake for each individual was added to usual (long-term) dietary folate intake (obtained in model 2). Usual dietary folate intake was estimated from model 2 as opposed to model 1 because this model accounts for previously documented folic acid overages (21, 22). The resulting model of total folate intake from dietary and supplemental sources was termed model 3.

Estimation of an adequate dose of supplemental folic acid for NTD prevention

Whereas Health Canada recommends that women preparing for a pregnancy consume a multivitamin supplement containing 400 μg folic acid to reduce the risk of NTDs, the US Institute of Medicine (IOM) recommends that women consume 400 μg synthetic folic acid/d from all sources (dietary and supplements) in addition to food folate from a varied diet to protect against NTDs (1, 24). To estimate the dose of supplemental folic acid that would ensure that most women (>90%) of childbearing age receive 400 μg folic acid/d (dietary and supplements), we added several potential doses of supplemental folic acid to dietary folic acid intake adjusted for predicted folic acid fortification overages (model 2). All nonpregnant and nonlactating females aged 14–50 y were included in this analysis.

Assessment of prevalence of inadequacy by risk factor

The CCHS 2.2 contains data on diabetes status (types 1 and 2), alcohol consumption, smoking status, and body mass index (BMI), which is the ratio of a subject's weight (in kg) to the square of height (in m). In model 2, the POFI for all adults was estimated and compared between *1*) alcohol consumers and nonconsumers (in the past year), *2*) diabetics (types 1 and 2) and nondiabetics, *3*) current daily smokers and nonsmokers, and *4*) obese (BMI ≥ 30) and nonobese individuals.

Correction for the bioavailability of folic acid and the definition of UL

The prevalence of inadequate intakes was determined by using either dietary (models 1 and 2) or total (model 3) folate intakes expressed in dietary folate equivalents (DFEs) (1). As suggested by the IOM, to account for differences in bioavailability between folic acid and food folate, DFEs were determined by using the following calculation (1):

$$\mathrm{DFE} = \mu\mathrm{g\ food\ folate} + (\mu\mathrm{g\ dietary\ folic\ acid} \times 1.7) + (\mu\mathrm{g\ supplemental\ folic\ acid} \times 2) \tag{1}$$

Supplements in the CCHS 2.2 survey were assumed to be consumed on an empty stomach, which resulted in a larger conversion factor than that of dietary folic acid (2 compared with 1.7) (1). Whereas folic acid was converted to DFEs to estimate the POFI, the percentage of intakes above the UL was calculated as done by the IOM based on synthetic folic acid only, the rationale being that evidence suggests that excessive intakes of synthetic folic acid may precipitate or exacerbate neuropathy in individuals with vitamin B-12 deficiency (1). Hence, food folate was not included in the estimate of intakes above the UL (1). The UL for folic acid was set based on a Lowest Observed Adverse Effect Level, followed by the application of an uncertainty factor (1). Importantly, the adverse effect level was based on the masking of vitamin B-12 deficiency in adults; extrapolation was used to set ULs for children and adolescents (1).

Statistical analysis

All statistical analyses were performed with SAS software (version 9.1; SAS Institute Inc, Cary, NC). The SIDE program (version 1.11; Department of Statistics and Center for Agricultural and Rural Development, Iowa State University), as an SAS macro, was used to estimate the subjects' usual (long-term) dietary folate, total folate, and folic acid intake distributions by partially removing day-to-day variation from each individuals' intake estimated by using a second 24-h recall from a subset (n = 10,786) of respondents (25). SIDE was subsequently used to estimate the POFI among respondents, defined as the proportion of respondents with usual dietary (models 1 and 2) or total (model 3) folate intakes below their requirements by sex and age subgroups. This was performed by using the Estimated Average Requirement (EAR) cut-point method (17). The EAR is defined as the level of intake for a nutrient that meets the requirement for 50% of healthy individuals (defined by age and sex) in the population (17). Whereas there is no cutoff to define a high POFI, because of the strong relation between suboptimal intakes and birth defects, it is most concerning in women of childbearing age. Nonetheless, across the entire population, inadequacy means regularly consuming insufficient amounts to perform bodily functions and was based primarily on erythrocyte folate concentrations, which is an indicator of tissue folate stores (1). Because the EAR for folate is based on DFEs, this unit was used to estimate the POFI. SIDE was also used to estimate the proportion of individuals with usual folic acid intakes above the UL. Recognizing the limitations of using the UL as a strict risk assessment cutoff, it is only inferred that intakes below the UL are safe (26).

