

# Socioeconomic, Lifestyle and Dietary Factors Associated with Dietary Supplement Use during Pregnancy

Camille Pouchieu<sup>1\*</sup>, Rachel Lévy<sup>1,2</sup>, Céline Faure<sup>1,2</sup>, Valentina A. Andreeva<sup>1</sup>, Pilar Galan<sup>1</sup>, Serge Hercberg<sup>1,3</sup>, Mathilde Touvier<sup>1</sup>

**1** Nutritional Epidemiology Research Team, Sorbonne Paris Cité Research Center, Inserm U557, Inra, Cnam, Paris 13 University, SMBH Paris 13, Bobigny, France, **2** Reproductive Biology Unit-CECOS, Jean Verdier Hospital, Bondy, France, **3** Public Health Department, Avicenne Hospital, Bobigny, France

## Abstract

**Background:** Information on dietary supplement (DS) use during pregnancy is largely lacking. Besides, little is known about the share of DS use as self-medication versus such use following a physician's advice/prescription. Our aim was to evaluate DS use and its socioeconomic, lifestyle and dietary correlates among pregnant women participating in the French NutriNet-Santé cohort study.

**Method:** Data were collected by self-administered web-based questionnaires. Food intake was assessed by repeated 24 h dietary records. 903 pregnant women provided data on their DS use (both "regular" DS and medication containing mainly vitamins/minerals). Supplement users were compared to non-users by unconditional logistic regression.

**Results:** DS use—in general and as regards folic acid in particular—was positively correlated with age, being primiparous, having higher income and belonging to a higher socioprofessional category. DS users had significantly higher dietary intakes of most vitamins and minerals. The proportion of DS users (e.g., those reporting use at least three days a week) increased significantly with the trimester of pregnancy (58.0%, 62.2% and 74.5%, respectively). 50.2% of women in their 1st trimester used folic acid. The proportion of iron users tripled from the 1st to the 3rd trimester (18.5 to 63.9%). DS use was prescribed or recommended by a physician in 86.7% of the cases.

**Conclusion:** This study provided new and detailed information on DS use and its correlates during pregnancy. Even in this relatively well-educated population, folic acid supplementation at the beginning of pregnancy was inadequate and was associated with socioeconomic and demographic disparities.

**Citation:** Pouchieu C, Lévy R, Faure C, Andreeva VA, Galan P, et al. (2013) Socioeconomic, Lifestyle and Dietary Factors Associated with Dietary Supplement Use during Pregnancy. PLoS ONE 8(8): e70733. doi:10.1371/journal.pone.0070733

**Editor:** Shannon M. Hawkins, Baylor College of Medicine, United States of America

**Received:** April 30, 2013; **Accepted:** June 27, 2013; **Published:** August 13, 2013

**Copyright:** © 2013 Pouchieu et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Funding:** The NutriNet-Santé cohort study is funded by the following public institutions: Ministère de la Santé, Institut de Veille Sanitaire (InVS), Institut National de la Prévention et de l'Éducation pour la Santé (INPES), Fondation pour la Recherche Médicale (FRM), Institut National de la Santé et de la Recherche Médicale, Institut National de la Recherche Agronomique (INRA), Conservatoire National des Arts et Métiers (CNAM) and Paris 13 University. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors have declared that no competing interests exist.

\* E-mail: c.pouchieu@uren.smbh.univ-paris13.fr

## Introduction

Pregnancy is a physiologically-specific period during which the needs for some nutrients increase. While the nutrient requirements of the general population can be met by an adequate diet, risk of suboptimal micronutrient intake is common during pregnancy [1] and supplements might be useful to meet dietary requirements for specific key nutrients. In France as in several other countries, 0.4 mg/day of folic acid is recommended before the conception, at the beginning of pregnancy to reduce the risk of neural tube defects (NTD), and also later during pregnancy, to prevent megaloblastic anemia in the mother [2–7]. The 2011 incidence of NTD in France was estimated at 1.0 case per 1000 births [8], while upwards of 200 cases per year could be prevented by improving folic acid intake [9]. This has led some countries to proceed with large-scale dietary folic acid fortification programmes [10]. The prevalence of anemia in developed countries (due to iron deficiency in 2/3 of the cases) is estimated at around 5% before

pregnancy and is tripled during pregnancy [11]. Anemia is a risk factor for preterm delivery, low birth weight and cognitive impairment in the infant [12,13]. Vitamin D deficiency has been associated with the risk of pre-eclampsia, gestational diabetes, preterm delivery, low birth weight, and low fetal bone mineral content [14]. Iodine deficiency is associated with maternal and fetal goiter, cretinism, intellectual impairments, neonatal hypothyroidism, increased risk of miscarriage and infant mortality [15]. Thus, folic acid, iron, vitamin D and iodine supplementation at moderate doses is recommended for pregnant women at risk of deficiency. In contrast, other systematic supplementation is not necessary in the absence of specific pathological situations and some supplements should even be avoided [16]. Excessive intake of retinol [17] or vitamin E [18], for example, may have serious deleterious effects on fetal development. According to the Developmental Origins of Health and Disease (DOHaD) concept [19], exposure to nutritional factors in utero is likely to have major

health consequences in later life, notably through epigenetic mechanisms [20,21].

Despite being of major public health concern, little information is available regarding dietary supplement (DS) use in pregnant women worldwide [4,22–26]. Some studies conducted in various countries have suggested that DS use may be more frequent in older [24,27,28], well-educated [24,25,27,28], non-smoking and primiparous women [24]. However, information is lacking about differences in nutrient intake from food between pregnant DS users and non-users. If DS use is indeed associated with different sociodemographic, economic, lifestyle, and dietary factors, an accurate assessment of these associations is necessary in order to better target the nutritional recommendations regarding pregnant women's supplementation with specific nutrients.

Our objectives were: 1) to investigate the demographic, socioeconomic, lifestyle and dietary correlates of overall and folic acid DS use in pregnant women included in the NutriNet-Santé cohort study; and 2) to assess the role of physicians in the motives for DS purchases and the proportion of self-medicating users.

## Methods

### Study population

Worldwide, the NutriNet-Santé study is the first large-scale population-based prospective cohort study that is exclusively Internet-based. It aims at elucidating the relationships between nutrition and chronic disease risk, as well as defining the determinants of eating behaviour [29]. It was launched in France in May 2009. Adults ( $\geq 18$  y) living in France and having access to the Internet are recruited via mass-media campaigns. The study was approved by the Institutional Review Board of the French Institute for Health and Medical Research (IRB Inserm n°0000388FWA00005831) and the “Commission Nationale de l'Informatique et des Libertés” (CNIL n°908450 and n°909216). Written informed consent was obtained from all subjects.

