Published in final edited form as:

J Acad Nutr Diet. 2017 September ; 117(9): 1429–1436. doi:10.1016/j.jand.2017.04.002.

Is Nutrient Content and Other Label Information for Prescription Prenatal Supplements Different from Nonprescription Products?

Leila G. Saldanha, PhD, RD, FAND,

Scientific Consultant, Office of Dietary Supplements, National Institutes of Health, 6100 Executive Blvd MSC 7517, Room 3B01, Bethesda, MD 20892, Phone: (301)435-2920, Fax: (301)480-1845, saldanhl@mail.nih.gov

Johanna T. Dwyer, DSc, RD,

Senior Nutrition Scientist (contractor), Office of Dietary Supplements, National Institutes of Health, 6100 Executive Blvd MSC 7517, Room 3B01, Bethesda, MD 20892, Phone: 301-435-2920, Fax: 301-480-1845, DwyerJ1@od.nih.gov

Karen W. Andrews, BS,

US Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory, 10300 Baltimore Avenue, Building 005, Beltsville, MD 20705, Phone: 301-504-0710, Fax: 301-504-0713, karen.andrews@ars.usda.gov

LaVerne L Brown, PhD,

AAAS Science & Technology Policy Fellow, Office of Dietary Supplements, National Institutes of Health, 6100 Executive Blvd MSC 7517, Room 3B01, Bethesda, MD 20892, Tel: (301)435-2920, Fax: (301)480-1845, laverne.brown@nih.gov

Rebecca B. Costello, PhD,

Scientific Consultant, Office of Dietary Supplements, National Institutes of Health, 6100 Executive Blvd MSC 7517, Room 3B01, Bethesda, MD 20892, Phone: 301-435-2920, Fax: 301-480-1845, costellb@od.nih.gov

Abby G. Ershow, ScD, RD,

Office of Dietary Supplements, National Institutes of Health, 6100 Executive Blvd MSC 7517, Room 3B01, Bethesda, MD 20892, Phone: 301-435-2920, Fax: 301-480-1845, abby.ershow@nih.gov

Pavel A. Gusev, PhD,

Corresponding author (reprint contact): Leila G Saldanha, PhD, RD, FAND, Scientific Consultant, Office of Dietary Supplements, National Institutes of Health, 6100 Executive Blvd MSC 7517, Room 3B01, Bethesda, MD 20892. saldanhl@mail.nih.gov.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflicts of Interest:

Leila G. Saldanha, PhD, RD, FAND, Karen W. Andrews, BS; Rebecca B. Costello, PhD; Abby G. Ershow, ScD, RD; Pavel A. Gusev, PhD; Constance J. Hardy, MS, RD; and Pamela R. Pehrsson, PhD have no conflict of interest including grants, honoraria, advisory board membership, or shareholdings. Johanna T. Dwyer, DSc, RD has no conflicts other than stock in pharmaceutical companies, some of which produce dietary supplements.

All authors are employed by the Federal government. Doctors Ershow and Pehrsson, and Ms. Hardy are Federal employees.

US Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory, 10300 Baltimore Avenue, Building 005, Beltsville, MD 20705, Phone: 301-504-0710, Fax: 301-504-0713, pavel.gusev@ars.usda.gov

Constance J. Hardy, MS, RD, and

Interdisciplinary Scientist, Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5001 Campus Drive, College Park MD 20740-3835, Phone: 240-402-1433, Fax: 301-436-2636, Constance.Hardy@fda.hhs.gov

Pamela R. Pehrsson, PhD

US Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory, 10300 Baltimore Avenue, Building 005, Beltsville, MD 20705, Phone: 301-504-0710, Fax: 301-504-0713, pamela.pehrsson@ars.usda.gov

Abstract

Background—Prenatal supplements are often recommended to pregnant women to help meet their nutrient needs. Many products are available making it difficult to choose a suitable supplement, as little is known about their labeling and contents to evaluate their appropriateness.

Objective—To determine differences between prescription and nonprescription prenatal supplements available in the US regarding declared nutrient and non-nutrient ingredients, and the presence of dosing and safety-related information.

Design—Using two publicly available databases with information about prenatal supplement products, information from prescription and nonprescription product labels were extracted and evaluated. For the 82 prescription and 132 nonprescription products, declared label amounts of seven vitamins and minerals, and docosahexaenoic acid (DHA), the presence of other non-nutrient components, and the presence of key safety and informational elements as identified in two DHHS Office of Inspector General (OIG)'s 2003 reports were compiled and compared.

