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PATTERN OF MULTIVITAMIN USE: PREVALENCE AND PREDICTORS AMONG PREGNANT WOMEN IN NEW MEXICO

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THESIS

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Pattern of Multivitamin Use: Prevalence and Predictors among Pregnant Women in New Mexico

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ABSTRACT

Background: Prenatal vitamin use is recommended as a necessary supplement prior to conception and throughout pregnancy. Multivitamin use in early pregnancy can significantly reduce risks for birth defects: cardiovascular defects,[1, 2] limb defect,[3-5] urinary tract abnormalities,[4, 6] orofacial clefts,[7, 8] and neural tube defects (NTDs). [2, 9-16] Sixty-nine to seventy-eight percent of women take vitamins after pregnancy recognition, while only 23-35% of women in the U.S. start to use vitamins before pregnancy recognition.[17-19] Rates of NTDs by ethnicity demonstrat that Hispanics have the highest prevalence (4.2 per 10,000 births) than Non-Hispanics. (Non-Hispanic Black or African American: 3.2 per 10,000 births; Non-Hispanic Whites: 2.6 per 10,000 births).[20] **Objectives:** To explore the prevalence rates of multivitamin use during pregnancy and to find out the predictors of vitamin use using an established cohort in New Mexico. **Methods:** This is a cross-sectional analysis which used data from the "Safety of Medication and Perception of Teratogenicity

(SMART)" study. Patients in the SMART study were recruited from 5 University of New Mexico affiliated prenatal clinics. Patients were considered vitamin users if they took vitamins at least 4 times a week. Based on the different time exposure to vitamins, vitamin use was further categorized into three groups: pre-conceptional vitamin users, vitamin users after pregnancy recognition, and vitamin non-users. Chi square and ANOVA were used to identify potential predictors including sociodemographic characteristics, lifestyle characteristics, medical and reproductive health, and medication use. For multivariate analysis, ordinal logistic regression and polychotomous logistic regression model were used. **Results:** Most pregnant women (71.9%) in the sample began to take vitamins regularly after pregnancy recognition. Earlier vitamin use in pregnancy was significantly associated with pregnancy planning independent of other maternal characteristics. Education level and health insurance status revealed a significant interaction with respect to vitamin use. Lastly, almost one third (32.1%) of women in this study had a history of adverse pregnancy outcomes and 45.0% of women had at least one medical condition. Vitamin non-users were more likely to have experience of adverse pregnancy outcomes in prior pregnancies compared to women who used vitamin after pregnancy recognition. **Implication:** This study highlights the importance of promoting vitamin use in New Mexico in women of childbearing years prior to conception and in early pregnancy, given the finding that less than one third of women used vitamins during the pre-conceptional period. Public health strategies should also include the promotion of pregnancy planning.

Key word: Vitamin, Pregnant women, Predictors, Prevalence, Ordinal Logistic Regression, Polychotomous Logistic Regression

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CHAPTER I: INTRODUCTION

Background

Multivitamins are considered as a necessary supplement for pregnant women.[21] They contain a wide range of supplements including water-soluble/fat soluble vitamins (e.g. vitamin A, vitamin B, folic acid) and minerals, most of which have been recommended for prenatal use in the U.S.[22, 23] Women can benefit from using prenatal multivitamins during pregnancy. For instance, the risks of having preterm birth and preeclampsia can be reduced.[24, 25] Prior evidence indicated that prenatal multivitamin supplementation can provide protective effects against a series of birth defects including cardiovascular defects,[1, 2] limb defects,[3-5] orofacial cleft,[7, 8] urinary tract anomalies,[4, 6] congenital hydrocephalus,[26] respiratory tract defects,[26] and omphalocele.[27] In addition, periconceptional use of prenatal multivitamins containing folic acid is associated with decreased risk for Neural Tube Defects (NTDs).[2, 9-16]

Among many birth defects, NTDs, a structural birth defect, are one of the most severe congenital malformations in human beings.[28] NTDs are a series of malformation of the developing brain and spinal cord, and it occurs when there is an incomplete closure of the neural tube within a month of fertilization.[29] Anencephaly and spina bifida are the most common NTDs, and they affected around 300,000 newborns worldwide.[30] In the U.S., the number of NTD affected pregnancies decreased after the introduction of food fortification in 1998. A CDC report analyzed data from 23-poplation-based surveillance systems and comparing the prevalence of NTD before and after folic acid

fortification (1995-1996 vs. 1999-2000), suggesting that the average annual number of NTD-affected pregnancies was 3,020, comparing to 4,130 before food fortification.[31] However, the recent national data from 14 states showed that anencephaly and spina bifida still affected 859 and 1460 babies each year in the U.S., respectively.[32, 33] The causes of NTDs can be either environmental or genetic, but the causative mechanism of NTDs is still unclear and poorly studied.[28, 34] However, a majority of current clinical studies found that periconceptional multivitamin supplementation containing folic acid can have a protective effect against neural tube defects.[2, 9-16] In addition, a meta-analysis summarized the findings and showed that the overall effect of periconceptional use of multivitamin plus folate was significantly effective in protecting against NTDs.[29]

In the U.S., the prevalence of multivitamin use during pregnancy has been documented by previous studies and ranges from 68.8-78%.[19, 35] Unfortunately, the prevalence of regular prenatal multivitamin use (at least 3 times per week) is reported 53.8%.[36] Although a study using data from the National Maternal and Infant Health Survey (NMIHS) showed that the prevalence rate of multivitamin regular use was 82.5% in pregnancy.[37] This prevalence combined mineral use with multivitamin use and therefore might amplify the estimation of prevalence of multivitamin use in pregnancy.

While the majority of women initiate multivitamin use after pregnancy recognition, only 24.0% of women reported having ever used multivitamins during periconceptional period[35]- the most crucial period for organogenesis.

Multivitamin use during the first semester might be higher, but still in sufficient (29.3%).[38] With regard to multivitamin regular use during periconceptional period, the prevalence of periconceptional multivitamin regular users (at least 3 times per week) was reported around 21.0%.[36] Before recognition of pregnancy, studies showed that only 26% of women reported using multivitamins regularly (at least 3 times a week).[37] Two Centers for Disease Control and Prevention (CDC) reports using data from Pregnancy Risk Assessment Monitoring System (PRAMS) suggested that the prevalence of pre-conception multivitamin use was 23-45.2%.[18, 39]

Unplanned pregnancies may account for the difference in prevalence rates of multivitamin use between periconceptional period and after the recognition of pregnancy.[40] Women with unintended pregnancies become aware of their pregnancies at a later gestational age than women who planned their pregnancies.[41] As a result, the time of multivitamins exposure during periconceptional period may be delayed for women who did not plan a pregnancy.

Difference in prevalence of multivitamin use among pregnant women was also found among different racial groups. Only 25.6% and 67.0% African American use multivitamins in periconceptional period and later in pregnancy, respectively. On the other hand, 55.0% and 84% non-Hispanic white mothers use multivitamins in these two periods.[37, 42] For Hispanics, a national investigation using data from the Behavioral Risk Factor Surveillance System (BRFSS) showed that 66.4% of Hispanic pregnant women reported having

ever used multivitamins since pregnancy.[19] Data obtained from the National Birth Defects Prevention study showed that the prevalence of periconceptional intake of folic acid-containing supplements is only 30% among Hispanics, which is the lowest comparing to other racial groups (Non-Hispanic White: 66%; Non-Hispanic Black: 39%).[43]

Some evidences show that Hispanic women might have a high rate of adverse pregnancy outcome comparing to non-Hispanic white women. Before the introduction of mandatory food fortification in 1998, it has been documented that the prevalence of NTD is almost 3 times higher among infants of Hispanic women than that for non-Hispanic white women.[44-46] Although the overall trend of NTD prevalence has declined since fortification, the prevalence of NTD is still greater in Hispanics (4.17 per 10,000), comparing to non-Hispanics (Non-Hispanic Black or African-American: 2.64 per 10,000; Non-Hispanic Whites: 3.22 per 10,000)[20] Also, a CDC report using data from the Pregnancy Risk Assessment Monitoring System (PRAMS) found that the prevalence of having a low birth weight infant was higher among Hispanics than Non-Hispanic white women.[47] Moreover, a cross-sectional study used data from the National Birth Defects Prevention Study and found that foreign-born Hispanics had a higher risk of delivering babies with spina bifida than US-born Hispanics, and the higher prevalence of NTDs was also found among recent immigrants from foreign countries.[48] In addition, a low or deficient level of folic acid are found among Hispanic women because they are more likely to become pregnant relatively soon after giving birth.[49] The national vital statistics

reports in 2005 showed that Hispanic women have a higher birth rate and often had children at an older age.[50]

The lack of knowledge about benefits of vitamin use among Hispanic women might at least partially explain the higher prevalence of NTDs in Hispanics compared to Non-Hispanic Whites and African American women. However, there are also other factors that might account for a higher prevalence rate. Environmental exposures might be a contributing factor. For instance, pesticide exposure might be higher among Hispanic women, especially women involved in the farm labor, as demonstrated in some prior studies.[51] A population-based case-control study among Mexican-born Hispanics demonstrated that cigarette smoke, including second-hand exposure, significantly increased risk of NTDs.[52] Cultural norms and fatalism could also be a potential explanation for high prevalence of NTDs at birth. Religious beliefs, one important component of Hispanic culture norms, make it possible that Hispanic women are less likely to abort their children regardless of possible birth defects. Moreover, in fatalistic attitudes among Hispanics, they might believe that life events are predetermined. Therefore, Hispanic mothers may be less likely to participate in prenatal screening. As a result, Hispanic mothers might be more likely to deliver babies with NTDs than Non-Hispanic mothers.

There is a great need to compare the prevalence of periconceptional and preconception multivitamin regular use among Hispanics vs. non-Hispanic Whites, which can help us estimate the difference in the vitamin use between

Hispanic women and other racial groups. In addition, understanding specific predictors can identify those Hispanic women who are at risk of not using prenatal multivitamin. This is important as culturally–sensitive interventions can be developed and promote early vitamin use in pregnancy among Hispanic women.

Special Aims

The main purpose of this research is to investigate the prevalence of regular multivitamin use among different racial/ethnic groups of pregnant women and to describe the maternal characteristics of regular vitamin users. Specifically, the following aims are proposed:

Aim 1) To determine the differences in the prevalence of multivitamin regular use (at least 4 times per week) in preconception period (at least one month before last menstrual period) and in pregnancy (after pregnancy recognition) between Hispanic and non-Hispanic pregnant women.

Hypothesis 1: we hypothesize that the prevalence of preconception multivitamin regular use will be lower in Hispanic than in Non-Hispanic women.

Aim 2) To examine the predictors (e.g. ethnicity, education level, insurance status, age, marital status, pregnancy intention, smoking status, alcohol use, recreational drug use, parity, gravidity, a family history of birth defects, the use of prescription medications) of not preconception multivitamin regular use from an established cohort of pregnant women in New Mexico.

Hypothesis 2: we hypothesize that pregnant women who did not use multivitamins in preconception period are more likely to be Hispanics, less educated, younger, uninsured, unmarried, had an unintended pregnancy intention, are foreign born, multiparous, multigravida, speaking Spanish, current smokers, periconceptional binge drinker, recreational drug user, without a family history of birth defects, and use less than 2 kinds of prescription medications.

CHAPTER II: LITERATURE REVIEW

The literature review for this study is organized into following sections: (1) the benefit of using multivitamin during pregnancy and periconceptional period; (2) the prevalence of multivitamin use among pregnant women; 3) predictors of multivitamin use; 4) definition of multivitamin use in periconceptional period and early pregnancy in different studies; 5) a review of economic evaluations on food fortification and folic acid use.

The Benefit of Multivitamin Use in Pregnancy

We systematically reviewed the benefits of multivitamin supplementation use in pregnancy and summarized contents as following categories: cardiovascular defects, limb defects, urinary defects, orofacial defects, neural tube defects, and other defects and adverse perinatal adverse outcomes.

Cardiovascular Defects

There are many types of cardiovascular defects, such as transposition of great arteries (TGA), hypoplastic left heart syndrome (HLHS), atrioventricular septal defect (ASD). In the U.S., it has been estimated that TGA, HLHS, and ASD occurred 1 cases in 3,333 births, 1 case in 2,122 births, and 1 case in 4,344 births.[32] It also accounts for a major cause of infant deaths.[53] Some studies showed a significant association between the use of multivitamin containing folic acid in pregnancy and occurrence of cardiovascular defects of infants.[1, 2] One randomized clinical trial from Hungary found that the risk of congenital cardiovascular malformations (e.g. ventricular septal defect, aortic stenosis, patent ductus arteriosus) was significantly lower among women daily used

periconceptional multivitamins with 0.8 mg folic acid at least one month before conception.[2] A population-based case-control study from the U.S. also confirmed that the periconceptional multivitamin use (any multivitamin use 3 month before to 3 months after conception) can reduce the risk of congenital heat defects (OR=0.60-0.97).[1] In contrast, a case-control study collected data from Slone Epidemiology Unit Birth defects Study, tested a series of selected birth defects but did not find a significant association between preconceptional multivitamin supplementation (2 month before last menstrual period) and risks of conotruncal defects.[4] This result is consistent with the Baltimore-Washington Infant Study (BWIS), a large case-control study, which showed no protective effect of multivitamin use during the first 5 weeks of gestation.[54] These two contradicting results may be due to differential maternal recall of multivitamin use in the Slone Epidemiology Study or the fact that the interview in BWIS study was conducted prospectively before the infant's birthday while other studies respectively interviewed mothers after the delivery of infants.

Limb Defects

There are two major types of limb defects: upper limb (e.g. arms) defects and lower limb (e.g. leg) defects. There are approximately 1,500 babied in the U.S. born with upper limb defects and 750 with lower limb defects for each year.[33] Periconceptional use of multivitamin can also provide a protective effect against limb defects. A few case-control studies suggested that women who used multivitamin periconceptionally (from 3 months before conception until 3 months after pregnancy) could significantly reduce (OR=0.3-0.64) the risk of

developing infants with limb defects.[3, 5] One of the case-control studies specified that this protective effect was significant in transverse limb defects but not in other limb defects, such as preaxial and postaxial deficiencies.[5] In addition, a meta-analysis conducted by Canada showed that use of multivitamin supplements before during the first trimester of pregnancy provided consistent protection against limb defects (OR=0.48, 95% CI=0.30-0.76).[55] However, a case-control study conducted in Boston, Philadelphia, and Toronto during 1993-1996 did not find a significant reduction in limb defects among women who used multivitamins regularly before and in the first trimester use[4] The reason might be due to non-population based subject ascertainment and selection bias.

Urinary Tract Anomalies

In the United States, congenital malformation of the genitourinary system caused 518 deaths per 100,000 live infant per year.[56] Several studies have been done and demonstrated that periconceptional multivitamin use could significantly reduce the risk of urinary tract anomalies, such as rental agenesis, obstructive congenital abnormalities of the urinary system.[4, 6, 57] Of note, the risk reduction become smaller when multivitamin use was limited to the second or third trimester, which was reported by a case-control study, using data from the Slone Epidemiology Unit Birth defects Study.[4] A randomized double-blind controlled trial from Hungary was conducted and found that the daily periconceptional use (at least one month before conception and at least until the date of the second missed menstrual period) of multivitamin containing 0.8 mg of folic acid can significantly reduce the rate of urinary tract abnormalities.[57]

However, the same author did not find this association in a follow up case-control study.[2] The protective effect of periconceptional multivitamin use might be attenuated due to potential selection bias.

Orofacial Clefts

cleft lip with or without cleft palate (CLP) and cleft palate alone (CP) are two kinds of main orofacial clefts, and it has been reported that CLP and CP affected approximately 1 in 941-1000 and 1 in 1574-2500 infants, respectively.[32, 58] Mixed findings have been found with regarding to the protective effect of multivitamin use and occurrence of orofacial clefts. Some studies reported that the risk reduction for CLP but not for not in CP among women who used multivitamins regularly during periconceptional period (3 months before through 3 months after conception),[10, 58] while other studies found a reduction for CP but not for CLP.[59] In addition, one case-control study reported that the greatest reduction in the risk of CLP occurred with periconceptional multivitamin use (28 days before through 28 days after conception).[4] Also, there are other studies showing that the risks of both CP and CLP can be reduced by using multivitamin periconceptionally (one month before through two months after conception).[60] On the contrary, there is one case-control study which did not find any significant associations between the periconceptional multivitamin supplementation containing folic acid and reducing risk of CP or CLP.[61] Recall bias might be a problem in this study when women were asked to report multivitamin use that occurred up to more than one year before the time of interview.

NTD (Neural tube defects)

NTD is a severe structural defect due to the incomplete closure of the neural tube within a month of fertilization.[29] The most common types of NTD are anencephaly and spina bifida. Infants born with anencephaly usually die within the first few hours/days after delivery, while a majority of infants born with spina bifida grow to adulthood exhibiting only physical disability but having normal neurobehavioral development.[22] The medical costs for the first year of life for a child with spina bifida was $52,415.[62] It is still unclear of the causative mechanism, but there are extensive studies which suggested that the use of periconceptional multivitamin supplementation (from 3 months before and through 3 months after conception) can have a protective effect against NTDs.[2, 9-16] A randomized double-blind prevention trial was conducted in 7 countries and find that periconceptional multivitamin containing folic acid (4 mg folic acid per day) can reduce recurrence risk of NTDs, but whether lower doses had same protective effect was unknown.[9] Another randomized trial suggested that a daily dosage of 0.36 mg of folic acid could still be as protective as a daily dosage of 4 mg of folic acid [15]. Moreover, one case-control study from California found that there was a significant reduction associated with periconceptional multivitamin use (from 3 months before and through 3 months after conception) for NTD.[10] Due to different study design and multivitamin supplementation measurement, some studies, however, did not find a protective effect of periconceptional multivitamin supplementation on preventing neural tube defects.[14, 63-65]

Other Defects and Adverse Perinatal Outcomes

There are a number of studies which evaluated other birth defects and adverse pregnancy outcomes. A population-based case-control study found that periconceptional use (3 months before pregnancy through the first trimester of pregnancy) of multivitamin could reduce the risk for omphalocele, an abdominal wall defect.[66] However, the precision of this study was limited by small sample size in case-infants, which only 72 cases were ascertained. A population-based Atlantic Birth Defects Case-Control study examined the associations of periconceptional multivitamin use (from 3 months before pregnancy through the first 3 months of pregnancy) and respiratory tract defects, pyloric stenosis, anal atresia, but none of them yielded a significant result.[26]

The association of preterm birth and multivitamin use is also studied. Case-control studies suggested that its risk could be reduced approximately 1.6-2 folds with multivitamin supplement use during pregnancy.[38, 67] Surprisingly, a case-control study reported that multivitamin use during the third trimester was increased risk of preterm birth.[68] The interpretation of this result, however, needs to be caution, and the mechanism is unclear.

The association between adverse pregnancy outcome (miscarriage, ectopic pregnancy, and stillbirth) and the use of multivitamin containing folic acid during periconceptional period was also studied, but none of them was reported significantly associated with periconceptional multivitamin supplementation use.[9, 69, 70]

Preeclampsia is considered to a pregnancy-related disorder, and it remains a significant health problem in obstetric population. A prospective cohort study was designed to detect factors of preeclampsia in the United States, and the results showed that the periconceptional multivitamin use was associated with 45% of reduction in preeclampsia risk comparing to nonusers.[71] Another study found that regular multivitamin use in the periconceptional period was significantly associated with reduced risk of preeclampsia among normal-weight women.[24] However, more studies need to be done in this area in order to further confirm this result.

In addition to preeclampsia, periconceptional multivitamin supplementation (not specifically defined) can also significantly reduce the incidence of pregnancy-induced vertigo, nausea, and vomiting, which reported by a randomized placebo-controlled trial.[72]

The Prevalence of Multivitamin Use

Prevalence of Multivitamin Use Anytime in Pregnancy

There is a variation in the prevalence of using multivitamins during pregnancy. In the United States, it was previously reported in 1998 that 53.8% of women from the National Maternal and Infant Health Survey reported using either multivitamin and minerals 3 times per week after pregnancy recognition.[36] After the introduction of mandatory folic acid fortification, the prevalence rate went up and ranges from 68.8-78% in 2009.[19, 35]

In Europe, the prevalence of multivitamin use during pregnancy was reported as 76.2% in Portugal, which was highest comparing to other countries in Europe.[73] Unfortunately, the comparability of the data on the prevalence of multivitamin use was undermined by combining minerals use with multivitamins. Besides, there were another two studies estimating prevalence by combining multivitamins and minerals. One study suggested that 30.8% of participants using multivitamins minerals during pregnancy,[74] while another study broken down the prevalence rate and specified it into three trimesters periods, revealing that 23.3%, 14.1%, and 18.6% of women used multivitamin-mineral during the first trimester, second semester, and third trimester, respectively.[68] In addition, in Australia, the prevalence rates of multivitamin use during pregnancy were between 18-35%[75, 76]. In Brazil, the prevalence of multivitamin use was 14% as reported.[77]

Prevalence of Multivitamin Use in Periconceptional Period

In the U.S., the prevalence of periconceptional multivitamin (begin before pregnancy and continue to use in pregnancy) was reported as 21-23.8%.[35, 36] There were also studies which attempted to specify the time frame of multivitamin exposure during periconceptional period. A Pregnancy Exposure and Preeclampsia Prevention Study (PEPPS) found that 47% of women took multivitamins/prenatal vitamin at least once per week during periconceptional period (from 3 months before pregnancy through the first 3 months of pregnancy).[78] Recall bias might impact on the prevalence rate estimation in this study while women were asked to remember multivitamin use 3 months before pregnancy. A National Birth Defects Prevention (NBDP) Study further

examined periconceptional multivitamin use (one month before LMP and through the month after LMP) and pregnancy intention and found that 35.7% of women who did not plan for the pregnancy used periconceptional multivitamin, while the prevalence of periconceptional multivitamin use among women who had a pregnancy intention was reported as 59%.[79] In Canada, a cross-sectional analysis conducted in Toronto Hospital and the Mount Sinai Hospital found that only 28% of women reported using multivitamin supplementation containing acid during periconceptional period (at least 4 weeks prior to conception until 8 weeks after conception).[80] Additionally, preconception multivitamin use-multivitamin use during the month before pregnancy- was also studied. Data from PRAMS showed that the prevalence of preconception multivitamin regular users (≥ at least 4 times per week) was 23.0-43.6%.[18, 39, 47 81]

In Europe, a study from Demark using data from Danish National Birth Cohort and found that 65% of women had used multivitamins in periconceptional period (4 weeks before LMP through the 8 weeks after LMP).[24] The high prevalence is because of the fact that Caucasian women accounted for most of this population in Denmark and they were more prone to use periconceptional multivitamins. To the contrast, two other studies, one from Sweden using women who attended antenatal care units and another from Norway using Medical Birth Registry, found that 15.9-19% of women used vitamin during periconceptional period (not specifically defined: before pregnancy and during pregnancy).[49, 82] Regarding to preconception multivitamin use, one study from Hungary reported that the prevalence of

preconception multivitamin regular use was 43.8%.[83] However, all the data on multivitamin use were based on self-reports from voluntary participants, which might have a potential selection bias.

