Published in final edited form as:
Int J Public Health. 2009 ; 54(2): 78–87. doi:10.1007/s00038-009-8103-8.

Predictors of multivitamin use during pregnancy in Brazil

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Summary

Objectives—The study aimed at identifying predictors of multivitamin use during pregnancy in Brazil.

Methods—Birth registry data of 1,774 infants at maternity hospitals in Brazil were used. The effects of maternal health and fertility risk indicators, enabling factors and other maternal characteristics on multivitamin use were evaluated both pooled and stratified by African ancestry.

Results—About 14 % of the women used multivitamins during pregnancy. Number of previous live births, maternal age and education, number of ultrasound exams and year of pregnancy had significant effects on multivitamin use in the group reporting African ancestry. Maternal acute illnesses and education had significant effects on use in the group without African ancestry. Significant geographic variation in multivitamin use was observed in both groups.

Conclusions—The study identifies several risk indicators, health care access and enabling factors that are predictive of multivitamin use with differences by African ancestry. The study highlights the importance of increasing the awareness of women of childbearing age of the benefits of multivitamin use and identifies barriers that need to be addressed to promote use.

Keywords

Multivitamins; reproductive health; health behavior; prenatal health; South America

Multivitamin use during pregnancy is a commonly suggested intervention to improve general maternal and fetal health. In the US, women of childbearing age are encouraged to take a multivitamin containing folic acid or a folic acid supplement primarily to obtain the minimum recommended dose of 0.4 mg folic acid to prevent neural tube defects. However, only 33 % of women of child bearing age take regularly vitamin supplements containing folic acid, while more than 95 % of pregnant women take such a supplement at or during pregnancy.[1,2] Other vitamins have also been linked to preventing certain birth defects.[3] Prenatal use of

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Declaration on conflict of interest The authors have no conflict of interest in this work.

multivitamins may also have positive effects on fetal growth, birth weight and early child development.[4,5]

Information about multivitamin use during pregnancy is less available for less developed countries including Brazil in part due to limited national survey data. Two studies have reported multivitamin use rates during pregnancy ranging from <17 % to 37 % in the mid 1990s in few Brazilian cities.[6,7]

Understanding the health, demographic and socioeconomic determinants of multivitamin use during pregnancy is important for identifying interventions and informing health policies to improve utilization rates. Multivitamin use during pregnancy is likely to be affected by the woman's health preferences, perceptions of her pregnancy risks and the benefits and risks of multivitamin use and enabling factors to obtain multivitamins. Limited research exists on the contributions of these factors to multivitamin use, especially in less developed countries, where multivitamin use rates are markedly lower than developed countries. Multivitamin use has been reported to vary by maternal race, age, education and fertility history, yet most of the variation in utilization remains unexplained.[3,7–9] Most of the previous studies used data sources with limited information on proxy measures for health risks, preferences and risk/benefit perceptions. Further, few studies have estimated well specified multivariate models that simultaneously assess the effects of several potential contributors and account for confounding biases.

This study evaluates the effects of several health, demographic, socioeconomic and healthcare factors on the demand for multivitamins during pregnancy in Brazil using multivariate regression models. A primary contribution of this paper is identifying simultaneously the effects of several important characteristics and risk factors, several of which were omitted in previous studies, on multivitamin use in the largest country in South America. The study has significant implications for informing public health initiatives aimed at improving multivitamin use rates in Brazil and other countries.

We evaluate multivitamin use anytime during pregnancy as the primary outcome given that multivitamins as a combined dietary supplement have been found in several studies to affect birth and child health outcomes and given that effects on certain outcomes such as preterm birth or child neurological development are not necessarily limited to use during the first trimester. As a sensitivity analysis, we evaluate multivitamin use during the first trimester of pregnancy during which several congenital anomalies such as NTDs and oral clefts occur. We also evaluate the use of supplements containing folic acid (including folic acid-only supplements) during the first trimester given the preventive effects of folic acid on NTDs.

Given that access to healthcare, health information, health risks and preferences may vary by race, it is important to evaluate the demand function both pooled and stratified by race. Previous studies provide support to differences in health behaviors and outcomes by race.[5] Therefore, we evaluate the demand for multivitamins both pooled and stratified by African ancestry based on maternal report of the ancestries of the infant.

METHODS

Data and Study Sample

The study used birth record data collected by ECLAMC, a research program of birth defects surveillance in South America.[10] ECLAMC involves a large number of health professionals (primarily pediatricians) who monitor all births in their hospitals to identify and enroll newborns with birth defects into ECLAMC. An infant born without birth defects in the same hospital is matched to each affected newborn by date of birth and sex and also enrolled. Data

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is collected through a standard interview with the mother prior to discharge from the hospital after delivery and through abstraction from medical records. The same data collection instrument is used across all hospitals.[10]

The study sample included 1,774 mothers of liveborn infants without congenital malformations between 1995 and 2002 in 11 hospitals in Brazil. Adolescent mothers (<20 years) were excluded to avoid the analytical problems of simultaneous self-selection into vitamin use and other characteristics (e.g. school attendance and multivitamin use decisions of adolescent mothers may be affected by the same factors such as perceived health risks and time costs, yet some of these factors are unmeasured).