Results—Compared with nonprescription products, prescription products contained significantly fewer vitamins (mean $\pm$ SE, 9 ± 0.2 vs 11 ± 0.3 , $P<.05$) and minerals (4 ± 0.1 vs 8 ± 0.3 ; $P<.05$). Declared amounts of folic acid were higher in prescription products, while vitamin A, vitamin D, iodine, and calcium were higher in the nonprescription products. Amounts of iron, zinc, and DHA were similar. Virtually all products contained levels of one or more nutrients that exceeded the RDAs for pregnant and/or lactating women. Product type also affected ingredients added. Fewer prescription products contained botanical ingredients (6% prescription vs. 33% nonprescription) and probiotics (2% prescription vs. 8% nonprescription). Only prescription products contained the stool softener docusate sodium

Conclusions—Our analysis of prenatal supplements indicates that prescription and nonprescription supplements differ in terms of declared composition and nutrient strength, but have labels that are similarly sparse regarding aspects of usage such as dosing information.

descriptive phrases

Prenatal supplements; labeling; prescription; nonprescription; nutrients

National surveys in the United States (US) report that pregnant women are at risk of dietary deficiency in several key nutrients such as calcium, iron, folate, and vitamin D.^{1, 2} For example, per data reviewed in the 2015–2020 Dietary Guidelines for Americans, dietary intakes from food sources alone among pregnant women were 24% below the Estimated Average Requirement (EAR) for calcium, 26% for vitamin A, 29% for folate, 30% for vitamin C, 90% for vitamin D, 94% for vitamin E, and 96% for iron.^{2, 3} Based on these types of data, guidance from government and professional organizations often suggest the use of a prenatal vitamin supplement to help meet nutrient needs during pregnancy.^{1, 2, 4, 5}

The prevalence of prenatal supplement use among pregnant women in the US is high, with estimates ranging from 78 to 92%.^{6–8} Prenatal supplements are products formulated to meet the nutrition needs of women who are pregnant or planning to become pregnant; however, there is little information in the scientific literature on what these products contain. In the US, prenatal supplements can be obtained with and without a prescription through a variety of channels, including online on the internet, over-the-counter in supermarkets, in pharmacies, and community health departments.

A prescription is required for reimbursement by private and public health insurance programs, and therefore providers often make prenatal supplements available by prescription. As the name suggests, nonprescription prenatal supplements are products available without a prescription, such as those sold over-the-counter. In the US, virtually all nonprescription prenatal supplements are marketed and labeled as dietary supplements. A dietary supplement is a product that contains dietary ingredients, such as vitamins, minerals, herbs or other botanicals, amino acids, fatty acids, metabolites, and extracts, and is regulated as a food by the US Food and Drug Administration (FDA).⁹

Since there is no mandatory registration for either prescription or nonprescription prenatal supplements, no complete listing of these products is available. However, two publicly-accessible databases contain information on their labeling and content. These databases are available through the National Library of Medicine's (NLM) web portal. The Dietary Supplement Label Database (DSLDD) catalogs virtually all information printed on dietary supplement product labels marketed in the US, and consumed by participants in recent National Health and Nutrition Examination Surveys (NHANES).¹⁰ The DSLDD reflects only what is printed on labels. Information captured include the name and form of active and inactive ingredients, amount(s) of active ingredient(s) and percent of daily value of nutrients, and information about the manufacturer/distributor of products, label claims, warning statements, along with a photograph of the entire label. It currently contains information from over 65,000 product labels out of an estimated 92,800 labels. The DSLDD is updated periodically, and ~1000 new labels are added to the database each month. DailyMed the official provider of label information for drugs marketed in the US, contains drug labeling information submitted to the FDA by the pharmaceutical industry.¹¹ It includes package inserts, strengthened warnings undergoing FDA review or minor editorial changes and other information about drugs. The labels are reformatted by the NLM to make them easier to read. DailyMed currently contains over 87,000 drug listings submitted to the FDA, including information on prescribed supplements.

Our objective was to determine if and how prescription and nonprescription prenatal supplements differed in their labeling and contents, with the intent to provide healthcare professionals with the information they could use in their practice.