In Australia, a cross-sectional analysis showed that 12.3% of women had used multivitamins during periconceptional period (3 months prior to pregnancy and during pregnancy).[76] Another cross-sectional survey from Australia found that 21.8% of women had used multivitamin during periconceptional period (not specifically defined: before and during pregnancy).[75]

Multivitamins vs. Prenatal Vitamins

Most studies assumed that prenatal vitamins and multivitamins are similar in contents. Information of multivitamins and prenatal vitamins in other studies was mixed, and multivitamin users were identified if women reported having taken multivitamin or prenatal vitamins.[35, 38, 47, 78, 79, 81] Therefore, we cannot separately specify the prevalence of prenatal vitamin use from these results. It is of note that there is one study from U.S. that investigated the prevalence of prenatal vitamin use among women at rural outreach clinics and reported that 92% of women had used prenatal vitamins during pregnancy.[84] For most of other studies, the use of prenatal vitamins was not separately specified to investigate the prevalence.

Predictors of Multivitamin Use

Studies identified examined the maternal characteristics of multivitamin users. Prenatal multivitamin users (use multivitamin anytime during pregnancy) were

more likely to be White[42, 47], better educated,[37, 42, 78, 85] older,[37, 42, 77, 82] married or cohabiting with a partner,[19, 37, 42, 78, 82] be primiparous,[77, 82] have a higher income,[19, 37, 42, 47] pregnancy intention,[79] and private health insurance.[47] Similar to multivitamin users during pregnancy, periconceptional multivitamin users are those who were non-smokers,[42, 82, 86] married,[42, 78, 82, 85, 86] older,[42, 82, 86] have a high socioeconomics status,[42, 86] better educated,[42, 78, 85, 86] primiparous,[75, 80, 82] normal BMI,[78] However, a population-based survey initiated by the Medical Birth Registry and the National Council on Nutrition and Physical Activity from Norway reported periconceptional multivitamin users were tended to be younger.[85] With regard to preconception, multivitamin use are more likely to be white,[47] older,[39, 47] more educated,[39] intended pregnancy,[47, 86] and have private health insurance.[47] To the contrary, the preconception non-multivitamin users are more likely to be Black,[81] younger,[81] less educated,[39] Medicaid recipients.[39, 81]

Definition of Multivitamin Use in Periconceptional Period and Early Pregnancy

Regular Use vs. Non-regular Use

Multivitamin use is assessed in various ways. First, women are often identified as multivitamin users if they use multivitamins at the time of assessment or reported having ever used multivitamins in pregnancy.[19, 24, 35, 38, 49, 76, 77, 79, 82, 84] However, this assessment does not take into consideration the frequency and duration of multivitamin use, and this could lead to overestimation of multivitamin regular use. It could be possible that women who had just used multivitamin once were also regarded as multivitamin users. There were some studies estimating multivitamin use among regular users.[36, 37, 42, 74, 78, 85] The

change in the definition from multivitamin users to multivitamin regular users did not cause large variation in prevalence of using multivitamins during pregnancy. In the U.S., the prevalence of using multivitamins during pregnancy was reported between 78.0% and 82.5%.[35, 37] Regarding to the prevalence of periconceptional multivitamin use in the U.S., one study reported that 23.8% of women reported having used multivitamin during periconceptional period,[31] while another study suggested that 21.0% of women reported regularly using multivitamins (3 days a week) during periconceptional period.[36]

Prescription vs. OTC Multivitamins

The main difference between prescription and OTC multivitamins is the amount of folic acid: while OTC multivitamins contain 400 micrograms dose, prescription multivitamins have 1000 micrograms. A majority of studies asked women to report their multivitamin use but did not further asked women whether the multivitamins they took was prescription or OTC multivitamins. Although some studies collected information of brand of multivitamin supplementations, it is often not reported and still unclear about prescription multivitamin as well as OTC multivitamin use among pregnant women. A few of studies, however, investigated prescription and OTC multivitamins among multivitamin users. One study from U.S. investigated women at rural outreach clinics and reported that 92% of women had used prescription prenatal vitamins during pregnancy, while 10.9% of women had used OTC multivitamins.[84]

Multivitamin vs. Single Vitamin

The use of single vitamin (e.g. vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, folic acid) along with multivitamin use was studied. It seems that a small proportion of women who took multivitamin took additional single vitamins: a population-based study from UK assessed frequency and amount of all single vitamins during pregnancy including vitamin A, vitamin C, and vitamin E, all of which were below 5%. [68] Contrary to other single vitamins, a large number of women who took multivitamin also took additional folic acid supplementations during pregnancy: it was reported that the prevalence of taking folic acid was between 71.4-78.7%.[68 75]

The Timing of Measuring Multivitamin Exposure among Pregnant Women

The time frames for multivitamin exposure during pregnancy and periconceptional period were defined differently. For pregnancy, multivitamin exposure was usually measured after women realized they were pregnant or used the last menstrual period as the beginning time point of pregnancy. There is a time gap between the last menstrual period and women's recognitions of pregnancies, and women may not realize they were pregnant even the fetus was developing. A population-based study combined these two time points by asking women if they used any multivitamins since their recognitions of pregnancies or last period menstrual.[35]

Periconceptional period in studies is often defined 28 days prior to the last menstrual period to after 28 days after the last menstrual period.[42] Some studies expanded the endpoint of periconceptional period to 8 weeks after last

menstrual period.[24, 49] In addition, some studies did not define an exact time for periconceptional period but defined periconceptional multivitamin users as women who reported having used multivitamin before LMP and continued in pregnancy.[35 36]

Economic evaluations on food fortification and folic acid use

Some studies evaluating the benefits of folic acid fortification in food in the U.S, showed that it was associated with an annual economic benefit of $312- $425 millions and that the cost savings (net reduction in direct costs) ranged from $88 to $145 millions per year.[87] Another cost-effectiveness analysis from the U.S. analyzed folic acid fortification policy and found that it could achieve $266,649 per QALY gains.[88] However, this study did not focus on pregnant women and NTDs. The outcomes in this study included myocardial infarctions and color cancer for males.

In the Netherlands, a cost-effectiveness analysis conducted from a societal perspective found periconceptional use of folic acid supplementation was cost-effective (€1800-4500 per QALYS).[89] However, this study did not include productivity loss as a component in their cost estimation. There is another pharmacoeconomic study from the Netherlands which conducted a cost-effectiveness analysis to evaluate the folic acid food fortification and prevention of NTDs from a societal perspective. That study found that fortification of bulk food with 140μg folic acid per 100g results in cost savings if the cost of enrichment does not exceed €5.5 million.[90] However, the result of

this study might not be comparable, because the cost estimation was estimated under a different health care market and health care system.

CHAPTER III: RESEARCH DESIGN

Study Population

This is a cross-sectional study using data from the "Safety of Medications and Perception of Teratogenicity (SMART)" study. SMART is a prospective multi-clinics study conducted at the University of New Mexico (UNM). Eligible participants were women who aged 18 or older and attended UNM-affiliated prenatal care clinics (UNMH Fetal Monitoring Clinics, Triage, General Obstetric/Gynaecological, Satellite Clinic-West Mesa, Satellite Clinic-South Broadway, Satellite Clinic-North Valley) in Albuquerque, NM, during 2008-2009. A written informed consent in English or Spanish was obtained before each interview. If women agreed to participate, a semi-structured interview was administrated by a trained bi-lingual interviewer fluent in English and Spanish in a private setting at the clinics. If women did not want to participate, they would be asked to give reasons for non-participation. Institutional Review Board (IRB) approval for this study was obtained from the UNM Research Review Committee (HRRC).

On an initially screening, 493 pregnant women who were consecutively chosen from UNM main hospital and satellite clinics were offered participation in the study. Among those, 404 women enrolled in SMART study (response rate=81.5%). The major reasons for non-participation were the time constrains and lack of interest in the study. For the purpose of this study, women who did not report their multivitamin use were excluded (n=2). Therefore, 402 women were included for the present analysis.

Measurements

Sociodemographic Characteristics

Sociodemographic characteristics, including maternal age (continuous), marital status (single/never married, married/living with spouse, not married but living with partner, separated from spouse, divorced, widowed), race (white Non-Hispanic, white Hispanic, black or African American, American Indian or Alaskan native, Asian or Asian American or Pacific Islander, some other group, prefer not to report), ethnicity (Hispanic/Latino/Spanish descent, other ethnical groups), level of education (less than high school graduate, high school education or GED, some college or vocational school, college degree, master/doctorate or professional degree), health insurance status (no insurance, employer-based insurance, self-purchased insurance, Medicaid, other public insurances), place of born (U.S. born, foreign born), years of staying in U.S for immigrants, language predominantly spoken at home (English, Spanish, some other language) were ascertained. In addition, if women described themselves as American Indian or Alaskan Native, they were further asked to specify whether they can identify a specific tribe or pueblo. Women were also asked whether their health insurance covered prescription drug or not. For women who reported having other public health insurances, they would be asked to specify whether it is Indian Health Service, Veteran Affair (VA), First Choice, UNM/UNM Care, or other types.

Lifestyle Characteristics

Interviewer asked participants to report their lifestyle characteristics including smoking, alcohol use, and illicit drug use. We firstly asked women whether

they smoked cigarettes or used tobacco at the time of the interview. If they answered “yes”, the number of cigarettes in a day was recorded. Otherwise, we asked them whether they have ever smoked more than 100 cigarettes and whether they stopped before or after recognition of pregnancy.

Regarding alcohol use, we asked women whether they have ever used alcohol. If women answered “yes”, the interview would ask them to specify the number drinks typically she feels the first effect of alcohol and the number of drinks she can hold before passing out of falling asleep. We ascertained periconceptional binge drinker by asking women how many times participants drank four or more drinks during a month around the LMP. In addition, the standardized TWEAK (Tolerance, Worried, Eye-opener, Amnesia, Kut down) with “hold” and “high” versions of the questionnaire was administrated.[91-93] The difference between the two versions is the cutoff point of “Tolerance”. In the “hold” version, tolerance was ascertained if a woman drank more than six drinks she could tolerate, while the cutoff point is three in the “high” version. For “Worried, we asked whether the woman’s close friends or relatives worry or complain about her drinking; for “Eye-opener”, we asked a woman whether she has taken a drink first thing in the morning to get herself going; for “Amnesia”, we asked a woman whether her friend or family member tell her about things she said or did while she was drinking that she could not remember; for “Kut down”, we asked a woman whether she felt a need to cut down on her drinking. To calculate TWEAK score, we gave each woman one point per question if they answered yes to a question regarding using alcohol as an eye opener in the morning, memory loss, or cutting down on alcohol. Two points would be given

to a woman if she responded yes to the question regarding “Worried” or she meets the cutoff point of “Tolerance”.

Additionally, the interviewer asked women their recreational drug use including marijuana/hashish, heroin, cocaine/crack, inhalants, methamphetamines, other recreational drugs. For each type of recreational drug, recreational drug users were asked to specify the exposure time, whether before pregnancy or one month prior to LMP or during the current pregnancy. Women were also asked whether they had taken methadone treatment and whether they had completed treatment before pregnancy or still undergone treatment during pregnancy. Questions about recreational drug use were introduced in January 2009. Therefore, information on recreational use for women who were recruited in 2008 was missing.

Medical and Reproductive Health

Information on medical and reproductive health was queried and confirmed by electronic medical records review: pre-pregnant weigh (pounds), pre-pregnant height (feet), gestational age at the time of interview, presence of medical conditions (if yes, women would be asked to specify the following medical conditions: hypertension, depression, diabetes, anxiety, seizure disorder, migraine headaches, thyroid disorder, rheumatoid arthritis, asthma or allergies, heart disease, cancer, hepatitis).

Questions about reproductive health included pregnancy planning (i.e., “Did you plan to get pregnant with this child?” The answers consist of three options:

"Yes"; "No, not now"; "No, not at any time"). At the beginning of this study, the first 42 study participants were not asked about their pregnancy planning, and there were additional 8 women who did report their pregnancy planning during the interview.

Other questions regarding reproductive health included a history of miscarriage, stillbirth, pregnancy termination, and ectopic pregnancy in a prior pregnancy, gravidity (number of pregnancies including current pregnancy), parity (number of live-born children), the date of the last menstrual period, a family history of birth defects. For a family history of birth defects, women would be firstly asked whether she or her members of immediate family or the immediate family of her baby's father had any babies with birth defects. If such history was reported, participants were asked to specify the following birth defects: Down syndrome, cleft lip or palate, neural tube defects, cystic fibrosis, heart defect, or other defects. We also investigated the presence of complications for current pregnancy including bleeding, high blood pressure, diabetes, and other complication and asked women whether they had morning sickness during the current pregnancy.

Vitamin and Dietary Supplement Use

All enrolled women were asked whether they had taken any vitamin, including multivitamin or single vitamin, prescription or over-the-count (OTC) vitamin, at least 4 times a week since they became pregnant. Also, women who reported using single vitamin or multivitamin were asked to specify brand name of vitamin and the time they had started vitamin use. Periconceptional vitamin

use was ascertained by asking women if they had taken vitamin at least 4 times per week during the month around their LMP.

Regarding dietary supplements, we asked a woman whether she took dietary supplements (including iron supplements) or herbal products on a regular basis since her last menstrual period. If she response “Yes”, we further asked her to specify the type of herbal products, the frequency of dietary supplement use, and reasons for taking it.

Medication Use

The use of medications during pregnancy was also ascertained. To begin with, we asked a woman whether she discussed safety of medications in pregnancy with any health care provider (physician, nurse-midwife, physician assistant, or pharmacist). Then, we asked women about the use of OTC and prescription medications since LMP. For OTC medication, following OTC medications were provided: acetaminophen, aspirin, ibuprofen, ketoprofen, naproxen, chlorpheniramine, benadryl, pseudoephedrine, kaopectate/pepto bismiol. Questions about prescription medications included pain/fever medication, nasal decongestants/allergy/cough medications, antidiarrheal, medication, and heart burn/dyspersia/antiemetic/laxative medications. For the attitudes of each medication use, we provided a five-point Likert type scale was used to assess the perception of teratogenicity.

In additional to medication use, we also investigated vaccine exposure since LMP (e.g. flu vaccine, other vaccine) and asked women to specify the types of

cravings or non-food item/strange good they took. Women were also asked about the use of fertility medications with current pregnancy (e.g. Clomid, Metrodin, Fertinex, or Pergonal).

Perinatal Outcomes

Perinatal data were abstracted from electronic medical records including pregnancy outcomes, i.e. live-born infant, spontaneous abortion (<20 gestational weeks), stillbirth (≥20 gestational weeks), termination, lost to follow-up. Date of delivery and gestational age at the end of pregnancy were also recoded. Type of delivery (vaginal-vertex, vaginal-breech, vaginal-transverse, cesarian section-primary, cesarian section-repeat) was obtained from medical records. Maternal complications in pregnancy included preeclampsia, pregnancy induced hypertension, oligohydramnios, infection or fever at delivery, gestational diabetes, and others, all of which were recorded in this database. For the live-born children, we recorded gender of the infant, birth weight (grams), birth length (centimeters), and birth head circumference (centimeters). In addition, the database also captured the neonatal complications (respiratory distress, hypoglycemia, tachypnea, bradycardia, sepsis, and others), diagnosis of major structural anomaly, the number of days for infant stay in hospital, and diagnosis of any abnormalities/conditions in the neonatal period.

Data Modifications

A multivitamin regular user was identified if a woman reported having taken vitamins at least 4 times per week. Based on the timing of the vitamin

exposure, we further categorized women into three study groups: 1) pre-conceptional vitamin regular users (women who reported having taken vitamins ≥4 times per week at least one month before their LMP); 2) vitamin regular users after pregnancy recognition (women who reported beginning to take vitamins or single vitamin at least 4 times per week since they became pregnant); 3) vitamin non-users (women who reported not having taken any vitamins before their last menstrual periods or since they became pregnant).

Potential predictors were identified from previous studies. We categorized predictors in the following manner: maternal age was categorized into categories (≥21 yrs, 21-30 yrs, >30 yrs); level of education was categorized into three levels (high school education or less, some college or vocational school, college degree or higher); marital status was recategorized into three categories (single/never married, married/living with partner, separated/divorced/widowed); for health insurance status, we made three categories (uninsured, employer-based or self-purchased insurance, Medicaid or other public insurance); language speaking was dichotomized as “Spanish” and “English and other language” (there were 6 women who speak other languages other than English and Spanish); for body mass index, the reported prepregnancy height and weight were used to estimate the BMI (kg/m^2) and then BMI was dichotomized as obese (BMI≥30) and nonobese (BMI<30).

For gravidity and parity, they were dichotomized into two categories (primigravida if gravidty=1 vs. multigravida if gravidity≥2) and (primiparous if parity=0 vs. multiparous if parity≥1), respectively. A woman was identified to

have a history of adverse pregnancy outcome if she reported having experienced miscarriage, stillborn, pregnancy termination, or ectopic pregnancy in previous pregnancies. For pregnancy planning, a woman was considered to have a planned pregnancy if she answered “yes” to the question “Did you plan to get pregnant with this child”, while a woman was regarded not having a planned pregnancy if she answered “no, not now” or “no, not at any time”.

For the family history of birth defects, a woman was identified to have a family history of birth defects if she reported at least one of the following birth defects in her family: Down syndrome, cleft lip or palate, NTD, cystic fibrosis, heart defect, or other defects. For BMI, we recoded it as a categorized variable. Women were classified as obese if BMI equal or larger than 30 or nonobese if BMI is smaller than 30.

For smoking, we categorized women into three groups: women who smoked less than 100 cigarettes in a lifetime and did not currently smoke were identified as non-smokers; women who smoked 100 or more cigarettes in a lifetime but stopped smoking before pregnancy recognition were identified as a former smoker who quit before pregnancy recognition; women who currently smoked or who smoked ≥100 cigarettes or more than 100 cigarettes in a lifetime but stopped cigarettes after pregnancy recognition were identified as smokers during pregnancy. For alcohol use, periconceptional binge drinkers were identified if women have drunk four or more on one occasion during a month around their LMP. For recreational drug use, women were identified as

recreational drug users if they reported using any of following recreational drugs one month prior to LMP or during pregnancy: marijuana, heroin/hashish, cocaine/crack, inhalant, methamphetamines, or other recreational drugs. In addition, we also investigated prescription medications use during pregnancy and categorized pill burdens as follow: no prescription medications at all, 1-2 prescription medications, more than 2 prescription medications.

Statistical Approaches

SAS 9.2 (Cary, NC) was used for all analysis. A descriptive statistics were performed to describe the maternal characteristics in the entire population. Also, the prevalence of vitamin use in each study group was estimated. For vitamin users, we further specified the type of vitamin whether it is OTC or prescription vitamins. The most common brands of vitamins were determined based on women's self reported information. The number of days of vitamin use per week was additionally calculated. For women who began to take vitamins after pregnancy recognition, the beginning gestational age of regular vitamin use was measured using the date of last menstrual period as a starting time point.

The distribution of maternal characteristics among study groups was compared by using chi square test for categorized variables and ANOVA for continuous variables. All the significant predictors ($p<0.2$) were then entered into a multivariate ordinal logistic regression model to determine the association between vitamin use and maternal characteristics after adjusting

for confounders. Cumulative odds ratio with 95% Confidence intervals were constructed.

In ordinal logistic regression, we treated the three study groups as categorical under the assumption that there is a natural ordering across different vitamin groups. Therefore, the analysis built a set of cumulative logits to interpret the outcome (vitamin use). In total, two logits were developed as follow: Group 1 versus (Group 2 and Group 3), (Group 1 and Group 2) versus Group 3. The final model was examined by performing a chi square score test in order to check the proportional odds assumption. If the assumption is violated, then an alternative model, polychotmous logistic regression, would be used.

A polychotomous logistic regression model is an extension of dichotomous logistic regression model when there are more than two categories in the dependent variable. Unlike an ordinal logistic regression model, the dependent variable is treated as a nominal and cannot be arranged in any meaningful natural ordering. In this case, the interest outcome measure in this analysis is the vitamin use in different time of pregnancy: pre-conceptional vitamin users, vitamin users after pregnancy recognition, and non-users. Therefore, a multinomial model was introduced to determine whether maternal characteristics differed across three study groups. We did not use a series of binary models because this approach will give less statistical power to the results and higher values of standard error.

In this model, vitamin regular users after pregnancy recognition were the reference group. The rational of choosing this group as a reference group is that it this group has the largest frequency of cases and it makes the greatest clinical sense. Based on the reference group, there were two multinomial logits for polychotomous logistic regression: pre-conceptional vitamin users relative to vitamin users after pregnancy recognition and non-users relative to vitamin users after pregnancy recognition. For each logit, odd ratios and 95% confidence intervals (CI) of each predictor were estimated from the regression parameters and their standard errors.

Additional analysis was conducted by using ordinal logistic regression and polychotomous logistic regression with vitamin use as the response variable in order to examine interaction terms between different predictors, including ethnicity and race, ethnicity and place of birth, ethnicity and language speaking, race and language speaking, race and place of birth, place of birth and language speaking, education and health insurance status, education and pregnancy plan. Significant interaction terms would then be involved for the multivariate analysis.