Empirical model

Multivitamin use was studied as a function of variables that may signal to the mother her health risks and the extent of fetal health endowments (health risk indicators), reflect availability of information from healthcare providers about the benefits of multivitamins and pregnancy risks (healthcare access indicators), affect access to multivitamins (enabling characteristics) as well as other potentially relevant characteristics including ancestry and pregnancy year (other factors). Health risk indicators included the following: an indicator for having a family member/relative to the child with one or more of the five most common birth defects (cleft lip and palate, neural tube defects (NTDs), Down syndrome, congenital heart disease and polydactyly), indicators for occurrence of maternal acute illnesses such as flu or rubella during pregnancy and chronic illnesses such as diabetes or hypertension, indicator for reporting any difficulty in conception and an indicator for occurrence of vaginal bleeding during the first trimester of pregnancy. These indicators may reflect additional health risks to the mother or to the prenatal care provider and increase the value of multivitamin use as an intervention to improve maternal health. Also included were number of previous live births, number of miscarriages and still births and maternal age. These factors measure fertility history which affects the woman's efficiency and experience in assessing and dealing with pregnancy risks, as well as her perceptions of the value of multivitamin use. Multivitamin use is expected to decrease with the number of previous live births (favorable experience) but increase with the number of previous miscarriages and stillbirths (adverse experience). Maternal age results in greater accumulation of experience and information for health production including further awareness of the value of multivitamins but may also reflect higher risks of adverse pregnancy outcomes (e.g. certain birth defects). Therefore, multivitamin use is expected to increase with maternal age. There were no measures of whether the pregnancy was planned or not.

The healthcare access indicators included the number of prenatal care visits as well as the number of ultrasounds that the mother received. A more frequent use of prenatal care and prenatal diagnostics (which represents a proxy measure for quality and intensity of prenatal care procedures) is expected to increase multivitamin use through identifying health risks that may benefit from multivitamin use as well as enhancing maternal knowledge of the benefits of multivitamins through the counseling provided by health professionals.

Enabling characteristics included maternal and father's schooling which provide higher income and reflect greater efficiency in health production, through increasing the access to and the effectiveness of processing health related information; [11] higher education is expected to increase multivitamin use. Employment status was also included as an enabling factor (through securing higher income which may increase multivitamin use). However, employment may increase the cost of dedicating time to prenatal health investment (expected to reduce multivitamin use). Therefore, the net effect of employment is theoretically ambiguous. No direct measures of family income were available.

Health behaviors may vary by race and ancestry due to potential differences in access to health care and health information. Indicators were included for the ancestries of the infant as reported by the mother.

Indicators for the state of birth were included to evaluate geographic variations in multivitamin use. Significant within and between-country geographic variations are commonly seen in health care utilization and behaviors. These may relate to differences in physician practice styles, availability of care, socioeconomics, and other factors. Significant variations in prescription rates of vitamins and other medications during pregnancy have been reported among several countries including Brazil.[12] Finally, indicators for pregnancy year were included to evaluate changes in multivitamin use through time.

Multivitamin use was measured as a binary indicator of taking any multivitamin or prenatal vitamin anytime during pregnancy. ECLAMC professionals collected data on medication use during pregnancy, including dietary supplements. The medications and dietary supplements were coded at ECLAMC using the Anatomical Therapeutic Chemical Classification System (ATC). The codes and text descriptions were used to identify the multivitamins and prenatal vitamins that were included in the multivitamin use measure. Tab. 1 includes a description of the primary maternal characteristics for the pooled sample and stratified by African ancestry and Tab. A1 in the Appendix includes a description of the other study variables (Tab. 1 here).

Statistical analysis

The demand function was estimated by a random effect logit model in order to account for the correlation of observations within hospitals of birth.[13] As sensitivity analysis, a fixed-effect logit model was estimated to account for unobserved effects at the level of hospital of birth (excluding the state indicators) that may be related to the studied demand predictors. We used a chow-type test to assess differences in the coefficients of regression variables by African ancestry and a Wald-type chi-square test to assess the joint significance of all model covariates.[13,14]

Results

About 14 % of the study sample reported multivitamin use during pregnancy. About 42 % (740 subjects) reported that the infant had African ancestry. There were overall no differences in multivitamin use, risk indicators and healthcare access indicators by African ancestry (marginally significant differences in rates of acute illnesses and number of live births). Lower rates of maternal and paternal education, paternal employment, and other ancestries were observed in the group with African ancestry. Significant differences in geographic location were observed by African ancestry.

Tab. 2 reports the odds ratios (ORs) and 95 % confidence intervals for the predictors in the multivitamin use function with significant effects for the pooled sample and/or when stratified by African ancestry. Tab. 2A includes the ORs of the other predictors that had marginally significant or insignificant effects. There were no significant differences in the regression coefficients by African ancestry using a chow-type test (p=0.49). However, in a specification that included interaction terms between African ancestry and selected variables that showed potential differences in effects by ancestry (acute illnesses, live births, all maternal age indicators, prenatal ultrasounds, all maternal education indicators, and all pregnancy year indicators), the coefficients of these interaction terms were jointly significant (p=0.03) (Table 2 here).

