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The Association between Maternal Vitamin Use and Preterm Birth in 24 States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2009-2010

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An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

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Abstract

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By Emily Osteen Johnston

OBJECTIVE: To examine the prevalence and association between maternal vitamin use one month prior to pregnancy and early (<34 weeks) or late (34-36 weeks) preterm birth by race/ethnicity.

METHODS: Data from the 2009-2010 Pregnancy Risk Assessment Monitoring System (PRAMS), a population-based surveillance initiative of the Centers for Disease Control and Prevention (CDC) and state health departments was used for the analysis. The states (n=24) included in the analysis maintained a weighted response rate of ≥65% and included a question from the PRAMS questionnaire that assessed maternal vitamin use one month prior to pregnancy. The study included women aged ≥18 years with a singleton birth (n= 57,348). Chi-square tests were performed to examine maternal and infant characteristics and logistic regression models were used to determine odds ratios and 95% confidence intervals for vitamin use as a predictor of preterm birth, adjusting for maternal race, parity, education, age, marital status, Medicaid recipient, WIC recipient, smoking status, and prepregnancy BMI.

RESULTS: Overall, 55% of women reported no vitamin use in the month prior to pregnancy while 37% reported using vitamins ≥4 times per week. After adjustment for covariates, there was no significant association between maternal vitamin use one month prior to pregnancy and early preterm birth. The association between maternal vitamin use 1-3 times per week and ≥4 times per week and late preterm birth was significant only among American Indian, Alaska Native, or Hawaiian women (aOR: 0.39 95% CI 0.20, 0.76; aOR: 2.49 95% CI 1.18, 5.24).

DISCUSSION: The prevalence of vitamin use one month prior to pregnancy reported in this study was consistent with previous research. Maternal vitamin use one month prior to pregnancy was not significantly associated with early preterm birth and maternal race/ethnicity moderated the relation between maternal vitamin use and late preterm birth.

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INTRODUCTION

Preterm birth (less than 37 weeks gestation) affects an estimated 1 out of 9 infants (11.7%) each year in the United States (1). The majority of preterm births (approximately 65-70%) are spontaneous, often occurring without a known cause (2, 3). Preterm infants face an increased risk of mortality compared to infants born at term, accounting for more than two-thirds (67.2%) of infant deaths each year (4). Surviving preterm infants, particularly the smallest and youngest, have an increased risk of neurodevelopmental disabilities, including cerebral palsy, hearing impairment, and retinopathy of prematurity (4-6). Furthermore, the yearly societal economic burden associated with preterm birth in the United States exceeds $26.2 billion (6). Another significant concern in the United States is the persistent racial disparity in preterm birth rates. In 2011, the preterm birth rate was 16.8% among non-Hispanic black women compared to 10.5% among non-Hispanic white women (1). Although reasons for racial disparities in preterm birth are likely multifactorial and not completely understood, research suggests that possible explanations may include genetic, psychosocial, and environmental factors (7).

With increasing recognition of the importance of implantation and placentation in relation to pregnancy outcomes, the focus on potential risk factors for preterm birth has expanded to include the period before, during, and soon after conception (8-10). Current evidence indicates that maternal nutritional status before and during early pregnancy may influence pregnancy outcomes (8, 11-14). For example, research indicates that daily consumption of 400 micrograms (mcg) of folic acid starting at least 1 month before conception through early pregnancy is estimated to prevent 50-70% of neural tube defects

(15). Research also suggests vitamin D is posited to serve an immunomodulatory function in pregnancy, and deficiency in maternal vitamin D status may activate the inflammatory pathway suggested to lead to preterm birth (16, 17). Maternal iron-deficiency anemia in early pregnancy has also been associated with preterm birth (18).

As with preterm birth, racial disparities are also present when comparing the nutritional status of non-Hispanic black and non-Hispanic white women of reproductive age (19, 20). A national cross sectional study found that the proportion of women who consumed a daily average of at least 400 mcg of folic acid from supplements was significantly lower among nonpregnant non-Hispanic black women (14%) than nonpregnant non-Hispanic white women (31%) (19). Additionally, another nationally representative study revealed that an estimated 80% of non-Hispanic black pregnant women were vitamin D insufficient compared to 13% of non-Hispanic white pregnant women (20).

National Health and Nutrition Examination Survey (NHANES) data from 1999–2000 indicated the prevalence of iron deficiency among non-Hispanic black women was significantly higher than non-Hispanic white women (19% versus 10%, respectively) (21). Furthermore, a previous analysis of the Pregnancy Risk Assessment Monitoring Systems data set for 26 states demonstrated that multivitamin use four or more times per week one month prior to pregnancy was lower among non-Hispanic black women (24%) than non-Hispanic white women (41%) (22).

There is limited research examining the association between vitamin use and preterm birth by race/ethnicity. A previous study conducted in the state of Massachusetts that assessed vitamin use and birth outcomes by race found that maternal multivitamin use may improve fetal growth and possibly gestational age among non-Hispanic black infants (8). Additional research that encompasses a broader geographic reach is critical to gain more insight as to whether differences in vitamin use may serve to explain some of the racial disparity in preterm birth rates. Therefore, the purpose of this study is to assess the prevalence of prenatal, folic acid, or multivitamin use one month prior to pregnancy and its associations with preterm birth by race/ethnicity using a population-based, multi-state sample.

Research Questions

The following research questions will guide this study:

1. What is the prevalence of prenatal, folic acid, or multivitamin use one month prior to pregnancy?
2. Is prenatal, folic acid, or multivitamin use one month prior to pregnancy associated with reduced odds of preterm birth?
3. Does race/ethnicity moderate the relation between prenatal, folic acid, or multivitamin use one month prior to pregnancy and preterm birth?

Hypotheses

The hypotheses of this study are that vitamin use one month prior to pregnancy is associated with reduction in the odds of early (<34 weeks) and late (34-36 weeks) preterm birth and that race/ethnicity moderates the relation between vitamin use and preterm birth.

LITERATURE REVIEW

Introduction

Vitamins are nutrients that are essential for cell function and development. Sufficient vitamin and mineral intake is particularly important both before pregnancy for the normal development of the embryo and during pregnancy as nutritional requirements increase to sustain fetal growth and maternal metabolism and tissue development (23, 24). This literature review provides an overview of vitamin use, preterm birth, and studies examining the relationship between vitamin use and preterm birth.

Vitamin Supplementation

According to the 1994 Dietary Supplement Health and Education Act, dietary supplements refer to a product intended to supplement the diet that contain one or more of the following ingredients: vitamins, minerals, herbs or other botanicals, or amino acids (25). With regard to the exposure of interest, this literature review will focus on the following vitamin supplements: multivitamins, prenatal vitamins, and folic acid vitamins. Multivitamins refer to supplements that contain a combination of vitamins (26). As no scientific or regulatory definitions currently exist, manufacturers determine both the types and levels of vitamins present in multivitamins (26). Prenatal vitamins are formulated for women who are pregnant or attempting to conceive and typically contain higher amounts of iron and folic acid than multivitamins. Increased amounts of iron are required during pregnancy to produce more blood and support the growth of the fetal-placental unit and as previously discussed, folic acid has been shown to decrease the risk of neural tube defects (15, 27).Whereas multivitamins often contain 18 mg of iron (the Dietary Reference Intake, or DRI for women of reproductive age), prenatal vitamins typically contain at least 27 mg of iron, the DRI for pregnant women (28). Similarly, while multivitamins normally contain 400 mcg of folic acid (the DRI for women of reproductive age), prenatal vitamins often contain at least 600 mcg of folic acid, the DRI for pregnant women (29). In addition to being found in multivitamins and prenatal vitamins, folic acid is available as a single supplement, often containing at least 400 mcg.