Power Calculation

The power calculation for this study was done in PASS 11 Software (Kaysville, Utah) for comparing two independent proportions. For this calculation, we set the alpha value (the probability of rejecting a true null hypothesis) as 0.05 and 0.2 for beta (the probability of accepting a false null hypothesis). Sample

allocation ratio was set as three, which is approximately the ratio between group 1 and group 2 in the present analysis.

Estimations of the required total sample size were based on previously reported prevalence of pre-conception multivitamin users and prevalence of multivitamin users during pregnancy. In reference to the former prevalence, data from PRAMS (Pregnancy Risk Assessment Monitoring System), the prevalence of preconception vitamin use (P1) is 23.0-43.6% in the U.S.[18, 39, 47 81] For the prevalence of regular multivitamin users during pregnancy, the prevalence was previously estimated to be 68.8-78.0%.[19, 35] Therefore, we assume that the difference in the proportion of multivitamin use between the study groups would be between 20% and 60%. As presented in Table 3.1, the required total sample size might vary from 24 to 225 depending of the difference in prevalence between study groups. In sum, a total sample size of 24-225 subjects will achieve more than 80% power to defect a difference between the effect sizes of 20-60% using the two-sided Z test at an alpha level 0.05. In this present analysis, a sample of 402 subjects will be sufficient and can achieve a power that more than 80%. To detect 20% difference, a group sample sizes of 252 could achieve 80% power.

CHAPTER IV: RESULTS

Description of the Study Population

Maternal characteristics of the total population were summarized in Table 4.1. The study population included 80.4% of Hispanics, 6.7% American Indian or Alaskan Native, and 5.7% Black or African American women. In terms of other demographic characteristics, a majority of women were immigrants (59.6%), identified Spanish as their primary language (60.7%), were married or living with a partner (71.6%), reported education less than high school (35.1%), and did not have any health insurance (48.8%). Additional analysis assessed the association between insurance status and ethnicity. Results of this analysis indicate a statistically significant association ($p<0.01$). Among women without health insurance, 98.5% of women were Hispanics and 1.5% of women were Non-Hispanics. Among women with public health insurance, more than half of participants (66.8%) were Hispanic women. For women have private insurance, the difference in ethnic distribution was small (Hispanic women, 55.1%; Non-Hispanic women, 44.9%). Of note, even though there more than half of women in this sample did not have any health insurance, all participants received free prenatal care through the UNM clinics.

The average gestational age for women to initiate prenatal care was 8.5±4.4 weeks after the last menstrual period. Most of the women (89.4%) received prenatal care in their first trimester (1-11 weeks after LMP), and 10.3% of women initiated prenatal care during the second trimester (12-24 weeks after LMP). There is one woman who reported starting prenatal care 29 gestational weeks. There were no differences in the mean gestational age at which

prenatal care was initiated between Hispanic (8.6±4.3 weeks) and Non-Hispanic (8.2±4.6 weeks) women (p=0.45).

Almost half of women (45.0%) reported the presence of medical conditions with diabetes being the most prevalent (20.1%). One third of the study population (32.1%) had a history of adverse pregnancy outcomes, such as miscarriage (32.1%), stillbirth (27.6%), terminated birth (7.5%), and ectopic pregnancy (1.8%) Regarding tobacco use, most of women (87.0%) were not current smokers or quit before pregnancy recognition, while only 13.0% of participants reported smoking during some point of pregnancy.

Binge drinking (i.e., at least one episode of consuming ≥4 drinks per occasion) during a month around the last menstrual period was reported by 23.1% of women. Over half of women (53.4%) reported using prescription medications during pregnancy, and 29.1% of women who used medications did not discuss their safety in pregnancy with a health care provider.

Among 200 women who were asked questions about illicit drug use, 55 (27.5%) reported lifetime use of at least one type of drugs and 11 (5.5%) women reported use during the month prior to LMP or during the current pregnancy. Among 352 who answered a question about pregnancy planning, 181 women (51.4%) reported unplanned pregnancy.

Vitamin Use Patterns

The vitamin use patterns were summarized in Table 4.2. In this population, 21.4% of women were identified as pre-conceptional vitamin users, 71.9% of women began to take vitamin after they realized they were pregnant, and 6.7% of women did not use any vitamins during pregnancy. Of note, there were three women who began to take vitamin regularly in pre-conceptional period but stopped taking after pregnancy recognition. All of the three women reported a family history of birth defects (two women with a family history of Down syndrome and the other woman with a family history of cleft lip/palate), but reasons for this behavior change were not captured by this study. Among vitamin users after pregnancy recognition, only one woman used a single vitamin (folic acid), while the rest reported multivitamin use. This woman was included into the study Group 2 for analysis. Among all vitamin users, 58.4% of women used OTC multivitamins and 30.9% of women reported using prescription multivitamins. The two most frequently identified brands of prenatal vitamin were Walmart® and Walgreen® prenatal vitamins. Both of these brands contain 800 microgram of folic acid. Other brands identified by participants included “One a day Prenatals”, “Natalcare Plus”, and “Flinestone vitamins”. On average, vitamins were taken 6 days (s.d=1.9) per week during the week before the interview. Among women who took vitamin after pregnancy recognition, the average initiation time was 9 weeks after the LMP.

Maternal Characteristics of Vitamin Use

The distributions of maternal characteristics among the three study groups were summarized in Table 4.3. Only 17.3% of Hispanics took vitamin in

pre-conceptional period, while most of them began to take vitamins only after pregnancy recognition. There was a significant difference in the distribution of education level among the three study groups. A decreasing trend of the proportion of women with a college degree or higher education was identified: 50% of women with a college degree or higher education were identified among pre-conceptional vitamin users, followed by vitamin users after pregnancy recognition (47.5%) and vitamin non-users (2.5%). Interestingly, the largest proportion of women with some college or vocational school education was identified among vitamin users after pregnancy recognition (66.3%), followed by pre-conceptional vitamin users (23.6%). Association between the three study groups with respect to vitamin use and health insurance was significant. The proportion of women who had Medicaid or other public insurance among pre-conceptional vitamin users (44.9%) was closed to the proportion in vitamin users after pregnancy recognition (49.0%). In sum, there were significant associations among the three study groups with respect to ethnicity, education level, health insurance, language speaking, and pregnancy planning. Maternal age, race, marital status, primigravida, nulliparous, place of birth, history of adverse pregnancy outcomes, presence of medical conditions, a family history of birth defects or adverse pregnancy outcomes, use of prescription medications, smoking status, periconceptional drinking, periconceptional drug use, were not significantly associated with vitamin use in this sample.

Ordinal Logistic Regression

Results of ordinal multivariate logistic regression with cumulative odds ratios (ORs) and 95% confidence intervals (95% CI) for each predictor were summarized in Table 4.4. Cumulative ORs represent increasing odds of being early vitamin users. The results of multivariate analysis showed that maternal age, race, history of adverse pregnancy outcomes, country of birth, and use prescription medications were not significant associated with vitamin use. Moreover, ethnicity, education level, health insurance, and language speaking became not significant after adjusting for other variables in the model. The only significant predictor associated with vitamin use was pregnancy planning, suggesting that the odds of being vitamin users at an earlier stage in pregnancy were 1.76 times higher for women who had pregnancy planning than those women who did not have a pregnancy planning.

Interactions between predictors were examined using the ordinal logistic regression model and results were summarized in Table 4.5. Of note, there were no women who identified themselves as Non-Hispanics and spoke Spanish at the same time. Therefore, the interaction between ethnicity and language speaking could not be calculated. The only significant interaction was identified between education level and insurance status ($p<0.05$), meaning that the effect of education on vitamin use varied by the level of health insurance status. Thus, the association between education and vitamin use was examined after stratification by insurance status. Results are presented in Table 4.5 (women without health insurance), Table 4.6 (women

with employer-based or self-purchased insurance), and Table 4.7 (women with Medicaid or other public insurance).

Results of the stratified analysis demonstrate that there were no associations between maternal education and vitamin use among women without health insurance and women who had private or self-purchased health insurance. However, among women with public health insurance, having a college degree or higher was associated with greater odds of early vitamin use (OR=14.45; 95% CI: 1.78-117.66) compared to women with a high school education or less.

Due to the limited sample size in each category of health insurance status, the present analysis explored the interaction between education and health insurance by categorizing health insurance into a dichotomous variable (any type of insurance vs. none). Results were presented in Table 4.8 and Table 4.9, respectively. Among women without insurance, education level was not a significant predictor. However, among women with any type of insurance, the odds of earlier vitamin use were greater among women with a college degree or higher than women with a high school education or less (OR=5.90, 95% CI:1.89-18.44).

Polychotomous Logistic Regression

The test for the proportional odds assumption resulted in a p=0.15. The null hypothesis for the proportional odds assumption is that the assumption is met. Given that p=0.15 is greater that a usually used cut-off point of p=0.1, the H_0 is

not rejected and once can conclude that the proportional odds assumption is met. However, given that the p-value was close so close to the cut-off point, polychotomous logistic regression was also conducted in additional to the ordinal logistic regression.

All the significant covariates identified in univariate analysis at $p<0.2$ were considered as potential predictors of vitamin use and were included in a polychotomous logistic regression. As shown in Table 4.10, in the first logit of the unadjusted polychotomous logistic regression (pre-conceptional vitamin users vs. vitamin users after pregnancy recognition), significant predictors were ethnicity, education, health insurance, pregnancy plan, language speaking, and use of prescription medications during pregnancy. Specifically, women who were pre-conceptional vitamin users were less likely to be Hispanics (OR=0.33, 95% CI=0.19-0.57), speak Spanish (OR=0.43, 95% CI=0.27-0.71), more likely to have a college degree or higher education (OR=4.94, 95% CI=2.44-10.00), have employer-based or self-purchased insurance (OR=3.90, 95% CI=1.97-7.75), and use ≥2 prescription medications (OR=2.33, 95% CI=1.14-4.78) compared to women to initiated vitamin use later in pregnancy. Maternal age, race, and history of adverse outcomes were not significant in this analysis ($p>0.05$). In the second logit (non-users vs. vitamin users after pregnancy recognition), race was the only significant predictor. Specifically, non-users were more likely to be in the “other” racial groups (OR=3.35, 95% CI=1.13-9.92) compared to vitamin users after pregnancy recognition after adjusting for other risk factors.

Results of multivariate polychotomous logistic regression were present in Table 4.11. After adjusting for ethnicity, race, education level, language speaking, history of adverse pregnancy outcomes, place of birth, and use of prescription medications during pregnancy, pregnancy planning was the only significant predictor of using vitamins before pregnancy recognition as compared to vitamin user after pregnancy recognition (OR=2.29, 95% CI=1.29-4.09). Race was no longer significant in multivariate analysis for comparison of non-users vs. users after pregnancy recognition. However, a history of adverse pregnancy outcomes became a significant predictor: non-users are more likely to have a history of adverse pregnancy outcomes comparing to vitamin users after pregnancy recognition (OR=3.04, 95% CI=1.16-7.98).

For interaction terms, Table 4.5 summarized the results and showed that there were no significant interaction effects between ethnicity and race, ethnicity and place of birth, race and language speaking, ethnicity and place of birth, place of birth and language speaking, education and health insurance status, education and pregnancy plan.

CHAPTER IV: DISCUSSION

Summary

This study found that most pregnant women (71.9%) in the sample began to take vitamins regularly after pregnancy recognition. For women who started to use vitamins after pregnancy recognition, the mean gestational age of initiating vitamin use was 9 weeks. Women on average took vitamins 6 times per week. However, only 21.4% of study participants began to take vitamins before pregnancy, thus had vitamin exposure in early gestation even before pregnancy recognition. Most women reported using OTC vitamins (54.2%), with two most popular brands being Walgreen® and Walmart® prenatal vitamins, both containing 800mg of folic acid.

Hispanics were less likely to use vitamin early in pregnancy than non-Hispanics; however, ethnic difference in vitamin use became non-significant after adjusting for other maternal characteristics. Unplanned pregnancy is a big public health issue: half of participants, similar to national estimates,[94] in this study identified their pregnancies as unintended. Earlier vitamin use in pregnancy was significantly associated with pregnancy planning independent of other maternal characteristics. In addition, education level and health insurance status revealed a significant interaction with respect to vitamin use. Among women with public health insurance, the odds of early vitamin use were greater among women with a college degree or higher education than women with a high school education or less than high school. In addition, almost one third (32.1%) of women in this study had a history of adverse pregnancy outcomes and 45.0% of women had at least one medical

condition. In multivariate analysis, vitamin non-users were more likely to have experience of adverse pregnancy outcomes in prior pregnancies compared to women who used vitamin after pregnancy recognition. This observation requires investigation in future studies.

Prevalence of Vitamin Use as Compared to Other Studies

In this study, 92.5% of women reported regularly using vitamin anytime during pregnancy. This prevalence rate is higher comparing to a cross-sectional study using data from the Behavior Risk Factor Surveillance System (BRFSS), in which 78% of women from 14 U.S. states and territories reported using multivitamins in pregnancy.[19] For vitamin use among Hispanics, the present study identified that 76.2% of Hispanics were vitamin users anytime during pregnancy, while this prevalence in the BRFSS study was 66.4%. Although the estimation used a national sample, the BRFSS database did not contain information on the duration of multivitamin use, doses, contents, or frequency of use.

In additional to BRFSS, vitamin use during pregnancy was also investigated using data from the National Maternal and Infant Health Survey (NMIHS). This national survey defined vitamin use as vitamin/mineral supplement use at least 3 days a week. This definition was somewhat comparable to the present study (vitamin use at least 4 times per week). There were two cross-sectional studies which conducted analyses based on the NMIHS data. One of these studies was limited to mothers of live-born infants and reported that 82.5% of women used vitamin anytime during pregnancy,[37] while the prevalence was 74.2%

when the sample included women with miscarriages or women who terminated their pregnanciesl.[36] However, both of the prevalence estimates included mineral supplement use. Therefore, women who reported using mineral supplements only could be also included in these prevalence estimates. These studies have not reported the prevalence of vitamin use among Hispanics though, which comprised the majority of the sample in the present study.

Prescription claim databases were also used to estimate the prevalence of vitamin use during pregnancy. A population-based study analyzed data from the Kaiser Permanete Medical Care Program (KPMCP) in North California and reported that 69.0% of women used vitamin during pregnancy. As compared to the results of the present study, prevalence in the KPMCP was lower.[35] The difference might be due to the different gestational age at the interview time. The KPMCP study recruited women at an earlier stage of pregnancy: the mean gestational age at study entry was less than 5 weeks, while the mean gestational age at current analysis was 30.7 weeks. The Pregnancy, Infection, and Nutrition (PIN) Study in North Carolina recruited women from four prenatal care clinics and reported that the prevalence of vitamin use anytime in pregnancy was 84%.[25] However, neither KPMCP study nor PIN study reported vitamin use among Hispanics. Information on the duration of vitamin use and frequency was not reported in these two studies.

Regarding vitamin use after pregnancy recognition, 71.9% of women in this present analysis began to take vitamin after pregnancy recognition, which is higher comparing to two previous prospective cohort studies in the U.S

(44.8-48.9%).[25, 35] One of these prospective cohort studies, however, interviewed women who were at 24-29 weeks of pregnancy, and it potentially excluded women at third trimester. Thus, the estimation of vitamin use might not include women at higher risk of adverse birth outcomes. For the other prospective cohort study, nearly half of women (49.4%) refused to participate in the study. Furthermore, among all the participants, there were 23.2% of women who did not complete an interview. Therefore, the result of vitamin use after pregnancy recognition might suffer from a selection bias.

With respect to vitamin use in early pregnancy/pre-conceptional period, only 21.4% of women reported using vitamin in this present study. Similar to this result, there were several Pregnancy Risk Assessment Monitoring System (PRAMS) reports which investigate the vitamin regular use (≥4 times per week) in pre-conceptional period. Centers for Disease Control and Prevention (CDC) introduced PRAMS in 1987, and PRAMS is an ongoing surveillance system in order to monitor maternal behaviors that occur before, during, and after pregnancy.[39] Several reports analyzed PRAMS data covered from 2000 to 2003 and reported that the prevalence of pre-conceptional vitamin regular user ranged from 25.0 to 45.2% based on 19 states in the U.S.[18, 39] Another PRAMS report limited the sample to women in Oklahoma and found the prevalence fell between this range (26.5%) from 2000 to 2003.[81] Unfortunately, the prevalence remained relatively unchanged. The latest PRAMS report summarized data for 2003-2004 from 26 states and demonstrated that 35.1% of women on average reported using vitamin in pre-conceptional period.[47] Similar to the result of PRAMS, a state report using data from the Missouri

Pregnancy Related Assessment and Monitoring System (MoPRA) found that the prevalence of pre-conceptional daily vitamin use was 29.7%.[86] These results are comparable to our findings.

However, the results from PRAMS and MoPRA analyses might be have limited generalizability since they only include women with live-born infants. Therefore, the prevalence of pre-conceptional vitamin users might be overestimated, given to a possibility that the sample did not include women who had a miscarriage or stillbirth and did not use prenatal vitamins during the pre-conceptional period. In addition, all the identified PRAMS reports and the MoPRA study did not investigate pre-conceptional vitamin use by race/ethnicity.

The prevalence of pre-conceptional vitamin use in this present analysis, to some extent, might reflect the prevalence of periconceptional vitamin use. The definition of periconceptional period varies across the studies and might refer to one month before and one month after the LMP or might include as many as three months before and after LMP. Women who reported using vitamin before pregnancy are more likely to continue using vitamin after they were pregnant. A cross-sectional study, which used data from the NMIHS, reported that the prevalence of periconceptional vitamin use (≥3 times per week during three months before and three months after pregnancy recognition) was 21%.[36] Similarly, a Kaiser Permanete Medical Care Program (KPMCP) prospective cohort study reported 23.8% prevalence.[35] Therefore, the prevalence of periconceptional vitamin use and pre-conceptional vitamin use were similar.

The difference in maternal characteristics might explain variability in the prevalence of periconceptional vitamin use. The PIN study reported that the prevalence of periconceptional vitamin use (before and during pregnancy) was 30.0%.[25] The higher prevalence rate of pre-conceptional vitamin use in PIN study can be explained by the fact that this study included women who only spoke English and that most of women (64.5%) in this study were Non-Hispanic whites. Moreover, women who planned the pregnancy might be more likely to use vitamin in periconceptional period. The NBDPS study demonstrated that the prevalence of periconceptional vitamin use among women who planned their pregnancy was 64.3%.[79]

There is also a difference in the prevalence of periconceptional vitamin use among different racial groups. For Hispanics, data obtained from the National Birth Defects Prevention Study (NBDPS) showed that the prevalence of periconceptional intake of folic acid-containing supplements is only 30% among Hispanics, which is the lowest compared to other racial groups (Non-Hispanic White: 66%; Non-Hispanic Black: 39%).[43] For other races, a secondary analysis using data from the Slone Epidemiology Center Birth Defects Study (SECBDS) showed that 55.0% of Non-Hispanic White women were periconceptional vitamin users (used vitamins ≥ 4 times per week during lunar months -1 to 1), while this prevalence was only 25.6% among African American women.[42]

There are many potential reasons for lower prevalence of vitamin use among Hispanic women compared to Non-Hispanic Whites. One possible explanation might be the lower awareness about benefits of folic acid in prevention of birth defects and other adverse perinatal outcomes among Hispanic women. A household survey conducted in predominantly Hispanics neighborhoods of inner-city Hartford, Connecticut demonstrated that 78% of Hispanics (both women and men) are not aware of NTDs, including spina bifida.[95] Another survey among Hispanic women of childbearing age conducted in Michigan and showed that nearly half of study participants (45%) did not know about the time window to prevent birth defects and 59% did not take daily multivitamins before pregnancy recognition.[96]

With respect to the type of vitamins, more than half of women (54.2%) used OTC vitamins during pregnancy, and 28.7% of women reported using prescription vitamins. This result was quite different from a previous prospective cohort study, which recruited pregnant women from rural outreach clinics in the U.S. The result showed that 92.0% of pregnant women used prescription prenatal multivitamins and 10.9% of them used OTC multivitamins.[84] This discrepancy might be due to the different sampling method. Glover's study recruited all the women from obstetric patients who were seen by private physicians, while a majority of study participants in our study came from the university-affiliated community clinics providing free prenatal care. The difference in the health insurance coverage could account for the discrepancy between the two studies. In Glover's study, all of the

participants had heath insurance (e.g. Medicaid, private insurance), while almost half of women (48.8%) in our study did not have any health insurance.

The average time of pregnancy recognition is 9.0 gestational weeks. The time interval between the LMP and the pregnancy recognition is a curial period for organogenesis. During the month of fertilization, cells along the dorsal surface of the embryo develops into a groove and then a hollow tube.[29] If this process is not completed, a neural tube defect develops. A number of prior studies suggested that periconceptional use of multivitamin supplementation containing folic acid (from 3 months before and through 3 months after conception) can significantly lower the risks of NTDs.[2, 9-16] It has been strongly recommended that all women of childbearing age should consume 400 μg of folic acid daily given that 50% of pregnancies are unplanned.[22] Regular multivitamin use (≥4 times per week) provides the recommended amount of folic acid.[39] Nevertheless, in the present study, the result showed that most women initiated vitamin regular use at 9 weeks after LMP, which is after the closure of neural tube (six weeks after the last menstrual period). In our study, there were only 21.4% of women who initiated vitamin use before pregnancy recognition.