In the group with African ancestry, multivitamin use decreased with difficulty in conception and first trimester bleeding (OR=0.4; marginally significant) and with previous live births

(OR=0.7 per live birth). Multivitamin use increased with maternal age (OR=2.4 and 3.0 for age groups 26-35 and ≥ 36 years, respectively, compared to younger mothers) and with receiving prenatal ultrasounds (OR=1.4 per ultrasound). Multivitamin use increased significantly with maternal education in this group [OR=by about 2.8, 3.8 and 4.7 for incomplete secondary (marginally significant), complete secondary and university education, respectively, compared to completed primary education]. Use also increased with reporting native ancestry (OR=1.8; marginally significant) and ancestry other than European, Native and African (OR=5.8; marginally significant) and among pregnancies occurring in 1996-1998 relative to 1994 (OR=8.4, 8.7 and 4.5 for 1996, 1997 and 1998 respectively). Finally, significant geographic differences in use were observed, with lower use in the states of Minas Gerais (OR=0.2) and Rio Grande do Sul (OR=0.1) relative to Sao Paulo.

In the group without African ancestry, multivitamin use decreased with acute illnesses during pregnancy (OR=0.5) and among mothers 26-35 years old compared to younger mothers (OR=0.6; marginally significant). Lower multivitamin use was observed among mothers who did not complete primary school compared to those who completed primary school (OR=0.5) but no significant effects were observed with higher maternal education. Higher multivitamin use was observed with father's education of less than complete primary school compared to completed primary school (OR=1.9; marginally significant). Similar to the group with African ancestry, multivitamin use increased with reporting an ancestry other than European, Native and African (OR=3.3). Lower multivitamin use was observed among pregnancies occurring in 2002 relative to 1994 (OR=0.1; marginally significant) and in pregnancies occurring in the state of Rio Grande do Sul relative to Sao Paulo (OR=0.1).

The estimated effects in the pooled model represented average effects of those estimated by ancestry, with significant effects observed for acute illnesses, pervious live births, prenatal ultrasounds, maternal education, reporting an ancestry other than European, Native and African and geographic location.

Tab. A3 in the Appendix lists the ORs and the 95 % confidence intervals for the predictors that had significant effects on the two alternative measures of using multivitamins and using folic acid supplements during the first trimester of pregnancy. Use of either supplement increased with number of prenatal ultrasounds and reporting an ancestry other than European, Native and African, decreased with number of previous live births, and was lower in the state of Rio Grande do Sul relative to Sao Paulo (see Tab. 2). The use of folic acid in the first trimester increased with the number of prenatal visits (OR=1.1). Maternal acute illnesses and education did not have significant effects on the use of either supplement during the first trimester.

Discussion

Several of the study predictors had estimated effects with the hypothesized sign including live births, maternal education and age (in the group with African ancestry), and number of prenatal ultrasounds. The estimated effects of difficulty in conception, acute illnesses and first trimester bleeding had unexpected signs (though some were only marginally significant). These risk factors may decrease the availability of healthy time to learn about or take multivitamins as well as financial resources to purchase multivitamins (through reducing income), and they also may be reversely affected by multivitamin use (e.g. women who take multivitamins might have fewer acute illnesses or first trimester bleeding), which would contribute to the unexpected sign, though there is no consistent evidence of such reverse effects. Observing a smaller number of significant predictors of first trimester use of multivitamins or folic acid supplements compared to multivitamin use anytime during pregnancy is likely due to their lower frequency.

An interesting observation is that family history of the five most common birth defects had no effect on multivitamin use or folic acid use during the first trimester. The strong evidence that folic acid use prevents NTDs had already been established prior to the study years, and preventive effects of multivitamin/folic acid use for other defects including oral clefts and some forms of congenital heart disease were also suggested during the study years. [15-19] Studying the effects of family history of birth defects that are influenced by vitamin deficiencies on multivitamin use and the role of prenatal care practices in counseling at-risk women is an important area for future research. A 1996 survey in six South American countries including Brazil showed that less than 1 % of the pregnant women reported folic acid as a beneficial vitamin during pregnancy, about 14 % reported having heard of folic acid and about 15 % took a supplement containing folic acid.[20] In 1995 in the US, about 5 % of women of childbearing age reported knowing that folic acid may prevent birth defects, 52 % reported hearing of folic acid and 25 % reported taking a folic acid supplement.[21] While the rates of hearing of folic acid increased over the past decade in the US to about 84 % among women of childbearing age, only 25 % reported knowledge of its benefits in preventing birth defects and 33 % reported regular use.[1] Increasing the awareness of women of childbearing age about the benefits of multivitamins has large public health significance in both developed and less developed countries.