Materials and Methods

The search features in the DailyMed and DSLD were used to identify and include all types and forms of prescription (n=82) and nonprescription (n=132) prenatal supplements listed in these databases as of September 2015. The LanguaL™ intended target group code [P0253] for pregnant and lactating women under the advance search feature was used to identify all prenatal supplements coded as “on market” in the DSLD, and the search term “prenat” to identify prescription prenatal products in DailyMed. Duplicate entries in the DSLD were deleted. Data extracted from labels and manually entered in Microsoft Excel 2016 included the labeling format, the number of vitamins and minerals used in formulating the products, the amounts of three vitamins (vitamin A, vitamin D, folate), four minerals (iodine, calcium, iron, and zinc) and docosahexaenoic acid (DHA) identified as shortfall nutrients and of special public health interest during pregnancy, and the presence of other substances (botanicals, probiotics, and the stool softener docusate sodium) of interest to practitioners. For this study, nutrients are defined as dietary ingredients with Daily Values (DVs) established by the FDA for labeling purposes. The FDA has established DVs for only 28 vitamins and minerals.¹² Institutional Review Board (IRB) approval was not required, as the data in this study is publicly available and did not involve research on human subjects. This study was deemed exempt under federal regulation 45 46.101 (b) CFR.

All labels were also coded for the presence of key safety and informational label content elements identified in the 2003 Office of the Inspector General (OIG) of the US Department of Health and Human Services (DHHS) reports.^{13, 14} A coding instruction sheet was created to ensure uniform scoring of labels. All data were entered by one individual and random samples of labels were sent to five other coders to verify the accuracy of the coding. Safety information coded included interactions, contraindications, possible side effects, and adverse reactions. An example of informational label content coded was minimum duration of time for which a supplement should be taken to see results.

Declared labeled values were compared with the “old” (established in 1990) and “new” (revised May 27, 2016) DVs established by the FDA for vitamin A, vitamin D, folate, iodine, calcium, iron and zinc for pregnant and lactating women.^{12, 15} Comparisons of product contents were also made with the current Recommended Dietary Allowances (RDAs) and the Tolerable Upper Intake Levels (ULs) established by the National Academies of Sciences, Engineering and Medicine's Food and Nutrition Board (FNB).³ The FDA has substantially revised the DVs used to report amounts of nutrients on food and dietary supplement labels. For example, the DV for pregnant and lactating women have been substantially lowered for vitamin A and folate and substantially increased for iron, vitamin D and iodine. Table 1 summarizes these recommendations.

Information from prescription and nonprescription prenatal supplement product labels compiled in Excel 2016 was analyzed using STATA version 14 (Stata Corp, College Station,

Texas). Pearson's chi-square tests were conducted to test differences in the presence of non-nutrient components, and a two-sample t-test and one-way ANOVA was used to determine if there were between-group differences in the number and declared nutrient amounts. Differences with a probability value of < 0.05 were considered statistically significant.

Results

Virtually all (94%) of the prenatal supplements in our study were multivitamin and minerals containing three or more vitamins and minerals. The remaining 6% were either DHA, vitamin only, or mineral only products. Fifty two percent of the products were in pill or tablet form, 20% as soft gel capsules, 13% as capsules and the remaining in other forms, such as liquid, powders, and gummies. One hundred percent of the prescription and 22% of the nonprescription prenatal supplements disclosed the amounts of all active or dietary ingredients they contained on the label. Although most of the prescription and nonprescription product labels provided all the FDA-required labeling information, such as the label warning statements for iron-containing dietary supplement, virtually none provided optional information such as the maximum dose, the minimum duration of use, or the bioavailability of ingredients listed as key label content elements in the OIG reports.

Table 2 shows that the 82 prescription prenatal products, compared to the 132 nonprescription products, contained significantly fewer vitamins (mean $\pm$ SE, 9 ± 0.2 vs 11 ± 0.3 $P = < .05$) and minerals (4 ± 0.1 vs 8 ± 0.3 , $P = < .05$). Declared label amounts of folate were higher in the prescription products, while vitamin A, vitamin D, iodine, and calcium were higher in the nonprescription products. Prescription and nonprescription products were similar in the labeled amounts of iron, zinc, and DHA. Figure 1 shows the wide range of the amounts of the seven nutrients and DHA declared on prescription and nonprescription product labels. The maximum labeled amounts in the prescription vs nonprescription products, respectively, were 7500 vs 10000 IU vitamin A; 1000 vs 4000 IU vitamin D; 1250 vs 1000 mcg folic acid; 250 vs 300 mcg iodine; 500 vs 1200 mg calcium; 65 vs 60 mg iron; 25 vs 32 mg zinc; and 400 vs 580 mg DHA. Many prescription and nonprescription supplements also contained levels of nutrients that exceeded the RDA and UL established by the FNB for pregnant women and lactating women. For example, as displayed in Table 1, virtually all the products that contained folate exceeded the RDA and UL established by the FNB for pregnant women and lactating women, virtually all exceeded the RDA for iron established for lactating women, and 67% of the prescription and 93% of the nonprescription products exceed the RDA for vitamin A established for pregnant women.

