Original Article

Use of micronutrient supplements among pregnant women in Alberta: results from the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort

**Maríel Fajer Gómez^{*†}, Catherine J. Field^{*†‡}, Dana Lee Olstad^{*†§}, Sarah Loehr^{*†},
Stephanie Ramage^{*†}, Linda J. McCargar^{*†} and the APrON Study Team¹**

^{*}Alberta Institute for Human Nutrition, University of Alberta, Edmonton, Alberta, Canada, [†]Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada, [‡]Department of Medicine, University of Alberta, Edmonton, Alberta, Canada, and [§]School of Public Health, University of Alberta, Edmonton, Alberta, Canada

Abstract

Maternal nutrient intake in the prenatal period is an important determinant of fetal growth and development and supports maternal health. Many women, however, fail to meet their prenatal nutrient requirements through diet alone and are therefore advised to consume nutrient supplements. The purpose of this study was to describe the use of natural health products (NHP) by pregnant women in each trimester of pregnancy. Women ($n = 599$) participating in the first cohort of the Alberta Pregnancy Outcomes and Nutrition (APrON) study completed an interviewer-administered supplement intake questionnaire during each trimester of pregnancy. NHP use was high, with >90% taking multivitamin/mineral supplements, and nearly half taking at least one additional single-nutrient supplement. Compliance with supplementation guidelines was high for folic acid (>90%), vitamin D (~70%) and calcium (~80%), but low for iron (<30%) and for all four nutrients together ($\leq 11\%$). On average, women met or exceeded the recommended dietary allowance for folic acid, vitamin D and iron from NHPs alone, with median daily intakes of 1000 μg , 400 IU and 27 mg, respectively. The median calcium intake was 250 mg d^{-1} . Up to 26% of women exceeded the tolerable upper intake level for folic acid and up to 19% did so for iron at some point of their pregnancy. Findings highlight the need to consider both dietary and supplemental sources of micronutrients when assessing the nutrient intakes of pregnant women.

Keywords: dietary supplements, pregnancy, vitamin D, folic acid, iron, calcium.

Correspondence: Dr Linda J. McCargar, Alberta Institute for Human Nutrition, University of Alberta, 4-126 Li Ka Shing Centre, 8606, 112 St, Edmonton Alberta, Canada T6G 2E1. E-mail: linda.mccargar@ualberta.ca

¹The individual members of the APrON research team are Bonnie J. Kaplan, Catherine J. Field, Deborah Dewey, Rhonda C. Bell, Francois P. Bernier, Marja Cantell, Linda M. Casey, Misha Eliasziw, Anna Farmer, Lisa Gagnon, Gerald F. Giesbrecht, Laki Goonewardene, David W. Johnston, Libbe Kooistra, Nicole Letourneau, Donna P. Manca, Jonathan W. Martin, Linda J. McCargar, Maeve O'Beirne, Victor J. Pop, Nalini Singhal.

Introduction

Maternal nutrient intake in the prenatal period is one of the most important determinants of fetal growth and development, and supports maternal health (Barker *et al.* 1993; Godfrey *et al.* 1996; Godfrey & Robinson 1998; Clausen *et al.* 2001; Oken *et al.* 2007). Inadequate maternal nutritional status, including

micronutrients, increases the risk of poor birth outcomes (Harding 2001; Fowles 2004; Moore *et al.* 2004; Moore & Davies 2005; Kind *et al.* 2006), and chronic disease in the offspring (Barker 2003); and obesity (Siega-Riz *et al.* 2004), hypertension (Frederick *et al.* 2005; Olafsdottir *et al.* 2006) and mortality (Allen 2000) in the mother. The challenge to maintain adequate nutrient intakes is particularly significant

for pregnant women, as requirements for several micronutrients may increase by as much as 50% to support maternal physiological adaptations and fetal growth and development (Picciano 2003; Carlson & Aupperle 2007). Although these increased nutrient requirements could theoretically be met through consumption of a healthy, balanced diet, the energy-dense diets commonly consumed in developed nations do not always contain sufficient micronutrients (Mathews *et al.* 1999; Bodnar & Siega-Riz 2002). Indeed, a number of studies have confirmed that many women fail to meet their nutrient requirements (Allen 2005; Haugen *et al.* 2008; Bhutta *et al.* 2009; Pinto *et al.* 2009) or food group recommendations (Fowler *et al.* 2012) during the prenatal period through diet alone.