The observed geographic differences in multivitamin use in this study were in accordance with differences in wealth between the included states. For instance, the average family income in the states of Minas Gerais, Rio Grande do Sul and Santa Catarina is lower than in the state of Sao Paulo by 16-39 %.[22] Geographic variation may also be in part due to differences in prenatal care practices which likely impact multivitamin use, as suggested by the increased use of multivitamins with the number of ultrasound tests. Another study has found an increase in multivitamin use among women in the US who reported receiving advice from their healthcare providers about multivitamins.[23] The international study of 22 countries including Brazil by the Collaborative Group on Drug Use during Pregnancy (CGDUP) found that up to 94 % of medications including vitamins taken during pregnancy were prescribed by health professionals including 73 % that were prescribed by obstetricians, with significant variation in prescription and medication use rates between countries.[12] Little is still known about the counseling that pregnant women and women of childbearing age receive on multivitamin use from health care providers in both less developed and developed countries. The lack of effects of number of prenatal visits on multivitamin use coupled to the positive effect of number of ultrasound tests suggests that counseling pregnant women about the benefits of multivitamins might not be a standard prenatal care practice in Brazil, and that it might vary by quality of prenatal care as well as identification of health problems. The increase in use of folic acid supplements during the first trimester with prenatal visits suggests that more counseling is provided on folic acid use than multivitamin use in Brazil. Further studies into the role of health care providers and geographic variation in use of multivitamins and folic acid supplements are needed.

There were small differences in multivitamin use by ancestry, yet the significant differences in effects of certain predictors of use suggest differences in access to health information and resources by ancestry. For instance, the very strong effects of maternal age and education on multivitamin use in the group with African ancestry but not in the group without African ancestry suggest a more heterogeneous access to information and resources within this group than the group without African ancestry. The large increase in use between 1995 and 1997 in the group with African ancestry suggests improved access to information. The overall similar geographic variation in use by ancestry suggests similarities in geographic effects on access to health care and information by ancestry. Differences in vitamin use by race have been observed in other countries such as the US.[2,24]

Some of the included risk indicators showed no significant effects (such as history of birth defects or number of miscarriages). This suggests that these factors are discounted in the decision to use multivitamins. This result can also be, in part, due to the low multivitamin use rate [slightly lower than rates (<17-37.5 %) reported in two other studies in Brazil, with differences likely due to the different geographic areas, time periods and multivitamin use measures]. [6,7] Multivitamin use might have been underreported due to recall bias, the open-ended format of the question on medications and dietary supplements during pregnancy, or data collection errors. However, the health professionals who conducted the interviews and recorded the data received similar training and used the same data collection instrument. While underreporting is expected to widen the confidence intervals of the odds ratios, it is not expected to bias the estimates of the odds ratios, assuming that underreporting is unrelated to the studied predictors. Obtaining similar results using the model with fixed effects for the hospital of birth indicates that the estimated demand effects are not biased by differences in interviewer characteristics or area-effects correlated with the hospital of birth.

The study sample may not be fully representative of all births in Brazil but it represents a large proportion of the birth population given the socioeconomic and geographic diversity of the birth samples at the study hospitals as can be seen in Tab. 1 and A1. Further, selecting the unaffected sample into the ECLAMC program involves matching by sex, date and hospital of birth to the affected sample, which enhances the representativeness of this sample by limiting systematic sample selection biases. The study sample was overall comparable to two large birth samples in 1993 and 2004 from the city of Pelotas in Southern Brazil on mean birth weight (3,144 versus 3,152 grams), rate of first time birth (35.7 % versus 35.9 %), and mean number of prenatal care visits (7.1 versus 7.9), providing support for the large representativeness of the study sample.[25] Unfortunately, the study sample could not be compared to the overall birth population in Brazil due to the lack of access to population-level indicators.

A few countries including the United States, Brazil, Canada, and Chile have introduced fortification of grain and flour and several studies have reported decreases in NTDs of up to 50 % post fortification.[26-28] Other countries have not mandated folic acid fortification yet due to concerns about potential safety issues at the population-level including primarily the possibility of masking B12 deficiency, though evidence remains overall inconsistent.[29,30] The lack of fortification programs in several countries further highlights the importance of further interventions and studies to address the use of multivitamins and folic acid supplements among pregnant women and women of childbearing age.

The study highlights the importance of increasing the awareness of women of childbearing age of the benefits of use of multivitamin use and of developing surveillance systems to evaluate changes in use over time through large and nationally representative samples. Such efforts are relevant for both developed and less developed countries. The study has important public health implications by identifying potential barriers and risk perception factors that need to be addressed in order to promote multivitamin use. For instance, more counseling may be needed for women who have had a previous live birth given their lower multivitamin use rates.

Risk indicators, healthcare access, enabling factors and geographic effects were found to contribute to multivitamin use during pregnancy. Further research is needed to understand the effects of risk indicators on multivitamin use, in particular whether perceived health risks might increase or reduce the propensity to use multivitamins. Certain health risks are of particular interest, including family history of birth defects, given the potential preventive effects of multivitamins and folic acid on some major birth defects. The practices of healthcare professionals in counseling women of childbearing age on multivitamin use deserve further investigation. Finally, further research is needed to identify other economic and information constraints for multivitamin use.