As shown in Figure 2, 100% of the nonprescription products were labeled as dietary supplements and declared dietary ingredients within the Supplement Facts Panel, which is the required labeling format for dietary supplements.^{15, 16} Forty-six percent of the prescription prenatal products had a Supplement Facts Panel, and the remaining 54% of prescription products listed the ingredients and their amounts. Eighty percent of the prescription and 37% of the nonprescription products had a label statement stating that the supplement was suitable for women before, during, and after pregnancy.

Figure 2 also shows that 17% of the prescription and none of the nonprescription products contained the stool softener drug docusate sodium. The most common labeled amount of docusate sodium was 50 mg per serving, which is 50% of the amount found in over-the-counter drug stool softener products. In addition, 6% of the prescription and 33% of the nonprescription products contained botanical ingredients. Furthermore, 2% of prescription and 8% of nonprescription products contained probiotics.

Discussion

All prenatal labels in our study appear to have met the mandatory labeling requirements established by the FDA, however, neither the prescription nor the nonprescription products had labels that provided the optional information that the OIG reports of 2003 considered adequate with respect to information on maximum dose or minimum duration of use, which might further contribute to safe use. Only 22% of the nonprescription prenatal supplements disclosed the amounts of all active or dietary ingredients declared on the label. This low percentage reflects the option given to manufacturers under FDA labeling regulations for dietary supplements to disclose (or not disclose) the level of a dietary ingredient when it is a component of a proprietary blend.^{16, 17}

Virtually all the prescription prenatal supplements evaluated carried a National Drug Code (NDC) number. These products although sold by prescription are not necessarily manufactured per pharmaceutical standards. The NDC number does not indicate that FDA's Center for Drugs (CDER) has verified and approved them under an application process. As CDER states on its website, possession of an NDC number does not indicate that the FDA has determined that a product is a drug.^{18, 19}

Many prescription prenatal supplements appear to be nonprescription products because they follow the nonprescription (or dietary supplement) labeling format. Our study shows that prescription products contained fewer nutrients (9 vs 11 vitamins and 4 vs 8 minerals) with some at lower (vitamins A and D, iodine and calcium), another at higher (folate) and the remaining nutrients (iron, zinc and DHA) at the same levels as the nonprescription prenatals. Recommendations on the optimal number of nutrients in a prenatal supplement in the US do not exist. To overcome possible maternal micronutrient deficiencies the United Nations Children's Fund (UNICEF), United Nations University (UNU) and the World Health Organization (WHO), in 1999, agreed on the composition of a multiple-micronutrient tablet.²⁰ This tablet provides 15 micronutrients; 800 mcg vitamin A, 70 mg vitamin C, 200 IU vitamin D, 10 mg vitamin E, 1.4 mg thiamin, 1.4 mg riboflavin, 18 mg niacin, 1.9 mg vitamin B6, 2.6 mcg vitamin B12, 400 mcg folic acid, 2 mg copper, 150 mcg iodine, 30 mg iron, 65 mcg selenium, and 15 mg of zinc. In the US, dietary supplement manufacturers tend to market the full spectrum of nutrients in multivitamin and mineral supplements. Having more nutrients, however, does not necessarily mean that a product is "better" in meeting shortfalls in the vitamin and mineral intakes during pregnancy and in improving health outcomes. Unfortunately, there is limited data on the benefits of multi-micronutrient supplementation during pregnancy on fetal and infant health outcomes in the US. In two systematic reviews on the benefits of iron and folic acid containing supplements in improving birth outcomes and health benefits in children, except for two studies conducted

in Western Europe., the remaining trials were conducted in low and middle-income countries.^{21, 22} These reviews provide little evidence to support the additional benefits of other micronutrients over and above that provided by iron and folic acid alone in these supplements.