Predictors of Vitamin Use as Compared to Other Studies

Race/Ethnicity

The sample in the present analysis included a large proportion of Hispanics women, but ethnic difference in vitamin use was non-significant after adjusting for other maternal characteristics. The review of published literature showed

that findings among different studies with respect to race/ethnicity are inconsistent. A cross-sectional analysis of the BRFSS data did not demonstrate that ethnicity was a significant predictor for vitamin use among pregnant women.[19] The analysis conducted in the MoPRA study also yielded non-significant results after adjusting for other predictors.[86] However, other studies reported race/ethnicity to be a significant predictor. A study from the Slone Epidemiology Center Birth Defects Study suggested that periconceptional vitamin users (-1 to +1 month around LMP) were more likely to be non-Hispanic Whites.[42] Another cross-sectional analysis, using data from the NMIHS, found that vitamin non-users were more likely to be African American and Asians. However, the NMIHS study mentioned above did not assess the effect of Hispanic ethnicity on vitamin use.[37]

In terms of predominant language, Spanish was not a significant predictor of vitamin use in the present study. This result contradicted the findings from a cross-sectional study which used data from the National Birth Defects Prevention Program (NBDPP). In that study, women who did not use vitamins in periconceptional period (3 months before conception and one month after conception) tended to speak Spanish. However, the difference in the proportion of women who spoke Spanish may cause this difference. There were only less than 5% of Spanish-speaking women (n=80) in the NBDPP study, and the odds ratio was quite wide (OR=2.0-7.2), while our population included 60% Hispanics. In addition, the present study explored the relationship between place of birth and vitamin use. A population-based case-control study, using data from California birth cohort, found that women

who were Mexico descents had an increased risk of having a NTD-affected pregnancy.[46] However, this study did not specify the place of birth for the participants. In this present analysis, this demographic characteristic was not a significant predictor of vitamin use in pregnancy.

Maternal Education

Education was not a significant predictor of vitamin use during pregnancy or in pre-conceptional period after adjusting for other maternal characteristics. The result might due to the small sample of women with a college degree of higher in our samples. However, our results are consistent with several cross-sectional studies in the U.S. A cross-sectional analysis, using the 2004 data from the BRFSS, found that education was not a significant predictor of vitamin use during pregnancy.[19] Another report using the MoPRA data also confirmed that education level was not significantly associated with pre-conceptional vitamin use (one month before pregnancy recognition) after adjusting other variables in the analysis.[86]

However, other studies found an association between vitamin use and higher education level. For vitamin use anytime in pregnancy, a national survey initiated by the Medical Birth Registry in Brazil and a cross-sectional analysis using data from Norwegian Mothers and Child Cohort Study (MoBa) found that vitamin users during pregnancy tended to have a college/university degree.[74, 77] For periconceptional vitamin use, a cross-sectional analysis using data from the Slone Epidemiology Center Birth Defects Study and the 2001 New South Wales Child Health Survey in Australia found that periconceptional vitamin

user (-1 to +1 month around LMP vs. -2 to +3 month around pregnancy recognition) were those women with higher education level or more years of education.[42, 97] In addition, a PRAMS data and a cross-sectional analysis using data from NMIHS found that women with at least 12 years of education were significantly more likely to be pre-conceptional vitamin users (≥4 times per week during the month before pregnancy) than women with less than high school education (<12 years of education).[39]

The present analysis observed a significant interaction between health insurance and education level in respect to vitamin use during early pregnancy. Among women with public insurance, patients with a college degree or higher education were more likely to be vitamin earlier users than women with only high school or less than high school education. Among women who had private insurance or did not have insurance, the present study did observe any significant association between education and vitamin earlier use in pregnancy. We did not find other studies which examined this interaction. Nevertheless, a PRAMS report used data from 19 states and found that pre-conceptional vitamin users (≥4 times per week during the month before pregnancy) were more likely to have a private health insurance and have more than 12 years of education, but it did not examine the interaction regarding pre-conceptional vitamin use.[39]

Health Insurance

Even though there was a significant interaction between health insurance and maternal education, health insurance status by itself was not a significant

predictor of pre-conceptional vitamin use in the present analysis. Prior reports for this association are inconsistent. A cross-sectional analysis, using data from MoPRA, examined the insurance status of pregnant women, but this predictor was not significant.[86] This result did not concur with the results of two PRAMS reports, which used data during 2000-2003 in Oklahoma and 2003-2004 in 26 states, respectively. One of these reports found that the highest prevalence of pre-conceptional vitamin users were women with private health insurance. The other study further adjusted all other demographic characteristics and found that pre-conceptional vitamin users were more likely to be women with private health insurance than women who were recipients of Medicaid.[47, 81] It is worthy mentioning that the MoPRA study only asked women whether they had insurance or not, but it did not specify the type of insurance, which might cause the different result. The difference in findings between the PRAMS reports and current study might be due to various maternal characteristics of the study population between PRAM and the SMART study. There were no other studies from Europe or Australia that investigated the vitamin use in earlier pregnancy and health insurance status because of the different national health care system.

Marital Status

With respect to marital status, this present analysis did not observe any significant difference among the three study groups. A survey of postpartum women in Toronto Hospital also did not detect a significant association. However, a number of analyses presented a contrast to this result, suggesting that married women or women living with a partner were more likely to be

vitamin earlier users during pregnancy,[19, 42, 78, 82, 85, 86] even though the maternal characteristics varied by different studies. It is noteworthy that the present analysis included a small number of women who were separated or divorced. This might cause a non-significant result.

Maternal Age

Maternal age, measured as a continuous variable, was non-significant in the present study. A cross-sectional study, recruiting women in the antenatal clinics and birth center in Australia, also measured maternal age as a continuous variable, but did not find it to be significant.[75] However, a prospective cohort study obtained data from the Pregnancy Exposure and Preeclampsia Prevention Study in the U.S. and found that maternal age as a continuous variable was a significant predictor of periconceptional vitamin use (-3 to +3 months around LMP) from a chi square test. However, this study did not calculate the odds ratio and did not adjust other maternal characteristics.

Even though the present analysis categorized this predictor into three age groups, the present analysis still did not detect a significant result. Another study in Canada surveyed postpartum women in Toronto Hospital and categorized maternal age as three groups (<16-25, 26-30, 31-35),[80] also suggesting a non-significant result and being consistent to an analysis using data from the BRFSS in 2004.[19] On the contrary, there were also some studies pointing out that older age group was associated with vitamin earlier use in pregnancy.[37, 39, 43, 47, 73, 81, 86] A potential reason for the different result between these studies and the present study is due to the various maternal

characteristics in different countries and areas. Also, the different way to categorize maternal age may account for the different result. A cross-sectional study in the U.S. conducted at MoPRA categorized women into two age groups (<20 years, ≥20 years) and detected a significant result with respect to pre-conceptional vitamin use.

Pregnancy Planning

Pregnancy planning identified by the present analysis was the only significant predictor that associated with earlier vitamin use. This finding confirmed the result from a cross-sectional study in the U.S. conducted at MoPRA. This study suggested that planning of pregnancy was significantly associated with pre-conceptional prenatal multivitamin intake (OR=2.04, 95% CI=1.45-2.94) when the study adjusted other maternal characteristics.[86] In addition, a study obtained data from PRAMS during 2003-2004 reported that the highest prevalence of pre-conceptional vitamin users were among women with pregnancy intention. However, the PRAMS did not report the strength of association.[47] For other studies in the U.S., analyses using data from BRFSS, NMIHS, and PRAMS did not involve pregnancy planning as a potential predictor of vitamin use.[19, 37, 39, 81]

Although there are differences in maternal characteristics between various populations in different countries, several studies from other countries also detected a significant association between earlier vitamin use and pregnancy planning. A cross-sectional study from Australia used data from a population-based survey (the 2001 New South Wales Child Health Survey)

and reported that women with an unplanned pregnancy (OR=0.15, 95% CI=0.08-0.26) were significantly less likely to take periconceptional folic acid supplementation (≥1 months before and 3 months after pregnancy recognition).[43] A survey conducted at the Department of Obstetrics and Gynecology and in the Pregnancy Care Centre in Hungary also confirmed this result: planning of pregnancy (OR=4.22, 95% CI=2.61-6.84) was significantly associated with periconceptional vitamin intake (before and during pregnancy).[83] Of note, in the survey, most participants (83.7%) had a pregnancy planning, which is higher than the present analysis. Also, the authors did not specifically defined periconceptional period. A cross-sectional analysis from Canada defined periconceptional period (≥ 4 weeks prior to conception until 8 weeks after conception) and surveyed a group of postpartum women in Toronto Hospital. The result also supported that unplanned pregnancy (OR=1.5, 95% CI=1.4-1.6) was significantly associated with a lack of folic acid use in periconceptional period.[80]

Interestingly, pregnancy planning was not statistically associated with vitamin use after pregnancy recognition in the present study. This result may support the result of a cross-sectional study in Portugal. The study recruited mothers of live-born infants from two primary hospitals in the North of Portugal, but it did not observe a significant association between pregnancy planning and multivitamin use in pregnancy (OR= 0.96, 95% CI=0.89-1.03). Admittedly, there were other studies that also investigated the predictors of vitamin use in pre-conceptional or periconceptional period,[74, 75, 77, 82, 85] but none of these

studies measured pregnancy planning for women or did not involve this predictor for multivariate analysis.

History of Adverse Perinatal Outcomes

In this study, vitamin non-users were more likely to have a history of adverse pregnancy outcomes comparing to vitamin users after pregnancy recognition (OR=3.04, 95% CI=1.16-7.98). This result contradicted to a cross-sectional study using data from the National Birth Defects Prevention Study (NBDPS). In this analysis, women who did not take vitamins in periconceptional period (3 months before conception and 1 month after conception) tended to have no previous miscarriage (OR=0.7 95% CI=0.5-0.9).[43] However, non-users in the present analysis were those who did not use vitamin anytime during pregnancy, while this NBDPS report limited vitamin non-users to women who did not use vitamin in periconceptional period. Moreover, the present analysis not only investigated miscarriage but also other previous adverse pregnancy outcomes, such as ectopic pregnancy, stillbirth, and elective pregnancy termination. Difference in maternal characteristics might also account for the discrepancy. All the women recruited from the NBDPS were mothers with live-born infants without major malformations. There were other studies which also investigated the association between vitamin use during pregnancy and previous adverse pregnancy outcomes. One report obtained data from the Birth Registry in Brazil examined the relationship between vitamin use during pregnancy and previous experience of miscarriages as well as stillbirths.[77] However, the result was insignificant. Also, a study surveyed women in the antenatal clinics and birth centre in Australia, but the association between periconceptional vitamin

use (before and during pregnancy) and a history of adverse pregnancy outcomes was not signfiicant.[75]

It is still unclear how previous adverse pregnancy outcomes associated with vitamin use in pregnancy. The most likely explanation is that those non-vitamin users did not use vitamin in the prior pregnancy either. However, the SMART study did not investigate the reasons of not taking vitamins. Therefore, neither of the two possibilities could be confirmed in this study.

Other Predictors

Other predictors associated with reproductive health included a family history of birth defects, presence of chronic conditions, parity, and gravidity. Unfortunately, none of them was significant in the present analysis. A prospective cohort study, analyzing data from the Pregnancy Exposure and Preeclampsia Prevention Study, also did not detect a significant relationship between a family history of preeclampsia or hypertension and periconceptional vitamin use (-3 to 3 months around LMP).[24] For the presence of chronic disease, although the SMART was inclusive of possible maternal medical conditions, the present analysis still did not detect a significant association. A prospective cohort study examined the presence of hypertension and periconceptional vitamin use, but the result was also not significant. A PRAM report examined data from 19 reporting areas during 2000 suggested that the association between the presence of gestational diabetes and pre-conceptional vitamin use was not significant.[39] For parity, there were controversies about the relationship between parity and vitamin earlier use in

pregnancy. One study in the U.S. used data from the National Birth Defects Prevention Study found that women who did not take vitamin in periconceptional period (-3 months to 1 month around conception) tended to be nulliparous.[43] Another study in Australia, analyzing data from the Victoria Survey of Recent Mothers 2000 and the 2001 NSW Child Health Survey, found a different result: periconceptional vitamin non-users (-2 to 3 months around pregnancy recognition) were multiparous.[97] The difference in maternal characteristics between two countries might create this discrepancy.

Smoking during pregnancy was not a significant predictor. There were several studies in the U.S. found that women who were not current smokers were tended to be vitamin users in pregnancy,[42, 43, 74, 86] but none of these studies specified the time point when women stopped smoking. For alcohol and recreational drug exposure in periconceptional period, the present analysis did not observe any significant relationship with vitamin earlier use in pregnancy. A study, using data from the National Birth Defects Prevention Study, also examined yielded a similar result.[43] Of note, this study focused on any alcohol and recreational drug exposure from the three months before conception through the time of delivery, while the present study limited drink exposure to binge drink (≥4 drinks on one occasion) and recreational drug in periconceptional period (the month around the last menstrual period).

Limitations

The first limitation of this study was that we relied on the self-reported information from women. There is a possibility of outcome misclassification,

because women might have had difficulty remembering their behaviors regarding vitamin use before the interview or early in pregnancy. Recall bias might cause missing values for some maternal characteristics and information of vitamin use patterns. For instance, some women did not identify their family history of birth defects or adverse pregnancy outcomes. However, comparing to maternal characteristic, the present study had more missing values for vitamin use patterns. Some women failed to identify the type or brand of prenatal vitamins. There were also some women who could not specify the date when they began to take vitamins. Similarly, due to the sensitive nature of some questions (e.g. marital status, recreational drug use, periconceptional binge drink), there is a possibility that women felt reluctant to report or might not report their maternal behaviors accurately. In addition, potential interview bias might also occur and impact on the validity of self-report information.

A second limitation of this study was that it did not capture the maternal characteristics and vitamin use patterns for all the participants due to the nature of the SMART study. The late introduction of some questions also caused missing values for the present analysis. For instance, more than half of participants did not have information on recreational drug use. Also, the SMART study did not investigate pregnancy planning for the first 42 women. The incomplete information of maternal characteristics might cause loss of valid sample size for the analysis, thus reducing the power to detect significant predictors. Furthermore, the SMART study did not capture all the relevant maternal characteristics for vitamin use during pregnancy. For example, this study did not ask women about their house income, while this demographic

characteristic is a potential predictor of using vitamins during pregnancy. Given to the large proportion of women without any health insurance and recipients of Medicaid, it is likely that the study population included a large number of women at low socioeconomic status. For vitamin use patterns, the SMART study did not follow up vitamin use after the baseline interview. Therefore, this analysis could not estimate the duration of vitamin use during the entire process of pregnancy. In addition, the SMART study did not ask participants about the reason of vitamin use or non-use.

The inclusion criteria of the SMART study affected the estimation of vitamin use among all the pregnant women for the present analysis. The SMART study ascertained eligible women with known pregnancy status, but it did not include women with miscarriages that occur prior to this study. It is important to explore their vitamin use during pregnancy, for most of these women might be vitamin non-users.

In terms of generazability, the present study might limit the findings to the women in New Mexico. The ethnic distribution was quite different from that in the BRFSS and the PRAMS, for there were a large proportion of Hispanics women in the present analysis. Additionally, the SMART study might not be fully representative of all pregnant women in New Mexico, for it only captured women who did attend UNM-affiliated prenatal care clinics.

Strengths

The first strength of this study is that the validity of data from the SMART study is high. There is a high degree of intended cooperation, given to the fact that this study had a high participation rate (81.5%). For non-participation, the SMART study also asked them to specify the reasons. All the interviewers in the SMART study have previous experience of conducting interviews, and all of them received a standardized training before the study. Thus, we have reduced the interviews bias at the minimum level. Moreover, we realized that there were a large number of Spanish-speaking women in New Mexico. Hence, all the interviewers are bi-lingual and fluent in English in order to eliminate the language barrier of communication.

The second strength of this study is that it provides comprehensive information of vitamin use pattern. Firstly, we estimated the prevalence of vitamin use on a regular basis, which is meaningful. Prior CDC report demonstrates that multivitamin use at least four times per week can provide the recommended amount of folic acid.[39] Secondly, we categorized vitamin use in different time of pregnancy and created three mutually exclusive vitamin user groups. Based on this classification, we compared the different in maternal characteristics among three groups. In addition, the study showed the type and the most popular brands among vitamin users. Thirdly, for vitamin users after pregnancy recognition, we attempted to estimate the time gap between the last menstrual period and the initiate time of vitamin use. Knowing this time gap could help us determine whether women missed the appropriate time for vitamin intake. Lastly, although this study did not capture women who had a miscarriage

before enrollment, the present analysis included women who had pregnancy ended in a stillbirth (no live birth; gestational age<20 weeks).

Thirdly, this is the first study which adopted an ordinal logistic regression model and polychotomous logistic regression model for the analysis. With the ordinal logistic regression model, we assumed that there was a natural ordering across three vitamin user groups, and we were able to identify the significant predictor associated with earlier vitamin use. The use of polychotomous logistic regression enables this study to compare the difference in maternal characteristics between pre-conceptional vitamin users and vitamin users after pregnancy recognition. Additionally, the present analysis is the first one which attempted to examine interactions between two predictors.

The fourth strength of this study is that the population in SMART study has an ethnically and socially-diverse sample. The present study is the first one which investigated vitamin use in pre-conceptional period and after pregnancy recognition using a sample primarily with Hispanic women.

Future Directions & Recommendations

For vitamin use among pregnant women, future studies should clearly define “pre-conceptional period”, “periconceptional period”, and “anytime during pregnancy”. The difference in these definitions can cause various results, including both prevalence and predictors. Also, future studies need to select the study population carefully. Only including mothers of live-born child might

overestimate the prevalence of vitamin use in pregnancy. It is highly possible that the prevalence could be lower if the sample also included women with a miscarriage. In addition, to ascertain vitamin use, it is meaningful to define a vitamin user as someone who takes multivitamins at least 4 times per week. This meets the recommended amount of folic acid to prevent NTDs, according to the CDC. Moreover, it is helpful to identify the type and brands of vitamins. Therefore, researchers can determine the components and estimate the amount of folic acid in each product. To ensure the compliance of vitamin intake during pregnancy, future studies need to follow up and estimate the duration of vitamin use. Last but not least, it is helpful to estimate the initiate time for vitamin use, especially for women who started vitamin use after pregnancy recognition. Women with late pregnancy recognition might miss the right time to initiate vitamin use for preventing NTDs.

With regard to the questionnaire design and interviews, future study may need to introduce Spanish or other foreign languages if the population includes minorities or foreign immigrants. Also, considering that some participants might fail to identify the type or brand of vitamins, researchers should provide a sample or bottles of vitamin products. Interviewers could also ask participants to show the vitamin products that they are using. To ascertain some sensitive maternal behaviors (e.g. alcohol use, recreational drug use), future studies can introduce biomarkers to certify the validity of self-report information. Lastly, the reasons of not taking vitamins need to be further studied. Previous experience of adverse pregnancy outcomes could mislead women into believing that vitamin use in pregnancy might account for adverse pregnancy outcomes.

Future studies need to assess the perception of vitamin use in pregnancy. Public health campaign might incorporate appropriate education program in order to change attitudes towards an earlier vitamin use during pregnancy.

Although the association between some maternal characteristics (e.g. education, maternal age, BMI, health insurance, marital status) and vitamin use were not significantly in the present study, it does not mean that these factors do not account for the prevalence of vitamin use in early pregnancy. The findings of the present study should be interpreted with caution. Future studies need to explore these findings by recruiting a larger sample size.

There is a great need to develop prevention strategies to educate pregnant women about benefits of prenatal vitamin use. Our study indicated that ethnic minorities may particularly benefit from such education efforts. To begin with, improving access to prenatal care for all pregnant women will facilitate greater utilization of prenatal vitamins. For women who have financial or other barriers to obtain vitamins, publicly funded clinics with free access to prenatal care should be widely available. Health insurance companies can add multivitamin into their prescription plans and formulary. Also, healthcare providers should play a pivotal role in education of women at reproductive age. Specifically, they should provide counseling to pregnant women and women who plan a pregnancy in order to improve the patient's knowledge of preventing NTDs and to inform them about the benefits of taking vitamins. A March of Dimes survey suggested that 89% of women would be more likely to take folic acid if advised by health care providers.[98] However, this survey also found that only 30% of

women who were aware of folic acid cite health care providers as the source of information about the benefits of folic acid use in pregnancy.[98] Therefore, there is a great need to incorporate healthcare providers as a part of the birth defects prevention programs. A physician-based intervention, conducted at Arkansas, suggested that a brief counseling from physicians can potentially reduce the risk of folate-preventable birth defects among their patients by as much as 11%.[99] Besides physicians, pharmacists may also contribute to the promotion of folic acid use among women of reproductive age by encouraging them to take multivitamins. Moreover, the mass media, including printed media, audio and visual media, Internet, can also serve to increase the awareness of vitamin use at reproductive age. Lastly, additional research is needed to ascertain the reasons of using or not using vitamins among pregnant women or women who might become pregnant. Health behavior models, such as Health Belief Model, Theory of Planned Behavior, may help to better understand the patient's decision making process with respect to vitamin use during pregnancy and earlier initiation of prenatal care.

In sum, this study highlights the importance of promoting vitamin use in early pregnancy among pregnant women in New Mexico, given to the finding that only less than one third of women used vitamins during the pre-conceptional period. The findings of this study can also provide an implication that public health strategies to ensure early use of vitamin during pregnancy should include the promotion of pregnancy planning.

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LIST OF TABLES

Table 2.1. Prevalence of Multivitamin Use in Pregnancy

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Dott M 2010 U.S.	Case-control study *Data from National Birth Defects Prevention study 1997-2002	N=4,094 mothers of live born infants born during 1997-2002	Periconceptional period: -1 month to +1 month around conception During pregnancy: not studied Multivitamin: multivitamin containing folic acid/prenatal multivitamin Frequency: not studied OTC & Rx: not studied Single vitamin: not studied	Periconceptional non-multivitamin users: 41% (992/2437) of women without pregnancy intent; 64.3% (1059/1648) of women with pregnancy intent	Potential selection bias exists when this study did not capture mothers whose current pregnancy ended in a miscarriage, stillbirth, or an infant with a major birth defect, potentially resulting in an underestimate of the impact of pregnancy intention on maternal behaviors. Also, this study may have recall bias.

