



West Middlesex University Hospital

## Multivitamins/Multiple Micronutrients in Pregnancy

Date of Search: 18/05/2016

Sources Searched: Medline, Embase, Cochrane Library, DynaMed

### Search History:

1. Medline; (multivitamin\* OR "multi vitamin\*").ti; 902 results.
2. Medline; pregn\*.ti; 193246 results.
3. Medline; exp PREGNANCY/; 785274 results.
4. Medline; 2 OR 3; 802571 results.
5. Medline; 1 AND 4; 170 results.
6. EMBASE; (multivitamin\* OR "multi vitamin\*").ti; 1110 results.
7. EMBASE; \*MULTIVITAMIN/; 1136 results.
8. EMBASE; 6 OR 7; 1646 results.
9. EMBASE; pregn\*.ti; 223390 results.
10. EMBASE; exp PREGNANCY/; 615992 results.
11. EMBASE; 9 OR 10; 660015 results.
12. EMBASE; 8 AND 11; 214 results.
13. EMBASE; 12 [Limit to: English Language]; 200 results.
14. Medline; exp PREGNANCY OUTCOME/; 45051 results.
15. Medline; 1 AND 14; 18 results.
16. Medline; vitamins.ti; 7465 results.
17. Medline; 4 AND 16; 382 results.
18. Medline; 14 AND 16; 17 results.
19. Medline; 17 [Limit to: (Document type Review)]; 61 results.
20. Medline; (multivitamin\* OR "multi vitamin\*").ti,ab; 3193 results.
21. Medline; 4 AND 20; 600 results.
22. Medline; 21 [Limit to: (Document type Review)]; 85 results.
23. Medline; (multi\* AND micronutrient\* AND supplement\*).ti; 107 results.
24. Medline; 4 AND 23; 49 results.
25. EMBASE; (multi\* AND micronutrient\* AND supplement\*).ti; 143 results.
26. EMBASE; 11 AND 25; 54 results.

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**Title:** Folic acid alone or multivitamin containing folic acid intake during pregnancy and the risk of gestational hypertension and preeclampsia through meta-analyses.

**Citation:** Obstetrics & gynecology science, Mar 2016, vol. 59, no. 2, p. 110-115, 2287-8572 (March 2016)

**Author(s):** Shim, Sang-Min, Yun, Yeo-UI, Kim, Yun Sook

**Abstract:** The objective of this study was to assess the effect of folic acid and multivitamin use during pregnancy on the risk of developing of hypertensive disorder of pregnancy. Two reviewers independently determined all prospective cohort study, retrospective cohort study, large population based cohort study, retrospective secondary analysis, and double blinded, placebo-controlled, randomized clinical trial published using PubMed Medline database, KERIS (Korea Education and Research Information Service), Scopus, and the Cochrane Central Register of controlled trials comparing before conception throughout pregnancy intake oral multivitamin containing folic acid or folic acid alone. Meta-analyses were estimated with odds ratios and 95% confidence intervals (CIs) using random effect analysis according to heterogeneity of studies. Data from six effect sizes from six studies involving 201,661 patients were enrolled. These meta-analyses showed multivitamin containing folic acid or folic acid alone was not significantly effective in reducing gestational hypertension or preeclampsia incidence (odds ratio, 0.91; 95% CI, 0.81 to 1.03) than the placebo. And the difference of effective sizes of preeclampsia and gestational hypertension according to two dependent variables, multivitamin and folic acid were not significant, respectively (point estimate, 0.66; 95% CI, 0.46 to 0.96). These meta-analyses demonstrate multivitamin containing folic acid or folic acid alone was not significantly effective in reducing gestational hypertension or preeclampsia incidence.

**Source:** Medline

**Full Text:**

Available from *National Library of Medicine* in [Obstetrics and Gynecology Science](#)

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Title: Pre-conception Folic Acid and Multivitamin Supplementation for the Primary and Secondary Prevention of Neural Tube Defects and Other Folic Acid-Sensitive Congenital Anomalies

**Citation:** Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC, June 2015, vol./is. 37/6(534-552), 1701-2163 (01 Jun 2015)

**Author(s):** Wilson R.D., Audibert F., Brock J.-A., Carroll J., Cartier L., Gagnon A., Johnson J.-A., Langlois S., Murphy-Kaulbeck L., Okun N., Pastuck M., null, Deb-Rinker P., Dodds L., Leon J.A., Lowel H.L., Luo W., MacFarlane A., McMillan R., Moore A., Mundle W., O'Connor D., Ray J., Van den Hof M.

**Language:** English, French

**Abstract:** OBJECTIVE: To provide updated information on the pre- and post-conception use of oral folic acid with or without a multivitamin/micronutrient supplement for the prevention of neural tube defects and other congenital anomalies. This will help physicians, midwives, nurses, and other health care workers to assist in the education of women about the proper use and dosage of folic acid/multivitamin supplementation before and during

pregnancy. EVIDENCE: Published literature was retrieved through searches of PubMed, Medline, CINAHL, and the Cochrane Library in January 2011 using appropriate controlled vocabulary and key words (e.g., folic acid, prenatal multivitamins, folate sensitive birth defects, congenital anomaly risk reduction, pre-conception counselling). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies published in English from 1985 and June 2014. Searches were updated on a regular basis and incorporated in the guideline to June 2014. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies. Costs, risks, and benefits: The financial costs are those of daily vitamin supplementation and eating a healthy folate-enriched diet. The risks are of a reported association of dietary folic acid supplementation with fetal epigenetic modifications and with an increased likelihood of a twin pregnancy. These associations may require consideration before initiating folic acid supplementation. The benefit of folic acid oral supplementation or dietary folate intake combined with a multivitamin/micronutrient supplement is an associated decrease in neural tube defects and perhaps in other specific birth defects and obstetrical complications. VALUES: The quality of evidence in the document was rated using the criteria described in the Report of the Canadian Task Force on Preventative Health Care (Table 1).

Summary Statement In Canada multivitamin tablets with folic acid are usually available in 3 formats: regular over-the-counter multivitamins with 0.4 to 0.6 mg folic acid, prenatal over-the-counter multivitamins with 1.0 mg folic acid, and prescription multivitamins with 5.0 mg folic acid. (III) Recommendations

1. Women should be advised to maintain a healthy folate-rich diet; however, folic acid/multivitamin supplementation is needed to achieve the red blood cell folate levels associated with maximal protection against neural tube defect. (III-A)
2. All women in the reproductive age group (12-45 years of age) who have preserved fertility (a pregnancy is possible) should be advised about the benefits of folic acid in a multivitamin supplementation during medical wellness visits (birth control renewal, Pap testing, yearly gynaecological examination) whether or not a pregnancy is contemplated. Because so many pregnancies are unplanned, this applies to all women who may become pregnant. (III-A)
3. Folic acid supplementation is unlikely to mask vitamin B12 deficiency (pernicious anemia). Investigations (examination or laboratory) are not required prior to initiating folic acid supplementation for women with a risk for primary or recurrent neural tube or other folic acid-sensitive congenital anomalies who are considering a pregnancy. It is recommended that folic acid be taken in a multivitamin including 2.6 µg/day of vitamin B12 to mitigate even theoretical concerns. (II-2A)
4. Women at HIGH RISK, for whom a folic acid dose greater than 1 mg is indicated, taking a multivitamin tablet containing folic acid, should be advised to follow the product label and not to take more than 1 daily dose of the multivitamin supplement. Additional tablets containing only folic acid should be taken to achieve the desired dose. (II-2A)
5. Women with a LOW RISK for a neural tube defect or other folic acid-sensitive congenital anomaly and a male partner with low risk require a diet of folate-rich foods and a daily oral multivitamin supplement containing 0.4 mg folic acid for at least 2 to 3 months before conception, throughout the pregnancy, and for 4 to 6 weeks postpartum or as long as breast-feeding continues. (II-2A)
6. Women with a MODERATE RISK for a neural tube defect or other folic acid-sensitive congenital anomaly or a male partner with moderate risk require a diet of folate-rich foods and daily oral supplementation with a multivitamin containing 1.0 mg folic acid, beginning at least 3 months before conception.

Women should continue this regime until 12 weeks' gestational age. (1-A) From 12 weeks' gestational age, continuing through the pregnancy, and for 4 to 6 weeks postpartum or as long as breast-feeding continues, continued daily supplementation should consist of a multivitamin with 0.4 to 1.0 mg folic acid. (II-2A) 7. Women with an increased or HIGH RISK for a neural tube defect, a male partner with a personal history of neural tube defect, or history of a previous neural tube defect pregnancy in either partner require a diet of folate-rich foods and a daily oral supplement with 4.0 mg folic acid for at least 3 months before conception and until 12 weeks' gestational age. From 12 weeks' gestational age, continuing throughout the pregnancy, and for 4 to 6 weeks postpartum or as long as breast-feeding continues, continued daily supplementation should consist of a multivitamin with 0.4 to 1.0 mg folic acid. (I-A). The same dietary and supplementation regime should be followed if either partner has had a previous pregnancy with a neural tube defect. (II-2A).

**Publication Type:** Journal: Article

**Source:** EMBASE

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**Title:** Multiple-micronutrient supplementation for women during pregnancy.

**Citation:** The Cochrane database of systematic reviews, Jan 2015, vol. 11, p. CD004905., 1469-493X (2015)

**Author(s):** Haider, Batool A, Bhutta, Zulfiqar A

**Abstract:** Multiple-micronutrient (MMN) deficiencies often coexist among women of reproductive age in low- to middle-income countries. They are exacerbated in pregnancy due to the increased demands, leading to potentially adverse effects on the mother and developing fetus. Though supplementation with MMNs has been recommended earlier because of the evidence of impact on pregnancy outcomes, a consensus is yet to be reached regarding the replacement of iron and folic acid supplementation with MMNs. Since the last update of this Cochrane review, evidence from a few large trials has recently been made available, the inclusion of which is critical to inform policy. To evaluate the benefits of oral multiple-micronutrient supplementation during pregnancy on maternal, fetal and infant health outcomes. We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (11 March 2015) and reference lists of retrieved articles and key reviews. We also contacted experts in the field for additional and ongoing trials. All prospective randomised controlled trials evaluating MMN supplementation during pregnancy and its effects on the pregnancy outcome were eligible, irrespective of language or the publication status of the trials. We included cluster-randomised trials, but quasi-randomised trials were excluded. Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. The quality of the evidence was assessed using the GRADE approach. Nineteen trials (involving 138,538 women) were identified as eligible for inclusion in this review but only 17 trials (involving 137,791 women) contributed data to the review. Fifteen of these 17 trials were carried out in low and middle-income countries and compared MMN supplements with iron and folic acid versus iron with or without folic acid.

Two trials carried out in the UK compared MMN with a placebo. MMN with iron and folic acid versus iron, with or without folic acid (15 trials): MMN resulted in a significant decrease in the number of newborn infants identified as low birthweight (LBW) (risk ratio (RR) 0.88, 95% confidence interval (CI) 0.85 to 0.91; high-quality evidence) or small-for-gestational age (SGA) (average RR 0.90, 95% CI 0.83 to 0.97; moderate-quality evidence), and a reduced rate of stillbirth (RR 0.91, 95% CI 0.85 to 0.98; high-quality evidence). No significant differences were shown for other maternal and pregnancy outcomes: preterm births (RR 0.96, 95% CI 0.89 to 1.03; high-quality evidence), maternal anaemia in the third trimester (RR 0.97, 95% CI 0.86 to 1.10), miscarriage (RR 0.89, 95% CI 0.78 to 1.01), maternal mortality (RR 0.97, 95% CI 0.63 to 1.48), perinatal mortality (RR 0.97, 95% CI 0.84 to 1.12; high-quality evidence), neonatal mortality (RR 0.98, 95% CI 0.90 to 1.07; high-quality evidence), or risk of delivery via a caesarean section (RR 1.03; 95% CI 0.75 to 1.43). A number of prespecified, clinically important outcomes could not be assessed due to insufficient or non-available data. Single trials reported results for: very preterm birth < 34 weeks, macrosomia, side-effects of supplements, nutritional status of children, and congenital anomalies including neural tube defects and neurodevelopmental outcome: Bayley Scales of Infant Development (BSID) scores. None of these trials reported pre-eclampsia, placental abruption, premature rupture of membranes, cost of supplementation, and maternal well-being or satisfaction. When assessed according to GRADE criteria, the quality of evidence for the review's primary outcomes overall was good. Pooled results for primary outcomes were based on multiple trials with large sample sizes and precise estimates. The following outcomes were graded to be as of high quality: preterm birth, LBW, perinatal mortality, stillbirth and neonatal mortality. The outcome of SGA was graded to be of moderate quality, with evidence downgraded by one for funnel plot asymmetry and potential publication bias. We carried out sensitivity analysis excluding trials with high levels of sample attrition (> 20%); results were consistent with the main analysis. We explored heterogeneity through subgroup analysis by maternal height and body mass index (BMI), timing of supplementation and dose of iron. Subgroup differences were observed for maternal BMI and timing of supplementation for the outcome preterm birth, with significant findings among women with low BMI and with earlier initiation of supplementation in the prenatal period. Subgroup differences were also observed for maternal BMI, maternal height and dose of iron for the outcome SGA, indicating a significant impact among women with higher maternal BMI and height, and with MMN supplement containing 30 mg of iron versus control receiving 60 mg of iron. The findings between subgroups for other primary outcomes were inconclusive.

MMN versus placebo (two trials): A single trial in the UK found no clear differences between groups for preterm birth, SGA, LBW or maternal anaemia in the third trimester. A second trial reported the number of women with pre-eclampsia; there was no evidence of a difference between groups. Other outcomes were not reported. Our findings support the effect of MMN supplements with iron and folic acid in improving birth outcomes. The findings, consistently observed in several systematic evaluations of evidence, provide a strong basis to guide the replacement of iron and folic acid with MMN supplements containing iron and folic acid for pregnant women in developing countries where MMN deficiencies are common among women of reproductive age. Efforts should be focused on the integration of this intervention in maternal nutrition and antenatal care programs in developing countries.