Acknowledgments

This work was supported by NIH grants 1R03DE018394-01 and U01 DE-017958.

References

1. Centers for Disease Control and Prevention (CDC). Use of dietary supplements containing folic acid among women of childbearing age--United States. MMWR Morb Mortal Wkly Rep 2005;54:955–8. [PubMed: 16195694]
2. Carmichael SL, Shaw GM, Yang W, et al. Correlates of intake of folic acid-containing supplements among pregnant women. Am J Obstet Gynecol 2006;194:203–10. [PubMed: 16389033]
3. Munger RG, Sauberlich HE, Corcoran C, Nepomuceno B, Daack-Hirsch S, Solon FS. Maternal vitamin B-6 and folate status and risk of oral cleft birth defects in the Philippines. Birth Defects Res A Clin Mol Teratol 2004;70:464–71. [PubMed: 15259036]
4. Fawzi WW, Msamanga GI, Urassa W, et al. Vitamins and perinatal outcomes among HIV-negative women in Tanzania. N Engl J Med 2007;356:1423–31. [PubMed: 17409323]
5. Wehby GL, Murray JC. The effects of prenatal use of folic acid and other dietary supplements on early child development. Matern Child Health J 2008;12:180–7. [PubMed: 17554612]
6. Fonseca MR, Fonseca E, Bergsten-Mendes G. Prevalence of drug use during pregnancy: a pharmacoepidemiological approach. Rev Saude Publica 2002;36:205–12. [PubMed: 12045802]
7. Mengue SS, Schenkel EP, Schmidt MI, Duncan BB. Factors related to use of medication during pregnancy in six Brazilian cities. Cad Saude Publica 2004;20:1602–8. [PubMed: 15608862]
8. Yu SM, Keppel KG, Singh GK, Kessel W. Preconceptional and prenatal multivitamin-mineral supplement use in the 1988 National Maternal and Infant Health Survey. Am J Public Health 1996;86:240–2. [PubMed: 8633743]
9. Jasti S, Siega-Riz AM, Cogswell ME, Hartzema AG, Bentley ME. Pill count adherence to prenatal multivitamin/mineral supplement use among low-income women. J Nutr 2005;135:1093–101. [PubMed: 15867287]
10. Castilla EE, Orioli IM. ECLAMC: the Latin-American collaborative study of congenital malformations. Community Genet 2004;7:76–94. [PubMed: 15539822]
11. Grossman M. On the Concept of Health Capital and the Demand for Health. J Polit Econ 1972;80:223–55.
12. Medication during pregnancy: an intercontinental cooperative study. Collaborative Group on Drug Use in Pregnancy (C.G.D.U.P.). Int J Gynaecol Obstet 1992;39:185–96. [PubMed: 1360913]
13. Wooldridge, JM. Econometric analysis of cross section and panel data. Cambridge and London: MIT Press; 2002.
14. Chow GC. Tests of Equality Between Sets of Coefficients in Two Linear Regressions. Econometrica 1960;38:591–605.
15. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. Lancet 1991;338:131–7. [PubMed: 1677062]
16. Czeizel AE, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. N Engl J Med 1992;327:1832–5. [PubMed: 1307234]
17. Shaw GM, Lammer EJ, Wasserman CR, O'Malley CD, Tolarova MM. Risks of orofacial clefts in children born to women using multivitamins containing folic acid periconceptionally. Lancet 1995;346:393–6. [PubMed: 7623568]
18. Shaw GM, O'Malley CD, Wasserman CR, Tolarova MM, Lammer EJ. Maternal periconceptional use of multivitamins and reduced risk for conotruncal heart defects and limb deficiencies among offspring. Am J Med Genet 1995;59:536–45. [PubMed: 8585581]
19. Botto LD, Khoury MJ, Mulinare J, Erickson JD. Periconceptional multivitamin use and the occurrence of conotruncal heart defects: results from a population-based, case-control study. Pediatrics 1996;98:911–7. [PubMed: 8909485]
20. Dutra GM, Rittler M. Awareness of the Benefit of Periconceptional Folic Acid Supplementation in South America. Community Genet 2000;3:71–6.