For this reason, the Institute of Medicine (IOM) recommends that pregnant women with an elevated risk of nutritional deficiencies consume a prenatal multivitamin/mineral supplement (Institute of Medicine 1992). In addition, all women are advised to ensure that they take a daily supplement containing 30 mg of elemental iron (Institute of Medicine 1992) and to obtain 600 µg of folic acid daily from a combination of dietary and supplemental sources (Institute of Medicine 1998). In keeping with these recommendations, several studies suggest that the use of vitamin and mineral supplements is high among pregnant women (Maats & Crowther 2002; Glover *et al.* 2003; Refuerzo *et al.* 2005; Bercaw *et al.* 2010). Very few studies have, however, reported the contribution that these products make to overall nutrient requirements. The largest study with 40 817 pregnant women recruited to investigate this issue

found that dietary supplements contributed substantially to the total nutrient intakes of pregnant women (Haugen *et al.* 2008), but it and others concluded that even with the use of supplements, pregnant women's intakes of several key nutrients remained inadequate (Arkkola *et al.* 2006; Haugen *et al.* 2008; Pinto *et al.* 2009). In particular, women appear to have difficulty meeting their elevated requirements for folic acid, vitamin D and iron in the prenatal period (Arkkola *et al.* 2006; Haugen *et al.* 2008; Pinto *et al.* 2009). In addition, although pregnant women appear to be meeting current recommended calcium intakes (Arkkola *et al.* 2006; Haugen *et al.* 2008; Pinto *et al.* 2009), there is disagreement as to whether supplemental calcium may benefit both maternal and fetal bone health (Chang *et al.* 2003; Janakiraman *et al.* 2003; Prentice 2000a, Prentice, 2000b) and whether it may help to prevent pre-eclampsia and its complications (Hofmeyr *et al.* 2003).

Dietary supplements, however, are not limited to vitamins and minerals. In Canada, vitamin and mineral supplements are classified and regulated as natural health products (NHPs), a classification that also includes herbal remedies, homeopathic medicines, traditional medicines, probiotics, essential fatty acids and amino acids (Health Canada 2003). Products bearing this designation may be purchased without a medical prescription and are therefore easily accessible to pregnant women. In many cases, however, the safety of these products in pregnancy is not well established, as several herbs, for instance, have been linked to harmful effects in pregnancy (Finkel & Zarlengo 2004; Dugoua *et al.* 2006a,b). It is

Key messages

- Most pregnant women consumed natural health products (NHPs).
- Women in our sample, on average, met or exceeded the recommended dietary allowance for folic acid, vitamin D and iron from NHPs alone.
- Folic acid intake from NHPs decreased from the first to the third trimester, while iron intake increased from the first to the third trimester.
- Compliance with Institute of Medicine supplementation guidelines for pregnancy was high for folic acid, vitamin D and calcium, but low for iron and for all four nutrients together.
- NHPs need to be considered in dietary assessments; and women should be counselled on their appropriate use during pregnancy.

therefore important to understand patterns of NHP usage among pregnant women.

Given that data are limited regarding the type, dose and frequency with which NHPs in general, and vitamin and mineral preparations in particular, are used by pregnant women, the objective of this study was to: describe the intake of micronutrient supplements (particularly those containing folic acid, vitamin D, calcium and iron) by pregnant women during each trimester of pregnancy, and compare this to current recommendations. We focused on folic acid, vitamin D, calcium and iron because, as previously indicated, women's intake of these four nutrients is of particular concern during the prenatal period.

Materials and methods

Ethical approval

This study received ethics approval from the Health Research Ethics Board at the University of Alberta and the Conjoint Health Research Ethics Board in the Faculty of Medicine at the University of Calgary. Participants provided written, informed consent prior to enrolling in the study.

Participants

This study was part of The Alberta Pregnancy Outcomes and Nutrition (APrON) study, a pregnancy and birth cohort started in 2008 in Edmonton and Calgary, Alberta, Canada. The APrON study is investigating the impact of maternal nutrient status during pregnancy on maternal mental health, and on the health and development of the offspring. The current study includes data from the first 600 women recruited between June 2009 and June 2010.

Due to differences in the provision of obstetrical care within Edmonton and Calgary, recruitment strategies differed somewhat between the two cities. Pregnant women in Edmonton were recruited primarily through local media coverage, paid advertisements and posters placed in shopping malls and physician and midwives' offices. Research assistants also set up recruitment tables in shopping malls,

recreational centres and community fairs. A small number of women were recruited through physicians who agreed to inform their pregnant patients about the study. In Calgary, all pregnant women are referred to prenatal clinics. Nurses and research assistants met with women during their first visit to these prenatal clinics to ask if they would like to participate in the study. Some women were also approached at the time of their first or second ultrasound. Posters and media coverage were also used in Calgary. An APrON webpage was a useful recruiting tool in both cities.

Women were eligible to participate in APrON if they resided in Edmonton, Calgary or surrounding areas, were ≤ 27 weeks of gestation, ≥ 16 years of age and were able to speak and write in English. Participants were ideally enrolled during their first trimester of pregnancy and were asked to report once to the study clinic during each trimester. At study entry, a detailed questionnaire was used to collect information about demographics, lifestyle, medical history and current health status.