Several health organizations and initiatives recommend vitamin supplementation among women of reproductive age. The United States Public Health Service, the Centers for Disease Control and Prevention, the Institute of Medicine, and the 2010 Dietary Guidelines for Americans (managed by the U.S. Department of Agriculture and the U.S. Department of Health and Human Services) recommend that all women of childbearing age consume 400 mcg of folic acid daily (29-31). Additionally, Healthy People 2020, which is managed by the U.S. Department of Health and Human Services and provides evidence-based, ten-year national objectives to improve the health of Americans, also focuses on preconceptional nutrition. One of the objectives related to maternal, infant, and child health for Healthy People 2020 is to increase the percentage of women who take multivitamins or folic acid prior to pregnancy from 30.1% to 33.1% (32). The national baseline of 30.7% was established as a result of combining data from the 2007 Pregnancy Risk Assessment Monitoring System and the California Maternal and Infant Health Assessment.

Prevalence of Vitamin Use

A study using the Behavioral Risk Factor Surveillance System data from 2004 indicated that among nonpregnant women of reproductive age, 47% reported they were currently taking multivitamins (33). When multivitamin use was examined by race, 54% of non-Hispanic white women reported multivitamin use compared to 38% of non-Hispanic black women (33). A national cross sectional study using the National Health and Nutrition Examination Survey data from 2003-2006 found that, among nonpregnant women of reproductive age, 37% reported use of supplements containing folic acid within the last 30 days (34). Non-Hispanic white women (37%) were more likely report use of a supplement containing folic acid than non-Hispanic black women (18%) (34). The results of a national study for the years 2003-2005 and 2007 that surveyed pregnant and nonpregnant women 18-45 years of age found that approximately 40% of all women reported daily consumption of a multivitamin, a prenatal vitamin, or a folic acid supplement (35). When examined by race, the percentage of vitamin use was higher among white women (40%) than non-white women (36%) (35).

Preterm Birth

Preterm birth is generally defined as birth before 37 weeks of completed gestation. However, there is a lack of consensus on the terminology for standard gestational age categories for infants born in the period near to term (7). As outlined by the CDC's National Center for Health Statistics, this review will refer to births less than 34 weeks as early preterm and births between 34-36 weeks as late preterm (1). Approximately 72% of all preterm births are due to infants born late preterm, with the remainder of preterm births due to infants born early preterm (7).

Preterm birth represents a major public health concern in the United States, due to its high prevalence (11.7% in 2011) and significant contribution to infant mortality and morbidity. As stated previously, preterm birth is estimated to account for more than two-thirds (67.2%) of infant deaths each year and has been identified as a risk factor for long-term neurodevelopmental disabilities, including cerebral palsy as well as vision and hearing impairments (4, 6). Accordingly, reducing the prevalence of preterm birth has been identified as a national public health priority in the following health initiatives/reports: Healthy People 2020, the 2007 Institute of Medicine Report, and the 2008 Surgeon General's Conference (6, 32, 36).

Racial Disparity in Preterm Birth

The National Institutes of Health (NIH) defines health disparities as "differences in incidence, prevalence, morbidity, mortality and burden of diseases and other adverse health conditions that exist among specific population groups in the United States (37)." The prevalence of preterm births in the United States varies greatly by race and ethnicity

(38). An issue of particular concern in the United States is the racial disparity in preterm birth rates between non-Hispanic white and non-Hispanic black women. Non-Hispanic black women are approximately 1.6 times more likely to deliver a preterm infant than non-Hispanic white women (1). Furthermore, preterm-related infant mortality rates are an estimated 3.4 times higher for non-Hispanic black women than non-Hispanic white women (38). Despite decades of research and public health initiatives, this disparity remains relatively unchanged (39). Although contributing factors to this disparity are complex, possible explanations include genetic and environmental factors, access and quality of health care, psychosocial stress, poverty, and prevalence of co-morbidities (7).

Although the majority of interventions intended to reduce preterm birth have been introduced during pregnancy, the underlying pathophysiology for preterm birth, such as inflammation/infection, may have already been initiated (39). This may serve to explain why many previous interventions have failed to reduce preterm birth (39). Research indicates that maternal health profiles prior to conception differ significantly among non-Hispanic white women and non-Hispanic black women. A previous PRAMS analysis for 27 states indicated that non-Hispanic black women were more likely to report lower rates of multivitamin use and health counseling as well as higher rates of diabetes and hypertension prior to conception than non-Hispanic white women (22). More research is necessary to determine whether improving women’s health prior to conception and in early pregnancy holds promise for reducing the disparity in preterm birth.

Risk Factors for Preterm Birth

There are different types of preterm birth which have different etiologies and risk factors (38). The types of preterm birth include spontaneous labor with intact membranes, preterm premature rupture of the membranes (which, together, are referred to as spontaneous preterm births) and medically indicated preterm birth (2). As stated previously, the majority of preterm births (approximately 65-70%) are spontaneous (2).

Common causes for indicated preterm births include pre-eclampsia or eclampsia, and intrauterine growth restriction (2). Pathways suggested to lead to spontaneous preterm birth include stress, infection or inflammation, placental ischemia, and uterine overdistension (6). There are many maternal and pregnancy characteristics that have also been associated with preterm birth. Maternal characteristics associated with preterm birth include black race, low socioeconomic and educational status, low or high maternal age, single marital status, substance use, and medical conditions such as thyroid disease, asthma, diabetes, and hypertension (2). Pregnancy characteristics associated with preterm birth include previous preterm birth, a current pregnancy that is close in temporal proximity to a previous delivery, uterine overdistension, multiple gestations, vaginal bleeding caused by placental abruption or placenta preavia, extremes in amniotic fluid volume, intrauterine infection, and cervical length of ≤25 mm (2).

Association between Vitamin Use and Preterm Birth

Cziezel et al. assessed the effect of periconceptional (a term referring to the time period before and soon after conception) multivitamin supplementation on pregnancy outcomes in a randomized controlled trial conducted in Hungary (40). Participants were advised to take either a multivitamin supplement or a trace mineral supplement daily for at least one month before conception until the date of the second missed menstrual period. The multivitamin supplement contained four minerals (calcium, phosphorous, magnesium, and iron), three trace elements (copper, manganese, zinc), and 12 vitamins (one of which was folic acid). The trace element supplement contained the same amounts of zinc, copper, and manganese as the multivitamin, but also contained vitamin C. Although there were no significant differences in the incidence of preterm birth among the study groups, it is possible that results may have been obscured by the fact that both groups were exposed to trace elements.