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Burris HH 2009 U.S.	Cross-sectional study *Data source: the Slone Epidemiology Center Birth Defects Study	Control: random sample of Massachusetts births Case: Mothers of malformed infants	Periconceptional period: -1 to +1 around LMP During pregnancy: not studied Multivitamin: at least 2 water-soluble vitamins+2 fat-soluble vitamins Frequency: ≥4 times/week OTC & Rx: not mention Single vitamin: not mention Prenatal vitamin: not mention	Periconceptional multivitamin users: 55.0% of white women vs. 25.6% of black women	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Sullivan K 2009 U.S	Cross-sectional study *Data from Behavioral Risk Factor Surveillance System(BRFSS)	N= 788 pregnant women who were ascertained from 20, 263 women who aged from 18 to 44 years by 14 states and U.S territories	Periconceptional period: Not studied During pregnancy: studied but not defined Multivitamin: not defined Frequency: not studied OTC & Rx: not studied Single vitamin: not studied Prenatal multivitamin: not studied	Multivitamin users in pregnancy: 78% of pregnant women reported multivitamin use.	Women were asked whether they currently used multivitamin or not. Information about the duration of multivitamin use, dose, contents, and frequency was not collected

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Avalos LA 2009 U.S.	Prospective Cohort study *Data: women members in the Kaiser Permanente Medical Care Program (KPMCP)	N=1,061 women who was at their first pregnancy, speaking English, have pregnancy intentness and whose gestational age at the pregnancy test was less than or equal to 10 complete weeks	Periconceptional period: began prior pregnancy and in pregnancy (not specifically defined) During pregnancy: since become pregnant or LMP Multivitamin: multivitamin/prenatal vitamin Frequency: any use (not specifically defined) OTC & Rx: not studied Single vitamin: studied but not presented	Periconceptional multivitamin users: 23.8% (252/1061) During pregnancy: 68.8% (730/1061) Prenatal multivitamin users who begin to use multivitamin during pregnancy: 44.8% (475/1061) Multivitamin non-users: 31.2% (331/1061)	Multivitamin status is an important modifier in the relationship between pregnancy drinking and miscarriage: the risk of miscarriage was greatest for women who drank alcohol and reported no multivitamin supplementation

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Venkata P.S 2008 U.S.	Cross-sectional study *Data: Missouri Pregnancy Related Assessment and Monitoring System (MoPRA)	N=1,789 mothers in Missouri who delivered the previous 2-6 months	Pre-conceptional period: one month before became pregnant During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: 1-3/4-6/7 times per week OTC & Rx: not studied Single vitamin: studied but not presented	Pre-conceptional multivitamin users: 29.7% (every day a week), 5.0% (4-6 times per week), 10% (1-3 times per week)	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Catov JM 2007 U.S.	Prospective Cohort study *Data from the Pregnancy Exposure and Preeclampsia Prevention Study	N=1,823 women who enrolled at less than 16 weeks and followed through the postpartum visit	Periconceptional period: 6 months which included prior to conception, at the time of conception immediately after conception (not specifically defined) During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: at least once/week OTC & Rx: not studied Single vitamin: not studied	Periconceptional multivitamin users: 47%	The study relied on self-reported multivitamin use. Also, This study lack of information on the brand or dose of supplement periconceptional vitamin supplementation is associated with preterm birth (<34 weeks) has been reported by others

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
D'Angelo D et al 2007 U.S.	Cross-sectional study *Data from Pregnancy Risk Assessment Monitoring System(PRAMS) During 2003-2004	Women from 26 PRAMS reporting areas	Preconceptional period: before pregnancy (1 month before, 3 months, 12 months before pregnancy) Periconceptional period & During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: at least 4 times/week OTC & Rx: not studied Single vitamin/prenatal vitamin: not studied	Pre-conceptional multivitamin users: 35.1% (26.7% in Arkansas – 43.6% Rhode Island)	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
CDC (not listed) 2007 U.S.	Cross-sectional study *Data from Pregnancy Risk Assessment Monitoring System(PRAMS) During 2000-2003	Women from PRAMS in Oklahoma	Preconceptional period: during the month before pregnancy Periconceptional period & During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: at least 4 times/week OTC & Rx: not studied Single vitamin/prenatal vitamin: not studied	Pre-conceptional multivitamin users: 26.5%	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Suellentrop et al 2006 U.S.	Cross-sectional study *Data from Pregnancy Risk Assessment Monitoring System(PRAMS) During 2000-2003	Women from 19 PRAMS reporting areas	Pre-conceptional period: during the month before pregnancy Periconceptional period & During pregnancy: not studied Multivitamin: not defined Frequency: at least 4 times/week OTC & Rx: not studied Single vitamin/prenatal vitamin: not studied	Pre-conceptional multivitamin users: 23.0% in Arkansas to 45.2% in Maine	Sectional bias may exist because only women with live infants were included

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Carmichael 2006 U.S.	Cross-sectional analysis *Data from the National Birth Defects Prevention Study	N=2518 women with estimated delivery dates from 1997-2000	Pre-conceptional period: not studied Periconceptional period: 3 month before conception/one month after conception Earlier pregnancy: the second and third month after conception Later pregnancy: during the fourth month or later during pregnancy Multivitamin: multivitamin/prenatal vitamin: folic acid supplementation Frequency: not defined OTC & Rx/prenatal vitamin: not studied	Periconceptional vitamin non-users: 53% Earlier pregnancy: 35% Later pregnancy: 8%	Participants were mothers of live-born infants without major malformation

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Glover et al 2003 U.S	Prospective cohort study	N=578 participants from four rural outreach clinics between August 1999 and November 2001	Periconceptional period: not studied During pregnancy: since LMP Multivitamin: not defined Frequency: studied but not presented OTC & Rx: separately reported (Rx multivitamin was defined as a prenatal vitamin) Single vitamin: vitamin C was reported Prenatal multivitamin: not studied	Multivitamin users in pregnancy: 92% (prescribed prenatal vitamin) vs. 10.9% (OTC multivitamins) Vitamin C users in pregnancy: 2.4% (14)	Information about the duration of multivitamin use, dose, contents, and frequency was not mentioned

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Vahratian 2004 U.S.	Cross-sectional analysis *Data: Pregnancy, Infection, and Nutrition (PIN) study	Women who were at 24-29 weeks of pregnancy from 4 prenatal care clinics in central North Carolina	Periconceptional period: Before and during pregnancy (not specifically defined) During pregnancy: any time during pregnancy up until the time of interview or recruitment (24-29 gestational weeks) Multivitamin: not defined Frequency: studied but not presented OTC & Rx/prenatal vitamin: not studied Single vitamin: folate, vitamin A, vitamin C was studied but not reported	Periconceptional multivitamin users: 30% Prenatal multivitamin users: 54%	Frequency of multivitamin use, type of multivitamin was not studied in this analysis

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Williams LM 2000 U.S.	Cross-sectional study *Data from Pregnancy Risk Assessment Monitoring System (PRAMS) 2000	N=32,479 women who were identified from 19 states and U.S territories	Pre-conceptional period: during the month before pregnancy Periconceptional period & During pregnancy: not studied Multivitamin: not defined Frequency: at least 4 times/week OTC & Rx/prenatal vitamin: not studied Single vitamin: not studied	Pre-conceptional multivitamin users: 25.0%--40.7%	Because data are self-reported 2--8 months after delivery, responses might be subject to recall bias, particularly for behaviors and experiences that occurred before the pregnancy

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Wu T 1998 U.S	Cross-sectional study *Data from the National Maternal and Infant Health Survey	N=12,465 women were identified from livebirth, fetal death, infant death certifications from the National Maternal and Infant Health Survey	Periconceptional period: -3 to +3 months around pregnancy recognition During pregnancy: 3 months after pregnancy recognition Multivitamin: not defined Frequency: at least 3 times/week OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin A, vitamin C, folic acid were studied but not reported	Periconceptional multivitamin/mineral users: 21% Multivitamin/mineral users during pregnancy: 53.8%	Multivitamin and mineral supplements were combined and could not be separated for further analysis

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Scholl TO 1997 U.S.	Prospective cohort study	N=1,430 low income, urban women who entered prenatal care during the first and second trimesters and who had singleton pregnancies.	Periconceptional period: Not studied During pregnancy: after pregnancy recognition Multivitamin: prenatal multivitamin/mineral supplements Frequency: not studied OTC & Rx: not studied Single vitamin: not studied	Multivitamin/supplements users during pregnancy: 80.4% 29.3% (418/1430) at the first trimester vs. 730 51.0% (730/1430) during the second trimester	Multivitamin and mineral supplements were combined, and there was insufficient information on the use of multivitamin such as type of multivitamin, frequency, or length of ingestion

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Milunsky 1989 U.S.	Cross-sectional analysis	N=22,776 pregnant women who had a either maternal serum a-fetoprotein(MSAFP) screen or an amniocentesis around 16 weeks of gestation	Periconceptional period: -3 to +3 months around LMP During pregnancy: 3 months after LMP Multivitamin: not defined Frequency: studied but not reported OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin A, vitamin C, vitamin E, folic acid were studied but not reported	Periconceptional multivitamin users: 31.9% (n=7261) Multivitamin non-users: 12.9% (n=2927)	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Yu SM 1996 U.S.	Cross-sectional study *Data from the National Maternal and Infant Health Survey	N=9,953 women who delivered live infants in the 1988 National Maternal and Infant Health Survey	Periconceptional period: not studied During pregnancy: after pregnancy recognition Multivitamin: not defined Frequency: ≥3 times/week OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin A, vitamin C, vitamin E, folic acid were studied but not reported	Multivitamin-mineral supplement users: 82.5% (67% of Black mothers vs. 84% of White mothers)	Multivitamin and mineral supplements were combined,

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Tam LE 2004 Canada	Cross-sectional analysis	N=383 postpartum women in Toronto Hospital and the Mount Sinai Hospital	Periconceptional period: at least 4 weeks prior to conception until 8 weeks after conception During pregnancy: not studied Multivitamin: not defined Frequency: not studied OTC & Rx/prenatal vitamin: not studied Single vitamin: not studied	Periconceptional multivitamin users: 28%	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Alwan NA 2010 United Kingdom	prospective cohort study	N=1,274 women who aged at 18-45 years with low-risk pregnancies were prospectively recruited at 8-12 weeks of gestation from the Leeds Teaching Hospital maternity unit between 2003 and 2006	Periconceptional period: not studied During pregnancy: from the first trimester to the third trimester Multivitamin: not defined Frequency: not studied OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin A, B6, B12, C, D, E were studied but not prevalence rate was reported	Multivitamin-mineral supplement users during pregnancy: 23.3 % (293/1274) in the first trimester, 14.1% (177/1274) in the second trimester, and 18.6% (79/425)*. * Only 425 women had information on supplement intake in the third trimester.	Data on using multivitamin-mineral preparation was mixed and could not be separated.

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
KÄLLÉN 2003 Sweden	Prospective Cohort study	N=3675 women who were at their first visit to the antenatal care unit and return questionnaire around gestational week 28.	Periconceptional period: before pregnancy and the first two months after pregnancy (not specifically defined) During early pregnancy: first two months Multivitamin: not defined Frequency: not studied OTC & Rx/prenatal vitamin: not studied Single vitamin: not studied	Periconceptional multivitamin users: 19.3% (2525/3675) Multivitamin user during early pregnancy: 7.8% (286/3675) of women used vitamin only in early pregnancy.	The study explored the relationship between vitamin use, smoking, and nausea and vomiting of pregnancy, but it does not focus on the predictors of the use of multivitamin/vitamin

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Catov JM 2009 Denmark	Prospective Cohort study *Data from Danish National Birth Cohort	N=26,601 women who were recruited in Danish National Birth Cohort and completed revised recruitment form	Periconceptional period: -4 wks to +8 wks around LMP During pregnancy: not studied Multivitamin: not defined Frequency: at least once/week OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin A, B1, B12, B6, B12, C, D, E, and folic acid were studied but prevalence rates were not reported	Periconceptional multivitamin users: 65% (18,551/26601)	Regular periconceptional multivitamin use is associated with a reduced risk of preeclampsia among normal-weight women

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Paulik E 2009 Hungary	Cross-sectional study *Data from a self-administrated questionnaire (response rate=69.8%)	N=349 voluntary pregnant women who were at the Department of Obstetrics and Gynecology and in the Pregnancy Care Center	Periconceptional period: not studied During pregnancy: not defined Preconception period: Not defined Multivitamin: not defined Frequency: not defined OTC & Rx: not studied Single vitamin: folic acid	Preconception multivitamin regular users: 43.8% (153/349) Preconception folic acid regular users: 31.5% (110/349) Multivitamin regular users in pregnancy: 48.4% (141/349) Folic acid regular users in pregnancy: 40.4% (141/349)	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Haugen M 2008 Norway	Cross-sectional study *Data from Norwegian Mothers and Child Cohort Study(MoBa)	N=40,817 Pregnant women in Norway who were 17-18 weeks of gestation and participates in study between February 2002 and February 2005	Periconceptional period: not studied During pregnancy: first 4-5 months Multivitamin: not defined Frequency: never/<1/1-7 times per week OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin A, B1, B12, B6, B12, C, D, E, and folic acid were studied but prevalence rates were not reported	Multivitamin users in the first 4-5 months of pregnancy: 16.3%	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Vollest SE 2000 Norway	Prospective cohort study	N=1,140 Norwegian women who aged 18-45 years	Periconceptional period: before or during the first 2-3 months of their last recent pregnancies During pregnancy: not defined Multivitamin: not defined Frequency: daily or almost daily/less frequent than daily/ almost daily/never OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin B, folic acid	Periconceptional multivitamin users (daily or almost daily): 19.8% Periconceptional Vitamin B users: 3.6% Periconceptional folic acid users: 2.4%	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Lunet N 2008 Portugal	Cross-sectional analysis from a case-control study	N=836 mothers who were interviewed 24-72 hours after delivery at two major public hospitals in the North of Portugal	Periconceptional period: not studied, During pregnancy: without exactly refer to exact trimester Multivitamin: not defined Frequency: not studied OTC & Rx/prenatal vitamin: not studied Single vitamin: folic acid	Multivitamin uses in pregnancy: 76.2% Folic acid users in pregnancy: 55.4%	Frequency of multivitamin use and the content of multivitamin was not mentioned in this study;

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Nilsen RM 2008 Norway	Cross-sectional Analysis *Data from Medical birth registry of Norway	N=226,724 women who have been recorded by Medical Birth Registry of Norway from 1998 through 2004	Periconceptional period: before and during pregnancy (not specifically defined) During pregnancy: not defined Multivitamin: multivitamin alone/folic acid alone/both folic acid and multivitamin Frequency: not studied OTC & Rx: not studied Single vitamin/prenatal vitamin: not studied	Periconceptional multivitamin and/or folic acid users: 15.9% Multivitamin and/or folic acid users in pregnancy: 27.3%	The prevalence of using each supplement type can not be separated from the data

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Forster D 2009 Australia	Cross-sectional survey	N=588 women were approached in the antenatal clinic and the birth centre at around 36-38 weeks gestation	Periconceptional period: before and during pregnancy (not specifically defined) During pregnancy: not defined Multivitamin: folic acid alone/folic acid with multivitamin/folic acid with other vitamin Frequency: does/day and length of time were recorded OTC & Rx/prenatal vitamin: not studied Single vitamin: folic acid, vitamin B6	Periconceptional multivitamin users: 7.8% (46/587) Multivitamin users not before pregnancy but during pregnancy: 26.9% (158/587)	A combination of folic acid and multivitamin intake in different time of pregnancy was provided.

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Maats FH 2002 Australia	Cross-sectional study(Hospital-based sample)	N=211 women who were 26 weeks gestation or more	Periconceptional period: during the three months prior to pregnancy During pregnancy: from the 1st trimester to the 3rd trimester. Multivitamin/: not defined Frequency: studied but not reported OTC & Rx/prenatal vitamin: not studied Single vitamin: folic acid alone or folic acid combined with multivitamins	Periconceptional multivitamin users: 26 (12%) Multivitamin users in pregnancy: 33(16%) in the first trimester, 37(18%) in the second trimester, 39(18%) in the third trimester, respectively.	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Prevalence	Comments
Wehby G 2009 Brazil	Cross-sectional analyses(Birth registry data)	N=1,774 mothers of liveborn infants without congenital malformations between 1995 and 2001 in Brazil	Periconceptional period: not studied During pregnancy: not defined Multivitamin: multivitamin/prenatal vitamin Frequency: any use during pregnancy (not specifically defined) OTC & Rx: not studied Single vitamin: not studied	Multivitamin users in pregnancy: 14%	This study evaluate the demand for multivitamins both pooled and stratified by African ancestry based on maternal report of the ancestries of the infant

Table 2.2. Predictors of Multivitamin Use in Pregnancy

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Burris HH 2009 U.S.	Cross-sectional study *Data source: the Slone Epidemiology Center Birth Defects Study	Control: random sample of Massachusetts births Case: Mothers of malformed infants	Periconceptional period: -1 to +1 month around LMP During pregnancy: not studied Multivitamin: at least 2 water-soluble vitamins+2 fat-soluble vitamins Frequency: ≥4 times/week OTC & Rx: not mention Single vitamin: not mention Prenatal multivitamin: not mention	Periconceptional multivitamin users: white women, non-smokers, married, older, wealthier (annual household≥$45,000), and better educated (above high school education)	**Periconceptional: 28 days prior to the last menstrual period to after 28 days after the last menstrual period

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Sullivan K 2009 U.S.	Cross-sectional study *Data from Behavioral Risk Factor Surveillance System(BRFSS)	N=20, 263 women who aged from 18 to 44 years by 14 states and U.S territories	Periconceptional period: Not studied During pregnancy: studied but not defined Multivitamin: not defined Frequency: not studied OTC & Rx/prenatal vitamin: not studied Single vitamin: not studied Prenatal multivitamin: not studied	Multivitamin users during pregnancy: Higher Income (annual household≥$50,000) Marital status (married or previously married)	Based on 14 U.S states, the generalizability of the results is limited. Information about the duration of multivitamin use, dose, contents, and frequency was not collected

Author & Date	Study Design	Population	Assessment of Vitamin Use	Predictors	Comments
Venkata P.S 2008 U.S.	Cross-sectional study *Data: Missouri Pregnancy Related Assessment and Monitoring System (MoPRA)	N=1,789 mothers in Missouri who delivered the previous 2-6 months	Pre-conceptional period: one month before became pregnant During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: 1-3/4-6/7 times per week OTC & Rx: not studied Single vitamin: studied but not presented	Periconceptional multivitamin regular users (≥4 times/week): Intended pregnancy, high house income (≥35,000), married, non-smoker, more educated (≥12 years), older (≥20 years)	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Predictors	Comments
D'Angelo D et al 2007 U.S.	Cross-sectional study *Data from Pregnancy Risk Assessment Monitoring System(PRAMS) During 2003-2004	Women from 26 PRAMS reporting areas	Preconceptional period: before pregnancy (1 month before, 3 months, 12 months before pregnancy) Periconceptional period & During pregnancy: not studied Multivitamin: not defined Frequency: at least 4 times/week OTC & Rx: not studied Single vitamin/prenatal vitamin: not studied	Preconceptional multivitamin users: older (≥35 years), white women, intended pregnancy, had private health insurance	

Author & Date	Study Design	Population	Assessment of Vitamin Use	Predictors	Comments
CDC (not listed) 2007 U.S.	Cross-sectional study *Data from Pregnancy Risk Assessment Monitoring System(PRAMS) During 2000-2003	Women from PRAMS in Oklahoma	Preconceptional period: during the month before pregnancy Periconceptional period & During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: at least 4 times/week OTC & Rx: not studied Single vitamin/prenatal vitamin: not studied	Preconception Multivitamin non-users: Younger (<20 & 20-24) or, unmarried, < 12 years of education, no health insurance, enrolled in Medicaid	

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Carmichael 2006 U.S.	Cross-sectional analysis *Data from the National Birth Defects Prevention Study	N=2518 women with estimated delivery dates from 1997-2000	Preconceptional period: not studied Periconceptional period: 3 months before conception/one month after conception Earlier pregnancy: the second and third month after conception Later pregnancy: during the fourth month or later during pregnancy Multivitamin: multivitamin/prenatal vitamin: folic acid supplementation Frequency: not defined OTC & Rx/prenatal vitamin: not studied	Periconceptional vitamin non-users: race (nonwhite), language speaking (Spanish), education (low education), maternal age (younger<25), parity (nulliparous), smoke (current smoker), a history of miscarriage (no history of miscarriage)	Participants were mothers of live-born infants without major malformation

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Williams LM 2000 U.S.	Cross-sectional study *Data from Pregnancy Risk Assessment Monitoring System(PRAMS)	N=32,479 women who were identified from 19 states and U.S territories	Preconceptional period: during the month before pregnancy Periconceptional period & During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: at least 4 times/week OTC & Rx/prenatal vitamin: not studied Single vitamin: not studied	Preconceptional users: Education (>12 years), age (>35 years), non-Medicaid recipients	Because data are self-reported 2--8 months after delivery, responses might be subject to recall bias, particularly for behaviors and experiences that occurred before the pregnancy

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Catov JM 2007 U.S.	Prospective cohort study *Data from the Pregnancy Exposure and Preeclampsia Prevention Study	N=1,823 women who enrolled at less than 16 weeks and followed through the postpartum visit	Periconceptional period: 6 months which included prior to conception, at the time of conception immediately after conception (not specifically defined) During pregnancy: not studied Multivitamin: multivitamin/prenatal vitamin Frequency: at least once/week OTC & Rx: not studied Single vitamin: not studied .	Periconceptional multivitamin users: higher level of education, married, of normal body mass index (18.5-24.9), and to have participated in moderate or vigorous physical activity in the year before becoming pregnancy	The study relied on self-reported multivitamin use. Also, This study lack of information on the brand or dose of supplement

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Yu S 1996 U.S.	Cross-sectional study *Data: National Maternal and Infant Health Survey	N=9953 women who delivered live infants in the 1988 National Maternal and Infant Health Survey	Periconceptional period: not studied During pregnancy: after pregnancy recognition Multivitamin: not defined Frequency: ≥3 times/week OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin A, vitamin C, vitamin E, folic acid were studied but not reported	Multivitamin non-users before pregnancy: black, unmarred, age<30 or 20<age<34, less than or only have a high school education, Multivitamin non-users during pregnancy: black/Asia, younger, low education, unmarried, smoking status. age, race (white), socioeconomics married status (married), education	The self-report nature of the mothers' questionnaire data poses certain limitations to the study