Supplement use

A supplement intake questionnaire (SIQ) was developed for the APrON study. It was based on questionnaires used in previous studies (Centers for Disease Control and Prevention 2006; Csizmadia *et al.* 2007; Statistics Canada 2004) and adapted for use with pregnant women. The SIQ was pilot-tested with a panel of nutrition experts and with the first 50 APrON participants during their first and second visits to assess its efficiency and the level of detail collected. Following pilot testing, columns were added to the initial questionnaire to facilitate reporting of changes in products, dosages and frequency at follow-up visits, rather than asking participants to complete a new SIQ each time.

The final version of the SIQ contained three sections: multivitamins/minerals, single-nutrient supplements, and other herbal products, probiotics, homeopathic remedies and traditional medicines. In the first section, a list of 20 commonly consumed multivitamins/minerals was provided. The second provided a list of 23 single-nutrient supplements, and

the third contained a list of 43 herbal products, probiotics, homeopathic remedies, traditional medicines and animal-derived products. Health Canada defines vitamins as essential substances, in small quantities, for the normal functioning of metabolism in the body, which cannot usually be synthesised in the body but occur naturally in certain foods (Health Canada 2003). Minerals defined as 'an inorganic solid with a definite and predictable chemical composition and physical properties' (Health Canada 2003). Herbal remedies were defined as medication prepared from plants or plants material (Health Canada 2003). 'Homeopathic medicines are manufactured from or contain as medicinal ingredients only those substances or sources referenced in the *Homeopathic Pharmacopoeia* of the United States, the *Homöopathische Arzneimittel*, the *Pharmacopée française* or the *European Pharmacopoeia*' (Health Canada 2003). Traditional medicines were defined as 'the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures' (Health Canada 2003). Probiotics were defined as 'a monoculture or mixed-culture of live micro-organisms that benefit the microbiota indigenous to humans,' amino acids were defined as 'a class of organic molecules containing amino and carboxylic groups, forming the chief constituents of proteins found in a plant or a plant material, an alga, a bacterium, a fungus or a non-human animal material,' and essential fatty acids are fatty acids that 'cannot be synthesised in the body' (Health Canada 2003).

For the purposes of this study, any NHP that contained more than one vitamin or mineral was included in the multivitamin/mineral category. If a NHP contained only one vitamin or mineral, it was included in the single supplement category. The exception was when a single supplement contained additional vitamins or minerals that aid in absorption and/or metabolism of the primary micronutrient. For example, supplements containing calcium with vitamin D were included in the single supplement category. In addition, if a multivitamin/mineral contained items from other NHP categories such as essential fatty acids or probiotics it was still classified as a multivitamin as this was its primary function.

Following enrolment, APrON participants completed the SIQ once during each trimester of pregnancy to report current NHP intake. A timeframe for 'current' intake (i.e. past week, past month) was not provided and therefore was subject to participant interpretation. In each section, the interviewer placed a check mark beside any NHPs that the women were currently taking. Additional space was provided in each section to record the name of any NHPs taken but not listed, and their corresponding natural product number (NPN) or drug identification number (DIN). Health Canada assigns a NPN or a DIN to all NHPs that have met its standards for quality, safety and efficacy (Health Canada 2003). Women reported the dosage and frequency of consumption for each product, as well as the place of purchase of herbal products, probiotics, homeopathic remedies, traditional medicines and animal-derived products. Additionally, women were asked to bring the containers or labels for all of the NHPs that they were taking for verification by study personnel. If a participant forgot, an email was sent to remind participants to bring the containers/labels to their next visit; or they were telephoned at home and asked to provide these details over the telephone.

NHP database

An Excel database (Microsoft Office 2007; Microsoft Corp., Redmond, WA, USA) containing the nutrient values of more than 400 NHPs was developed and was continuously updated throughout the study. To facilitate data entry, NPNs and DINs were used to identify products within the APrON database. These NPN/DINs were then located within Health Canada's Natural Health Products Database, and their formulations were entered into the APrON database. For products that did not have a NPN or DIN, ingredients were recorded from product labels and where necessary from manufacturer/supplier websites. In a small number of cases (estimated at <10% of sample), the most common formulations of NHPs were used as a default. For example, if the vitamin/mineral content of a prenatal multivitamin/mineral was unknown, the formulation of the most common prenatal

multivitamin/mineral used by participants was documented for that participant.

A second database was simultaneously developed in which every NHP code for products consumed by each participant during each trimester was recorded. When data collection concluded, the two databases were merged into an Access database (Microsoft Office 2007), providing a comprehensive and detailed profile of the content of all NHPs that participants reported consuming during each trimester of pregnancy, and the dosage and frequency of consumption.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences for Windows version 17.0 (SPSS Inc., Chicago, IL, USA). Analysis of variance (ANOVA) was used to compare mean intakes between trimesters for continuous variables and Bonferroni *post-hoc* tests were performed when results were statistically significant. Reported intakes of folic acid, vitamin D, calcium and iron were compared to IOM recommendations for dietary and supplemental intakes during pregnancy using ANOVA and Bonferroni *post-hoc* tests when results were statistically significant. The chi-square statistic was used to test for differences involving categorical variables. All statistical tests were performed at the $P < 0.05$ level of significance.