A prospective cohort study in North Carolina assessed preconceptional (defined as intake anytime before pregnancy), prenatal (intake anytime during pregnancy up until the time of interview or recruitment, which occurred between 24-29 weeks), and periconceptional (a combination of prenatal and preconceptional) multivitamin use and risk of preterm birth (<37 weeks) (11). Preconceptional multivitamin use (compared with nonuse) was inversely associated with preterm birth (adjusted risk ratio: 0.50 95% confidence interval [CI] 0.20, 1.25) (11). However, the number of women categorized as preconceptional users (n=93) was relatively small compared to periconceptional users (n=661) and prenatal users (n = 982) and among the preconceptional users, only five women delivered a preterm infant. After adjustment for maternal race, marital status, parity, self-reported maternal health status during pregnancy, vomiting during pregnancy, dietary intake (assessed by estimated energy intake as well as estimated daily iron intake and folate intake per 1,000 kcal), the risk of preterm birth for periconceptional and prenatal users increased to 1.10 and 1.14, respectively, signifying little to no association (11). As results indicate there is little association independent of iron and folic acid, Vahratian et al. may have over controlled for factors likely to represent the mechanism through which vitamin use influences preterm birth.

An observational study assessed the association between periconceptional multivitamin use and risk of preterm birth (<34 weeks and 34–<37 weeks) (14). Periconceptional multivitamin use was assessed at an average of 9.9 weeks gestation and was defined as multivitamin use within the last six months (not including use once the participant discovered they were pregnant). Catov et al. found that periconceptional multivitamin use was associated with a reduced risk of preterm birth at <34 weeks (adjusted odds ratio [aOR]: 0.29 95% CI 0.13, 0.64). However, periconceptional multivitamin use did not have an effect on the risk of preterm birth between 34–<37 weeks (14).

A retrospective cohort study in Massachusetts evaluated the relationship between periconceptional (defined as 28 days prior to the last menstrual period to 28 days after the last menstrual period) multivitamin use ≥4 times per week and birth outcomes with effect differences by race/ethnicity (8). Periconceptional multivitamin use was not associated with birth weight, gestational age, or weight for-gestational-age for non-Hispanic white women. However, periconceptional multivitamin use was associated with a 536-gram increased birth weight among non-Hispanic black women (p=0.001) (8). Although not significant, among non-Hispanic black women, multivitamin users had longer gestations

(1.5 days) than non-users ($p=0.71$) (8).

A large study in Denmark using the Danish National Birth Cohort (n=35,897) evaluated the timing and frequency of periconceptional (defined as 4 weeks before the last menstrual period through 8 weeks after the last menstrual period) multivitamin use on the risk of preterm birth (<37 weeks) (12). Results indicated that the relationship between periconceptional multivitamin use and preterm birth varied by prepregnancy Body Mass Index (BMI), a measure of body fat determined by weight and height. Regular multivitamin use (defined as vitamin use for 4–6 weeks out of the 6 week study interval) among women with a prepregnancy BMI <25 kg/m^2 was associated with reduced risk of a preterm birth (hazard ratio [HR]: 0.84 95% CI 0.73, 0.95), however, no comparable associations were shown for overweight women (BMI ≥ 25 kg/m^2) (12).

Summary

Published research suggests that vitamin use before and during early pregnancy may be important for reducing the risk of preterm birth and possibly, the racial disparity in preterm birth. However, there is limited research examining the relationship between maternal vitamin use prior to pregnancy and preterm birth by race/ethnicity. This study assesses the prevalence of prenatal, folic acid, or multivitamin use one month prior to pregnancy and its associations with preterm birth by race/ethnicity. This study also intends to examine whether race/ethnicity moderates the relation between prenatal, folic acid, or multivitamin use one month prior to pregnancy and preterm birth.

The hypotheses of this study are that vitamin use one month prior to pregnancy is associated with reduction in the odds of early (<34 weeks) and late (34-36 weeks) preterm birth and that race/ethnicity moderates the relation between prenatal, folic acid, or multivitamin use one month prior to pregnancy and preterm birth.

Table 1 Summary of studies of maternal vitamin use and preterm birth

Reference	Study Location Study Design & Sample	Intervention/Exposure	Outcome of interest	Association
Czeizel et al., 1994 (40)	Hungary Randomized Controlled Trial N=5,453	Daily multivitamin supplement or a trace element supplement beginning one month prior to conception until the second missed menstrual period	Preterm birth (not defined)	There were no significant differences in the incidence of preterm birth among the study groups.
Vahratian et. al., 2004 (11)	North Carolina Prospective Cohort N=2,010	Preconceptional (intake anytime before pregnancy), periconceptional (combination of prenatal and preconceptional) and prenatal multivitamin use	Preterm birth (<37 weeks)	Preconceptional vitamin use was associated with a reduced risk of preterm birth (adjusted risk ratio: 0.50 95% CI: 0.20, 1.25).
Catov et. al., 2007 (14)	Pennsylvania Prospective Cohort	Multivitamin use assessed at average of 9.9 weeks' gestation	Preterm birth (<34 weeks; 34–<37 weeks)	Periconceptional multivitamin use was associated with a reduced risk of preterm birth (<34 weeks)

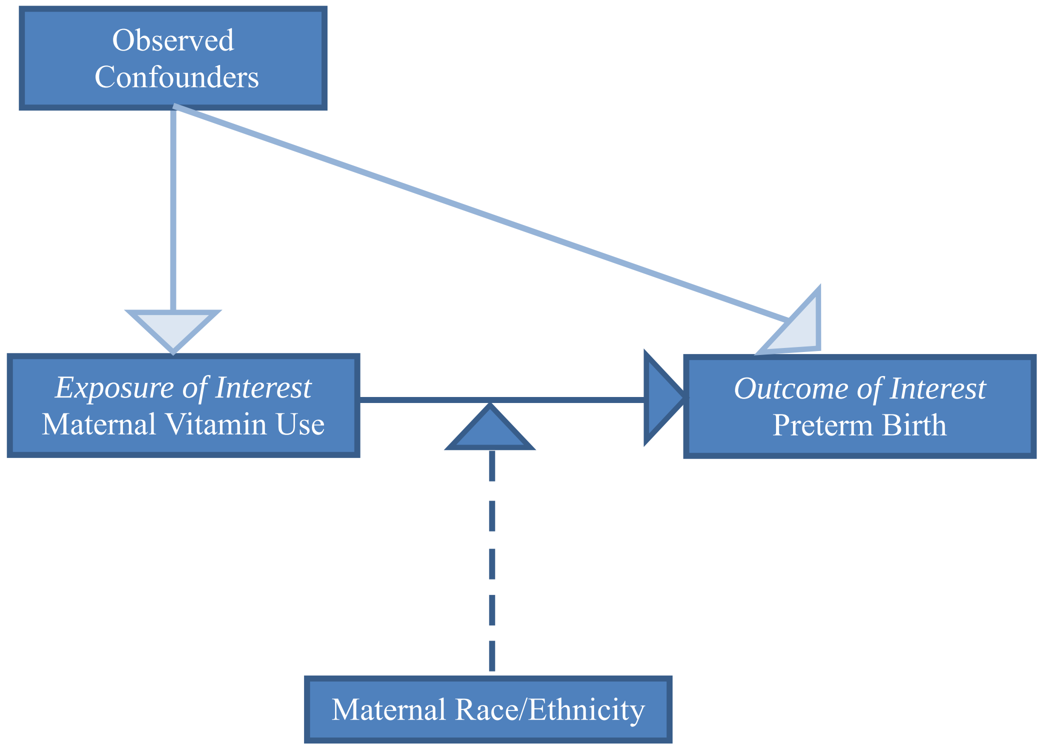
Table 1 Summary of studies of maternal vitamin use and preterm birth