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Tam LE 2004 Canada	Cross-sectional analysis	N=383 postpartum women in Toronto Hospital and the Mount Sinai Hospital	Periconceptional period: at least 4 weeks prior to conception until 8 weeks after conception During pregnancy: not studied Multivitamin: not defined Frequency: not studied OTC & Rx/prenatal vitamin: not studied Single vitamin: not studied	folic acid non users in pregnancy: unplanned pregnancy; lack of knowledge about folic acid Periconceptional folic acid/multivitamin users are more likely to be Jewish decent, parity (≥1)	marital status, education, family income were not significant

Author & Date	Study Design	Population	Assessment of Vitamin Use	Predictors	Comments
Paulik E 2009 Hungary	Cross-sectional study *Data from a self-administrated questionnaire (response rate=69.8%)	N=349 voluntary pregnant women who were at the Department of Obstetrics and Gynecology and in the Pregnancy Care Center	Periconceptional period: not studied During pregnancy: not defined Pre-conceptional period: Not defined Multivitamin: not defined Frequency: not defined OTC & Rx: not studied Single vitamin: folic acid	Pre-conceptional folic acid users: age (older), pregnancy planning Folic acid users in pregnancy: age (older), gestational age (younger)	Multivitamin use in pregnancy or preconception was correlated with folic acid use

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Nilsen RM 2008 Norway	Medical birth registry	N=226,724 women who have been recorded by Medical Birth Registry of Norway from 1998 through 2004	Periconceptional period: before and during pregnancy (not specifically defined) During pregnancy: not defined Multivitamin: multivitamin alone/folic acid alone/both folic acid and multivitamin Frequency: not studied OTC & Rx: not studied Single vitamin/prenatal vitamin: not studied	Periconceptional multivitamin users: order (≥25), married or cohabiting, primiparous, non-smoker multivitamin users during pregnancy have the same predictors	The prevalence of using each supplement type can not be separated from the data

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Vollest SE 2000 Norway.	Cross-sectional study *Data: a national survey initiated by the Medical Birth Registry and the National Council on Nutrition and Physical Activity	N=1,140 Norwegian women who aged 18-45 years	Periconceptional period: before or during the first 2-3 months of their last recent pregnancies During pregnancy: not defined Multivitamin: not defined Frequency: daily or almost daily/less frequent than daily/ almost daily/never OTC & Rx/prenatal vitamin: not studied Single vitamin: vitamin B, folic acid	Periconceptional multivitamin users: young (18-24), high education (university/college degree), married	Household was not significant(p=0.25) in multiple logistic regression result

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Forster D 2009 Australia	Cross-sectional survey	N=588 women were approached in the antenatal clinic and the birth centre at around 36-38 weeks gestation	Periconceptional period: before and during pregnancy (not specifically defined) During pregnancy: not defined Multivitamin: folic acid alone/folic acid with multivitamin/folic acid with other vitamin Frequency: does/day and length of time were recorded OTC & Rx/prenatal vitamin: not studied Single vitamin: folic acid, vitamin B6	Multivitamin non-users during pregnancy: unmarried/living with a partner, low income (annual house income<$30,000), Low education, parity (≥1)	The author did not undertook regression analysis to explore the predictor of the use of multivitamin during periconceptional period

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Waston 2006 Australia	Cross-sectional survey *Data: the Victoria Survey of Recent Mothers 2000 and the 2001 NSW Child Health Survey	N=1240 women who gave birth in Victoria	Periconceptional period: 1-2 months before pregnancy recognition+ 3 months after pregnancy recogntiion During pregnancy: after pregnancy recognition Multivitamin: folic acid supplementation Frequency: daily (7 times per week) OTC & Rx/prenatal vitamin: not studied	Folic acid non-users in periconceptional period: age (younger), education (lower education), income (less income), language speaking (Non-English speaking), marital status (unmarried), parity (multiparous), pregnancy planning (unplanned), living area (rural area)	

Author & Date	Study Design	Population	Assessment of Vitamin & Folic acid Use	Predictors	Comments
Haugen M 2008 Norway	Cross-sectional study *Data from Norwegian Mothers and Child Cohort Study(MoBa)	N=40,817 Pregnant women in Norway who were 17-18 weeks of gestation and participates in study between February 2002 and February 2005	Periconceptional period: not studied During pregnancy: first 4-5 months Multivitamin: not defined Frequency: never/<1/1-7 times per week OTC & Rx: not studied Single vitamin: vitamin A, B1, B12, B6, B12, C, D, E, and folic acid were studied but prevalence rates were not reported prenatal vitamin: not studied	Multivitamin users in pregnancy: age (≥25), BMI(≤24.9), smoking status during pregnancy (non-smokers), parity (primiparous), education (≥10 years of education)	Multivitamin use was combined with mineral use and other dietary supplements. It could not be separated from data

Author & Date	Study Design	Population	Assessment of Vitamin Use	Predictors	Comments
Lunet N 2008 Portugal	Cross-sectional analysis from a case-control study	N=836 mothers who were interviewed 24-72 hours after delivery at two major public hospitals in the North of Portugal	Periconceptional period: not studied, During pregnancy: without exactly refer to exact trimester Multivitamin: not defined Frequency: not studied OTC & Rx/prenatal vitamin: not studied Single vitamin: folic acid	Folic acid supplementation non-users during pregnancy: marital status (single), pregnancy planning (unplanned); Multivitamin users: education (less educated)	Frequency of multivitamin use and the content of multivitamin was not mentioned in this study;

Table 3.1. Sample size calculations for different effect sizes

Effect size	N1	N2	Total N	Power
20%	63	189	225	0.80
30%	28	84	112	0.82
40%	13	39	52	0.81
50%	9	27	36	0.83
60%	6	18	24	0.82

Two-sided Z tests were used with 1:3 ratio at alpha level 0.05
N1: required sample size for pre-conception multivitamin regular users
N2: required sample size for multivitamin regular users during pregnancy
Total N: the total required sample size in both groups
Effect size: the difference in the proportion of multivitamin user between the study groups

Table 4.1 Characteristics of the Study Population (N=402)

Maternal Characteristics	N (%)[a]
Hispanics	323 (80.4)
Race*	
White Non-Hispanic	49 (12.2)
White Hispanic	298 (74.3)
Black or African American	23 (5.7)
American Indian or Alaskan Native	27 (6.7)
Asian or Asian American or Pacific Islander	3 (0.8)
Some other group	1 (0.3)
Educational Level	
Less than high school graduate	141 (35.1)
High school graduate or GED	132 (32.8)
Some college or vocational school	89 (22.1)
College degree	28 (7.0)
Master, doctorate or professional degree	12 (3.0)
Marital Status	
Single, never married	95 (23.6)
Married, living with spouse	168 (41.8)
Not married, but living with partner	120 (29.9)
Separated	15 (3.7)
Divorced	4 (1.0)
Widowed	0
Health Insurance Status	
No insurance	196 (48.8)
Employer-based insurance	45 (11.2)
Self-purchased insurance	4 (1.0)
Medicaid	110 (27.4)
Other public insurance[b]	47 (11.7)
Language Speaking	
Spanish speaking	244 (60.7)
English speaking	152 (37.8)
Other language speaking	6 (1.5)
Country of Birth: U.S.	163 (40.6)
Primigravida	89 (22.2)
Nulliparous	130 (32.5)
History of Adverse Pregnancy Outcomes	129 (32.1)
Miscarriage (<20 wk of gestation)	110 (27.6)
Stillborn child (≥ 20 wk of gestation)	17 (4.3)
Terminated birth	30 (7.5)
Ectopic pregnancy	7 (1.8)
Presence of Chronic Condition(s)	181 (45.0)
Diabetes	81 (20.1)
Depression	26 (6.5)
Asthma or Allergies	35 (8.8)

Table 4.1 (Continued) Characteristics of the Study Population (N=402)

Maternal Characteristics	N (%)[a]
A Family History of Birth Defect(s) or Adverse Pregnancy Outcome	76 (19.3)
Down syndrome	12 (3.0)
Cleft lip or palate	4 (1.0)
Neural tube defect	5 (1.2)
Cystic fibrosis	0
Heart defect	6 (1.4)
Other[c]	63 (15.7)
Obesity (BMI≥30)	104 (25.9)
Pregnancy Planning	
Yes	171 (48.6)
No, not now	110 (31.3)
No, not at any time	71 (20.2)
Smoking Status	
Non-smoker	294 (73.3)
Past smoker, quit before pregnancy recognition	55 (13.7)
Past smoker, quit after pregnancy recognition	41 (10.2)
Current smoker	11 (2.7)
Periconceptional Binge Drinker	93 (23.1)
Periconceptional Recreational Drug User	11 (5.5)
Use of Prescription Medications during Pregnancy	
None	187 (46.6)
1-2 medications	165 (41.2)
More than 2 medications	49 (12.2)
Mean±s.d	
Maternal Age (yrs)	27.6±6.1
Gestational Age at Enrollment (wks)	30.7±8.0

[a] Sample size might vary due to missing values

[b] Other public insurance: UNM/UNM Care (7.0%, 28/402), Indian Health Service (1.0%, 4/402), First Choice (1.0%, 3/402)

[c] Other birth defect or adverse perinatal outcome: miscarriage (9.7%, 39/402), stillbirth (1.7, 7/402)

Table 4.2 Descriptive Statistics of Multivitamin Use Patterns (N=402)

Pattern of Use	N (%)
Three Study Groups	
Group 1-Pre-conceptional vitamin users	86 (21.4)
Group 2-Vitamin users after pregnancy recognition*	289 (71.9)
Group 3-Vitamin non-users	27 (6.7)
Prescription vs. OTC Multivitamin	
Prescription vitamins	116 (28.7)
OTC vitamins	219 (54.2)
Non-specified	40 (6.7)
The Most Common Brands of Vitamin**	
Wal-Mart prenatal vitamin	87 (21.6)
Walgreen prenatal vitamin	50 (12.4)
Mean±s.d	
Initiation of regular vitamin use (gestational weeks)***	9.0±7.2 wks
Number of days of vitamin use per week	6.0±1.9 days

***** There is only one woman who used single vitamin (folic acid) after pregnancy recognition, and she was still included in the Group 2.
****** The sample size is limited to group 1 and group 2
******* The sample size is limited to group 2

Table 4.3 Characteristics of the Study Participants by Vitamin Use

Maternal Characteristics	Group 1 (n=86)[a] %	Group 2 (n=289)[a] %	Group 3 (n=27)[a] %	*P value*
Hispanics	17.3	76.2	6.5	**<0.01**
Maternal age (yrs)				**0.16**
≤21 yrs	13.8	75.0	11.3	
21-30 yrs	24.7	69.6	5.7	
>30 yrs	21.1	73.4	5.5	
Race*				**0.20**
Whites	21.0	72.9	6.1	
Black or African American	17.4	78.3	4.4	
Some other groups	21.0	72.9	6.1	
Educational Level				**<0.01**
High school education or less	16.5	77.3	6.2	
Some college or vocational school	23.6	66.3	10.1	
College degree or higher	50.0	47.5	2.5	
Marital Status				0.44
Single, never married	20.0	72.6	7.4	
Married or with a partner	22.9	70.8	6.3	
Separated/divorced/widowed	5.3	84.2	10.5	
Health Insurance Status				**<0.01**
No insurance	17.7	76.0	6.1	
Medicaid or other public insurance	44.9	49.0	6.1	
Employer-based or self-purchased	18.5	73.9	7.6	
Spanish-Speaking	16.0	77.9	6.2	**<0.01**
Primigravida	23.6	70.8	5.6	0.79
Nulliparous	25.4	70.0	4.6	0.23
History of Adverse Pregnancy Outcomes	25.4	65.9	8.7	**0.15**
Presence of Chronic Condition(s)	22.7	69.1	8.3	0.40
A family History of Birth Defect(s)	26.3	67.1	6.6	0.53
Country of Birth: U.S	27.0	66.3	6.8	**0.07**
Obesity (BMI≥30)	25.4	67.7	6.9	0.32
Planned Pregnancy	26.9	66.7	6.4	**0.04**
Smoking Status				0.40
Non-smoker	20.8	72.1	7.1	
Past, quit before pregnancy recognition	30.9	61.8	7.3	
Smoker in pregnancy	15.4	80.8	3.9	
Periconceptional Binge Drinker	21.5	69.9	8.6	0.66
Periconceptional Recreational Drug User	18.2	81.8	0	0.52

Table 4.3 (Continued) Characteristics of Study Participants by Vitamin Use

Maternal Characteristics	Group 1 (n=86)[a] %	Group 2 (n=289)[a] %	Group 3 (n=27)[a] %	*P value*
Use of Prescription Medications during Pregnancy*				**0.16**
None	17.1	74.9	8.0	
1-2 types of medications	23.0	71.5	5.5	
More than 2 types of medications	32.7	61.2	6.1	
	Mean±s.d			
Maternal Age (yrs)	28.5±5.5	27.4±6.2	26.3±6.7	**0.18**
Gestational Age at Enrollment (wks)	31.2±7.8	30.5±8.1	31.6±7.3	0.63

[a] Sample size might vary due to missing values

Table 4.4 Predictors of Vitamin Use: Results of Multivariate Ordinal Logistic Regression Analysis*

Maternal Characteristics	ORs	95% CL	*P value*
Hispanics	0.68	0.29-1.61	0.38
Maternal age (yrs)			0.62
≤21 yrs	--	--	--
21-30 yrs	1.88	0.95-3.71	0.07
>30 yrs	1.27	0.61-2.65	0.53
Race			
Whites	--	--	--
Black or African American	0.77	0.28-2.13	0.61
Some other groups	0.33	0.11-1.04	0.06
Educational Level			
High school education or less	--	--	--
Some college or vocational school	1.06	0.56-2.04	0.86
College degree or higher	2.47	0.91-6.72	0.08
Health Insurance Status			
No insurance	--	--	--
Employer-based or self-purchased	1.42	0.46-4.46	0.54
Medicaid or other public insurance	0.82	0.38-1.78	0.61
Spanish-speaking	0.69	0.22-2.13	0.52
History of Adverse Pregnancy Outcomes	0.87	0.52-1.47	0.61
Country of Birth: U.S	0.76	0.24-2.44	0.64
Planned Pregnancy	**1.77**	**1.08-2.89**	**0.02**
Use of Prescription Medications during Pregnancy			
None	--	--	--
1-2 types of medications	1.52	0.89-2.59	0.13
More than 2 types of medications	2.17	0.94-4.99	0.07

***** All Odds ratios are adjusted for all variables in the table

Table 4.5 Interaction between Predictors in Ordinal Logistic Regression and Polychotomous logistic Regression Model

Interaction	Ordinal Logistic Regression P-value	Polychotomous Logistic Regression P-value
Ethnicity*Race	0.20	0.91
Ethnicity*Place of Birth	0.13	0.48
Ethnicity*Language Speaking	N.A	N.A
Race*Language Speaking	0.29	0.89
Race*Place of Birth	0.44	0.68
Place of Birth*Language Speaking	0.17	0.69
Education*Health Insurance Status	**0.01**	0.96
Education*Pregnancy Plan	0.69	0.85

Table 4.6 Predictors of Vitamin Use: Results of Multivariate Ordinal Logistic Regression Analysis among Women without Health Insurance*

Maternal Characteristics	ORs	95% CL	*P value*
Educational Level			
High school education or less	--	--	
Some college or vocational school	2.11	0.70-6.34	0.18
College degree or higher	0.24	0.03-2.17	0.20

* Odds ratio was adjusted for ethnicity, maternal age, race, language speaking, history of adverse pregnancy outcomes, country of birth, pregnancy planning, and use of prescription medications were adjusted.

Table 4.7 Predictors of Vitamin Use: Results of Multivariate Ordinal Logistic Regression Analysis among Women with Private Insurance *

Maternal Characteristics	ORs	95% CL	*P value*
Educational Level			
High school education or less	--	--	
Some college or vocational school	0.09	0.01-1.32	0.08
College degree or higher	0.33	0.02-6.73	0.47

* Odds ratio was adjusted for ethnicity, maternal age, race, language speaking, history of adverse pregnancy outcomes, country of birth, pregnancy planning, and use of prescription medications were adjusted.

Table 4.8 Predictors of Vitamin Use: Results of Multivariate Ordinal Logistic Regression Analysis among Women with Public Insurance *

Maternal Characteristics	ORs	95% CL	P value
Educational Level			
High school education or less	--	--	
Some college or vocational school	1.04	0.39-2.80	0.94
College degree or higher	**14.45**	**1.78-117.66**	**0.01**

* Odds ratio was adjusted for ethnicity, maternal age, race, language speaking, history of adverse pregnancy outcomes, country of birth, pregnancy planning, and use of prescription medications were adjusted.

Table 4.9 Predictors of Vitamin Use: Results of Multivariate Ordinal Logistic Regression Analysis among Women without Insurance*

Maternal Characteristics	ORs	95% CL	P value
Educational Level			
High school education or less	--	--	
Some college or vocational school	2.11	0.70-6.34	0.18
College degree or higher	0.24	0.03-2.17	0.20

* Odds ratio was adjusted for ethnicity, maternal age, race, language speaking, history of adverse pregnancy outcomes, country of birth, pregnancy planning, and use of prescription medications were adjusted.

Table 4.10 Predictors of Vitamin Use: Results of Multivariate Ordinal Logistic Regression Analysis among Women with Insurance*

Maternal Characteristics	ORs	95% CL	P value
Educational Level			
High school education or less	--	--	
Some college or vocational school	0.92	0.39-2.17	0.85
College degree or higher	**5.90**	**1.89-18.44**	**<0.01**

* Odds ratio was adjusted for ethnicity, maternal age, race, language speaking, history of adverse pregnancy outcomes, country of birth, pregnancy planning, and use of prescription medications were adjusted.

Table 4.11 Predictors of Vitamin Use: Results of Univariate Polychotomous Logistic Regression Analysis*

Maternal Characteristics	Group 1 vs. Group 2		Group 3 vs. Group 2	
	ORs	95% CL	ORs	95% CL
Hispanics	**0.33**	**0.19-0.57**	0.61	0.23-1.60
Maternal age (yrs)				
≤21 yrs	1.00	--	1.00	--
21-30 yrs	1.94	0.94-3.99	0.54	0.21-1.38
>30 yrs	1.57	0.72-3.39	0.50	0.18-1.40
Race				
Whites	1.00	--	1.00	--
Black or African American	0.77	0.25-2.35	0.67	0.09-5.26
Some other groups	1.54	0.64-3.69	**3.35**	**1.13-9.92**
Educational Level				
High school education or less	1.00	--	1.00	--
Some college or vocational school	1.67	0.92-3.02	1.89	0.80-4.47
College degree or higher	**4.94**	**2.44-10.00**	0.65	0.08-5.18
Health Insurance Status				
No insurance	1.00	--	1.00	--
Employer-based or self-purchased	**3.90**	**1.97-7.75**	1.28	0.56-2.96
Medicaid or other public insurance	1.06	0.62-1.84	1.55	0.41-5.91
Spanish-speaking	**0.43**	**0.27-0.71**	0.65	0.29-1.45
History of Adverse Perinatal Outcomes	0.67	0.41-1.10	1.17	0.49-2.79
Country of Birth: U.S	**1.76**	**1.08-2.82**	1.15	0.52-2.57
Planned Pregnancy	**1.95**	**1.15-3.30**	1.13	0.48-2.65
Use of Prescription medications during pregnancy				
None	1.00	--	1.00	--
1-2 medications	1.41	0.83-2.39	0.71	0.30-1.69
More than 2 medications	**2.33**	**1.14-4.78**	0.93	0.25-3.43

***** All Odds ratios are adjusted for all variables in the table

Table 4.12 Predictors of Vitamin Use: Results of Polychotomous Multivariate Logistic Regression Analysis*

Maternal Characteristics	Group 1 vs. Group 2		Group 3 vs. Group 2	
	ORs	95% CL	ORs	95% CL
Hispanics	0.62	0.24-1.59	0.87	0.13-5.70
Maternal age (yrs)				
≤21 yrs	1.00	--	1.00	--
21-30 yrs	1.57	0.68-3.63	0.41	0.13-1.29
>30 yrs	0.95	0.38-2.40	0.46	0.13-1.56
Race				
Whites	1.00	--	1.00	--
Black or African American	0.50	0.14-1.81	0.45	0.05-4.09
Some other groups	0.64	0.16-2.56	3.90	0.71-21.37
Educational Level				
High school education or less	1.00	--	1.00	--
Some college or vocational school	1.34	0.63-2.86	1.36	0.46-4.05
College degree or higher	2.73	0.92-8.07	0.70	0.06-7.81
Health Insurance Status				
No insurance	1.00	--	1.00	--
Employer-based or self-purchased	1.88	0.52-6.80	2.38	0.31-18.47
Medicaid or other public insurance	0.83	0.33-2.09	1.03	0.26-4.04
Spanish-speaking	0.37	0.09-1.58	0.34	0.03-3.46
History of Adverse Prenatal Outcomes	1.32	0.73-2.40	**3.04**	**1.16-7.98**
Country of Birth: U.S	0.32	0.07-1.47	0.20	0.02-1.91
Planned Pregnancy	**2.29**	**1.29-4.09**	1.31	0.52-3.29
Use of Prescription Medications during Pregnancy				
None	1.00	--	1.00	--
1-2 types of medications	1.52	0.81-2.84	0.75	0.28-2.02
More than 2 types of medications	2.00	0.80-5.01	0.46	0.05-4.19

***** All Odds ratios are adjusted for all variables in the table

APPENDICES

APPENDIX A Data Dictionary for SMART Study

Question	Variable name	Categories	Value
GENERAL INFORMATION			
Subject ID	subjID	Text	
Date of interview	dateint	Date (mm/dd/yy)	
Location of interview	locat	UNMH Fetal Monitoring Clinic (FMC) Triage General Satellite Clinic-West Mesa Satellite Clinic- South Broadway Satellite Clinic C Satellite Clinic D Other	1 2 3 4 5 6 7 8
Algorithm for assigning Subject IDs	**First two digits** –Location **Next two digits**- Year of interview **Last four digits**- Serial no.	**First two digits for location**: UNMH Fetal Monitoring Clinic (FMC) Triage General Satellite Clinic-West Mesa Satellite Clinic- South Broadway Satellite Clinic –North Valley Satellite Clinic D Other **Next two digits for year of interview:** 2008 **Last four digits for serial no.:**	10 20 30 41 42 43 44 50 08 0001-0124
If location is “Other”, please specify	locatot	Text	
Prenatal care provider’s last name	obgyn	Text	
Examiner’s last name	examln	Text	