Sample size

The APrON study is an ongoing cohort study. The researchers have analysed results of this first completed subsample ($n = 600$). A secondary analysis of participants who attended visits in each trimester ($n = 105$) was completed to determine potential differences between those who completed the entire study and those who joined in the second trimester or did not complete all three visits.

Results

Participant recruitment

Of the 600 women enrolled in the first cohort, one participant was excluded because she did not attend

any study appointments, leaving a total of 599 participants for the present study. Sample sizes differed by trimester due to later enrolment in the study, withdrawals or missed appointments. In total, 136 women completed the first visit, 575 completed the second and 516 completed the third. Complete supplement intake data were available for 105 women who attended all three visits. Demographic information varies due to some incomplete or missing answers.

Participant characteristics

Baseline characteristics of participants are presented in Table 1. At enrolment, the mean age of the women was 31 (± 4.3) years with a mean pre-pregnancy body mass index of 24.1 (± 4.9) kg m⁻². The majority of the women were Caucasian (81%) and were married or living common law (91%). Nearly 65% of subjects had a university degree (undergraduate or post-graduate) and about half reported an annual family income above \$100 000. Fifty-four per cent reported having had at least one previous pregnancy and the majority had planned their current pregnancy (77%).

Supplement use

The mean timing of SIQ completion was 10.7 ± 2.3 weeks in trimester 1, 19.2 ± 3.7 weeks in trimester 2 and 32.4 ± 1.4 weeks in trimester 3. Almost all women reported taking a multivitamin/mineral supplement at some point during their pregnancy (Table 2). Small but significant differences were observed in the reported intake of multivitamin/mineral supplements between trimesters, whereby 97% of participants reported their use in the first trimester, and 92% in the third trimester ($P = 0.01$). Many women also reported taking single-nutrient supplements: 45% during the first trimester and 55% by the third trimester ($P = 0.02$).

In all trimesters, a higher proportion of the micro-nutrient intake came from multivitamin/mineral supplements compared with single supplements. A significant difference between trimesters was observed with iron intake from multivitamins decreasing and intake from single supplements increasing ($P < 0.05$) (data not presented). No

Table 1. Characteristics of participants enrolled in APrON at study entry

Demographic variables (<i>n</i> = 599)	
Age (mean $\pm$ SD)	31.1 ($\pm$ 4.3)
Pre-pregnancy BMI (mean $\pm$ SD)	24.1 ($\pm$ 4.9)
Marital Status (%) [*]	
• Single / separated / divorced	3.3
• Married / common law relationship	90.5
Highest level of education (%) [*]	
• Less than high school	1.7
• High school	7.7
• Trade	19.3
• University – first degree	44.8
• Post-graduate	19.8
Ethnicity (%) [*]	
• Caucasian	81.0
• Chinese	2.5
• Latin American	2.3
• Black	1.2
• Other	6.2
Family annual income (%) [*]	
• Less than \$20 000	1.5
• \$20 000–\$39 000	4.0
• \$40 000–\$69 000	12.5
• \$70 000–\$99 000	23.3
• \$100 000+	50.8
Previous pregnancies (%) [*]	
• Yes	54.2
• No	40.0
Current pregnancy planned (%) [*]	
• Yes	76.5
• No	17.7
Assisted pregnancy (%) [*]	
• Yes	6.5
• No	87.5

APrON, Alberta Pregnancy Outcomes and Nutrition; BMI, body mass index; SD, standard deviation. ^{*}Column percentages do not always add up to 100% due to missing values.

Table 2. Daily intake of natural health products by APrON participants

First trimester (<i>n</i> = 136)		Second trimester (<i>n</i> = 575)		Third trimester (<i>n</i> = 516)		
Natural health products	<i>n</i> (%) [*]	Natural health products	<i>n</i> (%) [*]	Natural health products	<i>n</i> (%) [*]	<i>P</i> [†]
Multivitamin/mineral	132 (97) ^a	Multivitamin/mineral	551 (95) ^a	Multivitamin/mineral	475 (92) ^b	0.009 [‡]
Single nutrient	62 (45) ^a	Single nutrient	270 (46) ^a	Single nutrient	284 (55) ^b	0.015 [‡]
Herbal products	13 (9)	Herbal products	52 (9)	Herbal products	31 (6)	0.128
Essential fatty acids	15 (11) ^a	Essential Fatty Acids	76 (13) ^a	Essential Fatty Acids	93 (18) ^b	0.033 [‡]
Homeopathic remedies	2 (1)	Homeopathic remedies	9 (1)	Homeopathic remedies	4 (0.7)	0.476
Probiotics	6 (4)	Probiotics	18 (3)	Probiotics	20 (3)	0.691
No NHP intake	0	No NHP intake	10 (1)	No NHP intake	13 (1)	0.148

APrON, Alberta Pregnancy Outcomes and Nutrition; NHP, natural health product. ^{*}Column percentages do not always add up to 100% as some participants reported the use of ≥ 1 different natural health products. [†]*P* values for Chi-square statistic. [‡]Values within a row with different superscripts are significantly different.

significant differences were found between trimesters for folic acid, vitamin D or calcium.