Given that the sampling process for the CCHS 2.2 was complex and multistage, variance estimates were calculated by using the bootstrap balanced repeated replication technique. Briefly, a replicate weight was generated by randomly selecting a sample, with replacement, from the original sample and then applying all the performed adjustments to this selected sample. This exercise was repeated 500 times to generate 500 sample survey weights, which were then used to estimate variance. A P value < 0.05 was considered statistically significant in all analyses.

RESULTS

Dietary folate intake based on mandated (model 1) and predicted actual (model 2) fortification levels

In all DRI sex and age groups, the mean usual intake of dietary folate exceeded the EAR, regardless of whether intakes were modeled to predict folic acid fortification overages (**Table 1**). As illustrated in **Figure 1**, the POFI based on dietary folate intake alone was very low for children $\geq$14 y of age and virtually nonexistent when intakes were modeled to predict actual fortification levels. In model 1, all female age groups $\geq$14 y had a POFI >25%, which reached as high as 54% in females aged >70 y. However, when dietary folate intakes were modeled to predict actual intakes (model 2), the POFI fell to <20% in adolescent females and women aged $\leq$70 y. The POFI for females aged >70 y was 32.6% in model 2. Except for men aged >70 y, the POFI for males was <20% in model 1 and fell to <7.5% when data were modeled to consider folic acid fortification overages (model 2). The POFI for males aged >70 y was >30% in model 1 and fell to 13% in model 2.

Use of folic acid–containing supplements

Despite the fact that children had the lowest POFI of all age groups based on dietary folate intakes alone, they were the most likely of any of the sex and age categories to consume folic acid supplements (4–8 y; 38.7%) (Table 1). Among females of reproductive age, folic acid–containing supplements were consumed by 15.0%, 22.9%, and 29.2% of females aged 14–18, 19–30, and 31–50 y, respectively. Among females aged >70 y, 28.5% consumed a folic acid–containing supplement.

Total folate intake from dietary and supplemental sources (model 3)

The addition of folic acid from the use of folic acid–containing supplements to the dietary folate intake had little effect on the POFI across all sex and age categories, except for females aged >70 y; when the contribution of folic acid–containing supplements was added to dietary folate intake (model 3), the POFI among women aged >70 y was reduced from 32.6% to 24.6% (Figure 1). Of all the other sex and age categories, the reduction in POFI was $\leq$5% and highest in females aged 31–50 y (15.2–10%). In children and adolescents, the largest reduction in POFI was observed in females aged 14–18 y (13.2–11.3%). Only 17.7% of women of childbearing age (14–50 y) consumed $\geq$400 μg folic acid from fortified foods and supplements—the amount recommended by the IOM to minimize the risk of NTD.

TABLE 1
Prevalence of folic acid–containing supplement use and usual dietary folate intakes[1]