### Data collection

Participants fill in self-administered web-based questionnaires at baseline and then regularly during the follow-up. Several of the baseline questionnaires were tested and compared against traditional assessment methods (paper questionnaires or interviews by a dietitian) [30–32]. In the NutriNet-Santé study, 60388 women had completed the DS questionnaire.

**Pregnancy data.** At baseline and regularly over the follow-up, data on current pregnancy and due date were collected through health status questionnaires.

**Dietary supplement use.** The questionnaire regarding DS use was administered two months after baseline in the entire cohort. In our study, we considered as DS both regular DS and medicinal supplements mainly composed of vitamins and minerals, which are treated as pharmaceutical products in France. Participants were asked if they were currently taking any supplement at least 3 days a week. They were also asked to specify the type of DS using a list of 34 different nutrients and substances. They had to refer to the nutritional information on the packaging of the DS that they were currently taking. Circumstances of DS purchase (notably role of physicians versus self-medication) were also reported.

**Demographic, socioeconomic, lifestyle and behavioural data.** At baseline, self-administered questionnaires were used to collect data on demographic, socioeconomic and lifestyle characteristics, including age, geographical region, marital status, number of children, educational level, socioprofessional category, and income.

**Dietary data.** Each year, the participants are asked to complete three non-consecutive self-administered web-based 24 h dietary records, the days for which are randomly assigned during a two-week period (two days during the week and one day during the weekend). All foods and beverages consumed at breakfast, lunch, dinner and at all other occasions are recorded. For foods with potentially high nutrient variability, participants are also asked to provide the brand name. The participants are asked to estimate the portion size for each reported food and beverage item using validated photographs [33]. Daily dietary intakes of energy and nutrients are then calculated using the NutriNet-Santé food composition table, which includes more than 2500 different foods.

Knowledge of official nutritional recommendations as provided in the French National Nutrition and Health Programme (PNNS) was also assessed. Finally, a specific questionnaire was used to assess the opinion and behaviour of women as regards organic food.

### Statistical analyses

All women who entered the cohort before September 2012 and had completed the DS questionnaire while pregnant were included in the present study ( $n = 903$ ).

We estimated the proportion of DS users overall and according to the trimester of pregnancy. Types of DS as well as circumstances of purchase were also described.

DS users (overall and specifically regarding folic acid) and non-users were compared by age-adjusted unconditional logistic regression analyses, regarding their sociodemographic characteristics (age, geographical region, marital status, number of children, education, income, and socioprofessional category), knowledge of official nutritional recommendations and organic food consumption. Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

The mean daily intake of dietary micro- and macro-nutrients was compared via logistic regression between DS users and non-users after adjustment for age, number of 24 h records and energy intake. Only women who provided at least one dietary record during their pregnancy and who were normo-energy reporters according to the Goldberg criteria [34] were included in this part of the analysis.

A P-value  $< 0.05$  was considered significant in all statistical tests. All tests were two-sided. Analyses were carried out with SAS software (Release 9.1, SAS Institute Inc., Cary, NC, USA).

## Results

Among the 903 pregnant women included in this study, 31% were in the 1<sup>st</sup> trimester of pregnancy, 36% in the 2<sup>nd</sup>, and 33% in the 3<sup>rd</sup> at the time of the DS questionnaire completion. Sociodemographic characteristics of the study population are presented in Table 1. The average age of the participants was  $31.7 \pm 4.07$  years. A high proportion of pregnant women (64.9%) used DS at least three days a week. The corresponding proportion among the non-pregnant women of childbearing age in the cohort was only 29.1% (data not shown). The proportion of DS users increased significantly with the trimester of pregnancy (58.0%, 62.2% and 74.5% in the first, second and third trimester, respectively).

### Demographic, socioeconomic and behavioural correlates of overall and folic acid dietary supplement use

As compared with non-users (Table 1), pregnant women who used DS were more likely to be older, to live in the Paris

**Table 1.** Demographic, socioeconomic and lifestyle correlates of dietary supplement use in pregnant women of the NutriNet-Santé cohort study.