Essential fatty acids were also used by 11% of women in the first trimester and 18% in the third trimester (*P* = 0.03). There were no significant differences between trimesters in the reported intake other NHPs including herbal products, homeopathic remedies and probiotics. No participants reported intake of traditional medicines and only one participant reported intake of amino acids during the first and second trimester, while no amino acids were reported in the third trimester. Therefore traditional medicines and amino acids were not included in Table 2.

In a secondary analysis of only women who completed all three visits (*n* = 105), a similar pattern of intake was observed where multivitamin/mineral supplement intake decreased and single-nutrient supplement intake increased; however, differences were not significant. In the secondary analysis of *n* = 105, 98% of participants reported multivitamin/mineral supplements in the first trimester, and 91% in the third trimester (*P* = 0.10). In addition, 44% of participants reported taking single-nutrient supplements in the first trimester, 50% in the second trimester and 60% in the third trimester (*P* = 0.083).

Contribution of NHPs to meeting dietary nutrient intake recommendations

Daily reported intakes of folic acid, vitamin D, calcium and iron from NHPs in each trimester are presented in Table 3 and compared to IOM dietary

Table 3. Daily intake of key micronutrients from natural health products by AP-ON participants.

Micronutrient	First trimester (<i>n</i> = 136)		Second trimester (<i>n</i> = 575)		Third trimester (<i>n</i> = 516)		<i>P</i> *
	RDA	Mean $\pm$ SD	Median (min, max)	Mean $\pm$ SD	Median (min, max)	Mean $\pm$ SD	
Folic acid (μ g)	600 μ g	1225 $\pm$ 866	1 000 (0, 6 000 μ g)	1353 $\pm$ 1110	1000 (0, 7100 μ g)	1228 $\pm$ 1029	0.126
(% RDA)		204 $\pm$ 144		225 $\pm$ 184		204 $\pm$ 171	
Vitamin D (IU)	600 IU	789 $\pm$ 1302	400 (0, 12 600 IU)	645 $\pm$ 670	400 (0, 6000 IU)	746 $\pm$ 1002	0.084
(% RDA)		131 $\pm$ 217		107 $\pm$ 111		124 $\pm$ 166	
Calcium (mg)	1000 mg	313 $\pm$ 313	250 (0, 2 300 mg)	339 $\pm$ 297	250 (0, 2300 mg)	352 $\pm$ 339	0.421
(% RDA)		31 $\pm$ 31		33 $\pm$ 29		35 $\pm$ 33	
Iron (mg)	27 mg	28 $\pm$ 17 ^a	27 (0, 160 mg)	30 $\pm$ 21 ^a	27 (0,187 mg)	39 $\pm$ 33 ^b	<0.001 [†]
(% RDA)		104 $\pm$ 61		112 $\pm$ 76		143 $\pm$ 124	

AP-ON, Alberta Pregnancy Outcomes and Nutrition; Max, maximum; Min, minimum; RDA, recommended dietary allowance (Institute of Medicine 1998, 2001); SD, standard deviation. **P* value for analysis of variance used to compare mean supplement intake between trimesters. [†]Significant differences for iron between groups determined by Bonferroni *post-hoc* tests. Values within a row with different superscripts are significantly different

recommendations. Average folic acid intake from NHPs as reported by participants was greater than 200% of the recommended dietary allowance (RDA) for the gestational period in each trimester. No significant differences were observed between trimesters. The mean reported intake of vitamin D from NHPs also exceeded the RDA, with no significant differences between trimesters. Non-dietary calcium intake during pregnancy met approximately one-third of dietary recommendations, and did not differ by trimester. Iron intake from NHPs, by contrast, did differ between trimesters as intake during the third trimester was significantly greater than intake in the first and second trimesters. During the first trimester 104% of the RDA was met through the use of NHPs, and 112% in the second trimester. This increased to 143% by the third trimester ($P < 0.001$).

Compliance with supplementation guidelines

The IOM guidelines for folic acid supplementation were met by 97% of participants during the first trimester of gestation, decreasing significantly by the third trimester to 91% ($P = 0.02$) (Table 4). The proportion of participants who met IOM supplementation guidelines during the gestational period for vitamin D and calcium was ~70% and ~80%, respectively, with no differences between trimesters. Compliance with iron supplementation guidelines was also significantly different between trimesters, with 15% of participants meeting the guideline in the first trimester, and 29% during the third ($P < 0.001$). Compliance with supplementation guidelines for all four micronutrients was $\leq 11\%$ across trimesters, with no significant differences between trimesters. Demographic characteristics of participants who met supplementation guidelines for the four micronutrients in at least one trimester ($n = 103$), compared with those who did not, are presented in Table 5. Significant differences were observed according to level of education and ethnicity ($P = 0.05$).