Reference	Study Location Study Design & Sample	Intervention/Exposure	Outcome of interest	Association
	N=1,823 women			(aOR: 0.29, 95% CI: 0.13, 0.64).
Burris, et. al., 2010 (8)	Massachusetts Retrospective Cohort N=2,509 mother-infant pairs	Periconceptional multivitamin use (defined as 28 days prior to the last menstrual period [LMP] to 28 days after the LMP)	Gestational age and weight-for-gestational age as a measure of fetal growth	After adjustment, multivitamin use was associated with an increased birth weight (536 g) among black infants (p=0.001). Although not significant, multivitamin use was associated with longer gestations (1.5 days) among non-Hispanic black women.
Catov, et. al.,	Denmark	Periconceptional multivitamin use:	Preterm birth	Regular periconceptional

Table 1 Summary of studies of maternal vitamin use and preterm birth

Reference	Study Location Study Design & Sample	Intervention/Exposure	Outcome of interest	Association
2011 (12)	Prospective cohort N=35,897	defined as 4 weeks before the LMP through 8 weeks after the LMP	(<37 weeks)	multivitamin use was associated with reduced risk of preterm birth among women with a prepregnancy BMI <25 kg/m^2 (HR: 0.84 95% CI 0.73, 0.95).

Figure 1 Directed acyclic graph showing the relation between maternal vitamin use and preterm birth with maternal race/ethnicity as a potential moderator. Observed confounders include maternal race, parity, education, age, marital status, Medicaid recipient, WIC recipient, smoking status, and prepregnancy BMI.



METHODS

Data Source

A secondary analysis of the Pregnancy Risk Assessment Monitoring System (PRAMS) data set was performed for the years 2009-2010. Access to PRAMS data from the Centers for Disease Control and Prevention and exemption from the Emory Institutional Review Board was granted prior to beginning this study. PRAMS is a population-based surveillance system that was established in 1987 by the Centers for Disease Control and Prevention (CDC) to reduce infant mortality and low birth weight (41). PRAMS provides information on maternal experiences and behaviors before, during, and soon after pregnancy (41). Currently, forty states and New York City participate in PRAMS, representing an estimated 78% of all live births in the United States (42).

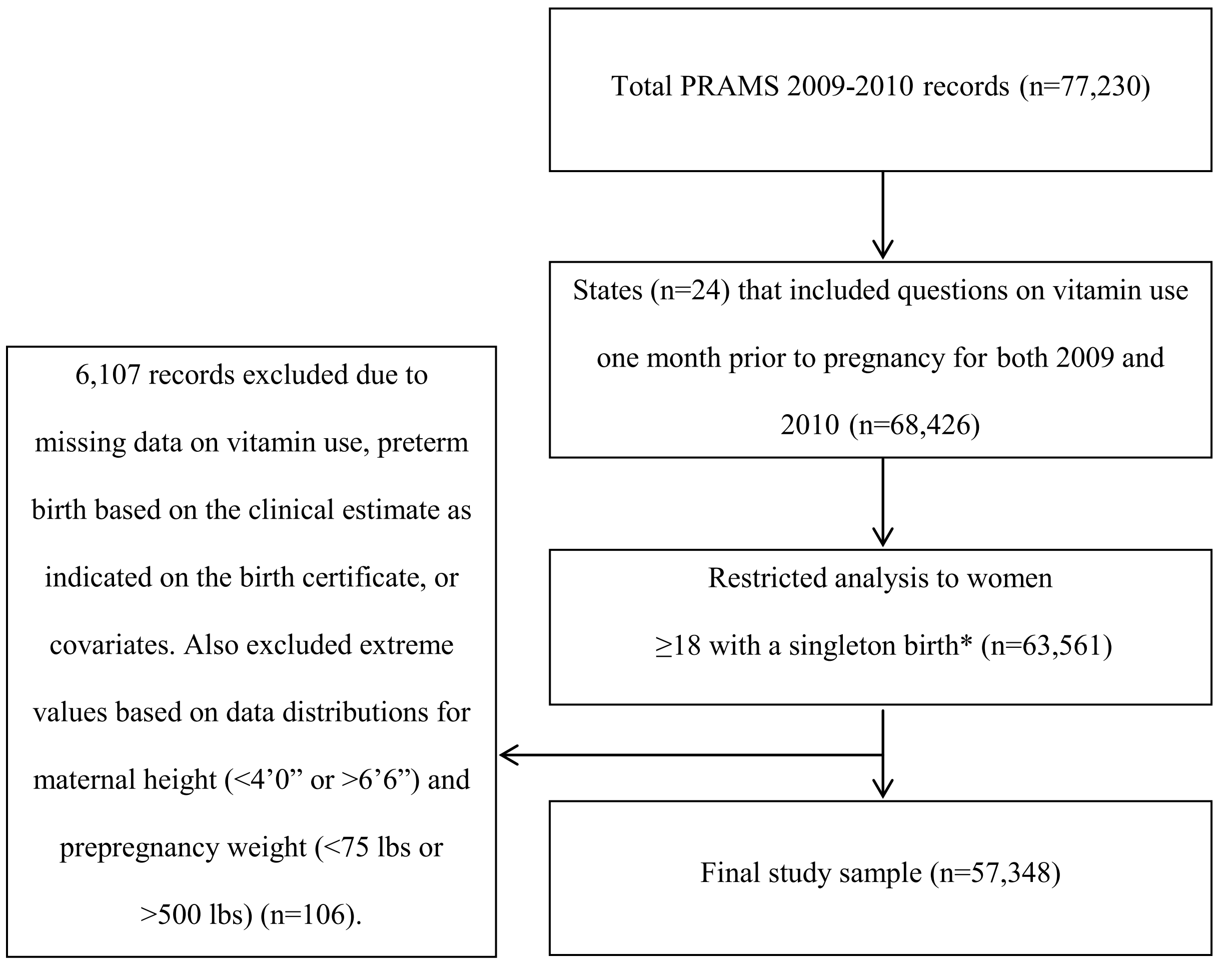
Each month, participating states draw a stratified systematic sample (obtained from the state's birth certificate file) of 100 to 250 women who have had a recent live birth, resulting in annual sample sizes that range from 1,000 to 3,400 (42). To ensure that sufficient data are available for analysis, the majority of states participating in PRAMS oversample women in smaller populations with elevated risks for preterm birth, such as women with low birth weight infants. PRAMS' standardized method of data collection includes a mailed survey sent approximately 2-4 months after delivery along with an introduction to PRAMS and an informed consent form. The informed consent document indicates to respondents that their names will not appear on any PRAMS reports, confidentiality will be maintained to the extent of the law, and that their responses will be used only for research. In the case of non-response to repeated mailing attempts, a telephone survey is initiated. The telephone survey is administered using Computer Assisted Telephone Interviewing (CATI), a software package used to confirm that all interviewers present instructions and questions in a standardized manner that is consistent with the mailed questionnaire.

The survey is comprised of 56 core questions included in all participating states' surveys, as well as state-specific questions. The PRAMS core questionnaire assesses various maternal characteristics, behaviors, and health, as well as infant development and health. Participants' responses on the surveys are linked to birth certificate data. PRAMS data are weighted to adjust for the sampling design, noncoverage, and nonresponse. PRAMS' standardized surveys and methodology allow for analyses to be conducted on a multistate level.