|  | All Pregnant women |      | Supplement Non-Users |      | Supplement Users <sup>1</sup> |      | Age adjusted logistic regression analyses |                |
|--|--------------------|------|----------------------|------|-------------------------------|------|---|----------------|
|  | (n = 903)          |      | (n = 317)            |      | (n = 586)                     |      | OR  | p <sup>2</sup> |
|  | n                  | %    | n                    | %    | n                             | %    |   |                |
| Age <sup>3</sup>   | 31.7               | 4.07 | 31.1                 | 4.22 | 32.1                          | 3.94 | 1.06 [1.02–1.10]                          | 0.001          |
| Geographical region  |                    |      |                      |      |                               |      |   | 0.0007         |
| Paris metropolitan area  | 198                | 21.9 | 46                   | 14.5 | 152                           | 25.9 | 1.00                                      |                |
| North  | 66                 | 7.3  | 33                   | 10.4 | 33                            | 5.6  | 0.26 [0.09–0.77]                          |                |
| North-West   | 142                | 15.7 | 48                   | 15.1 | 94                            | 16.0 | 0.61 [0.38–0.99]                          |                |
| Center   | 225                | 24.9 | 76                   | 24.0 | 149                           | 25.4 | 0.61 [0.40–0.95]                          |                |
| South-West   | 71                 | 7.9  | 27                   | 8.5  | 44                            | 7.5  | 0.52 [0.29–0.93]                          |                |
| North-East   | 97                 | 10.7 | 37                   | 11.7 | 60                            | 10.2 | 0.52 [0.31–0.89]                          |                |
| South-East   | 89                 | 9.9  | 42                   | 13.2 | 47                            | 8.0  | 0.35 [0.20–0.59]                          |                |
| Corsica & overseas depts/territories                           | 15                 | 1.7  | 8                    | 2.5  | 7                             | 1.2  | 0.26 [0.09–0.77]                          |                |
| Marital Status   |                    |      |                      |      |                               |      |   | 0.6            |
| Married or living with partner                                 | 847                | 93.8 | 295                  | 93.1 | 552                           | 94.2 | 1.00                                      |                |
| Single   | 56                 | 6.2  | 22                   | 6.9  | 34                            | 5.8  | 0.84 [0.48–1.48]                          |                |
| Number of children   |                    |      |                      |      |                               |      |   | 0.003          |
| 0  | 518                | 57.4 | 171                  | 53.9 | 347                           | 59.2 | 1.00                                      |                |
| 1  | 262                | 29.0 | 97                   | 30.6 | 165                           | 28.2 | 0.70 [0.50–0.97]                          |                |
| 2 & more   | 123                | 13.6 | 49                   | 15.5 | 74                            | 12.6 | 0.52 [0.34–0.82]                          |                |
| Education  |                    |      |                      |      |                               |      |   | 0.4            |
| <12 years of schooling   | 37                 | 4.1  | 16                   | 5.0  | 21                            | 3.6  | 1.00                                      |                |
| >= 12 years of schooling                                       | 866                | 95.9 | 301                  | 95.0 | 565                           | 96.4 | 1.32 [0.67–2.60]                          |                |
| Income (€/month)   |                    |      |                      |      |                               |      |   | 0.0004         |
| <1670  | 71                 | 7.9  | 35                   | 11.0 | 36                            | 6.1  | 1.00                                      |                |
| 1670–3130  | 328                | 36.3 | 134                  | 42.3 | 194                           | 33.1 | 1.35 [0.81–2.27]                          |                |
| >3130  | 504                | 55.8 | 148                  | 46.7 | 356                           | 60.8 | 2.09 [1.25–3.50]                          |                |
| Socioprofessional category                                     |                    |      |                      |      |                               |      |   | 0.008          |
| Executive and intellectual professions                         | 322                | 35.7 | 94                   | 29.7 | 228                           | 38.9 | 1.00                                      |                |
| Intermediate professions                                       | 253                | 28.0 | 79                   | 24.9 | 174                           | 29.7 | 0.96 [0.67–1.39]                          |                |
| Employees  | 280                | 31.0 | 119                  | 37.5 | 161                           | 27.5 | 0.61 [0.43–0.87]                          |                |
| Manual workers, farmers and self-employed                      | 28                 | 3.1  | 14                   | 4.4  | 14                            | 2.4  | 0.42 [0.19–0.92]                          |                |
| Never employed   | 20                 | 2.2  | 11                   | 3.5  | 9                             | 1.5  | 0.45 [0.17–1.16]                          |                |
| Knowledge of official nutritional recommendations <sup>4</sup> |                    |      |                      |      |                               |      |   | 0.1            |
| Poor (0–2)   | 191                | 21.2 | 78                   | 22.9 | 113                           | 19.0 | 1.00                                      |                |
| Average (3)  | 217                | 24.0 | 73                   | 23.2 | 144                           | 25.1 | 1.35 [0.90–2.02]                          |                |
| Good (4–5)   | 495                | 54.8 | 166                  | 53.9 | 329                           | 55.9 | 1.34 [0.94–1.89]                          |                |
| Organic food consumption <sup>5</sup>                          |                    |      |                      |      |                               |      |   | 0.2            |
| Never (avoid organic products)                                 | 191                | 25.5 | 79                   | 29.7 | 112                           | 23.2 | 1.00                                      |                |
| Indifferent to organic food                                    | 88                 | 11.7 | 32                   | 12.0 | 56                            | 11.6 | 1.18 [0.70–2.00]                          |                |
| Occasional consumption   | 239                | 31.9 | 75                   | 28.2 | 164                           | 34.0 | 1.53 [1.03–2.28]                          |                |
| Regular consumption  | 231                | 30.8 | 80                   | 30.1 | 151                           | 31.3 | 1.37 [0.92–2.05]                          |                |

<sup>1</sup>Dietary supplement users were defined as the subjects who used dietary supplement(s) at least 3 days a week at the time of the DS questionnaire.

<sup>2</sup>P for linear trend (with adjustment for age, number of children, income, and knowledge of nutritional recommendations) or overall P (for all other variables).

<sup>3</sup>Values are n % for all variables except for age where values are mean SD.

<sup>4</sup>From the French National Nutrition and Health Programme.

<sup>5</sup>Determined by multiple correspondence analysis of data from a questionnaire on organic food consumption (5 clusters defined by the first 3 discriminant axes). Because of missing values, the proportions of subjects were calculated with 483 supplement users and 266 non-users.

doi:10.1371/journal.pone.0070733.t001

metropolitan area, to have had no biological children, to have a higher income, and to occupy an executive/high-skilled position (compared to manual workers and low-skilled staff). The same correlates were statistically significant specifically for folic acid supplement use ( $P=0.02$  for age,  $0.01$  for geographical region,  $0.0001$  for number of children,  $0.001$  for income, and  $0.007$  for socioprofessional category, data not tabulated).

### Overall and specific DS use according to the trimester of pregnancy

The three substances most commonly reported were folic acid, iron and magnesium (Table 2). About half of the women used folic acid in the 1<sup>st</sup> trimester. The proportion of iron users tripled from the 1<sup>st</sup> to the 3<sup>rd</sup> trimester. 15.5% of women reported taking vitamin D supplements on a regular/daily basis (information about single-dose use was not available). The proportion of vitamin D users during pregnancy was respectively 16.9%, 14.8%, 15.4% and 9.8% in women who delivered during the spring, summer, fall and winter, respectively (data not shown). The proportion of pregnant women using iodine DS reached 25.6% in the 2<sup>nd</sup> trimester. Retinol supplement use reached 5.8% during the last trimester of pregnancy. Vitamin E supplements were used by 29.0% of women in the 2<sup>nd</sup> trimester. About 11% of the women reported taking herbal supplements.

### Circumstances of dietary supplement purchase

37 women were excluded from these analyses because of missing data. A very high proportion of pregnant women (86.7%) reported taking DS with a medical prescription or following physician advice (Table 3). The proportion of users of prescribed DS increased significantly from 67% in the 1<sup>st</sup> trimester to 76% in the 3<sup>rd</sup> trimester. 18.6% of pregnant women reported taking their supplements following advice of a pharmacist.

### Dietary intake associated with DS use

Among the 903 pregnant women included in this study, 74% ( $n=666$ ) provided dietary data during their pregnancy and were normo-reporters; thus they were included in the following analyses. Most of those participants (73%) provided three 24 h dietary records, 17% provided 2 dietary records and only 10% provided only 1 record. DS users had significantly higher dietary intakes of most vitamins and minerals (i.e. thiamin, riboflavin, vitamin B6, folic acid, beta-carotene, vitamin E, iron, magnesium and potassium) (Table 4). DS users had slightly lower intakes of vitamin D than did DS non-users. Regarding folic acid intake from food, only 181 (27%) pregnant women reached the recommended dose of 0.4 mg/day and this proportion was significantly higher in folic acid supplement users than in non-users (33% vs. 23%;  $P=0.002$ , data not tabulated).

## Discussion

The present study highlighted demographic, socioeconomic and lifestyle disparities associated with DS use. Users of DS in general and of folic acid in particular were slightly older and belonged to higher socioeconomic classes, consistent with reports from other developed countries [23,24,27,28,35,36]. Demographic and socioeconomic disparities associated with nutritional behaviour during pregnancy are of major public health importance as they are the precursors of socioeconomic inequalities regarding the health status of the next generation [37]. While some medicinal supplements recommended during pregnancy were partly reimbursed by social security/assistance programmes, the extra cost to the patient may deter DS purchases in low-income households.