**Source:** Medline

**Full Text:**

Available from *John Wiley and Sons* in [Cochrane Library, The](#)

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**Title:** Effect of multiple micronutrient versus iron-folate supplementation during pregnancy on intrauterine growth

**Citation:** Nestle Nutrition Institute workshop series, 2013, vol./is. 74/(53-62), 1664-2155 (2013)

**Author(s):** Ramakrishnan U., Grant F.K., Imdad A., Bhutta Z.A., Martorell R.

**Language:** English

**Abstract:** This review examines the effects of prenatal multiple micronutrient (MM) supplementation (>5 micronutrients) on intrauterine growth. We identified publications from 16 randomized controlled trials through PubMed and EMBASE database searches. Meta-analyses were performed by pooling results, and sub-analyses by timing of intervention and amount of iron were also done. The primary outcome measures were birthweight, low birthweight (LBW; <2,500 g) and small for gestational age (SGA). Prenatal MM supplementation significantly reduced the incidence of LBW (risk ratio, RR: 0.86; 95% CI: 0.81-0.92) and SGA (RR: 0.83; 95% CI: 0.73-0.95) compared to iron-folate supplementation; mean birthweight was significantly higher by 55 g for MM with borderline increases in gestational age. MM supplementation was associated with larger decreases in the risk of LBW and SGA in the subgroup of trials that used supplements containing 60 mg of iron, but were not statistically significantly different from those for trials that used 30 mg iron. Prenatal MM supplementation improved intrauterine growth and can be recommended instead of prenatal IFA supplements in settings where micronutrient deficiencies are common.

**Publication Type:** Journal: Article

**Source:** EMBASE

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**Title:** The effect of folic acid, protein energy and multiple micronutrient supplements in pregnancy on stillbirths

**Citation:** BMC public health, 2011, vol./is. 11 Suppl 3/(S4), 1471-2458 (2011)

**Author(s):** Imdad A., Yakoob M.Y., Bhutta Z.A.

**Language:** English

**Abstract:** Pregnancy is a state of increased requirement of macro- and micronutrients, and malnourishment or inadequate dietary intake before and during pregnancy, can lead to

adverse perinatal outcomes including stillbirths. Many nutritional interventions have been proposed during pregnancy according to the nutritional status of the mother and baseline risk factors for different gestational disorders. In this paper, we have reviewed three nutritional interventions including peri-conceptual folic acid supplementation, balanced protein energy supplementation and multiple micronutrients supplementation during pregnancy. This paper is a part of a series to estimate the effect of interventions on stillbirths for input to Live Saved Tool (LiST) model. We systematically reviewed all published literature to identify studies evaluating effectiveness of peri-conceptual folic acid supplementation in reducing neural tube defects (NTD), related stillbirths and balanced protein energy and multiple micronutrients supplementation during pregnancy in reducing all-cause stillbirths. The primary outcome was stillbirths. Meta-analyses were generated where data were available from more than one study. Recommendations were made for the Lives Saved Tool (LiST) model based on rules developed by the Child Health Epidemiology Reference Group (CHERG). There were 18 studies that addressed peri-conceptual folic acid supplementation for prevention of neural tube defects (NTDs). Out of these, 7 studies addressed folic acid supplementation while 11 studies evaluated effect of folic acid fortification. Pooled results from 11 fortification studies showed that it reduces primary incidence of NTDs by 41 % [Relative risk (RR) 0.59; 95 % confidence interval (CI) 0.52-0.68]. This estimate has been recommended for inclusion in the LiST as proxy for reduction in stillbirths. Pooled results from three studies considered to be of low quality and suggest that balanced protein energy supplementation during pregnancy could lead to a reduction of 45% in stillbirths [RR 0.55, 95 % CI 0.31-0.97]. While promising, the intervention needs more effectiveness studies before inclusion in any programs. Pooled results from 13 studies evaluating role of multiple micronutrients supplementation during pregnancy showed no significant effect in reducing stillbirths [RR = 0.98; 95% CI: 0.88 - 1.10] or perinatal mortality [RR = 1.07; 95% CI: 0.92 - 1.25; random model]. No recommendations have been made for this intervention for inclusion in the LiST model. Peri-conceptual folic acid supplementation reduces stillbirths due to NTDs by approximately 41%, a point estimate recommended for inclusion in LiST.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:**

Available from *National Library of Medicine* in [BMC Public Health](#)

Available from *ProQuest* in [BMC Public Health](#)

Available from *National Library of Medicine* in [BMC Public Health](#)

Available from *BioMed Central* in [BMC Public Health](#)

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Title: Vitamin supplementation for preventing miscarriage.

**Citation:** The Cochrane database of systematic reviews, Jan 2011, no. 1, p. CD004073., 1469-493X (2011)

**Author(s):** Rumbold, Alice, Middleton, Philippa, Pan, Ning, Crowther, Caroline A

**Abstract:** Miscarriage is a common complication of pregnancy that can be caused by a wide range of factors. Poor dietary intake of vitamins has been associated with an increased risk of miscarriage, therefore supplementing women with vitamins either prior to or in early pregnancy may help prevent miscarriage. The objectives of this review are to determine the effectiveness and safety of any vitamin supplementation, on the risk of spontaneous miscarriage, maternal adverse outcomes and fetal and infant adverse outcomes. We searched the Cochrane Pregnancy and Childbirth Group Trials Register (21 June 2010). All randomised and quasi-randomised trials comparing one or more vitamins with either placebo, other vitamins, no vitamins or other interventions, prior to conception, periconceptionally or in early pregnancy (less than 20 weeks' gestation). At least two review authors independently assessed trials for inclusion, extracted data and assessed trial quality. We identified 28 trials assessing supplementation with any vitamin(s) starting prior to 20 weeks' gestation and reporting at least one primary outcome that was eligible for the review. Overall, the included trials involved 96,674 women and 98,267 pregnancies. Three trials were cluster randomised and combined contributed data for 62,669 women and 64,210 pregnancies in total. No significant differences were seen between women taking any vitamins compared with controls for total fetal loss (relative risk (RR) 1.04, 95% confidence interval (CI) 0.95 to 1.14), early or late miscarriage (RR 1.09, 95% CI 0.95 to 1.25) or stillbirth (RR 0.86, 95% CI 0.65 to 1.13) and most of the other primary outcomes, using fixed-effect models. Compared with controls, women given any type of vitamin(s) pre or peri-conception were more likely to have a multiple pregnancy (RR 1.38, 95% CI 1.12 to 1.70, three trials, 20,986 women). Taking any vitamin supplements prior to pregnancy or in early pregnancy does not prevent women experiencing miscarriage or stillbirth. However, women taking vitamin supplements may be more likely to have a multiple pregnancy. There is insufficient evidence to examine the effects of different combinations of vitamins on miscarriage, stillbirth or other maternal and infant outcomes.

**Source:** Medline

**Full Text:**

Available from *John Wiley and Sons* in [Cochrane Library, The](#)

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**Title:** Vitamin supply in pregnancy for prevention of congenital birth defects

**Citation:** Current Opinion in Clinical Nutrition and Metabolic Care, May 2011, vol./is. 14/3(291-296), 1363-1950;1473-6519 (May 2011)

**Author(s):** Czeizel A.E., Banhidy F.

**Language:** English

**Abstract:** Purpose of review: After the short summary of history of primary prevention of neural tube defects by folic acid or folic acid-containing multivitamin supplementation during the periconception period, the three main unsolved problems are highlighted. Recent findings: Both intervention trials and observational studies confirmed that this new primary

preventive method is effective - beyond the prevention of neural-tube defects - in the reduction of the most common structural birth defects: congenital cardiovascular abnormalities. Nevertheless, this important progress in the field of congenital abnormalities is not appreciated appropriately. The periconception supplementation of both folic acid alone and folic acid-containing multivitamin is useful; however, the available data indicate the higher efficacy of multivitamins in the primary prevention of neural-tube defects and congenital cardiovascular abnormalities. The optimal dose of folic acid is not known though this knowledge would be necessary from both a scientific and practical aspect. Summary: Periconception folic acid or folic acid-containing multivitamin supplementation has resulted in a breakthrough in the primary prevention of neural-tube defects, cardiovascular abnormalities and probably some other defects; however, extra efforts are necessary to eliminate folic acid or folic acid-containing multivitamin preventable congenital abnormalities. &#xa9; 2011 Wolters Kluwer Health Lippincott Williams & Wilkins.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *Ovid* in [Current Opinion in Clinical Nutrition and Metabolic Care](#)

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**Title:** Prenatal multivitamin supplementation and rates of pediatric cancers: a meta-analysis.

**Citation:** Clinical pharmacology and therapeutics, May 2007, vol. 81, no. 5, p. 685-691, 0009-9236 (May 2007)

**Author(s):** Goh, Y I, Bollano, E, Einarson, T R, Koren, G

**Abstract:** Prenatal supplementation of folic acid has been shown to decrease the risk of several congenital malformations. Several studies have recently suggested a potential protective effect of folic acid on certain pediatric cancers. The protective role of prenatal multivitamins has not been elucidated. We conducted a systematic review and meta-analysis to assess the potential protective effect of prenatal multivitamins on several pediatric cancers. Medline, PubMed, EMBASE, Toxline, Healthstar, and Cochrane databases were searched for studies published in all languages from 1960 to July 2005 on multivitamin supplementation and pediatric cancers. References from all articles collected were reviewed for additional articles. Two blinded independent reviewers assessed the articles for inclusion and exclusion. Rates of cancers in women supplemented with multivitamins were compared with unsupplemented women using a random effects model. Sixty-one articles were identified in the initial search, of which, seven articles met the inclusion criteria. There was an apparent protective effect for leukemia (odds ratio (OR)=0.61, 95% confidence interval (CI)=0.50-0.74), pediatric brain tumors (OR=0.73, 95% CI=0.60-0.88) and neuroblastoma (OR=0.53, 95% CI=0.42-0.68). In conclusion, maternal ingestion of prenatal multivitamins is associated with a decreased risk for pediatric brain tumors, neuroblastoma, and leukemia. Presently, it is not known which constituent(s) among the multivitamins confer this protective effect.

**Source:** Medline

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**Title:** Prenatal multivitamin supplementation and rates of congenital anomalies: a meta-analysis.

**Citation:** Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstétrique et gynécologie du Canada : JOGC, Aug 2006, vol. 28, no. 8, p. 680-689, 1701-2163 (August 2006)

**Author(s):** Goh, Y Ingrid, Bollano, Enkelejd, Einarson, Thomas R, Koren, Gideon

**Abstract:** The use of folic acid-fortified multivitamin supplements has long been associated with decreasing the risk of neural tube defects. Several studies have also proposed the effectiveness of these supplements in preventing other birth defects; however, such effects have never been systematically examined. We conducted a systematic review and meta-analysis to evaluate the protective effect of folic acid-fortified multivitamin supplements on other congenital anomalies. We searched Medline, PubMed, EMBASE, Toxline, Healthstar, and Cochrane databases for studies describing the outcome of pregnancies in women using multivitamin supplements that were published in all languages from January 1966 to July 2005. The references from all collected articles were reviewed for additional articles. Two independent reviewers who were blinded to the source and identity of the articles extracted data based on predetermined inclusion and exclusion criteria. Using a random effects model, rates of congenital anomalies in babies born to women who were taking multivitamin supplements were compared with rates in the offspring of controls who were not. From the initial search, 92 studies were identified; 41 of these met the inclusion criteria. Use of multivitamin supplements provided consistent protection against neural tube defects (random effects odds ratio[OR] 0.67, 95% confidence intervals [95% CI] 0.58-0.77 in case control studies; OR 0.52, 95% CI 0.39-0.69 in cohort and randomized controlled studies), cardiovascular defects (OR 0.78, 95% CI 0.67-0.92 in case control studies; OR 0.61, 95% CI 0.40-0.92 in cohort and randomized controlled studies), and limb defects (OR 0.48, 95% CI 0.30-0.76 in case control studies; OR 0.57, 95% CI 0.38-0.85 in cohort and randomized controlled studies). For cleft palate, case control studies showed OR 0.76 (95% CI 0.62-0.93), and cohort and randomized controlled studies showed OR 0.42 (95% CI 0.06-2.84); for oral cleft with or without cleft palate, case control studies showed OR 0.63 (95% CI 0.54-0.73), and cohort and randomized controlled studies showed OR 0.58 (95% CI 0.28-1.19); for urinary tract anomalies, case control studies showed OR 0.48 (95% CI 0.30-0.76), and cohort and randomized controlled studies showed OR 0.68 (95% CI 0.35-1.31); and for congenital hydrocephalus case control studies showed OR 0.37 (95% CI 0.24-0.56), and cohort and randomized controlled studies showed OR 1.54 (95% CI 0.53-4.50). No effects were shown in preventing Down syndrome, pyloric stenosis, undescended testis, or hypospadias. Maternal consumption of folic acid-containing prenatal multivitamins is associated with decreased risk for several congenital anomalies, not only neural tube defects. These data have major public health implications, because until now fortification of only folic acid has been encouraged. This approach should be reconsidered.

**Source:** Medline

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**Title:** Effect of multivitamin versus multivitamin-mineral supplementation on metabolic profiles and biomarkers of oxidative stress in pregnant women: A double-blind randomized clinical trial

**Citation:** Journal of Maternal-Fetal and Neonatal Medicine, July 2015, vol./is. 28/11(1336-1342), 1476-7058;1476-4954 (24 Jul 2015)

**Author(s):** Taghizadeh M., Samimi M., Kollahdooz F., Tabassi Z., Jamilian M., Asemi Z.

**Language:** English

**Abstract:** Objective: This study was designed to determine the favorable effects of received multivitamin versus multivitamin-mineral supplements on metabolic profiles and biomarkers of oxidative stress among Iranian pregnant women. Methods: This double-blind randomized-controlled clinical trial was conducted among 70 pregnant women, primigravida, aged 18-35 years old between 16 and 37 weeks gestation. Subjects were randomly assigned to receive either the multivitamin (n = 35) or multivitamin-mineral supplements (n = 35) for 20 weeks. Fasting blood samples were taken at baseline and after a 20-week intervention to measure lipid profiles and biomarkers of oxidative stress. Results: After 20 weeks of intervention, multivitamin-mineral supplementation resulted in a significant difference on serum triglycerides levels (changes from baseline in multivitamin-mineral group: +6.1 versus in multivitamin group: +45.9 mg/dl, p = 0.04) compared with the multivitamin group. In addition, increased concentrations of serum HDL-cholesterol (changes from baseline in multivitamin-mineral group: +0.1 versus in multivitamin group: -7.4 mg/dl, p = 0.02) and total glutathione (GSH) levels (changes from baseline in multivitamin-mineral group: +151.09 versus in multivitamin group: -116.21  $\mu\text{mol/l}$ , p = 0.003) were also seen in the multivitamin-mineral group compared with the multivitamin group. Conclusion: Supplementation of multivitamin-mineral compared to multivitamin supplementation for 20 weeks during pregnancy had beneficial effects on triglycerides, HDL-cholesterol and GSH levels.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *Taylor & Francis* in [Journal of Maternal-Fetal and Neonatal Medicine, The](#)

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**Title:** Multivitamin Versus Multivitamin-mineral Supplementation and Pregnancy Outcomes: A Single-blind Randomized Clinical Trial.