Safety concerns regarding the use of NHPs during gestation

Folic acid intake was above the tolerable upper intake level (UL) for approximately one quarter of pregnant

Table 4. Proportion of APrON participants meeting Institute of Medicine supplementation guidelines during pregnancy

Micronutrient	Recommended intakes from supplements	First trimester (<i>n</i> = 136)	Second trimester (<i>n</i> = 575)	Third trimester (<i>n</i> = 516)	<i>P</i> *
		%	%	%	
Folic acid	300 µg	97 ^a	95 ^a	91 ^b	0.021 [†]
Vitamin D	400 IU	74	71	68	0.275
Calcium	250 mg	79	83	81	0.559
Iron	30–60 mg [‡]	15 ^a	20 ^a	29 ^b	<0.001 [†]
All four micronutrients [§]		5	9	11	0.076

APrON, Alberta Pregnancy Outcomes and Nutrition. **P* value for chi-square statistic. [†]Values within a row with different superscripts are significantly different. [‡]For the purposes of this analysis, in each trimester, participants with an intake of 30 mg of iron or above were considered to be meeting guidelines. [§]Proportion of participants meeting the Institute of Medicine's supplementation guidelines (Institute of Medicine 1992) for folic acid, vitamin D, calcium and iron in each trimester.

women in each trimester with no significant differences between trimesters (Table 6). Significant differences were observed in the proportion of participants exceeding the UL for vitamin D between trimesters, where fewer women exceeded the UL during the second trimester (0.2%) when compared with the first and third trimesters (1%) ($P = 0.03$). No participants exceeded the UL for calcium in any trimester. The proportion of women who exceeded the UL for iron increased significantly from the first (4%) to the third trimester, in which 19% of participants reported intakes above the UL ($P < 0.001$).

Discussion

Results revealed that almost all women took multivitamin/mineral supplements throughout pregnancy, nearly half took single-nutrient supplements, and 11–18% took essential fatty acids. The use of other types of NHPs was not as common in our sample. These results are consistent with other studies in which the majority of pregnant women reported use of NHPs (Maats & Crowther 2002; Glover *et al.* 2003; Refuerzo *et al.* 2005; Bercaw *et al.* 2010). Other studies have documented a higher use of essential fatty acids (Haugen *et al.* 2008) and herbal products (Glover *et al.* 2003; Tsui *et al.* 2001) among pregnant women than observed in the present cohort. To our knowledge our study is the first to describe NHP use across the different trimesters of pregnancy. NHP use differed by trimester, in that multivitamin/mineral use

decreased as pregnancy proceeded, while the use of single-nutrient supplements was significantly higher by the third compared with the first trimester. A similar pattern of intake was observed in the subsample of participants with complete data for all three trimesters although the differences were not significant. This may have been due to the smaller sample size; however, it cannot be ruled out that the smaller sample of women in the first trimester may have affected the results. In addition, iron was the only micronutrient of the four examined that was significantly different in terms of intake from multivitamin/mineral supplements compared with single supplements across trimesters in the full sample.

Compared to IOM *dietary recommendations* for pregnancy, the majority of women exceeded the daily RDA for folic acid from NHPs alone. Moreover, more than 20% of participants exceeded the UL (1000 µg) for folic acid in each trimester of gestation. High doses of folic acid (5000 µg) are indicated where there is a personal or family history of neural tube defects (Wilson *et al.* 2007). Whether participants taking high doses of folic acid were prescribed such high amounts is unknown, but it is unlikely that this would constitute a large portion of this healthy cohort. Concerns regarding excess folic acid intake include the potential to mask symptoms of vitamin B12 deficiency, reduced effectiveness of antifolate drugs and promotion of colorectal cancer in susceptible individuals (Institute of Medicine 1998; Cole *et al.* 2007; Mason *et al.* 2007; Morris *et al.* 2007; Smith *et al.* 2008; Hirsch

Table 5. Demographic characteristic of APrON participants meeting Institute of Medicine supplementation guidelines during at least one trimester of pregnancy compared with those who did not meet the guidelines

	Participants meeting guidelines (n = 103)*	Participants not meeting guidelines (n = 497)	P†
Age, (mean ± SD)	30.8 (±3.2)	31.8 (±4.3)	0.178
Pre-pregnancy BMI (%)‡			
Underweight	1.9	3.0	
Adequate	64.1	61.4	
Overweight	19.4	17.1	
Obese	9.7	13.5	0.647
Marital status (%)‡			
Married/common law	89.3	90.7	
Single/separated/divorced	2.9	3.2	0.895
Highest level of education (%)‡			
Trade or below	20.4	30.2	
University or above	71.8	63.2	0.049
Ethnicity (%)‡			
Caucasian	73.8	82.5	
Others	17.5	10.9	0.048
Total annual income (%)‡			
Low income§	2.9	5.8	
High income	88.3	86.3	0.235
Previous pregnancies (%)‡			
Yes	49.5	54.9	
No	42.7	39.2	0.403
Current pregnancy planned (%)‡			
Yes	78.6	76.1	
No	14.6	18.1	0.408
Assisted pregnancy (%)‡			
Yes	9.7	5.8	
No	83.5	8.3	0.138