Besides, women with low income likely visit physicians less often and are might be less aware of nutritional recommendations compared to their more affluent counterparts.

The fact that women who already had children took fewer DS in general and folic acid in particular is also of major concern and has been observed in other countries [4,28,36]. This may be related to the fact that women who have already been pregnant in the past have fewer physician consultations in early pregnancy and/or are less compliant with the physician's recommendations.

Disparities between pregnant DS users and non-users also appeared as regards nutritional intake from food. Indeed, DS users had significantly higher dietary intakes of most vitamins and minerals, as previously reported in pregnant women [24] and in the general adult population [38]. A recent study in the Netherlands showed an inverse association between a Mediterranean diet rich in fruit, vegetables, fish, legumes and cereals and the risk of spina bifida in the offspring [39]. Thus, diet quality during pregnancy is of major public health importance. Our results highlight a combination of two risk factors (a poorer diet and an absence of supplementation for key nutrients) that may act synergically to increase the risk of disease in the foetus.

Whereas medical prescription or advice represented about 55% of DS use in the general NutriNet-Santé study [38], this proportion was much higher in pregnant women (86.7%), while self-medication with DS was still reported by about 15% of the pregnant women. This proportion was much lower than those documented in Australian and US studies [36,40]. To our knowledge, such data have not been published for other European countries. In our study, 18.6% of DS users reported taking their supplements following advice of a pharmacist. It has been suggested that some pharmacists might be ill-equipped to counsel pregnant women about these products, and an ethical issue stemming from the profit-motive may occur [41].

During pregnancy, the nutritional requirements for several key nutrients (folic acid, iron, vitamin D and iodine in particular) increase, hence, supplemental intake under medical supervision may be beneficial. In our study, only 27% of pregnant women reached the recommended folate intake of 0.4 mg/day with food only. In turn, folic acid was the most frequently used nutrient in DS in our study. The proportion of folic acid users was higher than that observed in the 2010 French perinatal survey (40% took folic acid supplements during pregnancy and 24% before and/or at the time of conception [42]) but much lower than in other developed countries [4,23,36,43,44]. The potential harm of systematic folic acid supplementation has been questioned, but a recent meta-analysis of 13 trials showed that folic acid supplementation did not increase cancer risk at any site [45]. One of the issues regarding folic acid supplementation is that unplanned pregnancies possibly miss the critical period during which supplementation would be beneficial. [10,46]

Iron requirements increase during pregnancy, especially over the last trimester [2,12]. The current recommendation is to prescribe iron supplementation if women are at risk of insufficiency [16]. This is consistent with our results: iron was the second most frequently used supplemental nutrient, and its use tripled between the first and the last trimester, reaching 64% of users. However, this proportion is lower than in other developed countries [23,28,47].

Next, the current practice in France is to prescribe a single dose of 100 000 IU of vitamin D at the sixth month of pregnancy notably when the last trimester would take place in the winter [16]. However, our DS questionnaire (designed for the general population) did not capture information about the use of single-dose vitamin D medication. Nonetheless, our study provides

**Table 2.** Overall and specific dietary supplement use in pregnant women of the NutriNet-Santé cohort study, according to the trimester of pregnancy<sup>1</sup>.

|  | All pregnant |      | 1 <sup>st</sup> |      | 2 <sup>nd</sup> |      | 3 <sup>rd</sup> |      | p <sup>2</sup> |
|--|--------------|------|-----------------|------|-----------------|------|-----------------|------|----------------|
|  | women        |      | trimester       |      | trimester       |      | trimester       |      |                |
|  | (n = 903)    |      | (n = 281)       |      | (n = 328)       |      | (n = 294)       |      |                |
|  | n            | %    | n               | %    | n               | %    | n               | %    |                |
| <b>Overall supplement use</b>              | 586          | 64.9 | 163             | 58.0 | 204             | 62.2 | 219             | 74.5 | 0.0001         |
| <b>Specific supplement use<sup>3</sup></b> |              |      |                 |      |                 |      |                 |      |                |
| Folic acid                                 | 406          | 45.0 | 141             | 50.2 | 144             | 43.9 | 121             | 41.2 | 0.07           |
| Iron                                       | 380          | 42.1 | 52              | 18.5 | 140             | 42.7 | 188             | 63.9 | <0.0001        |
| Magnesium                                  | 289          | 32.0 | 57              | 20.3 | 111             | 33.8 | 121             | 41.2 | <0.0001        |
| Vitamin B6                                 | 240          | 26.6 | 48              | 17.1 | 105             | 32.0 | 87              | 29.6 | <0.0001        |
| Thiamin                                    | 233          | 25.8 | 49              | 17.4 | 105             | 32.0 | 79              | 26.9 | 0.0002         |
| Riboflavin                                 | 229          | 25.4 | 46              | 16.4 | 103             | 31.4 | 80              | 27.2 | <0.0001        |
| Vitamin E                                  | 205          | 22.7 | 39              | 13.9 | 95              | 29.0 | 71              | 24.1 | <0.0001        |
| Vitamin B12                                | 197          | 21.8 | 46              | 16.4 | 83              | 25.3 | 68              | 23.1 | 0.02           |
| Zinc                                       | 187          | 20.7 | 41              | 14.6 | 83              | 25.3 | 63              | 21.4 | 0.004          |
| Vitamin B8                                 | 182          | 20.2 | 38              | 13.5 | 79              | 24.1 | 65              | 22.1 | 0.004          |
| Iodine                                     | 182          | 20.2 | 37              | 13.2 | 84              | 25.6 | 61              | 20.7 | 0.0007         |
| Pantothenic acid                           | 165          | 18.3 | 42              | 14.9 | 70              | 21.3 | 53              | 18.0 | 0.07           |
| Other minerals <sup>4</sup>                | 148          | 16.4 | 31              | 11.0 | 64              | 19.5 | 53              | 18.0 | 0.01           |
| Vitamin D                                  | 140          | 15.5 | 35              | 12.5 | 60              | 18.3 | 45              | 15.3 | 0.1            |
| Vitamin C                                  | 142          | 15.7 | 23              | 8.2  | 68              | 20.7 | 51              | 17.3 | 0.0001         |
| Niacin                                     | 134          | 14.8 | 37              | 13.2 | 51              | 15.5 | 46              | 15.6 | 0.6            |
| ω3 fatty acids                             | 99           | 11.0 | 20              | 7.1  | 47              | 14.3 | 32              | 10.9 | 0.02           |
| Calcium                                    | 92           | 10.2 | 17              | 6.0  | 36              | 11.0 | 39              | 13.3 | 0.02           |
| Other herbal supplement                    | 72           | 8.0  | 20              | 7.1  | 26              | 7.9  | 26              | 8.8  | 0.97           |
| Selenium                                   | 69           | 7.6  | 8               | 2.8  | 33              | 10.1 | 28              | 9.5  | 0.003          |
| Retinol                                    | 41           | 4.5  | 6               | 2.1  | 18              | 5.5  | 17              | 5.8  | 0.08           |
| Phosphorus                                 | 27           | 3.0  | 8               | 2.8  | 10              | 3.0  | 9               | 3.1  | 0.98           |
| Evening primrose, borage, or cod liver oil | 18           | 2.0  | 4               | 1.4  | 11              | 3.4  | 3               | 1.0  | 0.1            |
| Beta-carotene                              | 11           | 1.2  | 1               | 0.4  | 5               | 1.5  | 5               | 1.7  | 0.3            |
| Fluoride                                   | 11           | 1.2  | 3               | 1.1  | 3               | 0.9  | 5               | 1.7  | 0.7            |
| Acerola, guarana or cranberry supplement   | 10           | 1.1  | 3               | 1.1  | 5               | 1.5  | 2               | 0.7  | 0.6            |
| Vitamin K                                  | 6            | 0.7  | 2               | 0.7  | 3               | 0.9  | 1               | 0.3  | 0.7            |
| Fiber                                      | 4            | 0.4  | 3               | 1.1  | 1               | 0.3  | 0               | 0.0  | 0.6            |
| Ginseng                                    | 3            | 0.3  | 2               | 0.7  | 0               | 0.0  | 1               | 0.3  | 0.8            |
| Amino acids/proteins                       | 3            | 0.3  | 1               | 0.4  | 1               | 0.3  | 1               | 0.3  | 0.99           |
| Phytoestrogens                             | 2            | 0.2  | 2               | 0.7  | 0               | 0.0  | 0               | 0.0  | 0.99           |
| Lutein                                     | 1            | 0.1  | 0               | 0.0  | 0               | 0.0  | 1               | 0.3  | -              |