Some of these supplements (prescription and nonprescription) might be inappropriate when taken over an extended period since the declared levels exceeded the RDAs in many products and many products had levels of folic acid that exceeded the UL established by the FNB. However, the consequences of consuming multi-micronutrient prenatal supplements that exceed the RDAs is not well documented, as data on pregnant women in the US is limited. For example, the sample size for women who were pregnant in the 2007–2010 What We Eat in America (WWEIA) survey is small (only 133 respondents) so generalizing the data to all pregnant women in the US is limited.² While in 2000, the FNB has set the RDA for folic acid for pregnant women at 360 mcg and the UL between 480–600 mcg per day, based on a systematic review a recent US Preventive Service Task Force (USPSTF) recommends that all women planning or capable of pregnancy take a daily supplement containing 400 to 800 mcg of folic acid.²³

Many prenatal supplements also carried a label statement that the product could be taken before, during, and after a pregnancy, although some prenatal supplements may not be appropriate post-partum or during lactation, when nutrient requirements are different. For labeling purposes, the FDA has established only four sets of DVs; adults and children 4 years and older, children 1 through 3 years, infants 1 through 12 months, and pregnant women and lactating women. In establishing these DVs, the FDA selects the highest RDA value established by the FNB within each of these four age and condition groups. For example, most of the prescription and nonprescription products examined listed iron levels close to the new DV of 27 mg of iron per serving (which is the RDA for pregnant women), but almost three times the RDA for lactating women. Some multivitamin and mineral supplements also contained as much as 65 mg iron per serving (six times the iron requirements for women after pregnancy). To compensate for likely constipation associated with consuming such high levels of iron, some manufacturers may have added stool softeners such as docusate sodium to the prescription prenatal products; an ingredient not found in nonprescription products.

While manufacturers will have until July 26, 2018, to comply with the new FDA dietary supplement label regulations, healthcare professionals are likely to see manufacturers transition to the new label requirements before this compliance date.²⁴ Our study suggests that some manufacturers have started reformulating their products to meet these new DV levels even before the regulations were finalized for some nutrients such as iron (“old” 18 mg, “new” 27 mg), but not others. Although the folic acid DV was reduced from 800 mcg to 600 dietary folate equivalents (DFEs, or 360 mcg folic acid in the most recent FNB RDAs and new FDA DVs based on the FNB RDAs), prenatal product levels remained high (1000 mcg folic acid for prescription and 800 mcg for nonprescription supplements; far above the UL levels established by the FNB).

The DV units have also been revised in the new regulations. Consumers unaware of this change may not know how to compare products using the “old” DV units with those using the “new” DV units. They may resolve this dilemma by picking the product with the larger number for a nutrient, while not realizing the products contain equivalent amounts of that nutrient (e.g. 15 mcg vitamin D = 600 IU vitamin D). Healthcare professionals will need to educate consumers about these changes to ensure they make the correct product choices during the transition to the new labels.

While our study has strengths as the first known study that describes the differences in the labeling and nutrient contents between prescription and nonprescription prenatal supplements, it has some limitations. Only products listed in the DSLD and DailyMed rather than a random sample of all products available through all the channels were included in this study, as this list of products in the US is not available. However, our results appear to be consistent with the small number of other surveys on this topic. A 2009 study on the iodine content of prenatal multivitamins identified 127 nonprescription and 96 prescription prenatal products using the internet.²⁵ Of these, 87 nonprescription and 27 prescription products contained iodine. The number of products and the proportion of those containing iodine in that study is similar to those in our study. Only declared label amounts of prescription prenatal products were compared with the declared label amounts of nonprescription products. We did not compare labeled amounts with actual amounts, as data on how declared labeled amounts compare with analyzed values for prescription products are currently not available. This study is currently underway at the Nutrient Data Laboratory at the USDA and the results made public when completed. From information available on nonprescription prenatal supplements in the USDA’s Dietary Supplement Ingredient Database (DSID), it is likely that mean predicted analytical content met or exceeded label values for vitamin A, vitamin D, folic acid, iodine, calcium, iron and zinc.^{26, 27} In contrast, for thiamin and vitamin B₆, the estimated mean analytical content was below the declared labeled amounts. Literature on how declared labeled amounts compare with actual amounts is limited as there are challenges in reporting this information, which we have described in other publications.^{28–31} In a recent study, the amounts of 18 nutrients declared on adult multivitamin and mineral supplement product labels were compared with analyzed values.³¹ The mean measured content of all nutrients (except thiamin) exceeded labeled amounts. Regardless of the labeled amount, the predicted amounts exceeded labeled values by 1.5 – 13% for copper, manganese, magnesium, niacin, phosphorus, potassium, folic acid, riboflavin, and vitamins B₁₂, C, and E, and by ~25% for selenium and iodine. For thiamin, vitamin B₆, calcium, iron, and zinc the percentage differences ranged from 26.5% to 8.6%, 23.5% to 21%, 7.1% to 29.3%, 20.5% to 16.4%, and 21.9% to 8.1%, respectively. Since manufactures are required to meet label claims at the end of the product’s shelf-life or “use by date”, this may provide one explanation for the overages.