	Folic acid supplement consumption[2]	EAR	Unadjusted dietary folate intake (model 1)[3,4]	Adjusted dietary folate intake (model 2)[3,5,6]	Unadjusted contribution from dietary folic acid (model 1)[3]	Adjusted contribution from dietary folic acid (model 2)[3,6]
	%	*DFE*	*DFE*	*DFE*	*μg*	*μg*
Children and adolescents						
1–3 y (*n* = 2193)	30.7 ± 1.6	120	278 ± 104	331 ± 123	75 ± 35	108 ± 51
4–8 y (*n* = 3343)	38.7 ± 1.4	160	378 ± 100	472 ± 127	118 ± 35	170 ± 52
Male, 9–13 y (*n* = 2149)	24.0 ± 1.5	250	462 ± 125	573 ± 149	142 ± 43	206 ± 63
Female, 9–13 y (*n* = 2043)	22.2 ± 1.6	250	403 ± 113	498 ± 134	126 ± 33	180 ± 50
Male, 14–18 y (*n* = 2397)	13.8 ± 1.2	330	560 ± 179	699 ± 225	175 ± 57	254 ± 86
Female, 14–18 y (*n* = 2346)	15.0 ± 1.2	330	426 ± 147	516 ± 179	129 ± 49	183 ± 72
Men						
19–30 y (*n* = 1897)	17.6 ± 1.5	320	574 ± 167	686 ± 196	164 ± 56	236 ± 75
31–50 y (*n* = 2750)	19.3 ± 1.4	320	522 ± 160	624 ± 196	145 ± 53	205 ± 75
51–70 y (*n* = 2725)	26.0 ± 1.4	320	460 ± 151	543 ± 181	115 ± 54	164 ± 76
>70 y (*n* = 1601)	25.2 ± 1.9	320	390 ± 122	469 ± 147	100 ± 43	146 ± 64
Women						
19–30 y (*n* = 1915)	22.9 ± 1.6	320	407 ± 119	475 ± 133	107 ± 39	152 ± 59
31–50 y (*n* = 2851)	29.2 ± 1.7	320	406 ± 137	471 ± 155	101 ± 39	141 ± 56
51–70 y (*n* = 3407)	31.2 ± 1.3	320	378 ± 115	447 ± 142	90 ± 39	131 ± 57
>70 y (*n* = 2769)	28.5 ± 1.4	320	324 ± 104	388 ± 127	78 ± 36	114 ± 53

[1] EAR, estimated average requirement; DFE, dietary folate equivalents.
[2] Values are percentages ± SEs of individuals consuming at least one folic acid–containing supplement in the 30 d before the first 24-h recall.
[3] Values are means ± SDs calculated by using the Software for Intake Distribution Evaluation (version 1.11; Department of Statistics and Center for Agricultural and Rural Development, Iowa State University).
[4] Usual dietary folate intake (naturally occurring folate and synthetic folic acid from foods) based on mandated levels of fortification (model 1).
[5] Usual dietary folate intake (naturally occurring folate and synthetic folic acid from foods) based on estimates of folic acid fortification overages (model 2).
[6] Model 2 intake > model 1 intake (Student's paired *t* test, $P < 0.01$).

Less than 1% of women of childbearing age consumed ≥400 μg folic acid from dietary sources alone.

Based on dietary intakes alone, the percentage of Canadians with intakes above the UL was zero in all sex and age groups (**Table 2**). However, once supplemental folic acid consumption was included (model 3), 1.2–5% of individuals in each sex and age group exceeded the UL.

Estimation of an adequate dose of supplemental folic acid for NTD prevention

To estimate the dose of supplemental folic acid that would ensure that most women of childbearing age receive 400 μg synthetic folic acid/d, we considered several potential doses of supplemental folic acid that could be consumed over and above the amount of folic acid consumed as a fortificant in food (dietary) as determined by model 2 (**Table 3**). If all women aged 14–50 y consumed a folic acid–containing supplement daily, a minimum supplemental dose of 325 μg folic acid would ensure that 91.4% of women would consume ≥400 μg total synthetic folic acid (from dietary and supplemental sources) daily. In contrast, supplemental doses of 500 and 700 μg lead to 6.8% and 1.5% of females aged 14–18 and 19–50 y, respectively, with intakes above the UL.

Assessment of prevalence of inadequacy by risk factor

Adults who consumed alcohol had a lower POFI than did those who did not consume alcohol, whereas patients with diabetes had a higher POFI than did their nondiabetic counterparts (**Figure 2**). No difference in the POFI between smokers and nonsmokers or between obese and nonobese adults was observed.