<sup>1</sup>DS users were defined as the subjects who used dietary supplement(s) at least 3 days a week at the time of the DS questionnaire.

<sup>2</sup>Comparison of overall and specific DS use among pregnant women according to the trimester of pregnancy by unconditional logistic regression analysis adjusted for age.

<sup>3</sup>Nutrients and other substances were consumed alone or in combination in the same DS.

<sup>4</sup>Potassium, copper, lithium, manganese, chromium, and others.

doi:10.1371/journal.pone.0070733.t002

important data on regular vitamin D supplement use, which concerned 15.5% of pregnant women.

The World Health Organization recommends a dose of 250 µg/d of iodine for pregnant women if access to iodized salt cannot be guaranteed [48]. In France, no systematic iodine supplementation is practiced [16]. In our study, the proportion of pregnant women using iodine supplementation reached 25.6%

among those who were in their second trimester of pregnancy, as also observed in the US [15].

In contrast, several arguments encourage caution regarding supplement use as self-medication during pregnancy. They pertain to the potential toxicity associated with overdose of some nutrients or bioactive compounds and the potential deleterious effects of some herbal supplements, alone or when combined with certain

**Table 3.** Motives for dietary supplement purchase in pregnant women of the NutriNet-Santé cohort study.

| Motives for dietary supplement purchase <sup>2</sup>             | Pregnant women who used supplements <sup>1</sup> |      |
|--|--|------|
|  | n  | %    |
| With medical prescription or advice                              | 476  | 86.7 |
| With medical prescription  | 382  | 69.6 |
| Following medical advice   | 160  | 29.1 |
| Following advice of a pharmacist                                 | 102  | 18.6 |
| Following advice of a dietitian                                  | 6  | 1.1  |
| Following advice of another health professional                  | 31   | 5.6  |
| Following advice of a friend/family member                       | 45   | 8.2  |
| Discovered DS in the store by themselves                         | 25   | 4.6  |
| Read about the DS in a book                                      | 17   | 3.1  |
| Learned about the DS from the media (television, magazine, etc.) | 17   | 3.1  |
| Following advice received in the store (except in a pharmacy)    | 7  | 1.3  |
| Saw an advertisement   | 2  | 0.4  |
| Other circumstances  | 24   | 4.4  |
| Do not know  | 1  | 0.2  |

<sup>1</sup>DS users were defined as the subjects who used dietary supplement(s) at least 3 days a week at the time of the dietary supplement questionnaire. Data regarding circumstances of dietary supplement use were available for 94% of supplement users (i.e. 549 women out of 586).

<sup>2</sup>Several answers possible.

doi:10.1371/journal.pone.0070733.t003

medications [40,49]. Excessive retinol intake is associated with increased risk of teratogenicity [17,50] and retinol supplementation during pregnancy is not recommended. In our study, 5.8% of pregnant women used retinol supplements during the third trimester. A recent study showed that high maternal dietary and supplemental intake of vitamin E (>14.9 mg/day) was associated with a nine-fold increased risk of coronary heart disease in the offspring [18]. Thus, vitamin E DS use during pregnancy is of major concern. In our study, mean intake of vitamin E from food was 12 mg/day and nearly 30% of women used vitamin E supplements during the second trimester of pregnancy. 11% of the pregnant women used herbal supplements and only two women in this study took phyto-oestrogen supplementation.

To our knowledge, this epidemiologic study is the first which examined DS use and its correlates in French pregnant women. Its strengths include a substantial number of subjects, detailed evaluation of socioeconomic and lifestyle factors associated with DS use and detailed information on dietary intake.

Several limitations should be acknowledged. Caution is needed when extrapolating our results to pregnant women in general as this study was based on a sample of volunteers involved in an Internet-based cohort study on nutrition and health. Compared to pregnant women in the general French population, those participating in our study were older, better educated, and belonged to higher socioprofessional categories [42]. However, the direction of bias is predictable and suggests that supplement use in French pregnant women is probably slightly lower than what is observed in the present study. In addition, the major objective of this work was to investigate the associations between DS use and several individual-level correlates. Thus, the diversity of the sample (rather than its representativeness) is regarded the important parameter. Besides, this study included about 8% of women from lower socioprofessional categories (a population group that is usually difficult to reach), allowing us to perform between-class comparisons. Second, no information was available regarding folic

acid and other DS use before pregnancy, while this period is critical regarding NTD prevention. Third, the distinction between medically-assisted versus spontaneous and planned versus unplanned pregnancies could not be made in this study while these factors may influence DS use [51]. Fourth, longitudinal follow-up of DS use during pregnancy was not available in this study (women were divided according to trimester groups in a cross-sectional manner). Fifth, although three dietary records are appropriate to adequately estimate energy intake [52], they may not capture all of the variability of dietary intake during the entire pregnancy. Next, the nutrient doses from the DS were not quantified. Finally, no information was available regarding biomarkers of nutritional status or ethnicity in this study, since a specific authorization is required in France to collect such sensitive data.