Inclusion/Exclusion Criteria

States that included the question related to vitamin use one month prior to pregnancy from the PRAMS questionnaire (described below) with response rates of ≥65% for the years 2009-2010 were included in the analysis (figure 2).

Figure 2 Flow diagram of sample selection for Pregnancy Risk Assessment Monitoring System (PRAMS), United States, 2009-2010



*Except for the state of Vermont, for which plurality variable was not released

The 24 states that included a question evaluating vitamin use one month prior to pregnancy for both 2009 and 2010 were Alaska, Arkansas, Colorado, Delaware, Georgia, Hawaii, Maine, Maryland, Massachusetts, Minnesota, Missouri, Nebraska, New Jersey, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, Texas, Utah, Vermont, Washington, West Virginia, and Wyoming. Records with missing data on vitamin use, preterm birth based on the clinical estimate as indicated on the birth certificate, or covariates (discussed below) were excluded (n=6,107). Prepregnancy BMI was coded as missing for extreme values based on data distributions for maternal height (<4’0” or >6’6”) and prepregnancy weight (<75 lbs or >500 lbs) (n=106). The final study sample for analysis included 57,348 participants.

Exposure and Outcome Definitions

Maternal vitamin use one month prior to pregnancy was evaluated by the response to the question: “During the month before you got pregnant with your new baby, how many times a week did you take a multivitamin, a prenatal vitamin, or a folic acid vitamin?” Responses were coded as 0, 1-3, or ≥4 times per week. Women who reported 0 vitamins per week were identified as nonusers. The outcome of interest, preterm birth (<37 weeks gestation), was further defined as early (<34 weeks gestation) or late (34-36 weeks gestation) preterm birth and was based on the clinical estimate of gestational age at birth as indicated on the birth certificate.

Covariates

The covariates included in the analysis were previously established predictors for both vitamin use and preterm birth. Covariates from birth certificate data included maternal education, marital status, parity, race/ethnicity, and age. Education was assessed by the following statement “Check the box that best describes the highest degree or level of school completed at the time of delivery.” Responses were recoded into a variable that separated the mother’s level of education into <12 years, 12 years, or >12 years. Marital status was evaluated by the response to the question “Mother married? (At birth, conception, or any time between).” Parity was assessed by responses to the statement “Number of previous live births (do not include this child).” Responses were recoded as 0, 1, or ≥2. Race/ethnicity was determined by the responses to the following question and statement: “Mother of Hispanic origin?” and “Check one or more races to indicate what the mother considers herself to be.” If the response to the question “Mother of Hispanic origin?” was unknown, the respondent’s racial/ethnic identification defaulted to her selected race.

The prevalence of reported vitamin use ≥4 times per week one month prior to pregnancy was examined among various race groups and races were combined based on similar prevalence of reported vitamin use. Accordingly, American Indian, Alaskan Native, and Hawaiian races were combined into one category. Chinese, Japanese, and other Asian races (Asian Indian, Korean, Vietnamese, Other Asian, Guamanian, Samoan, and Other Pacific Islander) were also combined. Lastly, the race categories of other non-white and mixed race were combined into one category. The final designation of race/ethnicity includes the following categories: non-Hispanic white, non-Hispanic black, Hispanic, American Indian/Alaskan Native/Hawaiian, Asian race, or other. Maternal age (18-19, 20-24, 25-29, 30-34, 35-39, or ≥40 years) was determined by the mother’s date of birth as indicated on the birth certificate.

Covariates from the PRAMS core questionnaire included WIC recipient, Medicaid recipient, smoking status, and prepregnancy BMI. Women were identified as WIC recipients if they responded affirmatively to the following question “During your most recent pregnancy, were you on WIC (the Special Supplemental Nutrition Program for Women, Infants, and Children)?" Women were identified as Medicaid recipients if they selected "Medicaid" as a response for any of the following questions:

1) "During the month before you got pregnant with your new baby, were you covered by any of these health insurance plans?"
2) "Did any of these health insurance plans help you pay for your prenatal care?"
3) "Did any of these health insurance plans help you pay for the delivery of your new baby?"

Smoking status was evaluated by participants' responses to the following questions "In the 3 months before you got pregnant, how many cigarettes did you smoke on an average day?" and "In the last 3 months of your pregnancy, how many cigarettes did you smoke on an average day?" Response options ranged from: 1) 41 cigarettes or more 2) 21 to 40 cigarettes 3) 11 to 20 cigarettes 4) 6 to 10 cigarettes 5) 1 to 5 cigarettes 6) less than 1 cigarette 7) I didn't smoke then. Participants were classified as smokers, quitters or non-smokers. Women who reported smoking any cigarettes in the three months prior to pregnancy and in the last three months of pregnancy on the PRAMS questionnaire were categorized as smokers. Women who reported smoking any cigarettes three months before pregnancy but not in the last three months of pregnancy were categorized as quitters. Women who reported no smoking at both time points were categorized as nonsmokers.

Prepregnancy BMI (categorized as <18.5, 18.5-24.9, 25-29.9, and ≥30 kg/m^2), was calculated from maternal weight and height, which was obtained from the PRAMS questionnaire. Maternal weight and height were determined by the following questions "Just before you got pregnant with your new baby, how much did you weigh?" and "How tall are you without shoes?"

Analysis

SAS-callable SUDAAN version 9.3 (Research Triangle Institute, Research Triangle Park, North Carolina) was used to account for PRAMS' complex sampling design. Weighted percentages were calculated for all analyses. Chi-square tests were used to examine bivariate associations between maternal or infant characteristics and vitamin use. Logistic regression was used to obtain the crude odds ratios and 95% confidence intervals for vitamin use (versus non-use) by race. Logistic regression was also used to produce crude odds ratios and 95% confidence intervals for both early and late preterm birth versus term births (≥37 weeks' gestation) for selected maternal characteristics. Multivariate logistic regression was used to obtain the adjusted odds ratios and 95% confidence intervals for early and late preterm birth by race/ethnicity, controlling for vitamin use. Effect modification of race/ethnicity and vitamin use was assessed and found to be significant ($P<0.15$) only among late preterm births. As a result, each race/ethnic group was modeled separately for late preterm births. Final models were adjusted for maternal race, education, age, marital status, Medicaid recipient, WIC recipient, smoking status, prepregnancy BMI, and parity.

RESULTS

Table 2 presents the distribution of characteristics of the study population by vitamin use one month prior to pregnancy. Overall, 55% of women reported no vitamin use in the month prior to pregnancy while 37% reported using vitamins ≥4 times per week. Vitamin use ≥4 times per week was higher among Asian and non-Hispanic white women, as well as women who were older, more educated, married, and nonsmokers. Vitamin use ≥4 times per week was also higher among women who reported they did not receive WIC or Medicaid.

The prevalence of early and late preterm birth by maternal vitamin use can be seen in figure 3. The prevalence of early preterm birth was slightly higher among non-users (2.3%) compared to women who used vitamins 1-3 times per week (1.9%) and women who used vitamins ≥4 times per week (1.9%). The prevalence of late preterm birth by maternal vitamin use was highest among non-users (6.3%) followed by women who used vitamins ≥4 times per week (5.8%) and women who reported vitamin use 1-3 times per week (5.5%).