DISCUSSION

The results of this study suggest that, after the adjustment of food composition values for folic acid fortification levels higher than the minimally mandated level, the POFI in the Canadian population is low. In fact, in our reanalysis of the CCHS 2.2, only females aged >70 y had a POFI >20% when folic acid fortification overages in the food supply were accounted for (Figure 1). The mean usual dietary folate intake of females aged >70 y (388 ± 127 DFE, model 2) was similar to the median dietary intake of women of the same age (417 DFE) recently reported in the 2003–2006 National Health and Nutrition Examination Surveys (NHANES) (27). Furthermore, after fortification overages were accounted for, there was virtually no difference in the POFI (Figure 1), regardless of whether individuals consumed a supplement or not, except for women >70 y of age, in whom a modest reduction was observed (32.6–24.6%).

Our analysis suggests that there is no observable benefit of including folic acid in supplements designed for children aged <14 y and that regulatory guidance allowing for its inclusion should be reconsidered. Importantly, the POFI for children aged <14 y, regardless of how their dietary data were modeled, approached zero (Figure 1). Yet, young Canadians were the greatest consumers of folic acid–containing supplements, with

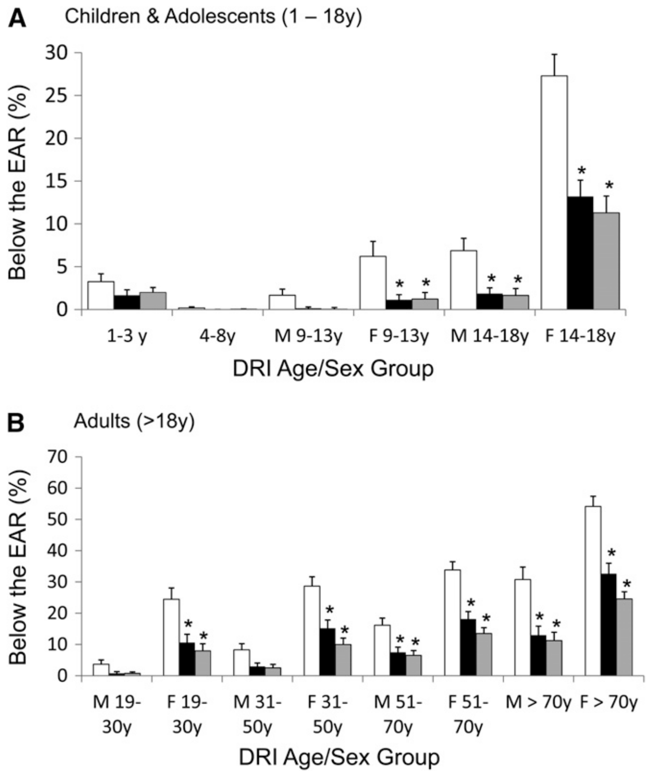

FIGURE 1. The prevalence of inadequacy in children (A) and adults (B) based on usual dietary folate intakes (naturally occurring folate and synthetic folic acid from foods). Folate nutrient composition data reflect the mandated fortification levels (model 1, open bars) compared with predicted actual dietary folate intakes (model 2, black bars). The gray bars represent the prevalence of inadequacy based on total folate intakes (model 2 plus supplemental folic acid intakes; model 3). Error bars represent the SE of the prevalence. Prevalence estimates <5% are shown despite the limitation of the Estimated Average Requirement (EAR) cut-point method at estimating tails of distributions (17). Note that the *y* axis of panel A covers a smaller range than that of panel B. A: 1–3 y (*n* = 2193); 4–8 y (*n* = 3343); male, 9–13 y (*n* = 2149); female, 9–13 y (*n* = 2043); male, 14–18 y (*n* = 2397); female, 14–18 y (*n* = 2346). B: male, 19–30 y (*n* = 1897); female, 19–30 y (*n* = 1915); male, 31–50 y (*n* = 2750); female, 31–50 y (*n* = 2851); male, 51–70 y (*n* = 2725); female, 51–70 y (*n* = 3407); male, >70 y (*n* = 1601); female, >70 y (*n* = 2769).*95% CI does not overlap with that of model 1 of the same sex and age category. DRI, Dietary Reference Intake.