**Citation:** International journal of preventive medicine, Apr 2014, vol. 5, no. 4, p. 439-446, 2008-7802 (April 2014)

**Author(s):** Asemi, Zatollah, Samimi, Mansooreh, Tabassi, Zohreh, Ahmad, Esmailzadeh

**Abstract:** Increased requirement and decreased dietary intakes of micronutrients during pregnancy might affect maternal health and pregnancy outcomes. This study was aimed to examine the effects of two types of multiple micronutrient supplementations on pregnancy outcomes in Kashan, Iran. In a randomized single-blind controlled clinical trial, 104 primigravid singleton pregnant women aged 18-30 years were randomly assigned to receive either a multivitamin (n = 51) or a multivitamin-mineral (n = 53) supplements for 20 weeks. Participants consumed supplements once a day at week 16 of gestation. Maternal anthropometric data as well as newborn's weight, height, head circumference and 5-min Apgar score were also determined. Independent samples t-test was used for comparing between-group means. Multivariate linear regression analysis was used to identify determinants of newborn's weight, height and head circumference. Women taking multivitamin-mineral supplements gained marginally less weight until week 28 than those taking multivitamin supplements (weight at week 28 of gestation:  $67.5 \pm 11.4$  vs.  $71.6 \pm 10.3$  kg,  $P = 0.06$ ). Mean body mass index at week 28 ( $25.8 \pm 4.0$  vs.  $28.4 \pm 3.7$  kg/m<sup>2</sup>),  $P = 0.001$  as well as at delivery ( $28.0 \pm 3.9$  vs.  $30.1 \pm 3.8$  kg/m<sup>2</sup>),  $P = 0.006$ ) was lower among women taking multivitamin-mineral supplements than those taking multivitamin supplements. Although no significant difference was seen in newborns' height and Apgar score between the two groups, mean birth weight ( $3.3 \pm 0.4$  vs.  $3.1 \pm 0.4$  kg,  $P = 0.04$ ) and head circumference ( $35 \pm 1.4$  vs.  $34 \pm 1.3$  cm,  $P < 0.0001$ ) of the infants whose mothers receiving multivitamin-mineral supplements were higher than those whose mothers received multivitamins. Multivitamin-mineral use by pregnant women was a significant predictor of infants' weight ( $\beta = 0.191$ ,  $P = 0.03$ ) and head circumference ( $\beta = 0.907$ ,  $P = 0.005$ ). In conclusion, we found that birth weight and head circumference was increased in infants whose mothers received multivitamin-mineral supplements for 5 months during pregnancy compared with infants whose mothers received multivitamin supplements.

**Source:** Medline

**Full Text:**

Available from *National Library of Medicine* in [International Journal of Preventive Medicine](#)

Available from *Free Access Content* in [International Journal of Preventive Medicine](#)

Available from *ProQuest* in [International Journal of Preventive Medicine](#)

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**Title:** Effect of antenatal multiple micronutrient supplementation of mothers on the birthweight of their infants

**Citation:** Journal of Paediatrics and Child Health, March 2012, vol./is. 48/(47-48), 1034-4810 (March 2012)

**Author(s):** Gathwala G.

**Language:** English

**Abstract:** Background: Multiple micronutrient deficiencies in pregnant mothers may contribute to low birthweight. Antenatal maternal micronutrient supplementation in undernourished pregnant women may result in improved birthweight and neonatal outcome. Objective: To evaluate the effect of antenatal multiple micronutrient supplementation of mothers on the birthweight of their infants. Method and Material: This randomised controlled trial was conducted in 560 pregnant women with a with singleton pregnancy attending the antenatal clinic. Those with fetal malformation on USG were excluded. Starting at 12-14 weeks of gestation, the control group mothers received ferrous sulfate (elemental iron 100 mg) and folic acid 500 mcg and the study group were given a multimicronutrient (MMN) supplement. The primary outcome was birthweight which was recorded using an electronic weighing scale. Results: Baseline maternal data and compliance with taking the supplements was comparable between the two groups. Mean birthweight was 120 g higher in MMN group compared to iron folic acid group ( $P < 0.05$ ). Low birthweight babies in MMN group were 29.8% compared to 38.4% in iron folic acid group showing an absolute risk reduction of 8.6% for low birthweight babies in MMN group compared to the iron folic acid group. The relative risk was 0.775 implying a 22.5% reduction of LBW in MMN group compared to the iron folic acid group. Number needed to treat (NNT) was 12, i.e., 12 cases needed to be supplemented with MMN to reduce one low birthweight. Conclusion: MMN supplementation of antenatal mothers starting at 12-14 weeks of gestation resulted improved birthweight and a 22.5% reduction in low birthweight babies.

**Publication Type:** Journal: Conference Abstract

**Source:** EMBASE

**Full Text:**

Available from *John Wiley and Sons* in [Journal of Paediatrics and Child Health](#)

Available from *John Wiley and Sons* in [Journal of Paediatrics and Child Health](#)

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**Title:** Impact of micronutrient supplementation during pregnancy on birth weight, duration of gestation, and perinatal mortality in rural western China: Double blind cluster randomised controlled trial

**Citation:** BMJ, November 2008, vol./is. 337/7680(1211-1215), 0959-8146;1756-1833 (22 Nov 2008)

**Author(s):** Zeng L., Dibley M.J., Cheng Y., Dang S., Chang S., Kong L., Yan H.

**Language:** English

**Abstract:** Objective: To examine the impact of antenatal supplementation with multiple micronutrients or iron and folic acid compared with folic acid alone on birth weight,

duration of gestation, and maternal haemoglobin concentration in the third trimester. Design: Cluster randomised double blind controlled trial. Setting: Two rural counties in north west China. Participants: 5828 pregnant women and 4697 live births. Interventions: Villages were randomised for all pregnant women to take either daily folic acid (control), iron with folic acid, or multiple micronutrients with a recommended allowance of 15 vitamins and minerals. Main outcome measures: Birth weight, length, and head circumference measured within 72 hours after delivery. Neonatal survival assessed at the six week follow-up visit. Results: Birth weight was 42 g (95% confidence interval 7 to 78 g) higher in the multiple micronutrients group compared with the folic acid group. Duration of gestation was 0.23 weeks (0.10 to 0.36 weeks) longer in the iron-folic acid group and 0.19 weeks (0.06 to 0.32 weeks) longer in the multiple micronutrients group. Iron-folic acid was associated with a significantly reduced risk of early preterm delivery (<34 weeks) (relative risk 0.50, 0.27 to 0.94, P=0.031). There was a significant increase in haemoglobin concentration in both iron-folic acid (5.0 g/l, 2.0 to 8.0 g/l, P=0.001) and multiple micronutrients (6.9 g/l, 4.1 to 9.6 g/l, P<0.001) groups compared with folic acid alone. In post hoc analyses there were no significant differences for perinatal mortality, but iron-folic acid was associated with a significantly reduced early neonatal mortality by 54% (relative risk 0.46, 0.21 to 0.98). Conclusion: In rural populations in China antenatal supplementation with iron-folic acid was associated with longer gestation and a reduction in early neonatal mortality compared with folic acid. Multiple micronutrients were associated with modestly increased birth weight compared with folic acid, but, despite this weight gain, there was no significant reduction in early neonatal mortality. Pregnant women in developing countries need sufficient doses of iron in nutrient supplements to maximise reductions in neonatal mortality. Trial registration: ISRCTN08850194.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *British Medical Journal (BMJ)* in [Patricia Bowen Library and Knowledge Service West Middlesex university Hospital](#)

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**Title:** Prevention of congenital abnormalities by periconceptional multivitamin supplementation.

**Citation:** BMJ (Clinical research ed.), Jun 1993, vol. 306, no. 6893, p. 1645-1648, 0959-8138 (June 19, 1993)

**Author(s):** Czeizel, A E

**Abstract:** To study the effect of periconceptional multivitamin supplementation on neural tube defects and other congenital abnormality entities. Randomised controlled trial of supplementation with multivitamins and trace elements. Hungarian family planning programme. 4156 pregnancies with known outcome and 3713 infants evaluated in the eighth month of life. A single tablet of a multivitamin including 0.8 mg of folic acid or trace

elements supplement daily for at least one month before conception and at least two months after conception. Number of major and mild congenital abnormalities. The rate of all major congenital abnormalities was significantly lower in the group given vitamins than in the group given trace elements and this difference cannot be explained totally by the significant reduction of neural tube defects. The rate of major congenital abnormalities other than neural tube defects and genetic syndromes was 9.0/1000 in pregnancies with known outcome in the vitamin group and 16.6/1000 in the trace element group; relative risk 1.85 (95% confidence interval 1.02 to 3.38); difference, 7.6/1000. The rate of all major congenital abnormalities other than neural tube defects and genetic syndromes diagnosed up to the eighth month of life was 14.7/1000 informative pregnancies in the vitamin group and 28.3/1000 in the trace element group; relative risk 1.95 (1.23 to 3.09); difference, 13.6/1000. The rate of some congenital abnormalities was lower in the vitamin group than in the trace element group but the differences for each group of abnormalities were not significant. Periconceptional multivitamin supplementation can reduce not only the rate of neural tube defects but also the rate of other major non-genetic syndromic congenital abnormalities. Further studies are needed to differentiate the chance effect and vitamin dependent effect.

**Source:** Medline

**Full Text:**

Available from *British Medical Journal (BMJ)* in [Patricia Bowen Library and Knowledge Service West Middlesex university Hospital](#)

Available from *Highwire Press* in [The BMJ](#)

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**Title:** Hungarian cohort-controlled trial of periconceptional multivitamin supplementation shows a reduction in certain congenital abnormalities.

**Citation:** Birth defects research. Part A, Clinical and molecular teratology, Nov 2004, vol. 70, no. 11, p. 853-861, 1542-0752 (November 2004)

**Author(s):** Czeizel, Andrew E, Dobó, Márta, Vargha, Péter

**Abstract:** The 1984-1991 Hungarian randomized controlled trial (RCT) of periconceptional multivitamin supplementation containing folic acid (0.8 mg) showed a significant reduction in the first occurrence of neural tube defects (NTDs), and of urinary tract and cardiovascular abnormalities, but no reduction in orofacial clefts. A controlled cohort trial was designed to confirm or deny these results. Supplemented women were recruited from the Hungarian Periconceptional Service using the same multivitamin as the Hungarian RCT. Unsupplemented pregnant women were recruited in the standard regional antenatal care clinics and were matched to each supplemented pregnant woman on the basis of age, socioeconomic status, place of residence, and year of pregnancy. A total of 3056 informative offspring were evaluated in each cohort. The occurrence of congenital cardiovascular malformations (31 vs. 50) was reduced (odds ratio [OR], 0.60; 95% confidence interval [CI], 0.38-0.96) in the supplemented cohort, accounted for mainly by ventricular septal defects (5 vs. 19; OR, 0.26; 95% CI, 0.09-0.72). There was no significant difference (14 vs. 19) in the

occurrence of urinary tract defects between the two cohorts, but stenosis/atresia of pelvic-ureteric junction (2 vs. 13) showed a significant reduction (OR, 0.19; 95% CI, 0.04-0.86). The protective effect of the folic acid-containing multivitamin for NTDs (one offspring in the supplemented vs. nine in the unsupplemented cohort) was confirmed (OR, 0.11; 95% CI, 0.01-0.91). There was, however, no protective effect on orofacial clefts or on multiple congenital abnormalities. The results of this cohort-controlled trial support the findings of the previous Hungarian RCT. The primary prevention of some major structural birth defects by multivitamins containing folic acid or by folic acid has great public health importance.

**Source:** Medline

**Full Text:**

Available from *John Wiley and Sons* in [Birth Defects Research Part A: Clinical and Molecular Teratology](#)

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**Title:** Periconceptional intake of vitamins and fetal death: a cohort study on multivitamins and folate.

**Citation:** International journal of epidemiology, Feb 2014, vol. 43, no. 1, p. 174-184, 1464-3685 (February 2014)

**Author(s):** Nohr, Ellen A, Olsen, Jorn, Bech, Bodil H, Bodnar, Lisa M, Olsen, Sjurdur F, Catov, Janet M

**Abstract:** Women planning to conceive are often advised to take multivitamins. Whether this affects the survival of the fetus is not known. We used data from 35 914 women in the Danish National Birth Cohort who at recruitment had reported the number of weeks of supplement use during a 12-week periconceptional period. A telephone interview provided information about maternal characteristics and data on fetal death came from registers. The associations between periconceptional multivitamin or folate-only use and early (<20 weeks) and late ( $\geq 20$  weeks) fetal death were estimated by hazard ratios (HR) with 95% confidence intervals (CI). Follow-up started at 8 completed weeks of gestation, and comparisons were made with no supplement use at any time during the periconceptional period. Any multivitamin use was associated with a small increased crude risk of fetal death [HR 1.12 (1.01-1.25)], which was restricted to early losses [HR 1.18 (1.05-1.33)] compared with late losses [HR 0.82 (0.62-1.10)]. Adjustment for maternal factors increased this excess risk further. Whereas regular users of multivitamins (4-6 weeks of 6) before conception had more early losses [HR 1.29 (1.12-1.48)], a decreased risk of late losses was indicated when use started after conception [HR 0.65 (0.39-1.09)]. Folate-only use was not associated with fetal death. Multivitamin use was associated with a modest increased risk of early fetal death. For late fetal death, regular supplement use after conception may decrease risk, but numbers were small. Further studies on preconceptional multivitamin use are needed to guide public health recommendations.