In conclusion, a wide variety of prescription and nonprescription prenatal supplements are marketed in the US, many with amounts that exceed the RDAs for pregnant women and lactating women, and many with labeled amounts that exceed the UL for folate. While the choice of a prenatal supplement may ultimately be determined not only by biological need but also by other factors, such as cost and coverage under insurance plans, qualified healthcare professionals who care for pregnant women should review product formulations,

to ensure that the higher levels are needed to compensate for nutrient deficiencies. Publicly accessible databases, such as the DSLD, DailyMed, and DSID provide healthcare professionals with ready access to this information, including images of the product labels. Finally, pregnant women should be encouraged to discuss the choice of a prenatal product with their healthcare provider to ensure that the product they select is appropriate to meet their nutrition needs.

Acknowledgments

The Office of Dietary Supplements, at the National Institutes of Health (NIH), funded this study. The DSLD is a collaborative project of the Office of Dietary Supplements and the National Library of Medicine at the NIH, with input from many federal stakeholders including most NIH institutes and centers, the U.S. Department of Agriculture's Agricultural Research Service, the Centers for Disease Control and Prevention's National Center for Health Statistics Division of Health and Nutrition Examination Surveys, and the U.S. Food and Drug Administration's Center for Food Safety and Applied Nutrition.

Source of Funding:

Office of Dietary Supplements, National Institutes of Health.

References

1. US Department of Health and Human Services; US Department of Agriculture. 2015–2020. Dietary Guidelines for Americans. 8. Washington, DC: US Dept of Health and Human Services; Dec. 2015 <http://health.gov/dietaryguidelines/2015/guidelines/>. [Accessed March 18, 2017]
2. 2015 Dietary Guidelines Advisory Committee. [Accessed March 18, 2017] Food and nutrient intakes, and health: current status and trends; Scientific Report of the 2015 Dietary Guidelines Advisory Committee. Part D. Chapter 1. p. 11 <http://health.gov/dietaryguidelines/2015-scientific-report/>.
3. Food and Nutrition Board. [Accessed March 18, 2017] Dietary reference intakes tables and application. <http://www.nationalacademies.org/hmd/Activities/Nutrition/SummaryDRIs/DRI-Tables.aspx>.
4. Academy of Nutrition and Dietetics. Position of the Academy of Nutrition and Dietetics: Nutrition and lifestyle for a healthy pregnancy outcome. *J Acad Nutr Diet*. 2014; 114:1099–1103. [PubMed: 24956993]
5. The American College of Obstetricians and Gynecologists. [Accessed March 18, 2017] Good health before pregnancy: Preconception care. <http://www.acog.org/Patients/FAQs/Good-Health-Before-Pregnancy-Preconception-Care>.
6. Branum AM, Bailey R, Singer BJ. Dietary supplement use and folate status during pregnancy in the United States. *J Nutr*. 2013; 143:486–492. [PubMed: 23365107]
7. Aronsson CA, Vehik K, Yang Y, et al. Use of dietary supplements in pregnant women in relation to sociodemographic factors - a report from The Environmental Determinants of Diabetes in the Young (TEDDY) study. *Public Health Nutr*. 2013; 16(8):1390–1402. [PubMed: 23452986]
8. Sullivan KM, Ford ES, Mokdad AH. Multivitamin use in pregnant and nonpregnant women: Results from the Behavioral Risk Factor Surveillance System. *Public Health Reports*. 2009; 124:384–390. [PubMed: 19445414]
9. 103D Congress (Public Law 103–417). [Accessed March 18, 2017] Dietary Supplement Health and Education Act of 1994. <http://www.gpo.gov/fdsys/pkg/BILLS-103s784es/pdf/BILLS-103s784es.pdf>.
10. National Institutes of Health. [Accessed March 18, 2017] The Dietary Supplement Label Database. <http://dslid.nlm.nih.gov/>.
11. National Institutes of Health. [Accessed March 18, 2017] DailyMed. <http://dailymed.nlm.nih.gov/>.
12. US Food and Drug Administration, HHS. Food labeling: Revision of the nutrition and supplement facts labels. *Federal Register*. 2016; 81(103):33982. [Accessed March 18, 2017] <https://>

www.federalregister.gov/articles/2016/05/27/2016-11867/food-labeling-revision-of-the-nutrition-and-supplement-facts-labels.