consumption reaching as high as 38.7% in children aged 4–8 y (Table 1). Currently in Canada, supplements designed for children contain doses of folic acid ranging from 100 to 400 μg/d. Whereas the percentage of all children aged <14 y with folic acid intakes above the UL was low, only children who consumed folic acid–containing supplements had folic acid intakes above the UL (Table 2). We caution that our conclusions about whether folic acid should be included in supplements designed for young children are not generalizable to other nutrients. Such an analysis was beyond the scope of this study.

The percentage of children consuming folic acid–containing supplements in the CCHS 2.2 is similar to that reported recently by Hennessy-Priest et al (28) from a cross-sectional convenience sample of preschool children (*n* = 254) from the province of Ontario (30%) but is somewhat lower than supplement consumption (with or without folic acid) reported in a NHANES III analysis of children aged 1–5 y (42–51%) (29). Hennessy-Priest et al reported that 7% of the preschoolers in their sample exceeded the UL for folic acid when supplement consumption was included (2% if not included) (28). When they assumed a folic acid overage of 200% in fortified foods, 12% of children exceeded the UL when supplement consumption was included (4% if not included) (28). Flynn et al (30), in their analysis of folate intakes across several European countries, concluded that high folic acid intakes in children were invariably associated with the consumption of supplements and with fortified foods (mainly fortified breakfast cereals), although they questioned the relevance of the UL for folic acid for children given that it was based on masking vitamin B-12 deficiency in adults.

Among adults, the contribution of folic acid from dietary sources was less than the UL for all age groups and both sexes regardless of how the dietary intake data were modeled (Table 2). This suggests that there is very little risk of folic acid intakes above the UL from dietary sources alone. Inclusion of folic acid supplements in the analysis leads to a small percentage of intakes (1.2–5%) above the UL, which agrees with other available Canadian data collected from regional or local convenience sampling (28, 31, 32). In their analysis of NHANES data from 2003 to 2006, Bailey et al (27) reported that 0.4–5.2% of adults had intakes above the UL. Furthermore, Yang et al (33), in their analysis of NHANES 2003–2006 data, showed that supplement consumption was solely responsible for intakes above the UL among adults.

Despite folic acid fortification of the food supply and estimated overages, the results from this study provide evidence to suggest that Canadian women of childbearing age should continue to consume a folic acid supplement for the prevention of NTD. From dietary sources alone, <1% of women of childbearing age in the CCHS 2.2 met the IOM's recommendation to consume 400 μg folic acid/d to prevent NTD. When supplement consumption data from these women were included in this analysis, only 17.7% of women consumed $\geq$400 μg folic acid/d. These data are consistent with recent reports from smaller local cross-sectional studies in Canada (31, 32). Furthermore, data herein suggest that the range of doses for a folic acid supplement that meets the IOM's recommendation for NTD prevention but do not result in folic intakes above the UL are between 325–500 and 325–700 μg/d for adolescent and adult females, respectively.

In the present study, we found that adults who did not consume alcohol had a higher POFI than did alcohol consumers. This observation was likely due to the fact that beer, the most commonly consumed alcoholic beverage in Canada (34), contains folate (35). Furthermore, no difference in the POFI existed regardless of whether an adult smoked or not or had a BMI > or <30 (Figure 2). However, before fortification of the food supply, smokers were more often reported to have inadequate folate intakes than were nonsmokers (1), and obese women of childbearing age had lower folate intakes than did nonobese women (36). Before fortification of the food supply, most dietary folate was consumed from foods belonging to the "vegetables and fruit" food group (37, 38). Because the consumption of fruit and vegetables is commonly associated with a cluster of many other healthy lifestyle characteristics, it makes sense that folate intakes before fortification were positively associated with healthful lifestyle characteristics (38–41). However, after fortification of the food supply, the largest reported component of dietary folate came from the "grains" group, specifically white-wheat flour, which is not associated with healthful lifestyle characteristics (37, 38).