**Source:** Medline

**Full Text:**

Available from *Oxford University Press* in [International Journal of Epidemiology](#); Note: ;  
Collection notes: To access please select Login with Athens and search and select NHS  
England as your institution before entering your NHS OpenAthens account details.  
Available from *Highwire Press* in [International Journal of Epidemiology](#)

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**Title:** Periconceptional multivitamin use and risk of preterm or small-for-gestational-age Births in the Danish National birth cohort

**Citation:** American Journal of Clinical Nutrition, September 2011, vol./is. 94/3(906-912), 0002-9165;1938-3207 (01 Sep 2011)

**Author(s):** Catov J.M., Bodnar L.M., Olsen J., Olsen S., Nohr E.A.

**Language:** English

**Abstract:** Background: The intake of periconceptional multivitamins may decrease the risk of preterm births (PTBs) or small-for-gestational-age (SGA) births. Objective: We related the timing and frequency of periconceptional multivitamin use to SGA births and PTBs and its clinical presentations (ie, preterm labor, premature rupture of membranes, and medical induction). Design: Women in the Danish National Birth Cohort (n = 35,897) reported the number of weeks of multivitamin use during a 12-wk periconceptional period. Cox regression was used to estimate the relation between any multivitamin use and PTBs (<37 wk) or SGA births (birth weight adjusted for gestational age >2 SDs below the mean on the basis of fetal growth curves). The timing (preconception and postconception) and frequency of use were also analyzed. Regular users (4-6 wk) and partial users (1-3 wk) in each period were compared with nonusers. Results: The association between periconceptional multivitamin use and PTBs varied according to prepregnancy overweight status (P-interaction = 0.07). Regular preconception and postconception multivitamin use in women with a prepregnancy BMI (in kg/m<sup>2</sup>) <25 was associated with reduced risks of a PTB (HR: 0.84; 95% CI: 0.73, 0.95) and preterm labor (HR: 0.80; 95% CI: 0.69, 0.94). No similar associations were shown for overweight women. The adjusted risk of an SGA birth was reduced in multivitamin users regardless of their prepregnancy BMI (HR: 0.83; 95% CI: 0.73, 0.95), with the strongest association in regular users in the postconception period. Conclusion: Regular periconceptional multivitamin use was associated with reduced risk of SGA births and PTBs in nonoverweight women. © 2011 American Society for Nutrition.

Publication Type: Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *Highwire Press* in [American Journal of Clinical Nutrition, The](#)  
Available from *Free Access Content* in [American Journal of Clinical Nutrition](#)

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**Title:** First trimester multivitamin/mineral use is associated with reduced risk of pre-eclampsia among overweight and obese women

**Citation:** Maternal and Child Nutrition, April 2016, vol./is. 12/2(339-348), 1740-8695;1740-8709 (01 Apr 2016)

**Author(s):** Vanderlelie J., Scott R., Shibl R., Lewkowicz J., Perkins A., Scuffham P.A.

**Language:** English

**Abstract:** The use of pregnancy-specific multivitamin supplements is widely recommended to support maternal homeostasis during pregnancy. Our objective was to investigate whether multivitamin use during pregnancy is associated with a reduced risk of pre-eclampsia. The effect of multivitamin use on incidence of pre-eclampsia in lean and overweight/obese women was analysed using data collected between 2006 and 2011 as part of the Environments for Healthy Living Project, Griffith University, Australia. A total of 2261 pregnancies were included in the analysis with pre-eclampsia reported in 1.95% of subjects. Body mass index (BMI)>25 was associated with a 1.97-fold [95% confidence interval (CI): 0.93, 4.16] increase in pre-eclampsia risk. First trimester multivitamin use was reported by 31.8% of women and after adjustment, was associated with a 67% reduction in pre-eclampsia risk (95%CI: 0.14, 0.75). Stratification by BMI demonstrated a 55% reduction in pre-eclampsia risk (95%CI: 0.30, 0.86) in overweight (BMI: 25-29.9) and 62% risk reduction (95%CI: 0.16, 0.92) in obese (BMI:>30) cohorts that supplemented with multivitamins in the first trimester of pregnancy. This finding may be particular to the Australian population and reflect inherent nutritional deficits. First trimester folate supplementation was found to reduce pre-eclampsia incidence [adjusted odds ratios (AOR) 0.42 95%CI: 0.13, 0.98] and demonstrated significance upon stratification by overweight status for women with BMI >25 (AOR 0.55 95%CI: 0.31, 0.96). These results support the hypothesis that multivitamin supplementation may be beneficial in reducing the incidence of pre-eclampsia during pregnancy and be of particular importance for those with a BMI >25.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *John Wiley and Sons* in [Maternal and Child Nutrition](#)

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**Title:** The association between third trimester multivitamin/mineral supplements and gestational length in uncomplicated pregnancies.

**Citation:** Women and birth : journal of the Australian College of Midwives, Feb 2016, vol. 29, no. 1, p. 41-46, 1878-1799 (February 2016)

**Author(s):** McAlpine, J M, Scott, R, Scuffham, P A, Perkins, A V, Vanderlelie, J J

**Abstract:** Widespread use of maternal micronutrient supplements have been correlated to gestational length and outcome in women predisposed to pre-eclampsia and preterm birth. However, research is yet to be conducted examining the influence of micronutrient supplements on outcomes at term in uncomplicated pregnancies. To analyse the relationship between third trimester micronutrient supplementation and gestation length at birth, demographics and maternal birthing outcomes in well women at term in a South East Queensland representative population. This research retrospectively analysed existing data pertaining to 427 uncomplicated, pregnancies birthing at the Gold Coast and Logan Hospitals using information gathered through the Environments for Healthy Living Study and Queensland perinatal data collection. Data were analysed using SPSS v20 by Chi square, ANOVA and regression analysis. Women in the third trimester taking individual zinc, folic acid or iron supplements in combination with a multivitamin were twice as likely to birth beyond 41 completed weeks (AOR 2.054, 95% CI 1.310-7.383, p=0.038) then those who did not take any supplement when controlled for established confounders. Non supplement users were found to experience a lower rate of post dates labour and requirements for induction (AOR 0.483, 95% CI 0.278-0.840, p=0.01). Length of gestation demonstrates significant associations with micronutrient supplementation practices. Well women consuming third trimester individual micronutrient supplements in addition to multivitamins experienced a longer gestation at term compared to women taking no micronutrients, increasing their risk for postdates induction of labour. Crown Copyright © 2015. Published by Elsevier Ltd. All rights reserved.

**Source:** Medline

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**Title:** Multivitamin supplementation during pregnancy and offspring adiposity: The healthy start study

**Citation:** Diabetes, June 2015, vol./is. 64/(A693), 0012-1797 (June 2015)

**Author(s):** Sauder K.A., Starling A.P., Kaar J.L., Shapiro A.L., Ringham B.M., Glueck D.H., Dabelea D.

**Language:** English

**Abstract:** Prenatal multivitamin (PNV) supplementation is recommended to improve maternal and neonatal outcomes. However, the effect of PNV on offspring early-life body composition and growth is unknown. This study examined the associations between PNV use in the preconception (3 months prior) and prenatal period with offspring adiposity at birth and 4-6 months postnatally, using data from Healthy Start, a pre-birth cohort study in Colorado. PNV use was assessed longitudinally via self-report. Offspring body composition was measured via air displacement plethysmography within 3 days of birth and at 4-6 months of age (median 5.2 months). Complete data at birth and at 4-6 months were available for 862 and 530 mother-offspring pairs, respectively. Multiple linear regression was used to assess the relationship between weeks of daily PNV use (mean 33.4, SD 13.6)

and offspring body composition (fat-free mass, fat mass, and percent fat mass), after adjustment for potential confounders (age, race/ethnicity, pre-pregnancy BMI, smoking, gestational age at birth, offspring sex, breastfeeding exclusivity prior to 4-6 month visit). PNV use was not associated with any measure of offspring body composition at birth. At 5 months postnatally, a significant interaction ( $p=0.02$ ) was detected between PNV use and breastfeeding exclusivity. Among exclusively breastfed offspring, PNV use was not associated with any measure of body composition. However, among offspring fed mixed or formula diets, the rate of increase in percent fat mass from birth to 5 months was inversely related to PNV use ( $p=0.01$ ). At 5 months, offspring fed mixed or formula diets had an average fat mass % of 29.0% if their mothers did not use PNV, but only 24.2% if mothers used daily PNV. In comparison, 5-month old offspring who were exclusively breastfed had 24.8% fat mass, regardless of maternal PNV use. **These results suggest that in the absence of exclusive breastfeeding, daily multivitamin use in pregnancy may reduce offspring adiposity.**

**Publication Type:** Journal: Conference Abstract

**Source:** EMBASE

**Full Text:**

Available from *Highwire Press* in [Diabetes](#)

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**Title:** Associations between multivitamin supplement use and alcohol consumption before pregnancy: Pregnancy risk assessment monitoring system, 2004 to 2008

**Citation:** Alcoholism: Clinical and Experimental Research, September 2013, vol./is. 37/9(1595-1600), 0145-6008;1530-0277 (September 2013)

**Author(s):** Weiss L.A., Chambers C.D.

**Language:** English

**Abstract:** Background: Approximately 50 to 70% of childbearing-aged women consume alcohol and up to 23% of pregnancies have some level of prenatal alcohol exposure. Methods: Using data from the Pregnancy Risk Assessment Monitoring System from 2004 to 2008, 111,644 women who completed questions relating to periconceptional alcohol use and multivitamin supplement use were included in the study. This study explored associations between periconceptional alcohol use and multivitamin supplementation use. Weighted multivariable logistic regression was used to explore associations, adjusting for maternal education, maternal ethnicity, maternal age, household income, and parity. Results: During the periconceptional period, a dose-dependent association was found where women who consumed alcohol (<3 drinks/wk, odds ratio [OR] = 0.76; 4 to 6 drinks/wk, OR = 0.60; 7 to 13 drinks/wk, OR = 0.49; >14 drinks/wk, OR = 0.39) and binged on alcohol (1 time, OR = 0.76; 2 to 3 times, OR = 0.66; 4 to 5 times, OR = 0.56; >6 times, OR = 0.50) were significantly less likely to take a multivitamin supplement compared with those that did not consume alcohol. Conclusions: These findings emphasize the importance of

periconceptional multivitamin supplement use, especially among alcohol-consuming women of childbearing age. &#xa9; 2013 by the Research Society on Alcoholism.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *John Wiley and Sons* in [Alcoholism: Clinical and Experimental Research](#)  
Available from *John Wiley and Sons* in [Alcoholism: Clinical and Experimental Research](#)

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**Title:** Observational study on the efficacy of the supplementation with a preparation with several minerals and vitamins in improving mood and behaviour of healthy puerperal women

**Citation:** Gynecological Endocrinology, August 2013, vol./is. 29/8(779-783), 0951-3590;1473-0766 (August 2013)

**Author(s):** Paoletti A.M., Orru M.M., Marotto M.F., Pilloni M., Zedda P., Fais M.F., Piras B., Piano C., Pala S., Lello S., Coghe F., Sorge R., Melis G.B.

**Language:** English

**Abstract:** We investigated whether a formulation containing vitamins and minerals (vit&min) could improve the worsening of mood changes occurring after delivery ("a.d."). The study was performed in 552 healthy non-anaemic puerperal women ("p.w") without risk factors for puerperal depression ("p.d"). They were at their first full-term pregnancy, and spontaneously delivered healthy newborns. The Edinburgh Depression Postnatal scale (EPDS) evaluates the psychological status of "p.w". EPDS was administered the 3rd (visit 1), 15th (visit 2) and 30th (visit 3) day "a.d.". An EPDS >12 indicates a major susceptibility to "p.d". At the same time intervals, haemoglobin, iron and ferritin (haematological parameters) levels were evaluated. After visit 1, the subjects were randomized to vit&min treatment (group A; N.274) or to calcium/vitamin D3 treatment (group B; N.278). In both groups haematological parameters significantly increased without differences between the groups. EPDS score improved in both groups, but in the group A, the EPDS decrease was significantly larger ( $p < 0.05$ ) in comparison to the group B. This effect is mainly evident in subjects with a basal EPDS >12. An early examination of psychological condition could select "p.w." with a high susceptibility to neuronal changes occurring postpartum. Vit&min favourably modulates brain functions antagonizing the evolution to "p.d". &#xa9; 2013 Informa UK Ltd. All rights reserved.

**Publication Type:** Journal: Article

**Source:** EMBASE

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**Title:** Maternal folic acid and multivitamin supplementation and risk of neural tube defects: A population-based registry study

**Citation:** European Journal of Epidemiology, August 2013, vol./is. 28/1 SUPPL. 1(S242-S243), 0393-2990 (August 2013)

**Author(s):** Gildestad T., Nordtveit T.I., Nilsen R.M., Daltveit A.K., Klungsoyr K., Oyen N., Vollset S.E.

**Language:** English

**Abstract:** Background: Several countries worldwide have implemented food fortification with folic acid to prevent neural tube defects. This health promotion strategy targets all fertile women and contributes to remove inequalities in maternal nutritional status. There are on-going debates about the benefits and risks of this strategy. Norway has no fortification with folic acid in flour, however, women are advised to take folic acid supplements prior to conception and in the beginning of their pregnancy to reduce neural tube defects. Objectives: The authors investigated the association between preconceptional use of folic acid and multivitamin supplementation on the risk of neural tube defects in non-terminated pregnancies in Norway. Methods: The study was based on data from 713,502 non-terminated pregnancies recorded in the population based medical birth registry of Norway during 1999-2010. Odds ratios adjusted by maternal age, marital status, maternal education level, parity, pregestational diabetes and epilepsy were calculated by logistic regression analyses. Results: From 1999 to 2010, use of folic acid supplements before pregnancy was reported for 17.5 % of the women, while use of multivitamin supplements before pregnancy was reported by 12.7 %. During the study period, there was an increase in reported use of folic acid and multivitamin supplements both before and during pregnancy. The increase in supplement use was much higher during pregnancy than before conception. Supplement use were generally more frequent among older women, mothers who had lower parity, who were married or cohabiting, women with a higher educational level and women who did not smoke at the time of their pregnancy. Mothers who used multivitamin supplements alone or in combination with folic acid before pregnancy, had a statistically significant risk reduction of having a child with neural tube defects compared with non-users (adjusted odds ratio = 0.62, 95 % confidence interval: 0.39, 0.98). Further, women who used folic acid supplements before pregnancy had an adjusted odds ratio of 0.74 (95 % confidence interval: 0.51, 1.09), relative to supplement non-users. Conclusion: In conclusion, the authors found that preconceptional use of multivitamins showed a statistically significant reduction on the occurrence of neural tube defects in this population based study of non-terminated pregnancies. Use of preconceptional folic acid was associated with a non-significant reduction in neural tube defects.

**Publication Type:** Journal: Conference Abstract

**Source:** EMBASE

**Full Text:**

Available from *ProQuest* in [European Journal of Epidemiology](#)

Available from *Springer Link Journals* in [European Journal of Epidemiology](#)

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**Title:** Multivitamin Supplementation During Pregnancy: Emphasis on Folic Acid and L-Methylfolate.