## Conclusion

This study provides new and detailed information on DS use and its correlates during pregnancy, highlighting socioeconomic differences in that dietary behaviour. In particular, women from lower socioeconomic classes were less likely to benefit from folic acid supplementation. 15% of pregnant women relied on self-medication. Even in this relatively well-educated and well-off population, folic acid supplementation at the beginning of pregnancy remained insufficient (only 50%), whereas only 27% of women reached the recommended 0.4 mg/day with food intake. In contrast, irrelevant supplementation practices have been identified (notably for retinol and vitamin E). It appears necessary to increase awareness among health professionals regarding the importance of recommending use of the right nutrient at the right moment (not only for the first but also for subsequent pregnancies; pre- and post-conception), while avoiding unnecessary (and even potentially hazardous) supplementation, with special attention paid to the lower socioeconomic strata.

**Table 4.** Daily dietary nutrient intake of pregnant women of the NutriNet-Santé study, overall and according to dietary supplement use.

|                                     | All <sup>1</sup> |        | Non-Users of supplements |        | Users of supplements <sup>2</sup> |        | p <sup>3</sup> |
|-------------------------------------|------------------|--------|--------------------------|--------|-----------------------------------|--------|----------------|
|                                     | (n = 666)        |        | (n = 237)                |        | (n = 429)                         |        |                |
|                                     | mean             | SD     | mean                     | SD     | mean                              | SD     |                |
| Energy (kcal)                       | 1999.1           | 459.3  | 1978.5                   | 463.5  | 2010.4                            | 457.0  | 0.4            |
| Alcohol (g)                         | 0.2              | 1.7    | 0.2                      | 1.8    | 0.2                               | 1.6    | 0.6            |
| Total carbohydrates (g)             | 222.1            | 58.0   | 218.5                    | 59.7   | 224.2                             | 57.0   | 0.2            |
| Simple carbohydrates (g)            | 110.6            | 37.3   | 107.5                    | 40.3   | 112.3                             | 35.5   | 0.07           |
| Starches (g)                        | 110.9            | 34.3   | 110.3                    | 34.3   | 111.2                             | 34.4   | 0.6            |
| Fiber (g)                           | 19.6             | 6.6    | 18.8                     | 6.3    | 20.0                              | 6.8    | 0.09           |
| Proteins (g)                        | 79.6             | 19.2   | 79.1                     | 18.3   | 80.0                              | 19.7   | 0.8            |
| Total lipids (g)                    | 87.0             | 26.4   | 86.7                     | 26.2   | 87.2                              | 26.5   | 0.3            |
| Saturated fatty acids (g)           | 37.7             | 12.9   | 38.0                     | 12.9   | 37.6                              | 12.9   | 0.07           |
| Monounsaturated fatty acids (g)     | 31.9             | 10.6   | 31.4                     | 10.4   | 32.2                              | 10.7   | 0.8            |
| All polyunsaturated fatty acids (g) | 11.3             | 4.6    | 11.2                     | 5.0    | 11.3                              | 4.3    | 0.8            |
| n-3 polyunsaturated fatty acids (g) | 1.2              | 0.6    | 1.2                      | 0.7    | 1.2                               | 0.6    | 0.5            |
| n-6 polyunsaturated fatty acids (g) | 9.3              | 4.2    | 9.3                      | 4.7    | 9.4                               | 3.9    | 0.9            |
| Thiamin (mg)                        | 1.3              | 0.5    | 1.3                      | 0.5    | 1.4                               | 0.5    | 0.01           |
| Riboflavin (mg)                     | 1.8              | 0.7    | 1.8                      | 0.6    | 1.9                               | 0.7    | 0.01           |
| Niacin (mg)                         | 17.9             | 6.4    | 17.4                     | 5.9    | 18.3                              | 6.6    | 0.2            |
| Pantothenic acid (mg)               | 5.5              | 1.7    | 5.4                      | 1.7    | 5.6                               | 1.7    | 0.3            |
| Vitamin B6 (mg)                     | 1.8              | 0.6    | 1.7                      | 0.6    | 1.8                               | 0.7    | 0.004          |
| Folate (µg)                         | 344.8            | 116.5  | 328.6                    | 111.3  | 353.7                             | 118.4  | 0.02           |
| Vitamin B12 (µg)                    | 4.7              | 5.7    | 5.1                      | 8.6    | 4.5                               | 3.1    | 0.2            |
| Retinol (µg)                        | 507.2            | 679.9  | 521.5                    | 747.9  | 499.2                             | 640.0  | 0.5            |
| Beta carotene (µg)                  | 3289.5           | 2562.0 | 2938.9                   | 2006.5 | 3483.1                            | 2805.9 | 0.02           |
| Vitamin C (mg)                      | 131.6            | 95.7   | 124.0                    | 63.1   | 135.8                             | 109.4  | 0.2            |
| Vitamin D (µg)                      | 2.5              | 1.9    | 2.7                      | 2.3    | 2.4                               | 1.5    | 0.03           |
| Vitamin E (mg)                      | 12.0             | 4.9    | 11.4                     | 5.2    | 12.3                              | 4.7    | 0.04           |
| Sodium (mg)                         | 2618.4           | 837.3  | 2584.6                   | 760.7  | 2637.1                            | 877.0  | 0.8            |
| Calcium (mg)                        | 1037.7           | 330.1  | 1008.9                   | 327.0  | 1053.6                            | 331.1  | 0.1            |
| Iron (mg)                           | 13.0             | 4.6    | 12.2                     | 4.0    | 13.4                              | 4.9    | 0.003          |
| Magnesium (mg)                      | 320.7            | 92.5   | 305.7                    | 78.4   | 329.0                             | 98.5   | 0.003          |
| Phosphorus (mg)                     | 1298.9           | 321.8  | 1278.7                   | 304.7  | 1310.0                            | 330.7  | 0.52           |
| Potassium (mg)                      | 3012.2           | 764.1  | 2905.3                   | 728.4  | 3071.3                            | 777.7  | 0.02           |
| Zinc (mg)                           | 10.6             | 3.2    | 10.4                     | 2.9    | 10.7                              | 3.4    | 0.6            |

<sup>1</sup>In pregnant women who provided at least one dietary record during their pregnancy.

<sup>2</sup>DS users were defined as the subjects who used dietary supplement(s) at least 3 days a week at the time of completion of the dietary supplement questionnaire.

<sup>3</sup>Unconditional logistic regression analyses adjusted for age, number of 24 h records and energy intake.

doi:10.1371/journal.pone.0070733.t004

## Acknowledgments

The authors thank Gwenael Monot, Paul Flanzy, Mohand Ait Oufella, Yasmina Chelghoum, and Than Duong Van (computer scientists), Florence Charpentier (dietitian), Anne-Sylvie Monot-Berroyer (communication assistant), Nathalie Arnault, Véronique Gourlet, Fabien Szabo, Laurent Bourhis, and Stephen Besseau (statisticians), and Rachida Mehroug (logistics assistant) for their technical contribution to the NutriNet-Santé study.