21. Centers for Disease Control and Prevention (CDC). Knowledge and use of folic acid by women of childbearing age--United States, 1995. MMWR Morb Mortal Wkly Rep 1995;44:716–8. [PubMed: 7675019]
22. Institute of Brazil for Geography and Statistics (IBGE). [April 2006]. at http://www.ibge.gov.br/)
23. Ahluwalia IB, Lawrence JM, Balluz L. Psychosocial factors associated with use of multivitamins by women of childbearing age. J Community Health 2007;32:57–69. [PubMed: 17269313]
24. Yang QH, Carter HK, Mulinare J, Berry RJ, Friedman JM, Erickson JD. Race-ethnicity differences in folic acid intake in women of childbearing age in the United States after folic acid fortification: findings from the National Health and Nutrition Examination Survey, 2001-2002. Am J Clin Nutr 2007;85:1409–16. [PubMed: 17490980]
25. Barros FC, Victora CG, Barros AJ, et al. The challenge of reducing neonatal mortality in middle-income countries: findings from three Brazilian birth cohorts in 1982, 1993, and 2004. Lancet 2005;365:847–54. [PubMed: 15752528]
26. Lopez-Camelo JS, Orioli IM, da Graca Dutra M, et al. Reduction of birth prevalence rates of neural tube defects after folic acid fortification in Chile. Am J Med Genet A 2005;135:120–5. [PubMed: 15846825]
27. Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity 1995-2002. Pediatrics 2005;116:580–6. [PubMed: 16140696]
28. De Wals P, Tairou F, Van Allen MI, et al. Reduction in neural-tube defects after folic acid fortification in Canada. N Engl J Med 2007;357:135–42. [PubMed: 17625125]
29. Mills JL, Von Kohorn I, Conley MR, et al. Low vitamin B-12 concentrations in patients without anemia: the effect of folic acid fortification of grain. Am J Clin Nutr 2003;77:1474–7. [PubMed: 12791626]
30. Wyckoff KF, Ganji V. Proportion of individuals with low serum vitamin B-12 concentrations without macrocytosis is higher in the post folic acid fortification period than in the pre folic acid fortification period. Am J Clin Nutr 2007;86:1187–92. [PubMed: 17921401]

Table 1

Description and distribution of primary maternal characteristics

Variable	Definition	Mean or %		
		Total sample (N=1774)	African ancestry (N=740)	No African ancestry (N=1034)
Multivitamin	Indicator (0,1) for any use of multivitamin/ prenatal vitamin during pregnancy (%)	13.9	13.6	14.0
Multivitamin in first trimester	Indicator (0,1) for any use of multivitamin/ prenatal vitamin during first trimester of pregnancy (%)	7.4	7.4	7.4
Folic acid in first trimester	Indicator (0,1) for any use of folic acid containing supplements during first trimester of pregnancy (%)	8.9	9.1	8.8
Birth defect history	Indicator (0,1) for reporting any child relatives with cleft lip and palate, congenital heart disease, neural tube defects, Down syndrome, or polydactyly (%)	6.1	5.9	6.2
Difficulty in conception	Indicator (0,1) for reporting difficulty in conception (%)	12.3	11.8	12.7
Acute illness	Indicator (0,1) for acute illnesses during pregnancy (%)	47.1	44.5*	49.0*
Chronic illness	Indicator (0,1) for any chronic illnesses during pregnancy (%)	17.5	18.5	16.7
First trimester bleeding	Indicator (0,1) for vaginal bleeding in 1st trimester (%)	8.2	8.2	8.1
Live births	Number of live births prior to birth of sampled subject	1.3 (1.5)	1.4* (1.6)	1.3* (1.4)
Miscarriages/stillbirths	Number of miscarriages and stillbirths prior to sampled subject	0.3 (0.7)	0.3 (0.7)	0.3 (0.7)
Maternal age 26-35 [a]	Indicator (0,1) for maternal age between 26 and 35 years inclusive (%)	45.1	46.9	43.8
Maternal age ≥36[a]	Indicator (0,1) for maternal age of 36 years or older (%)	11.8	10.8	12.5
Prenatal visits	Number of obtained prenatal visits	7.1 (3.0)	6.6 (2.4)	7.2 (2.9)
Prenatal ultrasounds	Number of ultrasound examinations obtained during pregnancy	2.1 (1.5)	2.1 (1.6)	2.1 (1.5)
Maternal education-Less than primary [b]	Indicator (0,1) for below primary school education (%)	44.8	48.5***	42.1***
Maternal education-Incomplete secondary [b]	Indicator (0,1) for incomplete secondary school education (%)	11.7	11.2	12.0
Maternal education-Secondary [b]	Indicator (0,1) for secondary school education (%)	19.6	19.3	19.7

Variable	Definition	Mean or %		
		Total sample (N=1774)	African ancestry (N=740)	No African ancestry (N=1034)
Maternal education-University [b]	Indicator (0,1) for university education (%)	9.0	7.7	10.0

Note: Standard Deviations are listed in parentheses;

[a]Reference category is maternal age between 20 and 25 years of age inclusive;

[b]Reference category is completed primary school;

* and *** indicate significant differences by African ancestry at $p<0.1$ and <0.01 respectively.