**Citation:** Reviews in obstetrics & gynecology, Jan 2011, vol. 4, no. 3-4, p. 126-127, 2153-8166 (2011)

**Author(s):** Greenberg, James A, Bell, Stacey J

**Source:** Medline

**Full Text:**

Available from *National Library of Medicine* in [Reviews in Obstetrics and Gynecology](#)

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**Title:** Association of periconceptional multivitamin use with reduced risk of preeclampsia among normal-weight women in the Danish National Birth Cohort.

**Citation:** American journal of epidemiology, Jun 2009, vol. 169, no. 11, p. 1304-1311, 1476-6256 (June 1, 2009)

**Author(s):** Catov, Janet M, Nohr, Ellen A, Bodnar, Lisa M, Knudson, Vibeke K, Olsen, Sjurdur F, Olsen, Jorn

**Abstract:** The timing and frequency of periconceptional multivitamin use may be related to the risk of preeclampsia. Women in the Danish National Birth Cohort (1997-2003) reported multivitamin or folate-only supplement use during a 12-week periconceptional period (from 4 weeks prior to 8 weeks after the last menstrual period). Preeclampsia cases were identified by using International Classification of Diseases, Tenth Revision, codes. Cox regression was used to estimate the association of frequency (weeks of use) and timing (preconception and postconception) of use with preeclampsia risk. Overall, there were 668 cases of preeclampsia (2.3%), and 18,551 women (65%) reported periconceptional multivitamin use. After adjustment, regular use (12 of 12 weeks) was related to a reduced risk of preeclampsia among normal-weight women. Compared with nonusers with a body mass index of 22 kg/m<sup>2</sup>, regular multivitamin users with the same body mass index had a 20% reduced risk of preeclampsia (hazard ratio = 0.78, 95% confidence interval: 0.60, 0.99). In addition, regular use in the postconception period only was associated with reduced risk, a relation that also appeared to be limited to women with a body mass index of <25 kg/m<sup>2</sup> (hazard ratio = 0.63, 95% confidence interval: 0.42, 0.93). Folate-only supplement use was unrelated to preeclampsia risk. Regular periconceptional multivitamin use was associated with a reduced risk of preeclampsia among normal-weight women, and the immediate postconception period appeared to be the relevant exposure window.

**Source:** Medline

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England as your institution before entering your NHS OpenAthens account details.  
Available from *Highwire Press* in [American Journal of Epidemiology](#)

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**Title:** Periconceptional folic acid and multivitamin supplementation for the prevention of neural tube defects and other congenital abnormalities.

**Citation:** Birth defects research. Part A, Clinical and molecular teratology, Apr 2009, vol. 85, no. 4, p. 260-268, 1542-0760 (April 2009)

**Author(s):** Czeizel, Andrew E

**Abstract:** The pioneering studies of Smithells et al. showed the reduction of recurrent neural-tube defects (NTD) after periconceptional folic acid-containing multivitamin supplementation. The Hungarian Periconceptional Service was established in 1984, and this primary health care system offered a chance to organize a randomized controlled trial to check whether the supplementation of a multivitamin containing 0.8 mg of folic acid during the periconceptional period is appropriate for the reduction of a first occurrence of NTD in the family. This found a reduction of approximately 90% of primary NTD. An unexpected finding was a significant reduction in the rate of congenital abnormalities overall: 20.6 per 1000 in the 'multivitamin' group, and 40.6 per 1000 in the 'trace-element-like' placebo group (RR = 0.53, 95% CI: 0.35-0.70). When the 6 cases of NTD were excluded, this difference in the rates of major congenital abnormalities between the two study-groups remained very highly significant ( $p < 0.0001$ ). Cardiovascular malformations and urinary tract defects were particularly affected. These findings were confirmed in the Hungarian cohort-controlled trial and by observational studies in other countries. Two questions remain to be answered. Is folic acid better alone or with multivitamins? What is the optimal dose of folic acid? Overall, the Hungarian experiences of periconceptional care have shown not only primary prevention of several severe congenital abnormalities but also a good cost-benefit balance. (c) 2009 Wiley-Liss, Inc.

**Source:** Medline

**Full Text:**

Available from *John Wiley and Sons* in [Birth Defects Research Part A: Clinical and Molecular Teratology](#)

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**Title:** Treatment response to standard of care for severe anemia in pregnant women and effect of multivitamins and enhanced antihelminthics

**Citation:** American Journal of Clinical Nutrition, March 2009, vol./is. 89/3(853-861), 0002-9165 (01 Mar 2009)

**Author(s):** Christian P., Shahid F., Rizvi A., Klemm R.D.W., Bhutta Z.A.

**Language:** English

**Abstract:** Background: Severe anemia (hemoglobin <70 g/L) in pregnancy may increase the risk of maternal and perinatal mortality. Objectives: We assessed response to standard treatment with high-dose iron-folic acid for 90 d and single-dose (500 mg) mebendazole among severely anemic pregnant women in periurban Karachi, Pakistan. In addition, we evaluated the efficacy of 2 enhanced treatment regimens. Design: We screened pregnant women (n = 6288) for severe anemia and provided them all with the standard treatment. To test the efficacy of 2 additional treatments, women were randomly assigned to standard treatment alone (control) or with 100 mg mebendazole twice daily for 3 d or 90 d of daily multivitamins or both using a 2 x 2 factorial design. Results: Prevalence of severe anemia was high (10.5%) during pregnancy. Prevalence of geohelminths and malaria was low. Treatment response was defined as hemoglobin >100 g/L at the 90-d or >25 g/L at the 60-d follow-up visit. The standard-of-care treatment resulted in a response rate of 49% at follow-up, although an adherence of >85% elicited a higher response (67%). The effect of the additional treatments was weak. Although response was higher in the enhanced groups than for the standard treatment at the final assessment, the differences were not statistically significant. However, hemoglobin concentration increased significantly in all groups and was higher in the enhanced mebendazole group compared with the standard group (P < 0.05). Conclusions: Iron deficiency was high in this population, and the standard-of-care treatment resulted in a treatment response of 50%, although better treatment adherence showed a higher response. Multivitamins and the enhanced mebendazole regimen had a modest benefit over and above the standard treatment. © 2009 American Society for Nutrition.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *Highwire Press* in [American Journal of Clinical Nutrition, The](#)  
Available from *Free Access Content* in [American Journal of Clinical Nutrition](#)

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**Title:** Adherence and tolerability of iron-containing prenatal multivitamins in pregnant women with pre-existing gastrointestinal conditions

**Citation:** Journal of Obstetrics and Gynaecology, 2009, vol./is. 29/7(594-598), 0144-3615;1364-6893 (2009)

**Author(s):** Gill S.K., Nguyen P., Koren G.

**Language:** English

**Abstract:** Summary Prenatal multivitamin supplements PMS are recommended during pregnancy. Suboptimal adherence in women experiencing gastrointestinal GI conditions is thought to be attributed to the high elemental iron content in PMS. This study sought to quantify adherence and tolerability of iron-containing PMS in women with pre-existing GI conditions by recruiting women who called the Motherisk Helpline. Women with n 36 and

without n 166 pre-existing GI conditions were randomised to either PregVit n 106 or Orifer F n 96. Monthly follow-up interviews were conducted to assess pill intake and GI adverse effects associated with PMS. The results of our study suggest that with the use of small size and low dose iron PMS, women with pre-existing GI conditions do not experience 1 more GI adverse effects, 2 lower adherence than women with no such conditions, and 3 may experience less severe nausea and vomiting of pregnancy. Supplementing with small tablets of low dose iron PMS should be considered. &#xa9; 2009 Informa UK Ltd All rights reserved.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

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**Title:** Prenatal multivitamins containing folic acid do not decrease prevalence of depression among pregnant women

**Citation:** Journal of Obstetrics and Gynaecology, July 2008, vol./is. 28/5(482-484), 0144-3615;1364-6893 (July 2008)

**Author(s):** Cho Y.J., Han J.Y., Choi J.S., Ahn H.K., Ryu H.M., Kim M.Y., Yang J.H., Nava-Ocampo A.A., Koren G.

**Language:** English

**Abstract:** Several studies have reported an association between depression and folic acid deficiency. We investigated whether intake of prenatal multivitamins containing folic acid (MVandFA) was associated with decreased rates of depression among pregnant women. A questionnaire was given to 1,314 low-risk pregnant women. Of them, 1,277 (97.2%) women completed the questionnaire. The overall prevalence of depression was 8.1%. Of 652 participants who did not take MVandFA, 9.4% had depression, whereas 6.9% of 624 women who had MVandFA had depression (p = 0.11). In a multivariate logistic regression analysis, family history of depression (adjusted OR 3.7; 95% CI 1.9-7.3) and premenstrual syndrome (adjusted OR 3.0, 95% CI 1.8-4.8) were identified as risk factors for depression during pregnancy. In conclusion, intake of MVandFA was not associated with lower rates of depression during pregnancy whereas family history of depression and personal history of premenstrual syndrome were significant risk factors. &#xa9; 2008 Informa UK Ltd.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *Taylor & Francis* in [Journal of Obstetrics and Gynaecology](#)

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**Title:** Folic acid and multivitamin supplement use and risk of placental abruption: a population-based registry study.

**Citation:** American journal of epidemiology, Apr 2008, vol. 167, no. 7, p. 867-874, 1476-6256 (April 1, 2008)

**Author(s):** Nilsen, Roy M, Vollset, Stein E, Rasmussen, Svein A, Ueland, Per M, Daltveit, Anne K

**Abstract:** The authors investigated a possible association of supplemental folic acid and multivitamin use with placental abruption by using data on 280,127 singleton deliveries recorded in 1999-2004 in the population-based Medical Birth Registry of Norway. Odds ratios, adjusted for maternal age, marital status, parity, smoking, pregestational diabetes, and chronic hypertension, were estimated with generalized estimating equations for logistic regression models. Use of folic acid and/or multivitamin supplements before or any time during pregnancy was reported for 36.4% of the abruptions (0.38% of deliveries) and 44.4% of the nonabruptions. Compared with no use, any supplement use was associated with a 26% risk reduction of placental abruption (adjusted odds ratio = 0.74, 95% confidence interval: 0.65, 0.84). Women who had taken folic acid alone had an adjusted odds ratio of 0.81 (95% confidence interval: 0.68, 0.98) for abruption, whereas multivitamin users had an adjusted odds ratio of 0.72 (95% confidence interval: 0.57, 0.91), relative to supplement nonusers. The strongest risk reduction was found for those who had taken both folic acid and multivitamin supplements (adjusted odds ratio = 0.68, 95% confidence interval: 0.56, 0.83). These data suggest that folic acid and other vitamin supplementation during pregnancy may be associated with reduced risk of placental abruption.

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**Title:** Association of periconceptional multivitamin use and risk of preterm or small-for-gestational-age births.

**Citation:** American journal of epidemiology, Aug 2007, vol. 166, no. 3, p. 296-303, 0002-9262 (August 1, 2007)

**Author(s):** Catov, Janet M, Bodnar, Lisa M, Ness, Roberta B, Markovic, Nina, Roberts, James M

**Abstract:** The authors' objective was to determine the relation between periconceptional multivitamin use and the risk of small-for-gestational-age (SGA: <5th percentile; 5th-<10th percentiles) or preterm (<34 weeks; 34-<37 weeks) births. Women in the Pregnancy Exposures and Preeclampsia Prevention Study (1997-2001) reported at enrollment their

regular multivitamin use in the past 6 months (n=1,823). Women were classified as users or nonusers in multinomial logistic models. After adjustment for race, age, education, enrollment gestational age, and household density, periconceptional multivitamin use was associated with a reduced risk of preterm births (<34 weeks) (odds ratio (OR)=0.29, 95% confidence interval (CI): 0.13, 0.64) and spontaneous preterm births (<34 weeks) (OR=0.40, 95% CI: 0.16, 0.99). Risk of SGA (<5th percentile) was marginally lower (OR=0.64, 95% CI: 0.40, 1.03) after adjustment for smoking, education, parity, enrollment gestational age, and body mass index. Prepregnancy body mass index modified this relation. Nonobese users had a reduction (OR=0.54, 95% CI: 0.32, 0.91) in risk of SGA (<5th percentile); there was no effect among obese women. There was no effect of multivitamin use on risk of preterm births (34-<37 weeks) or SGA (5th-<10th percentiles). Sensitivity analysis for unmeasured confounding by folate intake supported these findings. Study results indicate lower rates of severe preterm births and extreme SGA in women who report periconceptional vitamin use, although these should be considered cautiously until replicated.

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**Title:** No association between periconceptional multivitamin supplementation and risk of multiple congenital abnormalities: a population-based case-control study.

**Citation:** American journal of medical genetics. Part A, Nov 2006, vol. 140, no. 22, p. 2469-2477, 1552-4825 (November 15, 2006)

**Author(s):** Czeizel, Andrew E, Puhó, Erzsébet H, Bánhidly, Ferenc

**Abstract:** Two previous Hungarian intervention trials showed that periconceptional folic acid-containing multivitamin supplementation did not change the total (birth + fetal) prevalence of cases with multiple congenital abnormalities (MCAs). However, two US observational studies found an elevated risk for MCAs in the offspring of women who reported periconceptional use of multivitamins containing folic acid. These conflicting results stimulated us to evaluate the data set of the Hungarian Case-Control Surveillance of Congenital Abnormalities and to check the possible association between the use of periconceptional multivitamin supplementations and the total prevalence of cases with MCAs. Of 1,349 cases with MCA, 69 (5.1%) had mothers who used multivitamins during the second and third month of pregnancy. Of 2,405 matched controls without any defect, 126 (5.2%) had mothers who used multivitamin supplementation in early pregnancy. Of 21,494 malformed controls with isolated congenital abnormalities, 1,052 (4.9%) mothers received supplementation with multivitamins during the critical period of CAs including MCAs. There was no difference in the use of multivitamins among the study groups either in the total data set or at the evaluation of only prospective medically recorded data. Medically

recorded folic acid use without any multivitamins in the second and third gestational month showed some protective effect for MCAs. **In conclusion, our observational case-control study did not detect a folic acid containing multivitamins during the early pregnancy as a risk factor for MCAs.** (c) 2006 Wiley-Liss, Inc.