The crude associations for the relationship between race/ethnicity and vitamin use can be seen in table 3. Compared to non-Hispanic white women, non-Hispanic black women were less likely to use vitamins ≥4 times per week (crude odds ratio [cOR]: 0.43 95% CI 0.39, 0.47). Hispanic women and American Indian, Alaska Native, or Hawaiian women were also less likely to use vitamins ≥4 times per week than non-Hispanic white women (cOR: 0.52 95% CI 0.47, 0.59; 0.60 95% CI 0.48, 0.74). Asian women were slightly more likely to use vitamins ≥4 times per week than non-Hispanic white women, although this difference did not reach statistical significance (cOR: 1.10 95% CI 0.96, 1.25).

Maternal characteristics associated with early and late preterm birth are presented in table 4. There was a significant decrease in the odds of early preterm birth (<34 weeks) among women who used vitamins ≥4 times per week (cOR: 0.83 95% CI 0.72, 0.95) versus non-users. The association between maternal vitamin use 1-3 times per week or ≥4 times per week and late preterm birth was not statistically significant. Women who were smokers, non-Hispanic black, or less educated were more likely to experience a preterm birth at <34 weeks or 34-36 weeks.

Table 5 shows the association between maternal race/ethnicity and preterm birth, adjusting for vitamin use. Compared to non-Hispanic white women, non-Hispanic black women were more likely to experience early preterm birth (<34 weeks) (aOR: 2.59 95% CI 2.25, 2.99) as well as late preterm birth (aOR: 1.51 95% CI 1.30, 1.76. Hispanic women and American Indian, Alaska Native, or Hawaiian women were more likely to have an early preterm birth compared to non-Hispanic white women (aOR: 1.50 95% CI 1.24, 1.80; aOR: 1.50 95% CI 1.18, 1.89).

The association between maternal vitamin use and early and late preterm birth is presented in table 6. After adjustment for covariates, the relationship between maternal vitamin use 1-3 times per week (aOR: 0.92 95% CI 0.73, 1.16) and ≥4 times per week (aOR: 1.03 95% CI 0.89, 1.18) and early preterm birth was not statistically significant.

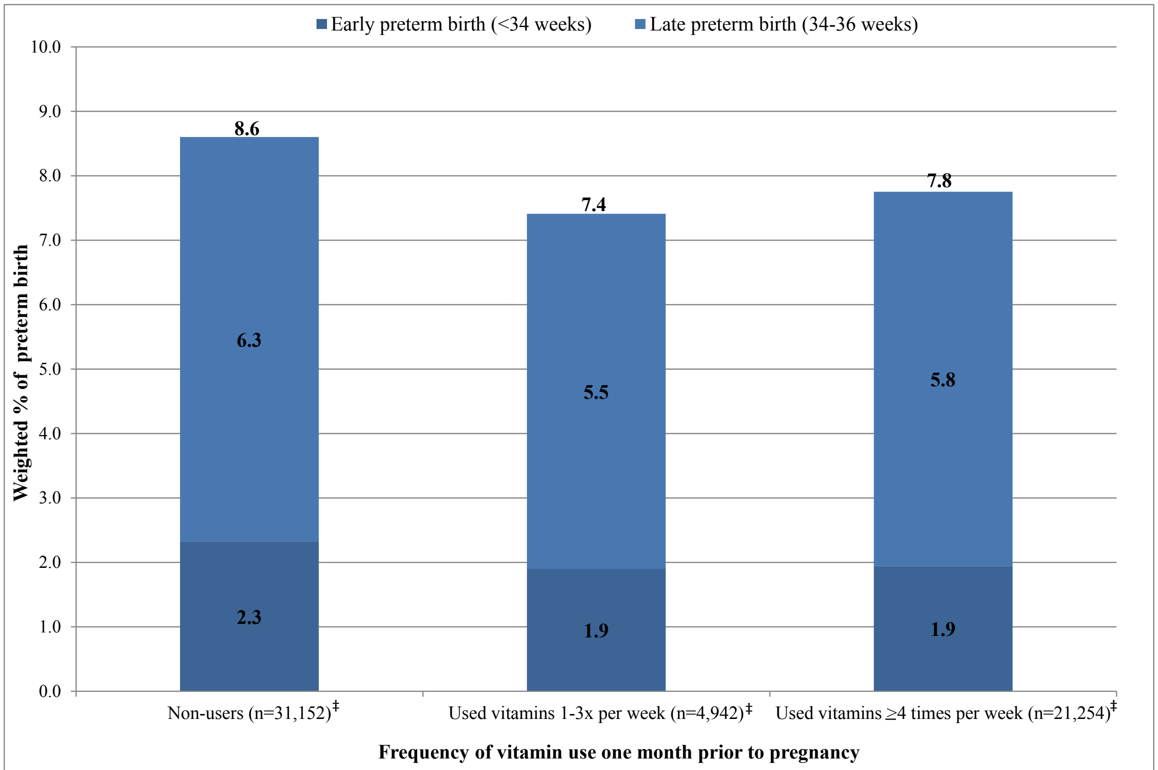
The association between maternal vitamin use and late preterm birth was not significant after adjustment for covariates except among certain racial/ethnic groups. Among American Indian, Alaska Native, or Hawaiian women, the odds of late preterm birth were lower among those who used vitamins 1-3 times per week (aOR: 0.39 95% CI 0.20, 0.76) whereas those who used vitamins ≥4 times per week had a greater odds of late preterm birth (aOR: 2.49 95% CI 1.18, 5.24).

Table 2 Distribution of maternal characteristics by vitamin use one month prior to pregnancy, PRAMS, 2009-2010, n=57,348‡

		Frequency of vitamin use one month prior to pregnancy			
	N‡	Non-users (n=31,152‡)	1-3 times/week (n=4,942‡)	≥4 times/week (n=21,254‡)	Chi-square *P* value
Maternal Characteristics					
Race/ethnicity (%)†					<0.001
Non-Hispanic White	32,844	49.3	8.7	42.0	
Non-Hispanic Black	7,621	66.1	9.9	24.1	
Hispanic	7,769	64.1	7.4	28.5	
American Indian/Alaskan Native/Hawaiian	2,842	67.2	9.4	23.4	
Asian race*	4,381	47.1	8.9	44.0	
Other	1,981	61.9	6.5	31.6	
Maternal Age (%)†					<0.001
18-19	3,794	80.2	4.7	15.2	
20-24	13,901	72.2	7.0	20.9	
25-29	17,146	53.4	8.7	37.9	
30-34	13,649	41.5	10.0	48.5	
35-39	7,151	38.4	10.8	58.8	
≥40	1,707	40.1	7.6	52.3	
Education (%)†					<0.001
<12 years	7,331	70.5	6.6	22.9	
12 years	16,065	68.7	6.8	24.5	
>12 years	33,952	44.3	9.9	45.8	
Married (%)†					<0.001
Yes	36,102	43.5	9.5	47.0	
No	21,246	73.8	7.0	19.2	
Medicaid Recipient (%)†					<0.001
Yes	9,147	65.4	8.1	26.5	
No	48,201	53.0	8.6	38.4	
WIC Recipient (%)†					<0.001
Yes	26,407	69.8	7.6	22.7	
No	30,981	42.3	9.4	48.3	
Maternal Smoking Status (%)†					<0.001
Nonsmoker	41,360	48.6	9.3	42.2	
Quitter	7,491	68.1	7.3	24.6	
Smoker	8,497	79.0	5.3	15.7	
Prepregnancy BMI (%)†					<0.001
<18.5	2,669	63.8	8.3	27.8	
18.5-24.9	28,501	50.3	8.6	41.2	
25-29.9	13,739	56.9	8.4	34.7	
≥30	12,439	60.5	8.7	30.8	
Previous Live Births (%)†					<0.001
0	24,248	53.3	7.1	39.6	
1	17,935	52.4	9.1	38.5	
≥2	15,165	59.5	10.0	30.6	