APrON, Alberta Pregnancy Outcomes and Nutrition; BMI, body mass index; SD, standard deviation. *Participants with a mean intake of $\geq 300 \mu\text{g}$ folic acid, $\geq 400 \text{ IU}$ vitamin D, $\geq 250 \text{ mg}$ calcium and $\geq 30 \text{ mg}$ of iron in ≥ 1 trimester were considered as meeting guidelines. †P value for Chi-square statistic. ‡Column percentages do not always add up to 100% due to missing data. §Low income cut-off point is \$40 000 per year for a family of four in a community with more than 500 000 habitants (Statistics Canada 2008).

et al. 2009). Folic acid supplementation during pregnancy has furthermore been associated with increased risk of asthma, obesity and insulin resistance in the offspring (Yajnik *et al.* 2008; Whitrow *et al.* 2009).

The same tendency to meet dietary recommendations via NHPs alone was evident for vitamin D. Notably, the proportion of participants who exceeded

the UL for vitamin D was low, at 1% in the first and third trimesters, and 0.2% during the second trimester. Given that there are limited frequently consumed dietary sources of vitamin D, and sunlight exposure is minimal in Canada between October and March (Webb *et al.* 1988), these findings pose few concerns.

Mean calcium intake from supplemental sources remained constant throughout gestation, representing approximately one-third of the RDA. Calcium intake from NHPs was similar to the amount suggested by the IOM, and no participants exceeded the UL for calcium in any trimester. Thus, dietary intake of calcium-containing foods is essential to meet the RDA. Calcium intake from NHPs appears to be at a reasonable level to supplement dietary intake and avoid interfering with iron absorption (Institute of Medicine 1992).

Women, on average, met the RDA for iron from NHPs in all trimesters of pregnancy. Supplementation increased significantly as pregnancy progressed, with the mean intake reaching 143% of the RDA by the third trimester. In addition a significant difference was noted in the proportion of supplemental iron coming from multivitamin/mineral supplements compared with single supplements with more coming from single supplements in the third trimester. Of note, almost 20% of participants exceeded the UL during the third trimester. Higher supplementation is recommended for women who develop iron-deficiency anaemia during pregnancy, which may explain the observed increase in iron supplementation in the second and third trimesters. Exceeding the UL for iron through supplements has been associated with gastrointestinal side effects, impaired zinc absorption and a potentially increased risk of vascular disease and cancer (Institute of Medicine 2001).

Compliance with IOM micronutrient *supplementation* recommendations was assessed for each of the four nutrients in each trimester. Folic acid supplementation guidelines (300 mcg daily) were met by almost all participants during the first trimester, with a small but significant decrease by the end of pregnancy. Vitamin D (400 IU) and calcium (250 mg) supplementation guidelines were met by fewer participants, at approximately 70% and 80% of participants, respectively. This finding contrasts to earlier studies

Table 6. Proportion of APrON participants exceeding the tolerable upper intake level of key micronutrients through natural health products during pregnancy

Micronutrient	Tolerable upper intake level	First trimester (<i>n</i> = 136)	Second trimester (<i>n</i> = 575)	Third trimester (<i>n</i> = 516)	<i>P</i> *
		%	%	%	
Folic acid	1000 µg	22	26	21	0.234
Vitamin D	4000 IU	1 ^a	0.2 ^b	1 ^a	0.026 [†]
Calcium	3000 mg	0.0	0.0	0.0	NS
Iron	45 mg	4 ^a	9 ^a	19 ^b	<0.001 [†]

APrON, Alberta Pregnancy Outcomes and Nutrition; NS, not significant. **P* value for Chi-square statistic. [†]Values within a row with different superscripts are significantly different.

where the proportion of participants meeting IOM supplementation guidelines was low (Millar 2004). Iron was the only nutrient for which the majority of women did not meet supplement recommendations. The IOM recommends 30 mg of iron supplementation daily during pregnancy. In this study $\leq 20\%$ of women met recommendations in the first and second trimesters, with a significant increase to 29% by the third trimester. Compliance with iron supplementation guidelines was also low in previous studies, and reported to be due to its gastrointestinal side effects (Hyder *et al.* 2002; Melamed *et al.* 2007; Nguyen *et al.* 2008). The women had median intakes for iron of 27 mg, which is equal to the RDA; however, the IOM supplementation guidelines recommend 30–60 mg day⁻¹. Thus, there is a small discrepancy between achieving both guidelines.