**Source:** Medline

**Full Text:**

Available from *John Wiley and Sons* in [American Journal of Medical Genetics Part A](#)

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**Title:** Periconceptual multivitamin use reduces the risk of preeclampsia

**Citation:** American Journal of Epidemiology, September 2006, vol./is. 164/5(470-477), 0002-9262;1476-6256 (September 2006)

**Author(s):** Bodnar L.M., Tang G., Ness R.B., Harger G., Roberts J.M.

**Language:** English

**Abstract:** The objective was to assess the independent effect of regular periconceptual multivitamin use on the risk of preeclampsia. Pregnant women (n = 1,835) enrolled in the Pregnancy Exposures and Preeclampsia Prevention Study (Pittsburgh, Pennsylvania, 1997-2001) at less than 16 weeks' gestation were asked whether they regularly used multivitamins or prenatal vitamins in the past 6 months. Women were classified as users or nonusers. The unadjusted prevalence of preeclampsia was 4.4% in nonusers and 3.8% in users. After adjustment for race/ethnicity, marital status, parity, prepregnancy physical activity, and income in a multiple logistic regression model, regular use of multivitamins was associated with a 45% reduction in preeclampsia risk compared with nonuse (odds ratio (OR) = 0.55, 95% confidence interval (CI): 0.32, 0.95). Prepregnancy overweight modified this effect. After confounder adjustment, lean multivitamin users had a 71% reduction in preeclampsia risk compared with lean nonusers (OR = 0.29, 95% CI: 0.12, 0.65). In contrast, there was no relation between multivitamin use and preeclampsia among overweight women (OR = 1.08, 95% CI: 0.52, 2.25). A sensitivity analysis for unmeasured confounding by fruit and vegetable intake supported these conclusions. If confirmed by others, these results suggest that regular use of a multivitamin supplement in the periconceptual period may help to prevent preeclampsia, particularly among lean women. Copyright © 2006 by the Johns Hopkins Bloomberg School of Public Health All rights reserved.

**Publication Type:** Journal: Article

**Source:** EMBASE

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**Title:** Multivitamin supplementation of HIV-positive women during pregnancy reduces hypertension

**Citation:** Journal of Nutrition, July 2005, vol./is. 135/7(1776-1781), 0022-3166 (July 2005)

**Author(s):** Merchant A.T., Msamanga G., Villamor E., Saathoff E., O'Brien M., Hertzmark E., Hunter D.J., Fawzi W.W.

**Language:** English

**Abstract:** Hypertension during pregnancy increases fetal growth retardation, preterm deliveries, and perinatal deaths, and yet its causes remain unclear. In HIV-infected women, preterm birth additionally increases the risk of HIV transmission to the infant, Oxidative stress and endothelial cell dysfunction of the placenta have been implicated in the development of hypertension during pregnancy. Vitamin intake can reduce oxidative stress and improve endothelial function. We therefore evaluated the effect of multivitamin (20 mg thiamine, 20 mg riboflavin, 25 mg B-6, 50 µg B-12, 500 mg C, 30 mg E, and 0.8 mg folic acid) and vitamin A supplements (30 mg beta-carotene plus 5000 IU preformed vitamin A) in relation to hypertension during pregnancy (systolic blood pressure > 140 mm Hg or diastolic blood pressure a 90 mm Hg at any time during pregnancy). In a double-blind, placebo-controlled, randomized, clinical trial, conducted among 1078 HIV-positive pregnant Tanzanian women, those who received multivitamins were 38% less likely to develop hypertension during pregnancy than those who did not [relative risk (RR) = 0.62, 95% CI 0.40-0.94, P = 0.03]. There was no overall effect of vitamin A on hypertension during pregnancy (RR = 1.00, 95% CI 0.66-1.51, P = 0.98). Hypertension during pregnancy was more likely in women with high baseline systolic blood pressure (>120 vs. <120 mm Hg) (RR = 6.02, 95%CI 2.59-13.97, P < 0.001), and those with higher mid-upper arm circumference (RR = 1.12, 95% CI 1.04-1.19, P = 0.002). Taking multivitamins containing vitamins B, C, and E during pregnancy may be an inexpensive and effective strategy to improve the health of the mother and baby. &#xa9; 2005 American Society for Nutritional Sciences.

**Publication Type:** Journal: Article

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**Title:** Reported multivitamin consumption and the occurrence of multiple congenital anomalies

**Citation:** American Journal of Medical Genetics, July 2005, vol./is. 136 A/1(1-7), 1552-4825 (01 Jul 2005)

**Author(s):** Yuskiv N., Honein M.A., Moore C.A.

**Language:** English

**Abstract:** The purpose of this case-control study was to determine whether multivitamin use is associated with the occurrence of multiple congenital anomalies (MCA). MCA case-infants were infants with two or more major birth defects affecting at least two different organ systems, with no recognized chromosome abnormality or single gene disorder. Control-infants were a random sample of live births with no major birth defects from the same population (metropolitan Atlanta) and time period (1993-1997) as the case-infants. Exposure to multivitamins, cereals, and supplements was ascertained from a maternal telephone interview and classified based on folic acid content. We compared women who used multivitamins three or more times per week with women who were not exposed to vitamins/cereals/supplements during the periconceptional period (3 months before pregnancy through the first trimester), adjusting for maternal age, education, race/ethnicity, first degree family history of a major birth defect, pre-pregnancy maternal body mass index, gravidity, and first trimester alcohol use and cigarette smoking. Periconceptional multivitamin use was associated with MCA among all infants (adjusted odds ratio [aOR] = 2.4, 95% confidence interval [CI] 0.9-6.7), and especially when analysis was limited to those with no family history of major defects (aOR = 4.0, 95% CI 1.3-12.8). MCA-infants with urinary obstructive defects were more common among multivitamin-exposed infants than among unexposed infants, but this defect did not occur within a consistent pattern of defects. While these findings provide some support for one previous study, the interpretation remains unclear given the proven protective effect of multivitamins containing folic acid on isolated neural tube defects and possibly other types of defects.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *John Wiley and Sons* in [American Journal of Medical Genetics Part A](#)

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**Title:** Multivitamin use and the risk of preterm birth

**Citation:** American Journal of Epidemiology, November 2004, vol./is. 160/9(886-892), 0002-9262 (01 Nov 2004)

**Author(s):** Vahratian A., Siega-Riz A.M., Savitz D.A., Thorp Jr. J.M.

**Language:** English

**Abstract:** Previous research suggests that multivitamin use before and during pregnancy can diminish diet-related deficiencies of certain micronutrients and potentially prevent preterm birth. To assess this association, the authors performed an analysis by using data from the

Pregnancy, Infection, and Nutrition Study (n = 2,010). Women were recruited at 24-29 weeks of pregnancy from four prenatal care clinics in North Carolina from August 1995 to June 2000. For women who took multivitamins prior to pregnancy, compared with nonusers, the adjusted risk ratio was 0.50 (95% confidence interval: 0.20, 1.25) for delivering preterm (<37 weeks). In contrast, prenatal and periconceptional use, compared with nonuse, were not related to preterm birth, with adjusted risk ratios of 1.1. Preconceptional multivitamin use was inversely associated with both early (<35 weeks; adjusted odds ratio = 0.59, 95% confidence interval: 0.12, 2.76) and late (35-36 weeks; adjusted odds ratio = 0.40, 95% confidence interval: 0.12, 1.40) preterm birth; findings were based on only two and three exposed cases, respectively. These results suggest that, compared with nonusers, women who take multivitamin supplements prior to conception may have a reduced risk of preterm birth, but further studies are needed with a larger sample of preconceptional users.

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**Title:** Periconceptional multivitamin supplementation and multimalformed offspring.

**Citation:** Obstetrics and gynecology, Dec 2003, vol. 102, no. 6, p. 1255-1261, 0029-7844 (December 2003)

**Author(s):** Czeizel, Andrew E, Medveczky, Erika

**Abstract:** To study the human teratogenic risk of a folic acid-containing multivitamin. We evaluated the data set of two Hungarian intervention studies: a randomized double-blind, controlled trial and a two-cohort, controlled study of the same folic acid-containing multivitamin in participants of the Hungarian periconceptional service. Of 2471 supplemented and 2391 unsupplemented women, 18 and 21, respectively, had multiple congenital abnormalities in the randomized, controlled trial. Of 3056 supplemented and unsupplemented pairs in the two-cohort, controlled study, 33 and 32, respectively, were affected with multiple congenital abnormalities. After the combination of two data sets, the number of cases with multiple congenital abnormalities was 51 in the supplemented group and 53 in the unsupplemented group (odds ratio 0.89; 95% confidence interval 0.45, 1.68). In addition, there was no difference in the occurrence of specified multiple congenital abnormality entities or of unidentified multimalformed informative offspring. We found no evidence that periconceptional folic acid-containing multivitamin supplementation either prevents or induces multiple congenital abnormalities.

**Source:** Medline

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**Title:** Periconceptional multivitamin folic acid use, dietary folate, total folate and risk of neural tube defects in South Carolina

**Citation:** *Annals of Epidemiology*, July 2003, vol./is. 13/6(412-418), 1047-2797 (July 2003)

**Author(s):** Thompson S.J., Torres M.E., Stevenson R.E., Dean J.H., Best R.G.

**Language:** English

**Abstract:** PURPOSE: To investigate whether dietary folate or multivitamin folic acid taken 3 months before conception and during the first 3 months of pregnancy reduces the risk of isolated occurrent neural tube defect (NTD)-affected pregnancies. METHODS: This population-based case control study conducted between 1992 and 1997 included 179 women with NTD-affected pregnancies and 288 randomly selected controls. Women completed a food frequency questionnaire and were interviewed about lifestyle behaviors, pregnancy histories and use of multivitamins. RESULTS: Use of 0.4 mg or more of multivitamin folic acid at least 3 times per week during the periconceptional period showed no statistically significant reduction in NTD risk [adjusted odds ratio (AOR) = 0.55, 95% confidence interval (CI) = 0.25, 1.22]. After adjusting for covariates, protective effects for NTDs were observed at the highest quartiles of dietary folate and total folate (daily dietary folate plus daily multivitamin folic acid); the respective odds ratios were 0.40 (95% CI = 0.19, 0.84) and 0.35 (95% CI = 0.17, 0.72). CONCLUSIONS: This study illustrates some of the difficulties in determining effects of folic acid and dietary folate in a population where the consumption of foods rich in folate and the use of multivitamins are increasing and the rate of NTDs is declining. Studies are needed to monitor future changes in folate levels and their effect on health. © 2003 Elsevier Inc. All rights reserved.

**Publication Type:** Journal: Article

**Source:** EMBASE

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**Title:** Maternal fever, multivitamin use, and selected birth defects: evidence of interaction?

**Citation:** *Epidemiology (Cambridge, Mass.)*, Jul 2002, vol. 13, no. 4, p. 485-488, 1044-3983 (July 2002)

**Author(s):** Botto, Lorenzo D, Erickson, J David, Mulinare, Joseph, Lynberg, Michele C, Liu, Yecai

**Abstract:** Multivitamin use has been associated with lower risks for some birth defects. We evaluated whether multivitamin use modified birth defect risks associated with febrile illness, a common and possibly teratogenic exposure. From the population-based Atlanta Birth Defects Case-Control Study (1968-1980) we selected seven defects (neural tube defects, cleft lip and palate, cardiac outflow tract defects, ventricular septal defects, atrial septal defects, omphalocele, and limb deficiencies) because of their inverse relation with multivitamin supplement use documented in previous analyses. We defined four exposure categories from combinations of multivitamin use (periconceptional use compared with no use) and febrile illness (early pregnancy compared with no illness). The reference category was no multivitamin use and no illness. Febrile illness with no multivitamin use was associated with generally increased risk for the seven defects and the combined group (odds ratio = 2.1, 1.7, 1.5, 1.9, 2.9, 4.4, 3.3, and 2.3, respectively). With multivitamin use, however, the risk estimates associated with febrile illness were generally lower (odds ratio = 0.6, 1.1, 0.0, 1.5, 0.0, 0.8, 0.0, and 0.8, respectively). Some of the associated 95% confidence intervals included one. The pattern of findings suggests that multivitamin use might decrease the risk associated with febrile illness.

**Source:** Medline

**Full Text:**

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**Title:** Overview of nausea and vomiting of pregnancy with an emphasis on vitamins and ginger

**Citation:** American Journal of Obstetrics and Gynecology, 2002, vol./is. 186/5(S253-S255), 0002-9378 (2002)

**Author(s):** Niebyl J.R., Murphy Goodwin T.

**Language:** English

**Abstract:** Patients suffering from nausea and vomiting of pregnancy (NVP) frequently do not receive therapy, in part because of fears of adverse effects of medications on the fetus. Several vitamin-based and herbal therapies have been shown to be effective and safe. Two randomized trials of vitamin B<sub>6</sub> have shown a benefit in reducing NVP. Women taking periconceptional multivitamins are less likely to have severe NVP. The combination of vitamin B<sub>6</sub> and doxylamine (previously marketed in the United States as Bendectin) has been shown to be safe for the fetus and effective in reducing NVP. Ginger was shown, in 2 studies, to reduce NVP. Vitamin B<sub>1</sub> (thiamine) deficiency can lead to Wernicke's encephalopathy in women with severe NVP. Replacement is needed for all women with vomiting of more than 3 weeks' duration. Prophylaxis with multivitamins and therapy with B<sub>6</sub>, with or without doxylamine, are safe and effective therapies for NVP.

**Publication Type:** Journal: Conference Paper

**Source:** EMBASE

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**Title:** Modelling the potential impact of population-wide periconceptional folate/multivitamin supplementation on multiple births.

**Citation:** BJOG : an international journal of obstetrics and gynaecology, Sep 2001, vol. 108, no. 9, p. 937-942, 1470-0328 (September 2001)

**Author(s):** Lumley, J, Watson, L, Watson, M, Bower, C

**Abstract:** To develop a model of the impact of population-wide periconceptional folate supplementation on neural tube defects and twin births. A hypothetical cohort of 100,000 pregnancies > or =20 weeks, plus terminations of pregnancy after prenatal diagnosis before 20 weeks. Application of pooled data on the relative risks for neural tube defects and twins following periconceptional folate from meta-analysis of the randomised trials. 1. Pregnancies with a neural tube defect (i.e. terminations of pregnancy, perinatal deaths, and surviving infants); 2. twin births (i.e. preterm births, perinatal deaths, postneonatal deaths, birth defects, cerebral palsy); 3. numbers needed to treat. The change in neural tube defects would be 75 fewer terminations (95% CI -47, -90), 30 fewer perinatal deaths (95% CI 18, -35), and 13 fewer surviving infants with a neural tube defect (95% CI -8, -16). The change in twinning would be an additional 572 twin confinements (95% CI -100, +1587), among whom there would be 63 very preterm twin confinements (95% CI -11, +174), 54 perinatal and postneonatal deaths (95% CI -9, +149), 48 surviving twins with a birth defect (95% CI -8, +133), and nine with cerebral palsy (95% CI -2, +26). The numbers needed to treat for the prevention of one pregnancy with a neural tube defect is 847, for the birth of one additional set of twins is 175, for the birth of one additional set of very preterm twins is 1587, and for the birth of an additional twin with any of the following outcomes (perinatal death, postneonatal death, survival with a birth defect, or survival with cerebral palsy) is 901. Monitoring rates of neural tube defects and twinning is essential as supplementation or fortification with folate is implemented.