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Table 2

Odds ratios (ORs) of the significant predictors of multivitamin use

Variable	Total sample		African ancestry		No African ancestry	
	OR	95% CI	OR	95% CI	OR	95% CI
Acute illness	0.7**	[0.5-0.9]	0.9	[0.5-1.6]	0.5**	[0.3-0.8]
Live births	0.8**	[0.7-0.96]	0.7**	[0.5-0.9]	0.9	[0.8-1.2]
Maternal age 26-35 [a]	1.0	[0.7-1.5]	2.4**	[1.3-4.4]	0.6*	[0.4-1.01]
Maternal age ≥36[a]	1.3	[0.7-2.3]	3.0**	[1.1-8.4]	1.0	[0.5-2.0]
Prenatal ultrasounds	1.2**	[1.04-1.3]	1.4**	[1.2-1.7]	1.1	[0.9-1.3]
Maternal education-Less than primary [b]	0.7	[0.4-1.3]	1.1	[0.4-3.0]	0.5**	[0.2-0.97]
Maternal education-Secondary [b]	1.9**	[1.1-3.4]	3.8**	[1.4-10.5]	1.5	[0.7-3.0]
Maternal education-University [b]	2.1**	[1.1-4.3]	4.7**	[1.3-16.6]	1.6	[0.6-4.0]
Other ancestry	3.4**	[1.5-7.5]	5.8*	[0.8-41.1]	3.3**	[1.3-8.3]
Pregnancy year 96 [c]	1.9	[0.8-4.5]	8.4**	[1.9-38.1]	0.8	[0.3-2.2]
Pregnancy year 97 [c]	1.9	[0.8-4.5]	8.7**	[1.9-40.5]	0.8	[0.3-2.2]
Pregnancy year 98 [c]	2.2*	[0.9-5.1]	4.5**	[1.02-19.6]	1.2	[0.4-3.4]
Minas Gerais [d]	0.3*	[0.1-1.1]	0.2**	[0.1-0.7]	0.3	[0.1-1.8]
Rio Grande do Sul [d]	0.1**	[0.03-0.3]	0.1**	[0.01-0.4]	0.1**	[0.02-0.3]
Wald Chi-square (df), p value	*105.6 (38), <0.0001*		*77.2 (37), <0.001*		*66.5 (37), <0.01*	

Note: 95% Confidence Intervals (CI) of the odds Ratios (ORs) of the predictors with significant effects at p<0.05 in at least one of the three models (pooled and stratified by race) are listed in brackets.

* and ** indicate p<0.1 and <0.05 respectively.

[a]Reference category is maternal age between 20 and 25 years of age inclusive;

[b]Reference category is completed primary school;

[c]Reference category is year 1994;

[d]Reference category is the state of Sao Paulo. Goodness of fit of the whole model including all the study covariates was evaluated by a Wald chi-square test for the significance of regression coefficients.

Table A1

Description and distribution of other study variables

Variable name	Definition	% Total sample (N=1774)	African ancestry (N=740)	No African ancestry (N=1034)
Father's education-Less than primary [b]	Indicator (0,1) for below primary school education (%)	44.6	48.9***	41.6***
Father's education-Incomplete secondary [b]	Indicator (0,1) for incomplete secondary school education (%)	10.7	11.2	10.3
Father's education-Secondary [b]	Indicator (0,1) for highest father's education of secondary school (%)	17.9	15.3**	19.8**
Father's education-University [b]	Indicator (0,1) for highest father's education of university education (%)	7.3	5.4**	8.6**
Maternal employment	Indicator (0,1) for maternal employment status (%)	42.8	41.2	43.9
Father's employment	Indicator (0,1) for father's employment status (%)	95.3	93.9**	96.2**
African ancestry	Indicator (0,1) for infant having African ancestry (%)	41.7	-	-
Native ancestry	Indicator (0,1) for infant having native ancestry (%)	53.6	43.4***	60.8***
European Latin ancestry	Indicator (0,1) for infant having Latin European ancestry (%)	57.4	58.6	56.6
European non-Latin ancestry	Indicator (0,1) for infant having non-Latin European ancestry (%)	19.0	9.7***	25.6***
Other ancestry	Indicator (0,1) for infant having other ancestry	2.6	1.5***	3.5***
Pregnancy year 95 [c]	Indicator (0,1) for pregnancy in 1995 (%)	8.6	7.2*	9.6*
Pregnancy year 96 [c]	Indicator (0,1) for pregnancy in 1996 (%)	10.7	10.0	11.2
Pregnancy year 97 [c]	Indicator (0,1) for pregnancy in 1997 (%)	10.3	8.0***	12.0***
Pregnancy year 98 [c]	Indicator (0,1) for pregnancy in 1998 (%)	11.6	10.5	12.4
Pregnancy year 99 [c]	Indicator (0,1) for pregnancy in 1999 (%)	13.8	14.2	13.4
Pregnancy year 00 [c]	Indicator (0,1) for pregnancy in 2000 (%)	16.1	15.5	16.5
Pregnancy year 01 [c]	Indicator (0,1) for pregnancy in 2001 (%)	19.1	23.4***	16.0***
Pregnancy year 02 [c]	Indicator (0,1) for pregnancy in 2002 (%)	4.2	5.3*	3.5*
Minas Gerais [d]	Indicator (0,1) for a sampled birth in the state of Minas Gerais (%)	15.1	29.9***	4.5***

Variable name	Definition	%		
		Total sample (N=1774)	African ancestry (N=740)	No African ancestry (N=1034)
Paraiba [d]	Indicator (0,1) for a sampled birth in the state of Paraiba (%)	3.0	6.2***	0.7***
Rio Grande do Sul [d]	Indicator (0,1) for a sampled birth in the state of Rio Grande do Sul (%)	23.6	15.8***	29.2***
Santa Catarina [d]	Indicator (0,1) for a sampled birth in the state of Santa Catarina (%)	22.8	12.0***	30.5***

Note:

[b]Reference category is completed primary school;

[c]Reference category is year 1994;

[d]Reference category is the state of Sao Paulo.