## Author Contributions

Conceived and designed the experiments: CP MT. Performed the experiments: CP MT SH. Analyzed the data: CP. Wrote the paper: CP. Supervised the study: MT. Contributed to the data interpretation and revised each draft for important intellectual content: RL CF VAA PG SH MT. Had primary responsibility for the final content: MT. Read and approved the final manuscript: CP RL CF VAA PG SH MT.

## References

- Blumfield ML, Hure AJ, Macdonald-Wicks L, Smith R, Collins CE (2013) A systematic review and meta-analysis of micronutrient intakes during pregnancy in developed countries. *Nutr Rev* 71: 118–132.
- Martin A. (2001) The “apports nutritionnels conseillés (ANC)” for the French population. *Reprod Nutr Dev* 41: 119–128. 10.1051/rnd:2001100.
- Lassi ZS, Salam RA, Haider BA, Bhutta ZA (2013) Folic acid supplementation during pregnancy for maternal health and pregnancy outcomes. *Cochrane Database Syst Rev* 3. Art. No: CD006896.10.1002/14651858.CD006896.pub2.
- McNally S, Bourke A (2012) Periconceptional folic acid supplementation in a nationally representative sample of mothers. *Ir Med J* 105: 236–8.
- Nilsen RM, Vollset SE, Gjessing HK, Magnus P, Meltzer HM, et al. (2006) Patterns and predictors of folic acid supplement use among pregnant women: the Norwegian Mother and Child Cohort Study. *Am J Clin Nutr* 84: 1134–1141.
- Vanderwijver S, Amsalkhir S, Van Oyen H, Moreno-Reyes R (2012) Determinants of folate status in pregnant women: results from a national cross-sectional survey in Belgium. *Eur J Clin Nutr* 66: 1172–1177.
- Candito M, Rivet R, Herbeth B, Boisson C, Rudigoz RC, et al. (2008) Nutritional and genetic determinants of vitamin B and homocysteine metabolisms in neural tube defects: A multicenter case-control study. *Am J Med Genet Part A* 146A: 1128–1133.
- EUROCAT (2012) Prevalence Tables. Available: <http://www.eurocat-network.eu/ACCESSPREVALENCEDATA/PrevalenceTables> (data uploaded 04/12/2012). Accessed 17 June 2013.
- AFSSA (2003) Enrichissement de la farine en vitamines B en France: proposition d'un programme-pilote. Available : <http://www.ladocumentationfrancaise.fr/var/storage/rapports-publics/044000441/0000.pdf>. Accessed 17 June 2013.
- Castillo-Lancellotti C, Tur JA, Uauy R (2012) Impact of folic acid fortification of flour on neural tube defects: a systematic review. *Public Health Nutr* 16: 901–911.
- Schlienger JL (2011) Dietary supplements during pregnancy: a review. *Medecine des Maladies Metaboliques* 5: 521–532.
- Milman N (2011) Iron in Pregnancy – How Do We Secure an Appropriate Iron Status in the Mother and Child? *Ann Nutr Metab* 59: 50–54. 10.1159/000332129.
- Alwan NA, Greenwood DC, Simpson NAB, McArdle HJ, Godfrey KM, et al. (2011) Dietary iron intake during early pregnancy and birth outcomes in a cohort of British women. *Hum Reprod* 26: 911–919.
- Li W, Green TJ, Innis SM, Barr SI, Whiting SJ, et al. (2011) Suboptimal vitamin D levels in pregnant women despite supplement use. *Can J Public Health* 102: 308–12.
- Stagnaro-Green A, Sullivan S, Pearce EN (2012) Iodine Supplementation during Pregnancy and Lactation. *JAMA* 308: 2463–2464.
- Haute Autorité de Santé (2006) Recommandations professionnelles. Comment mieux informer les femmes enceintes? Available : [http://www.has-sante.fr/portail/upload/docs/application/pdf/Infos\\_femmes\\_enceintes\\_fiche.pdf](http://www.has-sante.fr/portail/upload/docs/application/pdf/Infos_femmes_enceintes_fiche.pdf). Accessed : 30 April 2013.
- Schnorr CE, Morrone MdaS, Weber MH, Lorenzi R, Behr GA, et al. (2011) The effects of vitamin A supplementation to rats during gestation and lactation upon redox parameters: Increased oxidative stress and redox modulation in mothers and their offspring. *Food and Chem Toxicol* 49: 2645–2654.
- Smedts HP, de Vries JH, Rakhshandelroo M, Wildhagen MF, Verkleij-Hagoort AC, et al. (2009) High maternal vitamin E intake by diet or supplements is associated with congenital heart defects in the offspring. *BJOG: Intern J Obstet Gynaecol* 116: 416–423.
- Barouki R, Gluckman P, Grandjean P, Hanson M, Heindel J (2012) Developmental origins of non-communicable disease: Implications for research and public health. *Environ Health* 11: 1–42. 10.1186/1476-069X-11-42.
- Stegers-Theunissen RP, Obermann-Borst SA, Kremer D, Lindemans J, Siebel C, et al. (2009) Periconceptional Maternal Folic Acid Use of 400 µg per Day Is Related to Increased Methylation of the IGF2 Gene in the Very Young Child. *PLoS ONE* 4: e7845. 10.1371/journal.pone.0007845.
- Jaddoe VW (2008) Fetal nutritional origins of adult diseases: challenges for epidemiological research. *Eur J Epidemiol* 23: 767–71. 10.1007/s10654-008-9304-9.
- Picciano MF, McGuire MK (2009) Use of dietary supplements by pregnant and lactating women in North America. *Am J Clin Nutr* 89: 663S–667S.
- Branum AM, Bailey R, Singer BJ (2013) Dietary Supplement Use and Folate Status during Pregnancy in the United States. *J Nutr*. 10.3945/jn.112.169987.
- Haugen M, Brantsaeter AL, Alexander J, Meltzer HM (2008) Dietary Supplements Contribute Substantially to the Total Nutrient Intake in Pregnant Norwegian Women. *Ann Nutr Metab* 52: 272–280.
- Tarrant RC, Sheridan-Pereira M, McCarthy RA, Younger KM, Kearney JM (2011) Maternal and infant nutritional supplementation practices in Ireland: implications for clinicians and policymakers. *Ir Med J* 104: 173–7.
- Jensen CB, Petersen SB, Granström C, Maslova E, Molgaard C, et al. (2012) Sources and Determinants of Vitamin D Intake in Danish Pregnant Women. *Nutrients* 4: 259–272. 10.3390/nu4040259.
- Sullivan KM, Ford ES, Azrak MF, Mokdad AH (2009) Multivitamin use in pregnant and nonpregnant women: results from the Behavioral Risk Factor Surveillance System. *Public Health Rep* 124: 384–90.