TABLE 2
Percentage of individuals with folic acid intakes above the Tolerable Upper Intake Level (UL) based on usual dietary folic acid intake (model 1), overage-adjusted dietary folic acid intake (model 2), and total folic acid intake (model 2 plus supplemental folic acid; model 3)

		Percentage above the UL[1]		
	UL	Model 1[2]	Model 2[3]	Model 3[4]
	µg		%	
Children and adolescents				
1–3 y (*n* = 2193)	300	0	0	2.9 ± 0.6
4–8 y (*n* = 3343)	400	0	0	2.6 ± 0.5
Male, 9–13 y (*n* = 2149)	600	0	0	1.3 ± 0.3
Female, 9–13 y (*n* = 2043)	600	0	0	1.2 ± 0.4
Male, 14–18 y (*n* = 2397)	800	0	0	4.0 ± 0.8
Female, 14–18 y (*n* = 2346)	800	0	0	2.4 ± 0.5
Men				
19–30 y (*n* = 1897)	1000	0	0	1.2 ± 0.4
31–50 y (*n* = 2750)	1000	0	0	2.3 ± 0.5
51–70 y (*n* = 2725)	1000	0	0	3.3 ± 0.5
>70 y (*n* = 1601)	1000	0	0	4.2 ± 1.0
Women				
19–30 y (*n* = 1915)	1000	0	0	2.6 ± 0.5
31–50 y (*n* = 2851)	1000	0	0	5.0 ± 0.8
51–70 y (*n* = 3407)	1000	0	0	3.8 ± 0.5
>70 y (*n* = 2769)	1000	0	0	4.1 ± 0.6

[1] The Software for Intake Distribution Evaluation (version 1.11; Department of Statistics and Center for Agricultural and Rural Development, Iowa State University) was used to estimate usual dietary folic acid intakes in all models.
[2] Usual dietary folic acid intake (folic acid as a fortificant) based on mandated levels of fortification.
[3] Usual dietary folic acid intake (folic acid as a fortificant) adjusted for folic acid fortification overages.
[4] Usual dietary folic acid intake adjusted for folic acid fortification overages plus supplemental folic acid intake. Values are percentages ± SEs.

In this study, respondents with diabetes had a higher POFI than those without diabetes (Figure 2). This was likely due to the fact that patients with diabetes are encouraged to closely monitor their carbohydrate intake and to consume whole grains, which are not currently a vehicle for folic acid fortification in Canada (42). In fact, all Canadians are recommended to choose whole-grain

TABLE 3
Estimation of the prevalence of women consuming <400 *µ*g folic acid/d and above the Tolerable Upper Intake Level (UL) from all sources (dietary and supplemental) at different potential supplemental folic acid doses[1]

		Percentage above the UL[3]	
Supplemental folic acid dose	Prevalence <400 *µ*g[2]	Female, 14–18 y	Female, 19–50 y
	%	%	
0 *µ*g	99.8 ± 0.1	0 ± 0	0 ± 0
200 *µ*g	81.1 ± 2.3	0 ± 0	0 ± 0
250 *µ*g	56.0 ± 3.0	0 ± 0.1	0 ± 0
300 *µ*g	21.7 ± 2.6	0 ± 0.2	0 ± 0
325 *µ*g	8.6 ± 1.6	0.2 ± 0.2	0 ± 0
350 *µ*g	1.9 ± 0.6	0.4 ± 0.3	0 ± 0
375 *µ*g	0.1 ± 0.1	0.6 ± 0.4	0 ± 0
400 *µ*g	0 ± 0	1.0 ± 0.6	0 ± 0
500 *µ*g	0 ± 0	6.8 ± 1.9	0 ± 0
600 *µ*g	0 ± 0	34.8 ± 3.3	0 ± 0.1
700 *µ*g	0 ± 0	90.9 ± 2.4	1.5 ± 0.5
800 *µ*g	0 ± 0	100 ± 0	16.1 ± 2.5
900 *µ*g	0 ± 0	100 ± 0	76.2 ± 3.6
1000 *µ*g	0 ± 0	100 ± 0	100 ± 0