*Chinese, Japanese, Filipino, Other Asian (Asian Indian, Korean, Vietnamese, Other Asian, Guamanian, Samoan, and Other Pacific Islander)
†Based on weighted data
‡Based on unweighted data

Figure 3 Distribution of preterm birth by vitamin use one month prior to pregnancy, PRAMS, 2009-2010



Chi Square *P*-value=0.03

‡Based on unweighted data

Table 3 Association between maternal race/ethnicity and vitamin use one month prior to pregnancy, PRAMS, 2009-2010

Non-Hispanic White

Vitamin use one month prior to pregnancy	**Crude Odds Ratio (95% CI)**
0 vitamins/week	Ref.
1-3 vitamins/week	Ref.
≥4 vitamins/week	Ref.

Non-Hispanic Black

Vitamin use one month prior to pregnancy	**Crude Odds Ratio (95% CI)**
0 vitamins/week	Ref.
1-3 vitamins/week	0.85 (0.73, 0.99)
≥4 vitamins/week	0.43 (0.39, 0.47)

Hispanic

Vitamin use one month prior to pregnancy	**Crude Odds Ratio (95% CI)**
0 vitamins/week	Ref.
1-3 vitamins/week	0.66 (0.54, 0.80
≥4 vitamins/week	0.52 (0.47, 0.59)

American Indian/Alaskan Native/Hawaiian

Vitamin use one month prior to pregnancy	**Crude Odds Ratio (95% CI)**
0 vitamins/week	Ref.
1-3 vitamins/week	0.60 (0.42, 0.84)
≥4 vitamins/week	0.60 (0.48, 0.74)

Asian race*

Vitamin use one month prior to pregnancy	**Crude Odds Ratio (95% CI)**
0 vitamins/week	Ref.
1-3 vitamins/week	1.07 (0.87, 1.33)
≥4 vitamins/week	1.10 (0.96, 1.25)

Other

Vitamin use one month prior to pregnancy	**Crude Odds Ratio (95% CI)**
0 vitamins/week	Ref.
1-3 vitamins/week	0.60 (0.42, 0.84)
≥4 vitamins/week	0.60 (0.48, 0.74)

Ref=Reference group.
0 vitamins/week was selected as the referent group for vitamin use
Non-Hispanic white women were selected as the referent group for maternal race/ethnicity
*Chinese, Japanese, Filipino, Other Asian (Asian Indian, Korean, Vietnamese, Other Asian, Guamanian, Samoan, and Other Pacific Islander)

Table 4 Maternal characteristics associated with early and late preterm birth, PRAMS, 2009-2010

	Early preterm birth (<34 weeks) Unadjusted odds ratio (95% Confidence Interval)	*P*-value	Late preterm birth (34-36 weeks) Unadjusted odds ratio (95% Confidence Interval)	*P*-value
Maternal Characteristics				
Race/ethnicity		<0.001		<0.001
Non-Hispanic White	Ref.		Ref.	
Non-Hispanic Black	2.62 (2.27, 3.02)		1.52 (1.31, 1.77)	
Hispanic	1.51 (1.25, 1.83)		1.24 (1.01, 1.52)	
American Indian/Alaskan Native/Hawaiian	1.51 (1.20, 1.91)		1.39 (0.98, 1.98)	
Asian race*	1.13 (0.88, 1.46)		1.20 (0.92, 1.56)	
Other	1.75 (1.23, 2.47)		1.37 (0.92, 2.04)	
Vitamin Use One Month Prior to Pregnancy		0.01		0.26
0 times per week	Ref.		Ref.	
1-3 times per week	0.81 (0.64, 1.02)		0.87 (0.70, 1.07)	
≥4 times per week	0.83 (0.72, 0.95)		0.92 (0.80, 1.05)	
Maternal Age		<0.001		0.01
18-19	1.78 (1.33, 2.40)		0.97 (0.75, 1.24)	
20-24	1.26 (1.05, 1.51)		0.96 (0.81, 1.14)	
25-29	Ref.		Ref.	
30-34	1.14 (0.96, 1.34)		0.89 (0.75, 1.06)	
35-39	1.50 (1.22, 1.83)		0.97 (0.78, 1.20)	
≥40	1.21 (0.91, 1.76)		1.78 (1.25, 2.53)	
Education		<0.001		0.01
<12 years	1.44 (1.21, 1.70)		1.35 (1.11, 1.64)	
12 years	1.38 (1.19, 160)		1.13 (0.98, 1.30)	
>12 years	Ref.		Ref.	
Married	0.49 (0.44, 0.56)	<0.001	0.78 (0.69, 0.89)	<0.001
Medicaid Recipient	1.62 (1.36, 1.93)	<0.001	1.51 (1.27, 1.79)	<0.001
WIC Recipient	1.31 (1.15, 1.48)	<0.001	1.17 (1.03, 1.32)	0.02

Table 4 continued	**Early preterm birth (<34 weeks)** **Unadjusted odds ratio (95% Confidence Interval)**	***P*-value**	**Late preterm birth (34-36 weeks)** **Unadjusted odds ratio (95% Confidence Interval)**	***P*-value**
Maternal Smoking Status		<0.001		0.01
Nonsmoker	Ref.		Ref.	
Quitter	1.26 (1.01, 1.59)		0.91 (0.75, 1.10)	
Smoker	1.50 (1.28, 1.75)		1.22 (1.05, 1.41)	
Prepregnancy BMI		<0.001		0.01
<18.5	1.36 (1.04, 1.80)		1.63 (1.24, 2.15)	
18.5-24.9	Ref.		Ref.	
25-29.9	1.19 (1.02, 1.38)		1.03 (0.89, 1.21)	
≥30	1.72 (1.46, 2.03)		1.12 (0.95, 1.31)	
Previous Live Births		<0.001		0.02
0	1.32 (1.13, 1.53)		0.82 (0.70, 0.95)	
1	0.87 (0.74, 1.02)		0.83 (0.70, 0.99)	
≥2	Ref.		Ref.	