**Source:** Medline

**Full Text:**

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**Title:** Congenital heart defects, maternal febrile illness, and multivitamin use: a population-based study.

**Citation:** Epidemiology (Cambridge, Mass.), Sep 2001, vol. 12, no. 5, p. 485-490, 1044-3983 (September 2001)

**Author(s):** Botto, L D, Lynberg, M C, Erickson, J D

**Abstract:** We assessed the relation between febrile illness during pregnancy and cardiac defects in the offspring in a population-based case-control study in metropolitan Atlanta. Case infants (905) with cardiac defects were actively ascertained from multiple sources. Control infants (3,029) were infants without birth defects who were selected from birth certificates by stratified random sampling. We compared those whose mothers reported febrile illness from 1 month before pregnancy through the third month of pregnancy with those whose mothers reported no illness during the same period. Febrile illness was positively associated with the occurrence of heart defects in the offspring (odds ratio [OR] = 1.8; 95% confidence interval = 1.4-2.4). When influenzalike illness was the reported febrile illness, the OR was 2.1 (95% confidence interval = 0.8-5.5). The association with febrile illness was strongest for tricuspid atresia (OR = 5.2), left obstructive defects (OR = 2.7), transposition of the great arteries (OR = 1.9), and ventricular septal defects (OR = 1.8). These ORs were generally lower among mothers who used multivitamins during the periconceptual period.

**Source:** Medline

**Full Text:**

Available from *Ovid* in [Epidemiology](#)

Available from *Ovid* in [Epidemiology](#)

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**Title:** Maternal multivitamin use and orofacial clefts in offspring.

**Citation:** *Teratology*, Feb 2001, vol. 63, no. 2, p. 79-86, 0040-3709 (February 2001)

**Author(s):** Itikala, P R, Watkins, M L, Mulinare, J, Moore, C A, Liu, Y

**Abstract:** Cleft lip with or without cleft palate (CLP) and cleft palate alone (CP) affect approximately 1 in 1000 infants and 1 in 2,500 infants, respectively. Studies of the relation between orofacial clefts and multivitamins or folic acid have been inconsistent. We used data from a population-based case-control study involving 309 nonsyndromic cleft-affected births (222 with CLP, 87 with CP) and 3,029 control births from 1968 to 1980 to evaluate the relation between regular multivitamin use and the birth prevalence of orofacial clefts. We found a 48% risk reduction for CLP (odds ratio = 0.52, 95% confidence interval = 0.34-0.80) among mothers who used multivitamins during the periconceptual period or who started multivitamin use during the first postconceptional month, after controlling for several covariates. The risk reduction for CP was less than those for CLP (odds ratio = 0.81, 95% confidence interval = 0.44-1.52); however, a small number of CP cases limited interpretation. No risk reductions for CLP or CP were found for women who began multivitamin use in the second or third month after conception. The magnitude of the risk reduction in our study is comparable to those of other recent studies; our study does not support the contention that only large dosages of folic acid are needed to prevent orofacial clefts. More studies are needed to test the effects of multivitamins and varying dosages of folic acid on the recurrence and/or occurrence of orofacial clefts to provide information needed to determine possible prevention strategies. Published 2001 Wiley-Liss, Inc.

**Source:** Medline

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**Title:** Multivitamin supplementation and risk of birth defects.

**Citation:** American journal of epidemiology, Oct 1999, vol. 150, no. 7, p. 675-682, 0002-9262 (October 1, 1999)

**Author(s):** Werler, M M, Hayes, C, Louik, C, Shapiro, S, Mitchell, A A

**Abstract:** It is widely accepted that supplementation with folic acid, a B vitamin, reduces the risk of neural tube defects (NTDs). This case-control study tested the hypothesis that multivitamins reduce risks of selected birth defects other than NTDs. Infants with and without birth defects and aborted fetuses with birth defects were ascertained in the greater metropolitan areas of Boston, Philadelphia, and Toronto during 1993-1996. Mothers were interviewed within 6 months after delivery about a variety of factors, including details on vitamin use. Eight case groups were included: cleft lip with or without cleft palate, cleft palate only, conotruncal defects, ventricular septal defects, urinary tract defects, limb reduction defects, congenital hydrocephaly, and pyloric stenosis (n's ranged from 31 to 186). Controls were 521 infants without birth defects (nonmalformed controls) and 442 infants with defects other than those of the cases (malformed controls). Daily multivitamin supplementation was evaluated according to gestational timing categories, including periconceptual use (28 days before through 28 days after the last menstrual period). Odds ratios (ORs) below 1.0 were observed for all case groups except cardiac defects, regardless of control type. For periconceptual use, ORs with 95% confidence intervals that excluded 1.0 were estimated for limb reduction defects using both nonmalformed controls (OR = 0.3) and malformed controls (OR = 0.2) and for urinary tract defects using both nonmalformed controls (OR = 0.6) and malformed controls (OR = 0.5). Statistically significant ORs for use that began after the periconceptual period were observed for cleft palate only and urinary tract defects. These data support the hypothesis that periconceptual vitamin supplementation may extend benefits beyond a reduction in NTD risk. However, other than folic acid's protecting against NTDs, it is not clear what nutrient or combination of nutrients might affect risk of other specific defects.

**Source:** Medline

**Full Text:**

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England as your institution before entering your NHS OpenAthens account details.  
Available from *Highwire Press* in [American Journal of Epidemiology](#)

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**Title:** Use of multivitamin/mineral prenatal supplements: Influence on the outcome of pregnancy

**Citation:** American Journal of Epidemiology, July 1997, vol./is. 146/2(134-141), 0002-9262 (15 Jul 1997)

**Author(s):** Scholl T.O., Hediger M.L., Bendich A., Schall J.I., Smith W.K., Krueger P.M.

**Language:** English

**Abstract:** The objective of this study was to examine the association of prenatal multivitamin/mineral supplement use during the first and second trimesters of pregnancy by low income, urban women in the Camden Study (1985-1995, n = 1,430) and preterm delivery (<37 completed weeks) and infant low birth weight (<2,500 g). Prenatal supplement use was corroborated by assay of circulating micronutrients at entry to care (no differences) and week 28 gestation (increased concentrations of folate and ferritin for supplement users). Compared with women who entered care during the first or second trimester but did not use prenatal supplements, supplement use starting in the first or second trimester was associated with approximately a twofold reduction in risk of preterm delivery. After controlling for potential confounding variables, risk of very preterm delivery (<33 weeks' gestation) was reduced more than fourfold for first trimester users and approximately twofold when use dated from the second trimester. Infant low birth weight and very low birth weight (<1,500 g) risks were also reduced. Risk of low birth weight was reduced approximately twofold with supplement use during the first and second trimester. Diminution in risk was greater for very low birth weight infants, amounting to a sevenfold reduction in risk of very low birth weight with first trimester supplementation and a greater than sixfold reduction when supplement use started in the second trimester. Thus, in low income, urban women, use of prenatal multivitamin/mineral supplements may have the potential to diminish infant morbidity and mortality.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *Oxford University Press* in [American Journal of Epidemiology](#); Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details. Available from *Highwire Press* in [American Journal of Epidemiology](#)

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**Title:** Does periconceptional multivitamin use reduce the risk for limb deficiency in offspring?

**Citation:** Epidemiology (Cambridge, Mass.), Mar 1997, vol. 8, no. 2, p. 157-161, 1044-3983 (March 1997)

**Author(s):** Yang, Q, Khoury, M J, Olney, R S, Mulinare, J

**Abstract:** There is accumulating evidence that periconceptional multivitamin use may prevent the occurrence of some birth defects other than neural tube defects. Using data

from the population-based Atlanta Birth Defects Case-Control Study, we investigated the possible association between periconceptional multivitamin use and the occurrence of limb deficiency. We examined the periconceptional use of multivitamins among mothers of 117 babies with nonsyndromic limb deficiency who were liveborn or stillborn to residents of metropolitan Atlanta from 1968 to 1980 and among mothers of 3,029 control babies born without birth defects who were randomly selected through birth certificates. We found that children whose mothers were periconceptional multivitamin users had a lower risk of having a limb deficiency [odds ratio (OR) = 0.47; 95% confidence interval (CI) = 0.23-0.97]. This protective effect, however, was mostly seen for transverse limb deficiency (OR = 0.30; 95% CI = 0.07-1.32) and not for longitudinal deficiency (including preaxial and postaxial deficiencies; OR = 1.03; 95% CI = 0.17-4.30). Adjustment for potential confounding factors did not change these findings. We found a trend of decreasing risk for all transverse limb deficiencies with earlier vitamin use. These data indicate that mothers' periconceptional multivitamin use may reduce the risk for some types of limb deficiency among their offspring. In addition, because we did not find the protective effect for all types of limb deficiency, the data may also indicate causal heterogeneity of limb deficiencies.

**Source:** Medline

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**Title:** Multivitamin supplementation and multiple births

**Citation:** American Journal of Medical Genetics, 1997, vol./is. 71/1(93-96), 0148-7299 (1997)

**Author(s):** Werler M.M., Cragan J.D., Wasserman C.R., Shaw G.M., David Erickson J., Mitehell A.A.

**Language:** English

**Abstract:** It is well established that maternal multivitamin supplementation reduces the risk of neural tube defects and evidence suggests that it may be associated with other reproductive outcomes. The present study was prompted by a report from a randomized trial in Hungary which showed a 40% increase in multiple births among periconceptional vitamin users. Retrospectively collected data on multivitamin supplementation were obtained on multiple and singleton births from three separate studies: Atlanta Birth Defects Case- Control Study (ABDCCS) malformed and nonmalformed infants born 1968-1980, California Birth Defects Monitoring Program (CBDMP) malformed and nonmalformed infants born 1987-1989, and Boston University Slone Epidemiology Unit Birth Defects Study (SEU-BDS) malformed infants born 1987-1994. Supplementation was divided into three mutually exclusive categories based on timing: 'periconceptional' use-before through at least the third month after conception; 'early' use-beginning in the first month and continuing through at least the third month after conception; and 'later' use-beginning in the second or third month after conception. For periconceptional use, four of five datasets showed a 30 to 60% greater prevalence of supplementation among mothers of multiple births. In contrast, this pattern was not evident for 'early' and 'later' use. Overall, the study findings are tentative, due to a lack of consistency across all five datasets and they should

not alter recent recommendations related to folate supplementation for the prevention of neural tube defects.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *John Wiley and Sons* in [American Journal of Medical Genetics](#)

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**Title:** Periconceptual multivitamin use and the occurrence of conotruncal heart defects: results from a population-based, case-control study.

**Citation:** *Pediatrics*, Nov 1996, vol. 98, no. 5, p. 911-917, 0031-4005 (November 1996)

**Author(s):** Botto, L D, Khoury, M J, Mulinare, J, Erickson, J D

**Abstract:** The preventive efficacy of the periconceptual use of multivitamins is well established for neural tube defects, much less so for other birth defects. We conducted a population-based, case-control study to assess the effects of multivitamin use on the risk for conotruncal defects, a group of severe heart defects that includes transposition of the great arteries, tetralogy of Fallot, and truncus arteriosus. From the population-based Atlanta Birth Defects Case-Control Study, we identified 158 case infants with conotruncal defects and 3026 unaffected, randomly chosen control infants, born from 1968 through 1980 to mothers residing in metropolitan Atlanta. Periconceptual multivitamin use was defined as reported regular use from 3 months before conception through the third month of pregnancy. We present the results of the crude analysis, because the multivariate model yielded essentially identical results. Mothers who reported periconceptual multivitamin use had a 43% lower risk of having infants with conotruncal defects (odds ratio [OR], 0.57; 95% confidence interval [CI], 0.33 to 1.00) than did mothers who reported no use. The estimated relative risk was lowest for isolated conotruncal defects (OR, 0.41; 95% CI, 0.20 to 0.84) compared with those associated with noncardiac defects (OR, 0.91; 95% CI, 0.33 to 2.52) or a recognized syndrome (OR, 1.82; 95% CI, 0.31 to 10.67). Among anatomic subgroups of defects, transposition of the great arteries showed the greatest reduction in risk (OR, 0.36; 95% CI, 0.15 to 0.89). Periconceptual multivitamin use is associated with a reduced risk for conotruncal defects. These findings could have major implications for the prevention of these birth defects.

**Source:** Medline

**Full Text:**

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Available from *Highwire Press* in [Pediatrics](#)

Available from *Free Access Content* in [Pediatrics](#)

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**Title:** Reduction of urinary tract and cardiovascular defects by periconceptional multivitamin supplementation

**Citation:** American Journal of Medical Genetics, March 1996, vol./is. 62/2(179-183), 0148-7299 (15 Mar 1996)

**Author(s):** Czeizel A.E.

**Language:** English

**Abstract:** The objective in the Hungarian randomised double-blind controlled trial was to study the preventive effect of periconceptional multivitamin supplementation on neural tube-defects and other congenital abnormalities. There were 2,471 and 2,391 informative offspring (prenatally diagnosed and terminated malformed fetuses, stillborn fetuses, and liveborn infants) in the multivitamin and placebo-like trace element groups, respectively. A single tablet either of a multivitamin containing 0.8 mg of folic acid or trace element supplement was given daily for at least one month before conception and at least until the date of the second missed menstrual period. The total rate of major congenital abnormalities was 20.6/1,000 in the multivitamin and 40.6/1,000 in the trace element group. After the exclusion of six cases of neural-tube defects in the trace element group the difference was very highly significant [ $P = 0.0003$ ; relative risk of 0.54 (95% CI 0.39, 0.76)]. Multivitamin supplementation appeared to result in a significant reduction in the rate of urinary tract abnormalities, mainly obstructive defects, and in the rate of sporadic cardiovascular malformations, mainly ventricular septal defects. This report is regarded as a hypothesis-generating study encouraging others to see if the result can be repeated.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

Available from *John Wiley and Sons* in [American Journal of Medical Genetics](#)

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**Title:** Does periconceptional multivitamin use reduce the risk of neural tube defects associated with other birth defects? data from two population-based case-control studies.