13. Rehnquist, R. [Accessed March 18, 2017] Dietary supplement labels: An assessment. OIG, HHS. 2003. OEI-01-01-00121, <https://oig.hhs.gov/oei/reports/oei-01-01-00121.pdf>.
14. Rehnquist, R. [Accessed March 18, 2017] Dietary supplement labels: Key elements. OIG, HHS. 2003. OEI-01-01-00120, Website <https://oig.hhs.gov/oei/reports/oei-01-01-00120.pdf>
15. US Food and Drug Administration, HHS. [Accessed March 18, 2017] Guidance for industry: a food labeling guide (15. Appendix G: Daily Values for infants, children less than 4 years of age, and pregnant and lactating women). <http://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/labelingnutrition/ucm064930.htm>.
16. US Food and Drug Administration, HHS. [Accessed March 18, 2017] Guidance for industry. A dietary supplement labeling guide. <http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/DietarySupplements/ucm070597.htm#4-34>
17. US Food and Drug Administration, HHS. [Accessed March 18, 2017] Nutrition labeling of dietary supplements. e-CFR. 21CFR101.36. http://www.ecfr.gov/cgi-bin/text-idx?SID=fdb14fc1ad4c9125549a45f13ed6eeeb&mc=true&node=se21.2.101_136&rgn=div8
18. US Food and Drug Administration, HHS. [March 18, 2017] NDC product file definitions. <http://www.fda.gov/Drugs/InformationOnDrugs/ucm254527.htm>.
19. US Food and Drug Administration, HHS. [Accessed March 18, 2017] Unapproved prescription drugs: Drugs marketed in the United States that do not have required FDA approval. <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/default.htm>
20. United Nations Children's Fund (UNICEF), World Health Organization (WHO), United Nations University (UNU). [Accessed March 18, 2017] Composition of a multi-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries. 1999. <http://apps.who.int/iris/handle/10665/75358>
21. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev*. 2015; 11:CD004905.
22. Devakumar D, Fall CHD, Sachdev HS, et al. Maternal antenatal multiple micronutrient supplementation for long-term health benefits in children: A systematic review and meta-analysis. *BMC Med*. 2016; 14:90. [PubMed: 27306908]
23. Viswanathan, M., Treiman, KA., Kish-Doto, J., et al. Folic Acid Supplementation: An evidence review for the US Preventive Services Task Force: Evidence Synthesis No.145. Rockville, MD: Agency for Healthcare Research and Quality; 2017. AHRQ publication 14-05214-EF-1.
24. US Food and Drug Administration, HHS. [March 18, 2017] Food labeling: Revision of the nutrition and supplement facts labels. <https://www.regulations.gov/document?D=FDA-2012-N-1210-0875>
25. Leung AM, Pearce EN, Braverman LE. Iodine content of prenatal multivitamins in the United States. *N Engl J Med*. 2009; 360(9):939–940. [PubMed: 19246372]
26. US Department of Agriculture. [Accessed March 18, 2017] Dietary Supplement Ingredient Database. <https://dietarysupplementdatabase.usda.nih.gov/>.
27. US Department of Agriculture. [Accessed March 18, 2017] Dietary Supplement Ingredient Database. Nonprescription prenatal multivitamin/mineral calculator. https://dietarysupplementdatabase.usda.nih.gov/ingredient_calculator/index_nonrx_prenatal.php.
28. Saldanha LG, Dwyer JT, Betz JM. Culinary spice plants in dietary supplement products and tested in clinical trials. *Adv Nutr*. 2016; 7(2):343–348. [PubMed: 26980817]
29. Saldanha LG, Dwyer JT, Andrews KW, et al. Feasibility of including green tea products for an analytically verified dietary supplement database. *J Food Sci*. 2015; 80(4):H883–888. [PubMed: 25817236]
30. Andrews KW, Schweitzer A, Zhao C, et al. The caffeine contents of dietary supplements commonly purchased in the US: Analysis of 53 products with caffeine-containing ingredients. *Anal Bioanal Chem*. 2007; 389:231–239. [PubMed: 17676317]
31. Dwyer JT, Holden J, Andrews K, et al. Measuring vitamins and minerals in dietary supplements for nutrition studies in the USA. *Anal Bioanal Chem*. 2007; 389:37–46. [PubMed: 17641882]

32. Andrews KW, Roseland JM, Gusev PA, et al. Analytical ingredient content and variability of adult multivitamin/mineral products: national estimates for the Dietary Supplement Ingredient Database. *Am J Clin Nutr.* 2017; 105(2):526–539. [PubMed: 27974309]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.
Distribution of declared individual nutrient amounts on prescription and nonprescription prenatal supplement product labels.