[1] All values are percentages ± SEs. The Software for Intake Distribution Evaluation (version 1.11; Department of Statistics and Center for Agricultural and Rural Development, Iowa State University) was used to estimate usual folic acid intakes.
[2] All females aged 14–50 y (*n* = 7112).
[3] *n* = 2345 for adolescent females (14–18 y; UL = 800 *µ*g); *n* = 4766 for adult females (19–50 y; UL = 1000 *µ*g).

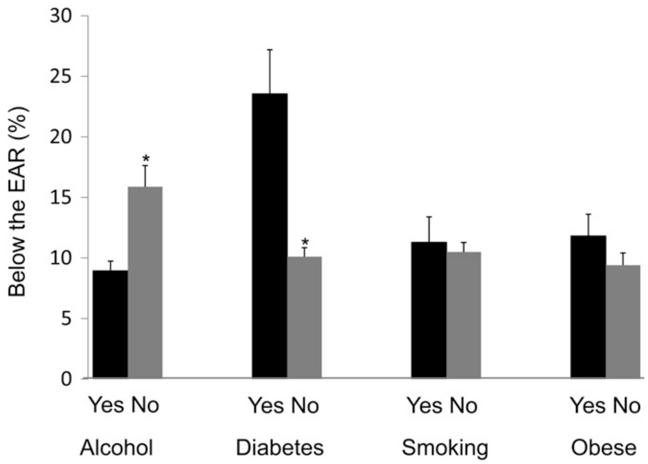

FIGURE 2. Prevalence of folate inadequacy in adults based on predicted actual dietary folate intake (model 2) and stratified by alcohol consumption [yes (*n* = 13,633) compared with no (*n* = 4374); in the past year], diabetes status [yes (*n* = 1536) compared with no (*n* = 18,357); types 1 and 2], smoking [yes = daily smoker (*n* = 4326) compared with no = nonsmoker (*n* = 14,826)], and obese status [yes (*n* = 3183) compared with no (*n* = 8567); BMI (in kg/m^2) $\geq$30]. Error bars represent the SE of the prevalence. *95% CI does not overlap with that of "yes" response for the same proposed risk factor. EAR, Estimated Average Requirement.

products more often (43). The effect that increased adherence to these recommendations or proposed changes to fortification regulations to include whole grains will have on the folate status of Canadians will require close monitoring.

One of the limitations of this study was the use of folic acid fortification overages based on a small number of fortified foods (*n* = 92) (22). However, as described in detail elsewhere, our sampling framework for selecting foods was systematic; we used national food consumption (FOODEX) and brand (ACNielson) data to identify the most commonly purchased fortified foods in Canada (22). In addition, the overall percentage overage that we reported in the aforementioned study is identical to that determined by Quinlivan and Gregory (21) in their estimation of the actual level of folic acid fortification in Canada based on changes reported in erythrocyte folate concentration before compared with after fortification of the food supply.

In summary, on the basis of the first nationally available dietary and supplement data in Canada in >30 y and estimates of the actual level of folic acid fortification, we conclude that, except for women aged >70 y, the POFI is low. Despite fortification, women of childbearing age are not consuming from dietary sources alone the amount of folic acid recommended to prevent NTDs. Data herein suggest that a folic acid supplement of 325–700 μg/d for adults and 325–500 μg/d for adolescents would serve to both maximally protect against NTDs and not provide intakes above the UL. Except for women aged >70 y, we saw little evidence that folic acid consumption from supplements modified the POFI among Canadians which fits with the commonly held perception that supplement users tend to be individuals whose diets are already folate-adequate. Given the low POFI in children aged <14 y and in adult males, consideration should be given to removing folic acid from supplements designed for these population subgroups in Canada.

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