*, ** and *** indicate significant differences by African ancestry at $p<0.1$, 0.05 and 0.01 respectively.

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Table A2

Odds ratios (ORs) of the other studied predictors on multivitamin use

Variable name	Total sample		African ancestry		No African ancestry	
	OR	95% CI	OR	95% CI	OR	95% CI
Birth defect history	1.4	[0.7-2.6]	1.9	[0.6-5.7]	1.2	[0.5-2.9]
Difficulty in conception	0.7	[0.4-1.2]	0.4*	[0.1-1.1]	0.8	[0.4-1.6]
Chronic illness	0.8	[0.5-1.2]	0.6	[0.3-1.2]	0.7	[0.4-1.3]
First trimester bleeding	0.6	[0.3-1.2]	0.4*	[0.1-1.03]	0.9	[0.4-2.0]
Miscarriages/stillbirths	0.9	[0.8-1.2]	1.1	[0.8-1.5]	0.8	[0.5-1.1]
Prenatal visits	1.0	[0.9-1.1]	0.9	[0.8-1.03]	1.0	[0.96-1.1]
Maternal education-Incomplete secondary [b]	1.5	[0.8-2.9]	2.8*	[0.9-9.0]	1.1	[0.5-2.4]
Father's education-Less than primary [b]	1.6*	[0.96-2.6]	1.3	[0.6-2.9]	1.9*	[0.97-3.6]
Father's education-Incomplete secondary [b]	1.3	[0.7-2.4]	2.0	[0.8-5.4]	1.0	[0.4-2.4]
Father's education-Secondary [b]	1.4	[0.8-2.4]	1.2	[0.5-3.1]	1.7	[0.8-3.4]
Father's education-University [b]	1.3	[0.7-2.5]	0.8	[0.2-2.6]	1.4	[0.6-3.3]
Maternal employment	1.1	[0.7-1.5]	1.2	[0.7-2.2]	1.1	[0.7-1.8]
Father's employment	1.7	[0.7-4.3]	1.2	[0.4-3.8]	3.1	[0.6-15.8]
African ancestry	0.9	[0.6-1.3]	-	-	-	-
Native ancestry	1.2	[0.8-1.8]	1.8*	[0.9-3.5]	1.2	[0.7-2.0]
European Latin ancestry	0.9	[0.6-1.3]	1.1	[0.6-2.1]	0.8	[0.5-1.4]
European non-Latin ancestry	1.0	[0.6-1.5]	0.6	[0.2-2.0]	1.1	[0.6-1.8]
Pregnancy year 95 [c]	0.8	[0.3-2.1]	2.6	[0.5-11.8]	0.4	[0.1-1.3]
Pregnancy year 99 [c]	1.6	[0.7-3.7]	3.2	[0.7-13.8]	0.9	[0.3-2.6]
Pregnancy year 00 [c]	1.2	[0.5-2.9]	1.6	[0.4-6.8]	0.8	[0.3-2.3]
Pregnancy year 01 [c]	0.8	[0.3-1.8]	1.3	[0.3-5.4]	0.5	[0.2-1.3]
Pregnancy year 02 [c]	0.4	[0.1-1.7]	1.3	[0.2-9.3]	0.1*	[0.01-1.2]
Paraiba [d]	1.5	[0.3-7.2]	1.6	[0.3-8.2]	2.3	[0.2-21.4]
Santa Catarina [d]	0.6	[0.2-1.5]	0.6	[0.2-2.1]	0.5	[0.2-1.7]

Note: 95% Confidence Intervals (CI) of odds ratios (ORs) that were marginally significant or insignificant are listed in brackets.

* indicates p<0.1.

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[b] Reference category is completed primary school;

[c] Reference category is year 1994;

[d] Reference category is the state of Sao Paulo.

Table A3

Odds ratios (ORs) of the significant predictors of first trimester use of multivitamins and folic acid supplements

Variable name	Multivitamins		Folic acid supplements	
	OR	95% CI	OR	95% CI
Live births	0.8**	[0.6-0.99]	0.7**	[0.6-0.9]
Prenatal visits	1.1	[0.98-1.2]	1.1**	[1.03-1.2]
Prenatal ultrasounds	1.2**	[1.1-1.4]	1.2**	[1.03-1.3]
Other ancestry	4.4**	[1.8-10.8]	2.7**	[1.2-6.4]
Rio Grande do Sul [a]	0.1**	[0.02-0.4]	0.1**	[0.03-0.5]
Wald Chi-square (df), p value	*77.0 (38), <0.001*		*78.6 (38), <0.001*	

Note: 95% Confidence Intervals (CI) of odds ratios (ORs) of the significant predictors of first trimester use of multivitamins and/or use of folic acid supplements at $p<0.05$ are listed in brackets.

** indicates $p < 0.05$.

[a] Reference category is the state of Sao Paulo. Goodness of fit of the whole model including all the model covariates was evaluated by a Wald chi-square test for the significance of regression coefficients.