*Chinese, Japanese, Filipino, Other Asian (Asian Indian, Korean, Vietnamese, Other Asian, Guamanian, Samoan, and Other Pacific Islander)
Ref.=Reference group

Table 5 Association between maternal race/ethnicity and preterm birth, PRAMS, 2009-2010

	Early preterm birth (<34 weeks)		**Late preterm birth (34-36 weeks)**	
	Adjusted Odds Ratio† (95% Confidence Interval)	***P*-value**	**Adjusted Odds Ratio† (95% Confidence Interval)**	***P*-value**
Race/ethnicity		0.24		0.49
Non-Hispanic White	Ref.		Ref.	
Non-Hispanic Black	2.59 (2.25, 2.99)		1.51 (1.30, 1.76)	
Hispanic	1.50 (1.24, 1.80)		1.23 (1.00, 1.51)	
American Indian/Alaskan Native/Hawaiian	1.50 (1.18, 1.89)		1.39 (0.97, 1.97)	
Asian race*	1.14 (0.88, 1.46)		1.20 (0.92, 1.56)	
Other	1.73 (1.22, 2.45)		1.36 (0.91, 2.03)	

Ref=Reference group
*Chinese, Japanese, Filipino, Other Asian (Asian Indian, Korean, Vietnamese, Other Asian, Guamanian, Samoan, and Other Pacific Islander)
†Adjusted for vitamin use one month prior to pregnancy

Table 6 Association between maternal vitamin use one month prior to pregnancy and preterm birth, PRAMS, 2009-2010

	Early preterm birth (<34 weeks) **Adjusted Odds Ratio†** **(95% Confidence Interval)**	***P*-value**
Vitamin use one month prior to pregnancy		0.67
0 vitamins/week	Ref.	
1-3 vitamins/week	0.92 (0.73, 1.16)	
≥4 vitamins/week	1.03 (0.89, 1.18)	

Ref=Reference group

†Adjusted for maternal race, education, age, marital status, Medicaid recipient, WIC recipient, smoking status, prepregnancy BMI, and parity

Vitamin use one month prior to pregnancy	**Late preterm birth (34-36 weeks)** **Adjusted Odds Ratio†** **(95% Confidence Interval)**	***P*-value**
Non-Hispanic White		0.90
0 vitamins/week	Ref.	
1-3 vitamins/week	1.02 (0.78, 1.33)	
≥4 vitamins/week	0.97 (0.81, 1.16)	
Non-Hispanic Black		0.67
0 vitamins/week	Ref.	
1-3 vitamins/week	0.91 (0.57, 1.46)	
≥4 vitamins/week	0.87 (0.64, 1.19)	
Hispanic		0.41
0 vitamins/week	Ref.	
1-3 vitamins/week	0.64 (0.33, 1.26)	
≥4 vitamins/week	1.02 (0.67, 1.55)	
American Indian/Alaskan Native/Hawaiian		<0.001
0 vitamins/week	Ref.	
1-3 vitamins/week	0.39 (0.20, 0.76)	
≥4 vitamins/week	2.49 (1.18, 5.24)	
Asian race*		0.25
0 vitamins/week	Ref.	
1-3 vitamins/week	0.88 (0.46, 1.69)	
≥4 vitamins/week	1.43 (0.87, 2.34)	

Table 6 continued	**Late preterm birth (34-36 weeks) Adjusted Odds Ratio† (95% Confidence Interval)**	
Other		0.41
0 vitamins/week	Ref.	
1-3 vitamins/week	0.41 (0.10, 1.66)	
≥4 vitamins/week	0.69 (0.31, 1.55)	

Ref=Reference group

†Adjusted for education, age, marital status, Medicaid recipient, WIC recipient, smoking status, prepregnancy BMI, and parity

*Chinese, Japanese, Filipino, Other Asian (Asian Indian, Korean, Vietnamese, Other Asian, Guamanian, Samoan, and Other Pacific Islander)

DISCUSSION

Overall, 55% of women reported no vitamin use in the month prior to pregnancy while 37% reported using vitamins ≥4 times per week. This finding is similar to an analysis of the 2004 Pregnancy Risk Assessment Monitoring Systems data set for 26 states, which found that multivitamin use ≥4 times per week one month prior to pregnancy was 35% (22). Although the prevalence of multivitamin use (47%) among nonpregnant women of reproductive age in a recent analysis of Behavioral Risk Factor Surveillance System data appears to be higher than the findings reported in this study, this is likely due to a difference in classification of the frequency of vitamin use, as BRFSS participants were categorized as either currently taking multivitamins or not currently taking multivitamins (33). Upon further examination, when vitamin use was classified as use or non-use for PRAMS participants, results were similar, given that 45% of respondents reported vitamin use in the month prior to pregnancy.

The results of this analysis do not support an association between maternal vitamin use in the month prior to pregnancy and early preterm birth. This finding differed from the results of a study by Vahratian et al. and Catov et.al, who found that preconceptional multivitamin use was associated with a significant reduction in the risk of early preterm birth (11). However, the number of preconceptional users in the study performed by Vahratian et al. was relatively small (n=93) and findings were based on only two cases of early preterm birth (<35 weeks). Additionally, both studies classified multivitamin use differently and more broadly than this study. For example, Vahratian et. al classified preconceptional multivitamin use as anytime before pregnancy and Catov et. al classified women as periconceptional multivitamins users if they indicated they used multivitamins at least once per week in the past 6 months (assessed at an average of 9.9 weeks gestation) (12). Differences in the measurement of maternal vitamin use may serve to explain other studies observed an association between maternal vitamin use and early preterm birth.

Race/ethnicity moderated the relation between maternal vitamin use one month prior to pregnancy and late preterm births, as evidenced by a significant association between maternal vitamin use and late preterm birth among American Indian, Alaska Native, or Hawaiian women. These findings are similar to an observational study in Massachusetts that found race/ethnicity moderated the relationship between maternal vitamin use and birth weight (8). Among white women, periconceptional multivitamin use was not associated with birth weight. However, among black women, multivitamin use was associated with a 536-gram increased birth weight ($p=0.001$).

This study has a number of potential limitations attributed to PRAMS' retrospective, cross sectional study design. As participants are surveyed 2–4 months following delivery, there is an increased likelihood of recall bias, given that participants report the frequency of vitamin use one month prior to pregnancy, which, by the time of receiving the survey, may have been at least a year ago for many respondents. There is also a possibility of information bias, given that vitamin use is self-reported. A study that examined the use of prenatal multivitamin/mineral supplements among pregnant women indicated that respondents tend to overestimate use (43).

There may be misclassification of some multiple births as singletons because the state of Vermont does not release data as to whether a birth was a singleton or multiple birth. However, National Vital Statistics System data indicate the proportion of multiple births in Vermont is relatively small compared to singleton births (3.4% versus 96.6%, respectively) and is comparable to the distribution of multiple and singleton births in the United States (3.5% versus 96.5%, respectively) (44, 45). Furthermore, Vermont data represent only 0.4% of all births included in the analysis. An additional limitation is that all preterm births were included in the analysis, as PRAMS does not distinguish between medically indicated and spontaneous preterm births, which may have different risk factors. A final limitation of the study was that BMI was used for as a measure for women 18-20, although BMI is typically reserved for adults 20 or older.

Strengths and Implications

This study has multiple strengths. First, PRAMS uses standardized methods for data collection, which allows for a multistate analysis. Additionally, because PRAMS collects a wide range of data, including clinical information, this analysis could control for important covariates. To my knowledge, this is the first research initiative that assesses the relationship between vitamin use and the risk of preterm birth by race/ethnicity on a multistate, population level. The results of this study indicate that further research is necessary on this topic, given that for some racial/ethnic groups, exposure to vitamins prior to pregnancy is significantly associated with late preterm birth in the opposite direction hypothesized. To minimize the potential for recall bias, large prospective cohort studies should be conducted to further examine the relationship between maternal vitamin use prior to conception and in early pregnancy and preterm birth. Ultimately, more research is necessary to identify modifiable health risk behaviors for preterm birth. This will allow for the planning of appropriate public health recommendations, services, and health education interventions to reduce the prevalence and racial disparities in preterm birth (46).

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