**Citation:** American journal of medical genetics, Jan 1996, vol. 61, no. 1, p. 30-36, 0148-7299 (January 2, 1996)

**Author(s):** Khoury, M J, Shaw, G M, Moore, C A, Lammer, E J, Mulinare, J

**Abstract:** The role of periconceptional folic acid in the prevention of neural tube defects (NTDs) is well established. However, it is not clear whether a protective effect exists for the subset of nonsyndromic NTD with other "unrelated" major structural birth defects (NTD-multiples). This question is important to investigate because of shared pathogenetic mechanisms between NTD and other types of birth defects, and because of the epidemiologic differences that have been shown between NTD-multiples and NTD-singles.

We analyzed data from two population-based case-control studies of NTDs, Atlanta 1968-1980, and California 1989-1991, to assess whether periconceptional multivitamin use reduces the risk of NTD-multiples. Maternal vitamin histories were assessed for 47 and 65 NTD-multiples cases and 3,029 and 539 control babies in Atlanta, and California, respectively. There was a substantial risk reduction associated with periconceptional multivitamin use (-3 to +3 months) for NTD-multiples (pooled odds ratio = 0.36, 95% C.I. 0.18-0.72) that persisted after adjustment for maternal race/ethnicity and education. Also, no specific types of NTDs or NTDs with specific defects explained the risk reduction with vitamin use. These data suggest that multivitamins reduce the risk of nonsyndromic NTD cases associated with other major birth defects. The implication of this finding for the role of vitamins in the prevention of non-NTD birth defects should be further explored.

**Source:** Medline

**Full Text:**

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**Title:** Maternal periconceptional use of multivitamins and reduced risk for conotruncal heart defects and limb deficiencies among offspring.

**Citation:** American journal of medical genetics, Dec 1995, vol. 59, no. 4, p. 536-545, 0148-7299 (December 4, 1995)

**Author(s):** Shaw, G M, O'Malley, C D, Wasserman, C R, Tolarova, M M, Lammer, E J

**Abstract:** We investigated whether a woman's periconceptional use of a multivitamin containing folic acid was associated with a reduced risk for delivering offspring with a conotruncal heart defect or a limb deficiency. Data were derived from a population-based case-control study of fetuses and liveborn infants with conotruncal or limb defects among a 1987-88 cohort of births in California. Telephone interviews were conducted with mothers of 207 (87.0% of eligible) conotruncal cases, 178 (82.0%) limb defect cases, and of 481 (76.2%) randomly selected liveborn nonmalformed control infants. Reduced risks were observed for maternal use of multivitamins containing folic acid from one month before until two months after conception. Odds ratios and 95% confidence intervals for any compared to no multivitamin use were 0.70 (0.46-1.1) for conotruncal defects and 0.64 (0.41-1.0) for limb defects. Controlling for maternal race/ethnicity, age, education, gravidity, alcohol use, and cigarette use resulted in a further reduction to the odds ratio for conotruncal defects, 0.53 (0.34-0.85), but not for limb defects. Among non-vitamin using women, consumption of cereal containing folic acid was also associated with reduced risk for both defects. Women who take multivitamins have 30-35% lower risk of delivering offspring with either conotruncal or limb defects. This association may not be attributable to folic acid specifically, but may be a consequence of other multivitamin components, or some unknown behaviors that highly correlate with regular use of a multivitamin. However, should the association prove causal, it offers an important opportunity for preventing thousands of serious birth defects.

**Source:** Medline

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**Title:** Risks of orofacial clefts in children born to women using multivitamins containing folic acid periconceptionally.

**Citation:** *Lancet* (London, England), Aug 1995, vol. 346, no. 8972, p. 393-396, 0140-6736 (August 12, 1995)

**Author(s):** Shaw, G M, Lammer, E J, Wasserman, C R, O'Malley, C D, Tolarova, M M

**Abstract:** Women are advised to take folic acid before they conceive as a precaution against neural-tube defects. However, the use of folic acid in preventing orofacial clefts is unknown. We investigated whether a woman's periconceptional use of multivitamins containing folic acid was associated with a reduced risk of orofacial clefts. We derived data from a population-based case-control study of fetuses and liveborn infants with orofacial anomalies among a 1987-89 cohort of births in California. We interviewed 731 (84.7%) of eligible mothers with orofacial cleft case infants and 734 (78.2%) mothers with non-malformed control infants. We found a reduced risk of orofacial clefts if the mother had used multivitamins containing folic acid during the period from one month before through two months after conception. The odds ratios ranged from 0.50-0.73 depending on cleft phenotype. Controlling for the potential influence of other variables did not substantially alter the results. Maternal daily consumption of cereal containing folic acid was also associated with a reduced risk of orofacial clefts. Women who used multivitamins containing folic acid periconceptionally had a 25-50% reduction in risk for offspring with orofacial clefts compared to women who did not use such vitamins. However, this association may not be attributable to folic acid specifically, but may be a consequence of other multivitamin supplement components, or behaviours, that are highly correlated with the use of multivitamins containing folic acid.

**Source:** Medline

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**Title:** Periconceptional multivitamin use in relation to the risk of congenital urinary tract anomalies.

**Citation:** *Epidemiology* (Cambridge, Mass.), May 1995, vol. 6, no. 3, p. 212-218, 1044-3983 (May 1995)

**Author(s):** Li, D K, Daling, J R, Mueller, B A, Hickok, D E, Fantel, A G, Weiss, N S

**Abstract:** To study the relation of maternal periconceptional vitamin use to the risk of a congenital urinary tract anomaly (CUTA), we conducted a case-control study using the Washington State Birth Defect Registry. We identified CUTA cases with no known

chromosomal abnormality in seven counties in western Washington State occurring between January 1, 1990, and December 31, 1991. We randomly selected a sample, as controls, of all infants delivered in five large hospitals in King County who did not have a birth defect and who were born in the same year as the cases. About 55% of all infants in King County and a smaller proportion of infants in the other six counties are delivered in these five hospitals. We interviewed mothers of 118 cases and 369 controls to obtain information about their vitamin use during the pregnancy and during the year before the conception. After adjustment for maternal race, family income, county of maternal residence, and birth year, we found that women who used multivitamins during the first trimester had only 15% the risk of bearing a child with a CUTA compared with women who did not take vitamins [odds ratio (OR) = 0.15; 95% confidence interval (CI) = 0.05-0.43]. The reduction was smaller for use restricted to the second or third trimesters (OR = 0.31; 95% CI = 0.09-1.02). Among women who used vitamins during the first trimester, vitamin use before conception was not associated with any further reduction in the risk, nor did there appear to be an association with the amount or brand of vitamin used.(ABSTRACT TRUNCATED AT 250 WORDS)

**Source:** Medline

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**Title:** Pregnancy outcomes in a randomised controlled trial of periconceptional multivitamin supplementation. Final report

**Citation:** Archives of Gynecology and Obstetrics, 1994, vol./is. 255/3(131-139), 0932-0067 (1994)

**Author(s):** Czeizel A.E., Dudas I., Metneki J.

**Language:** English

**Abstract:** The effect of periconceptional multivitamin/trace element supplementation on pregnancy outcomes was evaluated in a randomised controlled trial. The final data-base included 5,502 females with confirmed pregnancy. A multivitamin including 0.8 mg folic acid or a trace element were supplemented for at least 28 days before conception and continuing for at least until the second missed menstrual period. Number of pregnancies, terminations of pregnancies, four types of fetal deaths, livebirths including low birth weight, preterm birth and sex ratio were analysed. Periconceptional multivitamin supplementation increased fertility (higher rates of cumulative conceptions and multiple births), had no significant effect on the rate of different groups of fetal deaths, low birth weight and preterm birth in singletons. This primary preventive method can reduce the occurrence and recurrence of neural-tube defects and had no other significant effect on pregnancy outcomes except multiple births.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

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**Title:** The higher rate of multiple births after periconceptional multivitamin supplementation: an analysis of causes.

**Citation:** Acta geneticae medicae et gemellologiae, Jan 1994, vol. 43, no. 3-4, p. 175-184, 0001-5660 (1994)

**Author(s):** Czeizel, A E, Métneki, J, Dudás, I

**Abstract:** A randomized controlled trial of periconceptional multivitamin supplementation (including 0.8 mg folic acid--see the Materials and Methods section for the precise composition of the multivitamin and trace-element supplementation) was carried out for at least 28 days before conception. The trial was continued until at least until the second missed menstrual period to test the effectiveness of this new primary preventive method in the reduction of neural tube defects. However, other pregnancy outcomes were also evaluated. Of a total of 5,502 pregnant women, 4,846 births were analysed in the final data base. The rate of multiple births was significantly higher in the multivitamin group (3.8%) than in the placebo-like trace-element control group (2.7%), and in both groups exceeded the multiple birth rate of 2.2% in the Hungarian population at large. 7.3% of women in the multivitamin and 7.9% of women in the trace-element groups had received ovarian stimulation treatment (mainly clomiphene) for hormonal dysfunctions, eg. anovulation. Nonetheless, our study showed that periconceptional multivitamin supplementation, with or without ovarian stimulation, increases the rate of multiple births.

**Source:** Medline

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**Title:** Prevention of congenital abnormalities by periconceptional multivitamin supplementation

**Citation:** British Medical Journal, 1993, vol./is. 306/6893(1645-1648), 0959-8146 (1993)

**Author(s):** Czeizel A.E.

**Language:** English

**Abstract:** Objective - To study the effect of periconceptional multivitamin supplementation on neural tube defects and other congenital abnormality entities. Design - Randomised controlled trial of supplementation with multivitamins and trace elements. Setting - Hungarian family planning programme. Subjects - 4156 pregnancies with known outcome and 3713 infants evaluated in the eighth month of life. Interventions - A single tablet of a multivitamin including 0.8 mg of folic acid or trace elements supplement daily for at least one month before conception and at least two months after conception. Main outcome measures - Number of major and mild congenital abnormalities. Results - The rate of all major congenital abnormalities was significantly lower in the group given vitamins than in

the group given trace elements and this difference cannot be explained totally by the significant reduction of neural tube defects. The rate of major congenital abnormalities other than neural tube defects and genetic syndromes was 9.0/1000 in pregnancies with known outcome in the vitamin group and 16.6/1000 in the trace element group; relative risk 1.85 (95% confidence interval 1.02 to 3.38); difference, 7.6/1000. The rate of all major congenital abnormalities other than neural tube defects and genetic syndromes diagnosed up to the eighth month of life was 14.7/1000 informative pregnancies in the vitamin group and 28.3/1000 in the trace element group; relative risk 1.95 (1.23 to 3.09); difference, 13.6/1000. The rate of some congenital abnormalities was lower in the vitamin group than in the trace element group but the differences for each group of abnormalities were not significant. Conclusions - Periconceptional multivitamin supplementation can reduce not only the rate of neural tube defects but also the rate of other major non-genetic syndromic congenital abnormalities. Further studies are needed to differentiate the chance effect and vitamin dependent effect.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**

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Available from *Highwire Press* in [The BMJ](#)

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**Title:** Multivitamin/folic acid supplementation in early pregnancy reduces the prevalence of neural tube defects.

**Citation:** JAMA, Nov 1989, vol. 262, no. 20, p. 2847-2852, 0098-7484 (November 24, 1989)

**Author(s):** Milunsky, A, Jick, H, Jick, S S, Bruell, C L, MacLaughlin, D S, Rothman, K J, Willett, W

**Abstract:** We examined the relation of multivitamin intake in general, and folic acid in particular, to the risk of neural tube defects in a cohort of 23,491 women undergoing maternal serum alpha-fetoprotein screening or amniocentesis around 16 weeks of gestation. Complete questionnaires and subsequent pregnancy outcome information was obtained in 22,776 pregnancies, 49 of which ended in a neural tube defect. The prevalence of neural tube defect was 3.5 per 1000 among women who never used multivitamins before or after conception or who used multivitamins before conception only. The prevalence of neural tube defects for women who used folic acid-containing multivitamins during the first 6 weeks of pregnancy was substantially lower--0.9 per 1000 (prevalence ratio, 0.27; 95% confidence interval, 0.12 to 0.59 compared with never users). For women who used multivitamins without folic acid during the first 6 weeks of pregnancy and women who used multivitamins containing folic acid beginning after 7 or more weeks of pregnancy, the prevalences were similar to that of the nonusers and the prevalence ratios were close to 1.0.

**Source:** Medline

**Full Text:**

Available from *Journal of the American Medical Association (JAMA)* in [Patricia Bowen Library and Knowledge Service West Middlesex university Hospital](#)

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**Title:** The absence of a relation between the periconceptual use of vitamins and neural-tube defects

**Citation:** New England Journal of Medicine, 1989, vol./is. 321/7(430-435), 0028-4793 (1989)

**Author(s):** Mills J.L., Rhoads G.G., Simpson J.L., Cunningham G.C., Conley M.R., Lassman M.R., Walden M.E., Depp O.R., Hoffman H.J.

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**Abstract:** Whether taking multivitamins or folate around the time of conception can reduce a woman's risk of having a child with a neural-tube defect is controversial. To investigate this question, we examined the periconceptual use of vitamin supplements by women who had a conceptus with a neural-tube defect (n = 571), women who had had a stillbirth or a conceptus with another malformation (n = 546), and women who had a normal conceptus (n = 573). Women with conceptuses with neural-tube defects were identified either prenatally or postnatally and were matched to control mothers for gestational age. To minimize recall bias, we interviewed nearly all the women within five months of the diagnosis of a birth defect or the birth of the infant (mean, 84 days); information on vitamin use was obtained by an interviewer who was unaware of the outcome of pregnancy. The rate of periconceptual multivitamin use among the mothers of infants with neural-tube defects (15.8 percent) was not significantly different from the rate among mothers in either the abnormal or the normal control group (14.1 percent and 15.9 percent, respectively). After adjustment for potential confounding factors, the odds ratio for having an infant with a neural-tube defect among women classified as having had full supplementation with multivitamins was 0.95 as compared with the mothers of the abnormal infants (95 percent confidence interval, 0.78 to 1.14) and 1.00 as compared with the mothers of normal infants (95 percent confidence interval, 0.83 to 1.20). There were no differences among the groups in the use of folate supplements. The adjusted odds ratio for having an infant with a neural-tube defect among those receiving the recommended daily allowance of folate was 0.97 as compared with the mothers of abnormal infants (95 percent confidence interval, 0.79 to 1.18) and 0.98 as compared with the mothers of normal infants (95 percent confidence interval, 0.80 to 1.20). We conclude that the periconceptual use of multivitamins or folate-containing supplements by American women does not decrease the risk of having an infant with a neural-tube defect.

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