Question	Variable name	Categories	Value
Patient's phone number	patpn	Text	
DEMOGRAPHICS			
How old are you?	momage	Continuous	
What is your marital status now?	mommarit	Single, never married Married, living with spouse Not married, but living with partner Separated from spouse Divorced Widowed	1 2 3 4 5 6
Are you Hispanic, Latino or of Spanish descent?	mometh	Yes No	1 0
How do you describe yourself?	race	White Non-Hispanic White Hispanic Black or African American American Indian or Alaskan Native Asian or Asian American or Pacific Islander Some other group Prefer not to report	0 1 2 3 4 5 6
If race is American Indian or Alaskan Native, then specify	race3	Tribe Pueblo	1 2
If race is others, then specify	raceoth	Text	
What is the highest level in school you have completed?	momedlev	Less than high school graduate High school graduate or GED Some college or vocational school College degree Masters, doctorate or professional degree	1 2 3 4 5
What is your health insurance status?	momins	No insurance Employer-based insurance Self-purchased insurance Medicaid Other public	1 2 3 4 5

Question	Variable name	Categories	Value
		insurances	
If you have other public health insurance, then specify	momins5	Indian Health Service VA First Choice UNM/UNM Care	1 2 3 4
Does your insurance cover prescription drugs?	prescov	Yes No	1 0
Were you born in the Unites States?	usborn	Yes No	1 0
How long have you lived in the United States?	momyr	Continuous	
What language do you mostly use at home?	momlang	English Spanish Some other language	1 2 3
If some other language is used mostly at home, then specify	momlang3	Text	
Do you currently smoke cigarettes or use tobacco?	smkmom	Yes No	1 0
If yes, how many cigarettes do you usually smoke in a day?	smkpreg	Continuous	
If no, have you smoked >100 cigarettes in your life?	smkmp1	Yes No	1 0
If you have smoked >100 cigarettes in your life, when did you stop smoking?	smkstop	Before I became pregnant After I realized that I was pregnant	1 2
Have you ever drank alcohol?	havdrnk	Yes No	1 0
How many drinks typically can you hold before you feel high?	HIGH	Continuous	
How many drinks typically can you hold before passing out or falling asleep?	HOLD	Continuous	
What was the first day of your last menstrual period?	lmenst	Date (mm/dd/yy)	
During a month or so around your last menstrual period before	drink4m	Continuous	

Question	Variable name	Categories	Value
you got pregnant, how many times did you drink **4 or more drinks** on one occasion?			
During the year before you got pregnant, did close friends or relatives worry or complain about your drinking habits?	worry	Yes No	1 0
During the year before you got pregnant, did you ever take a drink first thing in the morning to get yourself going?	eyem	Yes No	1 0
During the year before you got pregnant, did a friend or family member tell you about things you said or did while you were drinking that you could not remember?	amnesm	Yes No	1 0
During the year before you got pregnant, did you feel you need to cut down on your drinking?	cutm	Yes No	1 0
TWEAK SCORE	tweak1 (High) tweak2 (Hold)	Continuous	
Algorithm for calculating TWEAK score	**<u>TWEAK HIGH</u>** **TOLERANCE**: 2, when no. of drinks >=3; 0 if no. of drinks <3 **WORRY**: Yes= 2 points; No= 0 pts. **EYEM:** Yes= 1 pt., No= 0 pt **AMNESM:** Yes= 1 pt., No= 0 pt **CUT:** Yes= 1 pt., No= 0 pt **<u>TWEAK HOLD</u>**		

Question	Variable name	Categories	Value
	TOLERANCE: 2, when no. of drinks >=6; 0 if no. of drinks <6 **WORRY**: Yes= 2 points; No= 0 pts. **EYEM:** Yes= 1 pt., No= 0 pt **AMNESM:** Yes= 1 pt., No= 0 pt **CUT:** Yes= 1 pt., No= 0 pt		
MEDICAL AND REPRODUCTIVE HEALTH			
What was your pre-pregnancy weight?	wtmpre	Continuous	
What was your pre-pregnancy height?	htmpre	Continuous	
Researcher Calculated BMI	BMI	Continuous	
Do you have a medical condition or problem that requires ongoing, periodic, or occasional treatment?	medcon	Yes No	1 0
If yes, specify Hypertension (High BP) Depression Diabetes Anxiety Seizure Disorder	 medcon1 medcon2 medcon3 medcon4 medcon5	 Yes No Yes No Yes No Yes No Yes No	 1 0 1 0 1 0 1 0 1 0

Question	Variable name	Categories	Value
Migraine headaches	medcon6	Yes No	1 0
Thyroid disorder	medcon7	Yes No	1 0
Rheumatoid Arthritis	medcon8	Yes No	1 0
Asthma or Allergies	medcon9	Yes No	1 0
Heart Disease	medcon10	Yes No	1 0
Cancer	medcon11	Yes No	1 0
Hepatitis	medcon12	Yes No	1 0
Other (s)	medcon13	Yes No	1 0
Specify the type of diabetes	diabetes	Gestational Type I Type II	1 2 3
If you have other medical condition, not listed, please specify	othcon	Text	
If diabetic, how likely do you think uncontrolled high blood sugar could harm your developing baby by causing birth defects or other serious health problems?	diabet1	Likert Scale	1-5
How likely do you think uncontrolled asthma could harm your developing baby by causing birth defects or other serious health problems?	asthma	Likert Scale	1-5

Question	Variable name	Categories	Value
Have you ever had gestational diabetes?	gestdia	Yes, in a previous pregnancy only Yes, in the current pregnancy only Yes, in a previous pregnancy and in the current pregnancy No, never had gestational diabetes No, never been pregnant before	1 2 3 4 5
Did you plan to get pregnant with this child?	planchld	Yes No, not now No, not at any time	1 2 3
Were you or your partner doing anything to try to prevent becoming pregnant with this child?	bcontr	Yes No	1 0
If Yes, which method were you using?	bcontr1	Condoms Diaphragm Birth control pills Withdrawal IUD Rhythm Depo Provera, Implanon or Norplant Other	1 2 3 4 5 6 7 8
If other method used, please specify	othmtd	Text	
Did you take any fertility drugs to help you get pregnant with this child, like Clomid, Metrodin, Fertinex, or Pergonal?	fertdrg	Yes No	1 0
If fertility drug taken, please specify	fertdrg1	Text	
Have you or members of your immediate family (mother or	bdefh	Yes No	1 0

Question	Variable name	Categories	Value
sisters) or the immediate family of your baby's father had any babies with birth defects (including babies that might not have survived)?			
If 'Yes', please specify Down syndrome	bdefhs1	Yes No	1 0
Cleft lip or palate	bdefhs2	Yes No	1 0
Neural tube defect	bdefhs3	Yes No	1 0
Cystic fibrosis	bdefhs4	Yes No	1 0
Heart defect	bdefhs5	Yes No	1 0
Other	bdefhs6	Yes No	1 0
If other, please specify	bdoth	text	
What is the date your baby is due to be born?	bdate	Date (mm/dd/yy)	
How was your due date estimated	dateest1, 2, and 3	Last menstrual period Ultrasound Physical exam	1 2 3
What is the gestational age of your baby?	gestage	Continuous	
How many times (including this pregnancy) have you been pregnant?	gravid	Continuous	
How many live-born children have you had?	parity	Continuous	
Have you ever had a miscarriage (<20 wk of gestation). If yes, how many?	miscrg	If no, then '0' If yes, then Continuous	
Have you ever had a stillborn child (≥ 20 wk of gestation). If yes, how many?	stillbrn	If no, then '0' If yes, then Continuous	
Have you ever had a pregnancy terminated?	termin	If no, then '0' If yes, then Continuous	

Question	Variable name	Categories	Value
If yes, how many?			
Have you ever had an ectopic pregnancy. If yes, how many?	ectop	If no, then '0' If yes, then Continuous	
For this pregnancy, how many weeks after your last menstrual period did you first think you were pregnant?	realize	Continuous	
For this pregnancy, how many weeks after your last menstrual period did you first go to see a doctor or other health care provider or go to the clinic for prenatal care?	prenwk	Continuous	
Have you had any complications in this pregnancy so far? Bleeding High blood pressure Diabetes Other	 bleed highbp diabet othcom	 Yes No Yes No Yes No Yes No	 1 0 1 0 1 0 1 0
If other, please specify	othcoms	Text	
Have you experienced morning sickness during this pregnancy?	mornsick	Yes No	1 0
USE OF MEDICATIONS AND SUPPLEMENTS DURING PREGNANCY			
Did you take a multivitamin regularly (4 times a week or more) during the month before your last menstrual period?	multivit	Yes No	1 0
Have you taken any **VITAMINS** regularly (4 times/week or more)	vitreg	Yes, multivitamins Yes, a single vitamin No	1 2 3

Question	Variable name	Categories	Value
since you became pregnant?			
If “Yes”, then specify	vitRx	Prescription OTC	1 2
If Brand name vitamin taken, then specify	vitregname	Text	
If “yes” when did you start taking vitamins?	vitdate vitwk	Date (mm/dd/yy) or 0 Continuous or 0	
How many days during the last week did you take vitamins?	vitdays	Continuous	
Have you taken any **DIETARY SUPPLEMENTS** (including iron supplements) or **HERBAL PRODUCTS** on a regular basis since your last menstrual period?	herbsup	Yes No	1 0
If ‘Yes’ to herbal products, please specify	herbsup1	Herbs Tablets or capsules Teas Other	1 2 3 4
If other, please specify	herboth	Text	
How often do you take them?	herboft	Regularly When I feel sick	1 2
If taken regularly, specify time	herbreg	Text	
Please specify any other dietary supplements or products and reason for taking it Product1,Reason/Condition Produc2,Reason/Condition Product3,Reason/Condition	 suppl1;reas1 suppl2;reas2 suppl3;reas3	Text	
Have you had any cravings for non-food items or really “strange” foods?	crave	Yes No	1 0
If ‘yes’ what did you crave, do you eat it, and	item 1	If no , then 0 If yes , then text	

Question	Variable name	Categories	Value
how often do you eat it?	howoft1	Text	
	eat1	Yes No	1 0
	item2	If no , then 0 If yes , then text	
	howoft2	Text	
	eat2	Yes No	1 0
	item3	If no , then 0 If yes , then text	
	howoft3	Text	
	eat3	Yes No	1 0
Have you ever taken recreational drugs?	recdrug	Yes No	1 0
If Yes, specify the recreational drug that you took			
Marijuana/Hashish	hashish	Before pregnancy 1 month prior to LMP or during this pregnancy	1 2
Heroin	heroin	Before pregnancy 1 month prior to LMP or during this pregnancy	1 2
Have you gone through methadone treatment?	methtrt	Never Completed treatment before pregnancy Undergoing treatment during current pregnancy	1 2 3 1 2
Cocaine/Crack	cocaine		

Question	Variable name	Categories	Value
Inhalants (Glue, solvent)	inhalant	Before pregnancy 1 month prior to LMP or during this pregnancy	1 2
Methamphetamines	methamp	Before pregnancy 1 month prior to LMP or during this pregnancy	1 2
Other (name)	recdrug1	Before pregnancy	
	when1	1 month prior to LMP or during this pregnancy Continuous	1 2
Other (name)	recdrug2	Before pregnancy	
	when2	1 month prior to LMP or during this pregnancy Continuous	1 2
		Before pregnancy 1 month prior to LMP or during this pregnancy	
If respondent used >=1 drug(s) 1 month prior to LMP or during this pregnancy	recdrugpreg	Yes No	1 0
Did you discuss the safety of medications in pregnancy with any health care provider (physician, nurse-midwife, physician assistant, or pharmacist)?	safdis	Yes No	1 0
Have you had any	vaccine	Yes	1

Question	Variable name	Categories	Value
vaccinations since your last menstrual period		No	0
If yes to vaccinations, then please specify			
Flu	vaccineF	Yes	1
		No	0
Other			
	vaccineO	Yes	1
		No	0
If vaccination other than flu, then specify	Othvacc	Text	
Have you taken any **medications PRESCRIBED by your doctor** or any other health care provider since your last menstrual period, even if you stopped taking them once you knew you were pregnant?	presmed	Yes No	1 0
During this pregnancy, did you take any **OVER-THE-COUNTER MEDICATIONS** (sold without prescription)?	otcmed	Yes No	1 0
If yes, please specify			
Pain/fever medications	pain	Yes	1
		No	0
Nasal Decongestants, Allergy, Cough Medications	allrgy	Yes	1
		No	0
Antidiarrheal Medications	antdiar	Yes	1
		No	0
Heartburn, Dyspepsia, Antiemetic, Laxative Medications	digesmed	Yes	1
		No	0
Antifungal Medications (taken for vaginal yeast infection or thrash)	antfungl	Yes	1
		No	0
	nicoreth	Yes	1
		No	0

Question	Variable name	Categories	Value
Nicotine Replacement Therapy (for smoking cessation)			
OTC Medications and their perceptions			
Acetaminophen (Tylenol)	tylenol	Yes No	1 0
	tylenolP	Likert Scale	1-5
Aspirin	aspirin	Yes No	1 0
	aspirinP	Likert Scale	1-5
Ibuprofen (Advil, Motrin)	ibuprof	Yes No	1 0
	ibuprofP	Likert Scale	1-5
Ketoprofen (Orudis)	ketopro	Yes No	1 0
	ketoproP	Likert Scale	1-5
Naproxen (Aleve)	naprox	Yes No	1 0
	naproxP	Likert Scale	1-5
Chlorpheniramine (Chlor-Trimeton)	chlorph	Yes No	1 0
	chlorphP	Likert Scale	1-5

Question	Variable name	Categories	Value
Benadryl	benadrl	Yes No	1 0
	benadrlP	Likert Scale	1-5
Pseudoephedrine (Sudafed)	sudafed	Yes No	1 0
	sudafedP	Likert Scale	1-5
Kaopectate, Pepto Bismol	clarzyr	Yes No	1 0
	clarzyrP	Likert Scale	1-5
	pepbsml	Yes No	1 0
	pepbsmlP	Likert Scale	1-5
If you took prescription medications regularly before you got pregnant, did you change the use of these medications when you realized you are pregnant?			
Did not take prescription medications regularly before pregnancy	usechngA	Yes No	1 0
Discontinued the use upon recognition of pregnancy	usechngB	Yes No	1 0
Decreased the use (dose or frequency)	usechngC	Yes No	1 0
Increased the use	usechngD	Yes No	1 0
Stayed the same, continued without any	usechngE	Yes No	1 0

Question	Variable name	Categories	Value
change			
If discontinued the use upon recognition of pregnancy, please specify medication name	usechng2	Text	
If decreased the use (dose or frequency), please specify medication name	usechng3	Text	
If Increased the use, please specify medication name	usechng4	Text	
If medication stayed the same, specify medication name	usechng5	Text	
If you changed the use of a medication upon recognition of pregnancy, why?	medchng	Provider recommendation Family or friend suggestion Self-initiated Financial constraints Other	1 2 3 4 5
If other, then specify	chngoth	Text	

Question	Variable name	Categories	Value
If a women plans a pregnancy or finds out that she is currently pregnant, she should	pregplan	Stop taking all medications immediately to protect the baby Continue taking only those medications that are absolutely necessary and check with her doctor to see if the medications are safe for the baby Continue taking necessary medications but reduce the dose or the number of days you take them to limit the amount that gets to the baby Continue with all medications as needed since medications are safe for the baby	1 2 3 4
When a woman uses medications regularly during pregnancy, how often can medications cause birth defects?	medbdef	Never Sometimes Often Very Often Always	1 2 3 4 5
Which statement best describes your view about women drinking alcohol during pregnancy?	pregalc	Pregnant women should abstain from drinking any alcohol (even small amounts) during pregnancy It is OK for a woman to have an occasional drink during pregnancy as long as it is not more often than once a week It is OK for a woman to have an occasional drink during pregnancy as long as it is not more often than one	1 2 3

Question	Variable name	Categories	Value
		drink per day It is OK for a woman to have an occasional drink during pregnancy as long as it is not more often than two drinks per day It is OK for a woman to drink during pregnancy as long as she does not drink hard liquor (i.e., vodka, whiskey, brandy) but only drinks wine or beer	4 5
During your current pregnancy, have you ever asked with anyone about the safety of medications you are taking for your baby?	safemed	Yes No	1 0
If yes, please specify: Your primary care doctor or provider Your OB/GYN doctor or midwife A pharmacist A member of your family, spouse A friend, partner Other Any other Hx provider	 safemed1 safemed2 safemed3 safemed4 safemed5 safemed6 safemed7	 Yes No Yes No Yes No Yes No Yes No Yes No Yes No	 1 0 1 0 1 0 1 0 1 0 1 0 1 0
If other, please specify	safeoth	Text	
Please check any sources below in which you have looked for			

Question	Variable name	Categories	Value
information about the safety of medications for your baby?			
	babyinfA	Yes	1
I have never looked at any of these sources about the safety of medications for my baby.		No	0
	babyinfB	Yes	1
An internet web site(s).		No	0
	babyinfC	Yes	1
A book.		No	0
	babyinfD	Yes	1
A magazine		No	0
	babyinfE	Yes	1
Pregnancy information telephone service/hotline (i.e., OTIS, Nurse Advisory Line)		No	0
	babyinfF	Yes	1
Other		No	0
	babyinfG	Yes	1
I have not had any questions about the safety of medications for my baby and have not looked at any of these sources.		No	0
	babyinfH	Yes	1
Clinic pamphlet or brochure		No	0
If checked an internet website, please specify the name of the website	babyinf2	Text	
If used any other source, please specify	babyinf6	Text	
Is the patient currently on Insulin	insulin	Yes	1
		No	0
Is the patient currently on any oral hypoglycemic ?	oralhypo	Yes	1
		No	0

Question	Variable name	Categories	Value
If yes, specify the type	sulfnylu	Yes No	1 0
	biguanid	Yes No	1 0
	TZD	Yes No	1 0
Perception regarding Insulin use	insulinP	Likert scale	1-5
Perception regarding Sulfonylurea (Oral Hypoglycemic) use	sulfnylP	Likert scale	1-5
Perception regarding Biguanid (Oral Hypoglycemic) use	bguanidP	Likert scale	1-5
Perception regarding Thiazolidinedione (Oral Hypoglycemic) use	TZDP	Likert scale	1-5
Is the patient currently on ICS	ICS	Yes No	1 0
Is the patient currently on BetaA	BetaA	Yes No	1 0
Is the patient currently on steriod	Steriod	Yes No	1 0
Perception regarding ICS use	ICSP	Likert scale	1-5
Perception regarding BetaA use	BetaAP	Likert scale	1-5
Perception regarding steroid use	SteriodP	Likert scale	1-5
Is the patient currently on Antipsychotics	Antipsychotics	Yes No	1 0
Is the patient currently on Nortiptyline	Nortiptyline	Yes No	1 0
Is the patient currently on Bupropion	Bupropion	Yes No	1 0
Is the patient currently on Citalopram	Citalopram	Yes No	1 0
Is the patient currently on Escitalopram	Escitalopram	Yes No	1 0
Is the patient currently on Fluoxetine	Fluoxetine	Yes No	1 0
Is the patient currently on Paroxetine	Paroxetine	Yes No	1 0
Is the patient currently on Sertraline	Sertraline	Yes No	1 0
Is the patient currently	Venlafaxine	Yes	1

Question	Variable name	Categories	Value
on Venlafaxine		No	0
Perception regarding Nortiptyline use	AntipsychoticsP	Likert scale	1-5
Perception regarding Antipsychotics use	NortiptylineP	Likert scale	1-5
Perception regarding Bupropion use	BupropionP	Likert scale	1-5
Perception regarding Citalopram use	CitalopramP	Likert scale	1-5
Perception regarding Escitalopram use	EscitalopramP	Likert scale	1-5
Perception regarding Fluoxetine use	FluoxetineP	Likert scale	1-5
Perception regarding Paroxetine use	ParoxetineP	Likert scale	1-5
Perception regarding Sertraline use	SertralineP	Likert scale	1-5
Perception regarding Venlafaxine use	VenlafaxineP	Likert scale	1-5
\Any comments?	comment	Text	
PERINATAL DATA ABSTRACTION			
Pregnancy outcome	pregoutc	Live-born infant Spontaneous abortion (no live birth; gestational age less than 20 weeks) Stillbirth (no live birth; gestational age 20 weeks or greater)Ectopic pregnancy Termination Lost to follow-up	1 2 3 4 5 6
Was this a multiple birth?	multbir	Yes, twins Yes, triplets No	1 2 3
Date of delivery or end of pregnancy?	pregend	Date (mm/dd/yy)	

Question	Variable name	Categories	Value
Cocaine present in Medical Record	CocianeMR	Yes No	1 0

Question	Variable name	Categories	Value
Gestational age at end of pregnancy	gestageE	Continuous	
Type of delivery?	deltype	Vaginal – vertex Vaginal – breech Vaginal – transverse Cesarian section-primary Cesarian section – repeat	1 2 3 4 5 6
If cesarian section, reason for surgical delivery?	csectn	Emergency Failure to progress through labor Elective (pre-planned) Not applicable Breech presentation	1 2 3 4 5
Maternal complications:			
Preeclampsia or toxemia	pretox	Yes No	1 0
High blood pressure	HBP	Yes No	1 0
Oligohydramnios	oligohyd	Yes No	1 0
Infection or fever at delivery	infect	Yes No	1 0
Gestational diabetes	gediabts	Yes No	1 0
Other	otcomp	Yes No	1 0