Findings that women met the RDA and/or exceeded the UL through intake of NHPs alone raise some concerns regarding potential effects on the future health of the offspring. NHPs are easily accessible by women with no requirement for a medical prescription. Women who take more than one NHP can easily exceed recommended micronutrient intakes. It is therefore important that health professionals counsel women about NHP use and consider both dietary and supplemental sources of micronutrients in their dietary assessments.

Adherence to IOM recommendations for all four nutrients simultaneously was low, at $\leq 11\%$ in each trimester. A total of 103 women met supplementation guidelines for all four micronutrients in at least one trimester of pregnancy. Adherence to supplementa-

tion guidelines among this group of women differed significantly according to level of education and ethnic background. Similar to the finding of the present study, it has been suggested that highly educated women may be more likely to follow supplementation guidelines (Haugen *et al.* 2008). The findings of the present study related to ethnicity were unexpected as other researchers have found that ethnic minorities are reportedly less compliant with dietary recommendations (Jasti *et al.* 2003). However, women in this sample tended to be highly educated and have a higher family income, including the women who were members of ethnic minorities. It is possible that these variables had a larger impact on the likelihood of following supplementation guidelines than ethnicity within this sample. Thus, dietary intervention may be most appropriately targeted to pregnant women with lower education levels.

Strengths and limitations

Given high rates of NHP use among pregnant women an important strength of this study was its development of an efficient system to capture and accurately quantify NHP intake among pregnant women in each trimester of gestation. Study findings testify to the utility of the SIQ together with the NHP database in enabling a more complete understanding of the NHP intakes of pregnant women. Nevertheless, as a self-reported questionnaire, the SIQ is subject to self-report bias. We partially overcame this limitation by asking women to bring in their supplement containers for objective verification by research staff. By asking

participants to complete the SIQ during each trimester of pregnancy, we also minimised the problem of recall bias.

It is important to note that dietary intake data were not available at the time of this report; however, dietary sources of folic acid, vitamin D and highly absorbable heme iron are somewhat limited. Furthermore, because the majority of women in our sample met or exceeded the RDA for folic acid, vitamin D and iron through NHPs alone, inclusion of dietary intake data would not have altered our overall findings. As seen in Table 3, there was a wide range of intakes of the four key micronutrients assessed. In each trimester, there were participants with null intake of these micronutrients from supplemental sources, while others reported very high intakes. Secondary to such excessive intakes, mean intakes of folic acid, vitamin D, iron and calcium may have been skewed to higher levels, and therefore the median intake may better reflect true intakes.

Other limitations of this study include our inability to assess the degree to which women remembered to take their supplements on a daily basis, and the small number of cases in which the exact nutritional composition of NHPs was not available. The demographic profile of participants may have influenced our overall results as they were older, primarily Caucasian and had a high socio-economic status. This is a limitation of human cohort studies and another similar study reported a sample with a similar demographic profile (Arkkola *et al.* 2006). While these results may not reflect the Alberta population as a whole, they still provide an important first description of NHP use across trimesters during pregnancy in Alberta women. It should also be noted that the two cities in this study are relatively affluent. Calgary and Edmonton had the highest and second highest average family income, respectively, for major cities in Canada for 2008 (Statistics Canada 2008). In addition, efforts were made to recruit a more diverse sample following this first group ($n = 600$), as other groups may have a lower prevalence or different patterns of NHP use. Finally, nutrient intakes may not necessarily reflect nutrient status due to factors such as genetics, impaired or enhanced intestinal absorption, endog-

enous synthesis, nutrient–nutrient interactions and drug–nutrient interactions.

Conclusions

The APrON cohort provided a unique opportunity to investigate NHP use during each trimester of pregnancy. The use of NHPs, assessed with a novel tool developed for this study, was high in this group of women, with >90% taking multivitamin/mineral supplements, and nearly half taking single-nutrient supplements. On average, women met or exceeded the RDA for folic acid, vitamin D and iron from NHPs alone. Compliance with IOM supplementation guidelines for pregnancy was high for folic acid, vitamin D and calcium, but low for iron and for all four nutrients together. Some differences by trimester were evident, most notably for folic acid, where the proportion of the sample consuming folic acid supplements decreased from the first to the third trimester, while iron exhibited an opposing trend, increasing from the first to the third trimester. Given that dietary sources of folic acid, vitamin D and highly absorbable heme iron are limited, findings suggest that NHP consumption may assist women to meet their elevated nutrient requirements during pregnancy. Women should be counselled on appropriate use of NHPs as 26% of participants exceeded the UL for folic acid at some point during their pregnancy and up to 19% did so for iron.

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Conflicts of interest

DLO received payment for manuscript preparation. The remaining authors declare that they have no conflicts of interest.

Contributions

CJF and LJM designed the study. MFG performed the study. SL and SR assisted with the implementation of the study. MFG and SL, SR analysed the data. MFG, CJF, DLO, SL, SR and LJM interpreted the data. MFG and DLO drafted the manuscript. CJF and LJM edited the manuscript. All authors read and approved the final manuscript.

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