Figure 2.
Percent of prescription and nonprescription prenatal supplement products containing specific label attributes.

Table 1

Old and new FDA Daily Values (DV's) for pregnant and lactating women; and comparison of nutrient amounts in prescription and nonprescription prenatal products with the current FNB recommendations for pregnant and lactating women¹

	Vit A IU ²	Vit D IU ³	Folic Acid mcg ⁴	Iodine mcg	Ca mg	Iron mg	Zn mg	DHA mg
FDA labeling DV's⁵								
Old	8000	400	800	150	1300	18	15	none
New	4333	600	360	290	1300	27	13	none
Percent of products containing nutrient								
Prescription prenatal products (n=82)	48	96	96	32	79	95	71	35
Nonprescription prenatal products (n=132)	91	92	92	68	86	88	90	39
Percent of supplements containing nutrient that exceeded the current FNB RDA for that nutrient⁶								
Current RDA for pregnant women	2567	600	360	220	1300	27	12	none
Prescription supplements	67	14	100	4	0	40	69	na
Nonprescription supplements	93	28	99	15	0	54	76	na
Percent of supplements containing nutrient that exceeded the current FNB RDA for lactating women⁷								
Current RDA for lactating women	4333	600	300	290	1300	10	13	None
Prescription supplements	3	14	100	0	0	99	69	na
Nonprescription supplements	53	28	99	4	0	96	76	na
Percent of supplements containing nutrient that exceeded the current FNB UL for pregnant and lactating women⁸								
Current UL range for pregnant & lactating women ⁷	9333–10,000	4000	480–600	900–1100	2500–3000	45	34–40	None
Prescription supplements	0	0	99	0	0	4	0	na
Nonprescription supplements	0	0	91	0	0	2	0	na

¹For labeling purposes, the Food and Drug Administration (FDA) has established only four sets of DV's: adults and children 4 years and older, children 1 through 3 years, infants 1 through 12 months, and pregnant women and lactating women. These DV's are based on the highest FNB recommended value within each age and gender category. The FDA and National Academies of Sciences, Engineering and Medicine's Food and Nutrition Board (FNB) have recently revised the units and conversion factors for reporting vitamins A and D, and folate. However, to make comparisons of amounts reported on labels with recommended intakes, the Table reports the amounts of these nutrients in units currently reported on product labels. A DV for DHA has not been established by the FDA or the FNB.

²the conversion factor of 1 IU = 0.3 mcg retinol was used, assuming the source of the vitamin A is retinol.

³the conversion factor of 1 IU = 0.025 mcg for cholecalciferol/ergocalciferol was used.

⁴the conversion factor of 1 mcg food folate = 0.6 micrograms folic acid was used, assuming all prenatal supplements are consumed with food and the source of folate is folic acid.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

the FDA published new labelling DV's on May 27, 2016. Manufacturers will have until July 26, 2018, to comply with the new regulations.

the Recommended Dietary Allowance (RDA) selected represents the highest value recommended for pregnant women. RDA is defined as average daily level of intake sufficient to meet the nutrient requirements of nearly all (97–98%) healthy people.

the RDA selected represents the highest value recommended for lactating women.

Highest Tolerable Upper Intake Levels (UL's) established by the FNB selected. Range represents the lowest and highest values established for pregnant and lactating women. UL is defined as the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population.

Table 2
Comparison of labeled nutrient and DHA amounts in prescription and nonprescription prenatal products.

	Vitamins	Minerals	Vit A IU	Vit D IU	Folic Acid mcg	Iodine mcg	Ca mg	Iron mg	Zn mg	DHA mg
Mean number (± SE) of vitamins and minerals and amount (± SE) of nutrients and DHA										
Prescription prenatal products (n=82)	9 (0.2) ^{a,§}	4 (0.1) ^a	3241 (199.0) ^a	462 (22.4) ^a	1009 (9.3) ^a	150 (4.8) ^a	172 (8.6) ^a	28 (0.8) ^a	18 (0.9) ^a	263 (13.8) ^a
Nonprescription prenatal products (n=132)	11 (0.3) ^b	8 (0.3) ^b	5001 (176.1) ^b	646 (58.1) ^b	800 (12.8) ^b	164 (6.7) ^b	368 (28.7) ^b	27 (0.8) ^a	18 (0.6) ^a	225 (19.1) ^a

[§]Different superscript letters indicate significant differences (p <0.05) between the declared level of a nutrient in the prescription vs. the nonprescription products, e.g., between vitamin A levels in the prescription vs. the nonprescription. Data analyzed using two-sample t-test and one-way ANOVA.