If “Other”, specify	otcomps	Text	
What was mother’s weight at the end of pregnancy?	endwt	Continuous	
What was mother’s weight gain during pregnancy?	wtgain	Continuous	
Is mother breastfeeding the infant?	brstfeed	Yes No N/A	1 0 2
Infant ID	infntID	Text	
Question	**Variable name**	**Categories**	**Value**
Sex of a child	sex	Boy Girl	1 2
Birth weight	bweight	Continuous	
Birth length	blength	Continuous	
Birth head circumference	bheadcf	Continuous	
Apgar Score 1 minute	Apgar1	Continuous	
Apgar Score 5 minute	Apgar5	Continuous	
Neonatal complications: Respiratory distress	respdist	Yes No	1 0
Hypoglycemia	hypglycm	Yes No	1 0
Tachypnea	tachypn	Yes No	1 0
Bradycardia	bradycd	Yes No	1 0
Sepsis	sepsis	Yes No	1 0
Other	otcompn	Yes No	1 0
If “Other”, specify	otcompns	Text	
Major structural anomaly diagnosed during the hospital stay?	stranom	Yes No	1 0
How many days was infant in the hospital?	hospdays	Continuous	
Was the infant in Intensive Care Unit?	infICU	Yes No	1 0

Did infant go home with the mother?	infhome	Yes No	1 0
If 'No', what is the reason?	infhomeN	Still in nursery Neonatal death Orphanage Other	1 2 3 4
If 'Other', specify reason	othomes	Text	
Any abnormalities/conditions diagnosed in neonatal period	abncon	Yes No	1 0
If Yes, specify	abncons	Text	
Notes	Notes	Text	

MAJOR DRUG CATEGORIES

Question	**Variable name**	**Categories**	**Value**
Nutrients and Nutritional Agents	nutrients	Yes No	1 0
Hematological Agents	hematolog	Yes No	1 0
Endocrine and Metabolic Agents	endocmetab	Yes No	1 0
Cardiovasculars	cardiovasc	Yes No	1 0
Renal and Genitourinary Agents	renalgenitour	Yes No	1 0
Respiratory Agents	respiratory	Yes No	1 0
Central Nervous System Agents	cns	Yes No	1 0
Gastrointestinal Agents	gastro	Yes No	1 0
Anti-Infectives, Systemic	antiinfect	Yes No	1 0
Biological and Immunological Agents	bioimmun	Yes No	1 0
Dermatological Agents	dermatol	Yes No	1 0
Ophthalmic and Otic Agents	ophthal	Yes No	1 0
Antineoplastic Agents	antineoplast	Yes No	1 0
Herbalife(Herbal Life)	Herbalife	Yes No	1 0

Fish Oil(Omega-3l DHA; Expecta; DHA Expecta; Omega fats)	Fish_Oil	Yes No	1 0
Chamomile (Manzanilla, German chamomile, Roman Chamomile)	Chamomile	Yes No	1 0
Valerian (Valeriana)	Valerian	Yes No	1 0
Primrose Oil (Evening primrose oil; Primrose pill; primrose oil capsule)	Primrose_Oil	Yes No	1 0
Cranberry (Cranberry extract, cranberry tea)	Cranberry	Yes No	1 0
Raspberry (Red Raspberry; Raspberry Leaf)	Raspberry	Yes No	1 0
Flax Seed	Flax_Seed	Yes No	1 0
Other Herb drug	Other_Herb	Yes No	1 0
If Yes, specify the name of herb	Herb_specify	Text	

APPENDIX B QUESTIONNAIRE OF THE SMART STUDY

GENERAL INFORMATION

1. Date of interview: __ /__ /__ (month/day/year)

2. Location of interview:
   _____

3. Prenatal care provider's last name:
   _____

4. Examiner's last name:
   _____

5. Patient's phone number: _____

DEMOGRAPHIC / LIFESTYLE INFORMATION

6. How old are you? _____ (years)

7. What is your marital status now?

   [ ] Single, never married

   [ ] Married, living with spouse

   [ ] Not married, but living with partner

   [ ] Separated from spouse

   [ ] Divorced

   [ ] Widowed

8. Are you Hispanic, Latino or of Spanish descent? [ ] Yes [ ] No

9. How do you describe yourself: (check all that apply)

   [ ] White, non-Hispanic or [ ] White, Hispanic

   [ ] Black or African American

   [ ] American Indian or Alaskan Native - Please specify [ ] tribe or [ ] pueblo

   [ ] Asian or Asian American or Pacific Islander

[ ] Some other group(s) – please specify: _____

[ ] Prefer not to report

10. What is the highest level in school you have completed?

[ ] Less than high school graduate

[ ] High school graduate or GED

[ ] Some college or vocational school

[ ] College degree

[ ] Masters, doctorate or professional degree

11. What is your health insurance status?

[ ] No insurance

[ ] Employer-based insurance

[ ] Self-purchased insurance

[ ] Medicaid

[ ] Other public insurances
([ ] Indian Health Service, [ ] VA, [ ] First Choice, [ ] UNM/UNMCARE)

11a. Does your insurance cover prescription drugs? [ ] Yes [ ] No

12. Were you born in the Unites States? [ ] Yes [ ] No

If 'Yes', go to question 13. If 'No', please answer questions 12a and 12b.

12a. Did you move to the United States:
[ ] With your parents when you were a child
[ ] When you were an adult (≥18 years old)

12b. How long have you lived in the United States: _____ years

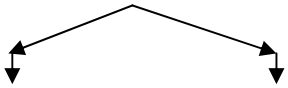
13. What language do you mostly use at home?

[ ] English

[ ] Spanish

[ ] Some other language – specify:_____ _____

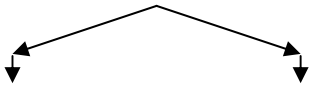
14. Do you currently smoke cigarettes or use tobacco?



[ ] Yes [ ] No

14a. How many cigarettes do you usually smoke in one day? _____

14b. Have you smoked >100 cigarettes in your life?



[ ] Yes [ ] No

14c. When did you stop smoking?
** Go to the next question*

[ ] Before I became pregnant

[ ] After I realized that I was pregnant

15. Have you ever drank alcohol in your life (e.g., beer, wine, hard liquor, mixed drinks)?

[ ] Yes [ ] No

If 'yes,' continue to questions 15a and 15b. If 'no,' continue to 21a.

15a. How many drinks does it take before you begin to feel the first effect of alcohol?
_____

15b. How many drinks typically can you hold before passing out or falling asleep?
_____

a. What was the first day of your last menstrual period ___/___/___ (mm/dd/yy)?

I would like you to think back to that period and tell me about your drinking at that time.

16. During a month or so around your last menstrual period before you got pregnant, how many times did you drink **4 or more drinks** on one occasion? _____

Now I want you to think of <u>12 months before you got pregnant</u> (a year prior to your LMP)

17. During the year before you got pregnant, did close friends or relatives worry or complain about your drinking habits?
[ ] Yes [ ] No

18. During the year before you got pregnant, did you ever take a drink first thing in the morning to get yourself going?
[ ] Yes [ ] No

19. During the year before you got pregnant, did a friend or family member tell you about things you said or did while you were drinking that you could not remember?
[ ] Yes [ ] No

20. During the year before you got pregnant, did you feel you need to cut down on your drinking?

[ ] Yes [ ] No

[TWEAK High: _____; TWEAK Hold: _____]

MEDICAL AND REPRODUCTIVE HEALTH

21a. What was your pre-pregnancy weight? _____ pounds

21b. What was your pre-pregnancy height? _____ feet/inches

[Researcher Calculated BMI: _____]

22. Do you have a medical condition or problem that requires ongoing, periodic, or occasional treatment?
[ ] Yes [ ] No

22a. If yes, check all that apply:

[ ] Hypertension (high blood pressure) [ ] Depression
[ ] Diabetes: [ ] Gestational [ ] Type I [ ] Type II
[ ] Anxiety [ ] Seizure disorder (i.e., epilepsy)
[ ] Migraine headaches [ ] Thyroid disorder
[ ] Rheumatoid arthritis
[ ] Asthma or allergies [ ] Heart disease
[ ] Cancer [ ] Hepatitis
[ ] Other(s) problem - specify: _____

If 'Yes' to diabetes, please answer questions 23 and 24. If 'No', skip to question 26.
If 'Yes' to asthma, please answer question 25. If 'No,' skip to question 26.

23. Have you ever had gestational diabetes?

[ ] Yes, in a previous pregnancy only

[ ] Yes, in the current pregnancy only

[ ] Yes, in a previous pregnancy and in the current pregnancy

[ ] No, never had gestational diabetes

[ ] No, never been pregnant before

24. How likely do you think uncontrolled high blood sugar could harm your developing baby by causing birth defects or other serious health problems? (circle one number)

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

25. How likely do you think asthma exacerbations requiring hospitalization or unscheduled clinic visits could harm your developing baby? (circle one number)

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

26. Did you plan to get pregnant with this child?

[ ] Yes [ ] No, not now [ ] No, not at any time

27. Were you or your partner doing anything to try to <u>prevent becoming pregnant</u> with this child?

[ ] Yes [ ] No

27a. If *Yes*, which <u>method</u> were you using?

[ ] Condoms [ ] Diaphragm [ ] Birth control pills

[ ] Withdrawal [ ] IUD [ ] Rhythm

[ ] Depo Provera, Implanon or Norplant [ ] Other: _____

28. Did you take any <u>fertility drugs</u> to help you get pregnant with this child, like Clomid, Metrodin, Fertinex, or Pergonal?
[ ] Yes [ ] No

28a. If *Yes*, which drugs did you use? _____

29. Have you or members of your immediate family (mother or sisters) or the immediate family of your baby's father had any babies with birth defects (including babies that might not have survived)?

[ ] Yes [ ] No

** If 'No', go to question 30. If 'Yes', please specify:*

Down syndrome	[ ] Yes	[ ] No
Cleft lip or palate	[ ] Yes	[ ] No
Neural tube defect	[ ] Yes	[ ] No
Cystic fibrosis	[ ] Yes	[ ] No
Heart defect	[ ] Yes	[ ] No
Other	[ ] Yes	[ ] No

If "Yes," please specify:_____

30. What was the **first day** of your last menstrual period?__ __ / __ __ /__ __ *(mm / dd / yy)*

31. What is the date your baby is due to be born: ___ ___ / ___ ___ / ___ ___ *(mm / dd / yy)*

31a. What is the gestational age of your baby? _____ weeks

31b. How was your due date estimated? By:

[ ] Last menstrual period
[ ] Ultrasound
[ ] Physical exam

32. How many times (including this pregnancy) have you been pregnant?

_____

If this is the 1st pregnancy put "1"for q. 32 and "0" for questions 33-37 & skip to question 37.

33. How many live-born children have you had? _____

If no live-born children or this is the first pregnancy, then put "0"

34. Have you ever had a miscarriage (<20 wk of gestation). If yes, how many?_____

If never had a miscarriage, put "0"

35. Have you ever had a stillborn child (≥ 20 wk of gestation). If yes, how many?_____

If never had a stillborn child, put "0"

36. Have you ever had a pregnancy terminated? If yes, how many?_____

If never had a termination, put "0"

37. Have you ever had an ectopic pregnancy. If yes, how many?_____

If never had an ectopic pregnancy, put "0"

38. For this pregnancy, how many weeks after your last menstrual period did you first think you were pregnant? _____

39. For this pregnancy, how many weeks after your last menstrual period did you first go to see a doctor or other health care provider or go to the clinic for prenatal care? _____

40a. Have you had any complications in this pregnancy so far?
(** Please check yes or no for each complication)*

- Bleeding [ ] Yes [ ] No
- High blood pressure [ ] Yes [ ] No
- Diabetes [ ] Yes [ ] No
- Other [ ] Yes [ ] No

40b. If "other", please specify: _____

41. Have you experienced morning sickness during this pregnancy?
[ ] Yes[ ] No

USE OF MEDICATIONS AND SUPPLEMENTS DURING PREGNANCY

42. Did you take a multivitamin regularly (4 times a week or more) during the month before your last menstrual period?

[ ] Yes [ ] No

43. Have you taken any **VITAMINS** regularly (4 times/week or more) since you became pregnant?

43a. [ ] Yes, multivitamins [ ] Yes, a single vitamin [ ] No

If 'Yes,' answer questions 43b-43e.

43b. [ ] Prescription [ ] OTC

43c. [ ] Brand name: _____

43d. When did you start taking vitamins?
_____ (mm/dd/yy) _____ (gestational weeks)

43e. How many days during the last week did you take vitamins? _____ (days/week)

44a. Have you taken any **DIETARY SUPPLEMENTS** (including iron supplements) or

HERBAL PRODUCTS on a regular basis since your last menstrual period?

[ ] Yes [ ] No

44b. If 'Yes' to herbal products, please specify: [ ] Herbs

[ ] Tablets or capsules

[ ] Teas

[ ] Other: _____

44c. How often do you take them? [ ] Regularly: _____ times per _____ or [ ] When I feel sick

Please specify any other dietary supplements or products and reason for taking it:

Product 1:_____ Reason/Condition: _____

Product 2: _____Reason/Condition: _____

Product 3: _____Reason/Condition: _____

44d. Have you had any cravings for non-food items or really "strange" foods?

[ ] Yes [ ] No

If 'yes' what did you crave, do you eat it, and how often do you eat it?

Item 1: _____ Eat it? [ ] Yes [ ] No; How often? _____

Item 2: _____Eat it? [ ] Yes [ ] No; How often? _____

Item 3: _____Eat it? [ ] Yes [ ] No; How often? _____

45. Have you ever taken any recreational drugs?

[ ] Yes [ ] No

If 'Yes' please specify the recreational drug name(s) and when it was used:

Check if taken:

[ ] Marijuana/Hashish: [ ] Before pregnancy

[ ] 1 month prior to LMP or during this pregnancy

[ ] Heroin: [ ] Before pregnancy
[ ] 1 month prior to LMP or during this pregnancy

Have you gone through methadone treatment?
[ ] Never
[ ] Completed treatment before pregnancy
[ ] Undergoing treatment during current pregnancy

[ ] Cocaine/Crack: [ ] Before pregnancy
[ ] 1 month prior to LMP or during this pregnancy

[ ] Inhalants (glue, solvent): [ ] Before pregnancy
[ ] 1 month prior to LMP or during this pregnancy

[ ] Methamphetamines: [ ] Before pregnancy
[ ] 1 month prior to LMP or during this pregnancy

[ ] Other: _____ [ ] Before pregnancy
[ ] 1 month prior to LMP or during this pregnancy

[ ] Other: _____ [ ] Before pregnancy
[ ] 1 month prior to LMP or during this pregnancy

46. Did you discuss the safety of medications in pregnancy with any health care provider (physician, nurse-midwife, physician assistant, or pharmacist)?

[ ] Yes [ ] No

47a. Have you had any vaccinations since your last menstrual period?

[ ] Yes [ ] No

47b. If *Yes* to vaccinations, please specify: [ ] Flu

[ ] Other: _____

48. Have you taken any **medications PRESCRIBED by your doctor** or any other health care provider since your last menstrual period, even if you stopped taking them once you knew you were pregnant?

[ ] Yes [ ] No

If 'Yes' please specify the medication name, reason for taking it, and <u>your perception</u> of how likely it is that this medication might be harmful for your baby if taken during pregnancy:

a. **Medication 1**:_____ Indication: _____

How likely do you think it is that this medication could harm your developing baby by causing birth defects or other serious health problems: (circle one number)

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

b. **Medication 2**:_____ Indication: _____

How likely is it that this medication could harm your developing baby by causing birth defects or other serious health problems: (circle one number)

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

c. **Medication 3**:_____ Indication: _____

How likely is it that this medication could harm your developing baby by causing birth defects or other serious health problems: (circle one number)

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

d. **Medication 4**:_____ Indication: _____

How likely is it that this medication could harm your developing baby by causing birth defects or other serious health problems: (circle one number)

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

e. **Medication 5**:_____ Indication: _____

How likely is it that this medication could harm your developing baby by causing birth defects or other serious health problems: (circle one number)

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

49. During this pregnancy, did you take any **OVER-THE-COUNTER MEDICATIONS** (sold without prescription)?

[ ] Yes [ ] No

Check all medications that you have actually taken since your last menstrual period, even if you stopped taking them once you knew you were pregnant. Then for medications you took since pregnancy, please specify your perception of how likely each medication is to cause birth defects or other problems for your baby.

Pain/Fever Medications:

Rate all medications**:**

	1 Not at all likely to harm	2 Unlikely to cause harm	3 Somewhat likely to harm	4 Likely to harm to cause harm	5 Very likely to harm
[ ] Acetaminophen (Tylenol)	1	2	3	4	5
[ ] Aspirin	1	2	3	4	5
[ ] Ibuprofen (Advil, Motrin)	1	2	3	4	5
[ ] Ketoprofen (Orudis)	1	2	3	4	5
[ ] Naproxen (Aleve)	1	2	3	4	5
[ ] Other medication – specify: _____	1	2	3	4	5

Nasal Decongestants, Allergy, Cough Medications:

Rate all medications**:**

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

[ ] Chlorpheniramine (Chlor-Trimeton) 1 2 3 4 5

[ ] Benadryl 1 2 3 4 5

[ ] Pseudoephedrine (Sudafed) 1 2 3 4 5

[ ] Claritin, Zyrtec 1 2 3 4 5

[ ] Other medication – specify:_____ 1 2 3 4 5

Antidiarrheal Medications:

Rate all medications**:**

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

Check if taken:

[ ] Kaopectate, Pepto Bismol 1 2 3 4 5

[ ] Loperamide (Imodium) 1 2 3 4 5

[ ] Other medication – specify: _____ 1 2 3 4 5

Heartburn, Dyspepsia, Antiemetic, Laxative Medications:

Rate all medications**:**

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

Check if taken:

[ ] Maalox, Mylanta Gas 1 2 3 4 5

[ ] Tums 1 2 3 4 5

[ ] Tagamet, Zantac, Axid, Pepcid 1 2 3 4 5

[ ] Colace 1 2 3 4 5

[ ] Correctol, Dulcolax, Ex-Lax 1 2 3 4 5

[ ] Senna, fiber products 1 2 3 4 5

[ ] Unisom 1 2 3 4 5

[ ] Other medication – specify:_____ 1 2 3 4 5

Antifungal Medications (taken for vaginal yeast infection or thrash):

Rate all medications**:**

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

Check if taken:

[ ] Vaginal cream or suppositories (Monistat, Vagistat, Femstat, Lotrim) 1 2 3 4 5

[ ] Other medication – specify:_____ 1 2 3 4 5

Nicotine Replacement Therapy (for smoking cessation):

Rate all medications**:**

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

Check if taken:

[ ] Nicotine gum, spray or inhaler 1 2 3 4 5

[ ] Nicotine patch 1 2 3 4 5

[ ] Other medication – 1 2 3 4 5

specify:_____

Other over-the-counter medications you have taken while pregnant:

Rate all medications**:**

1	2	3	4	5
Not at all likely to harm	Unlikely to cause harm	Somewhat likely to harm	Likely to harm to cause harm	Very likely to harm

Check if taken:

[ ] Other medication – specify: _____ 1 2 3 4 5

[ ] Other medication – specify: _____ 1 2 3 4 5

[ ] Other medication – specify: _____ 1 2 3 4 5

50. If you took prescription medications regularly before you got pregnant, did you change the use of these medications when you realized you are pregnant?

[ ] Did not take prescription medications regularly before pregnancy

[ ] Discontinued the use upon recognition of pregnancy. Medication_____

[ ] Decreased the use (dose or frequency). Medication: _____

[ ] Increased the use. Medication: _____

[ ] Stayed the same, continued without any change. Medication: _____

50a. If you changed the use of a medication upon recognition of pregnancy, why?

[ ] Provider recommendation

[ ] Family or friend suggestion

[ ] Self-initiated

[ ] Financial constraints

[ ] Other:

_____

Now I'm going to ask you about your thoughts about medication use during pregnancy in general. Please check the answer you think is the most appropriate for each question.

51. If a woman plans a pregnancy or finds out that she is currently pregnant, she should:

[ ] Stop taking all medications immediately to protect the baby

[ ] Continue taking only those medications that are absolutely necessary and

check with her doctor to see if the medications are safe for the baby

[ ] Continue taking necessary medications but reduce the dose or the number of days you take them to limit the amount that gets to the baby

[ ] Continue with all medications as needed since medications are safe for the baby

52. When a woman uses medications regularly during pregnancy, how often can medications cause birth defects?

[ ]	[ ]	[ ]	[ ]	[ ]
Never	Sometimes	Often	Very Often	Always

53. Which statement best describes your view about women drinking alcohol during pregnancy?

[ ] Pregnant women should abstain from drinking any alcohol (even small amounts) during pregnancy.

[ ] It is OK for a woman to have an occasional drink during pregnancy as long as it is not more often than once a week.

[ ] It is OK for a woman to have an occasional drink during pregnancy as long as it is not more often than one drink per day.

[ ] It is OK for a woman to have an occasional drink during pregnancy as long as it is not more often than two drinks per day.

[ ] It is OK for a woman to drink during pregnancy as long as she does not drink hard liquor (i.e., vodka, whiskey, brandy) but only drinks wine or beer.

54. During your current pregnancy, have you ever asked anyone about the safety of medications you are taking for your baby?

[ ] Yes [ ] No

54a. If yes, check any individuals who you have asked a question about the safety of any medications for your baby: (*Check all that apply to you*)

[ ] Your primary care doctor or provider

[ ] Your OB/GYN doctor or midwife

[ ] A pharmacist

[ ] A member of your family, spouse

[ ] A friend, partner

[ ] Other - specify:
_____

[ ] Any other heath care provider

55. Please check any sources below in which you have looked for information about the safety of medications for your baby? (*Check all that apply to you*)

[ ] I have never looked at any of these sources about the safety of medications for my baby

[ ] An internet web site(s).
Specify:_____

[ ] A book.

[ ] A magazine

[ ] Pregnancy information telephone service/hotline (i.e., OTIS, Nurse Advisory Line)

[ ] Other - specify:
_____

[ ] I have not had any questions about the safety of medications for my baby and have not looked at any of these sources.

[ ] Clinic pamphlet or brochure

56. NOTES/COMMENTS:

_____

_____

_____

_____

_____