- Arkkola T, Uusitalo U, Pietikainen M, Metsala J, Kronberg-Kippila C, et al. (2006) Dietary intake and use of dietary supplements in relation to demographic variables among pregnant Finnish women. *Br J Nutr* 96: 913–920.
- Hercberg S, Castetbon K, Czernichow S, Malon A, Mejean C, et al. (2010) The Nutrinet-Santé Study: a web-based prospective study on the relationship between nutrition and health and determinants of dietary patterns and nutritional status. *BMC Public Health* 10: 242. 10.1186/1471-2458-10-242.
- Touvier M, Mejean C, Kesse-Guyot E, Pollet C, Malon A, et al. (2010) Comparison between web-based and paper versions of a self-administered anthropometric questionnaire. *Eur J Epidemiol* 25: 287–296.
- Touvier M, Kesse-Guyot E, Mejean C, Pollet C, Malon A, et al. (2011) Comparison between an interactive web-based self-administered 24 h dietary record and an interview by a dietitian for large-scale epidemiological studies. *Br J Nutr* 105: 1055–1064. 10.1017/S0007114510004617.
- Vergnaud AC, Touvier M, Mejean C, Kesse-Guyot E, Pollet C, et al. (2011) Agreement between web-based and paper versions of a socio-demographic questionnaire in the NutriNet-Santé study. *Intern J Public Health* 56: 407–417. 10.1007/s00038-011-0257-5.
- Hercberg S, Decheeger M, Preziosi P. (2002) S.U.VI.MAX Portions alimentaires manuel-photos pour l'estimation des quantités. Paris: Editions polytechnica. 132 p.
- Black AE (2000) Critical evaluation of energy intake using the Goldberg cut-off for energy intake:basal metabolic rate. A practical guide to its calculation, use and limitations. *Int J Obes Relat Metab Disord* 24: 1119–1130.
- Woude P, Walle HE, Berg LT (2012) Periconceptional folic acid use: Still room to improve. *Birth Defects Res Part A: Clin Mol Teratol* 94: 96–101. 10.1002/bdra.22882.
- Forster DA, Wills G, Denning A, Bolger M (2009) The use of folic acid and other vitamins before and during pregnancy in a group of women in Melbourne, Australia. *Midwifery* 25: 134–146. 10.1016/j.midw.2007.01.019.
- Hanson M, Gluckman P, Ma R, Matzen P, Biesma R (2012) Early life opportunities for prevention of diabetes in low and middle income countries. *BMC Public Health* 12: 1025. 10.1186/1471-2458-12-1025.
- Pouchieu C, Andreeva V, Péneau S, Kesse-Guyot E, Lassale C, et al. (2013) Socio-demographic, lifestyle and dietary correlates of dietary supplement use in a large sample of French adults: results from the Nutrinet-Santé cohort study. *Br J Nutr* FirstView: 1–12. 10.1017/S0007114513000615.
- Vujkovic M, Steegers EA, Looman CW, Ocké MC, van der Spek PJ, et al. (2009) The maternal Mediterranean dietary pattern is associated with a reduced risk of spina bifida in the offspring. *BJOG* 116: 408–415.
- Tsui B, Dennehy CE, Tsourosunis C (2001) A survey of dietary supplement use during pregnancy at an academic medical center. *Am J Obstet Gynecol* 185: 433–437. 10.1067/mob.2001.116688.
- Boon H, Hirschhorn K, Griener G, Cali M (2009) The Ethics of Dietary Supplements and Natural Health Products in Pharmacy Practice: A Systematic Documentary Analysis. *Int J Pharm Pract* 17: 31–38.
- Ministère de l'Emploi du Travail et de la Santé, INSERM (2011) Enquête Nationale Périnatale 2010. Les naissances en 2010 et leur évolution depuis 2003. Available: [http://www.sante.gouv.fr/IMG/pdf/Les\\_naissances\\_en\\_2010\\_et\\_leur\\_evolution\\_depuis\\_2003.pdf](http://www.sante.gouv.fr/IMG/pdf/Les_naissances_en_2010_et_leur_evolution_depuis_2003.pdf). Accessed 30 April 2013.
- Barbour RS, Macleod M, Mires G, Anderson AS (2012) Uptake of folic acid supplements before and during pregnancy: focus group analysis of women's views and experiences. *J Hum Nutr Diet* 25: 140–147. 10.1111/j.1365-277X.2011.01216.x.
- Roy A, Evers SE, Campbell MK (2012) Dietary supplement use and iron, zinc and folate intake in pregnant women in London, Ontario. *Chronic Dis Inj Can* 32: 76–83.
- Vollset SE, Clarke R, Lewington S, Ebbing M, Halsey J, et al. (2013) Effects of folic acid supplementation on overall and site-specific cancer incidence during the randomised trials: meta-analyses of data on 50000 individuals. *Lancet* 381: 1029–36.
- Berry RJ, Bailey L, Mulinare J, Bower C, Folic Acid Working Group (2010) Fortification of flour with folic acid. *Food Nutr Bull* S22–35.
- Knudsen VK, Hansen HS, Ovesen L, Mikkelsen TB, Olsen SuF (2007) Iron supplement use among Danish pregnant women. *Public Health Nutr* 10: 1104–1110.
- WHO/UNICEF (2007) Reaching Optimal Iodine Nutrition in Pregnant and Lactating Women and Young Children. Available : [http://www.who.int/nutrition/publications/WHOSStatement\\_IDD\\_pregnancy.pdf](http://www.who.int/nutrition/publications/WHOSStatement_IDD_pregnancy.pdf). Accessed 30 April 2013.
- Buehler BA (2003) Interactions of herbal products with conventional medicines and potential impact on pregnancy. *Birth Defects Res Part B: Dev Reprod Tox* 68: 494–495.
- European Food Safety Authority (2006) Tolerable Upper Intake levels For Vitamins and Minerals by the Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) and Scientific Committee on Food (SCF). Available: <http://www.efsa.europa.eu/en/ndatopics/docs/ndatolerableuil.pdf>. Accessed 30 April 2013.
- Timmermans S, Jaddoe VW, Mackenbach JP, Hofman A, Steegers-Theunissen RP, et al. (2008) Determinants of folic acid use in early pregnancy in a multi-



ethnic urban population in The Netherlands: The Generation R study. *Preventive Medicine* 47: 427–432.

52. Ma Y, Olendzki BC, Pagoto SL, Hurley TG, Magner RP, et al. (2009) Number of 24-Hour Diet Recalls Needed to Estimate Energy Intake. *Ann Epidemiol* 19: 553–559.