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Micronutrient Variations Among US Young Women Using Oral Contraceptives

in NHANES 2011-2012

by

Sarah Hulse

A thesis

submitted in partial fulfillment

of the requirements for the degree of

Master of Public Health in the Department of Community and Public Health

Idaho State University

Spring 2018

Committee Approval

To the Graduate Faculty:

The members of the committee appointed to examine the thesis of Sarah Hulse find it satisfactory and recommend that it be accepted.

____

Ryan Lindsay, PhD, MPH
Major Advisor

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Committee Member

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Human Subjects Committee Approval

March 15, 2017

Sarah Hulse
Public Health
MS 8109

RE: regarding study number IRB-FY2017-210: Micronutrient Variations Among NHANES 2011-2012 Young Women Using Oral Contraceptives

Dear Ms. Hulse:

I agree that this study qualifies as exempt from review under the following guideline: Category 4: Collection or study of existing data. This letter is your approval, please, keep this document in a safe place.

Notify the HSC of any adverse events. Serious, unexpected adverse events must be reported in writing within 10 business days.

You are granted permission to conduct your study effective immediately. The study is not subject to renewal.

Please note that any changes to the study as approved must be promptly reported and approved. Some changes may be approved by expedited review; others require full board review. Contact Tom Bailey (208-282-2179; fax 208-282-4723; email: humsubj@isu.edu) if you have any questions or require further information.

Sincerely,

Ralph Baergen, PhD, MPH, CIP
Human Subjects Chair

NCHS Research Ethics Review Board (ERB) Approval*

Survey Name/Date	NCHS IRB/ERB Protocol Number or Description
NHANES 2017-2018	Protocol #2018-01 (Effective beginning October 26, 2017)
	Continuation of Protocol #2011-17 (Effective through October 26, 2017)
NHANES 2015-2016	Continuation of Protocol #2011-17
NHANES 2013-2014	Continuation of Protocol #2011-17
NHANES 2011-2012	Protocol #2011-17
NHANES 2009-2010	Continuation of Protocol #2005-06
NHANES 2007-2008	Continuation of Protocol #2005-06
NHANES 2005-2006	Protocol #2005-06
NHANES 1999-2004	Protocol #98-12
NHANES III	Institutional Review Board (IRB) approval and documented consent was obtained from participants
NHANES II	Underwent internal human subjects review, but IRB approval using current standards was not obtained.
NHANES I	Underwent internal human subjects review, but IRB approval using current standards was not obtained.
NHES	Underwent internal human subjects review, but IRB approval using current standards was not obtained.

* In 2003, the NHANES Institutional Review Board (IRB) changed its name to the NCHS Research Ethics Review Board (ERB).

Acknowledgments

"If it weren't for the last minute, nothing would get done."- Rita Mae Brown

A special thank you to my advisor, Dr. Ryan Lindsay. Your enthusiasm, support, patience, and mentorship through some of my hardest years is greatly appreciated. Thank you Dr. Cynthia Blanton and Rick Tivis for providing your expertise and support. It has been a pleasure to work with such an excellent team.

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List of Abbreviations

BRFSS	Behavioral Risk Factor Surveillance System
CDC	Centers for Disease Control and Prevention
MEC	Mobil examination centers
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NTD	Neural tube defects
OC (OCs)	Oral contraceptive(s)
PSU	Public sampling units
RDA (RDAs)	Recommended dietary allowance(s)
UL	Upper limit
WHO	World Health Organization

Micronutrient Variations Among US Young Women Using Oral Contraceptives

in NHANES 2011-2012

Thesis Abstract—Idaho State University (2018)

Women in the United States commonly use oral contraceptives (OCs), with highest use among young women. Interactions between OCs and nutrition-related biomarkers may result in poorer nutritional serum levels. However, interactions between OCs and micronutrients including folate, vitamin B12, iron, zinc, copper, and selenium, have not previously been studied on a nationally representative sample in the United States. This cross-sectional study uses NHANES 2011-2012 data to describe nutrition-related micronutrient laboratory levels, and potentially confounding factors such as dietary quality, dietary supplement use, ratio of family income to poverty, and health insurance, for US women ages 18-24 years, using OCs compared to those not using OCs. Chi-square tests and t-tests were used to determine significant difference between those using and not using OCs. Insignificant differences were found with serum folate, iron, and zinc. Selenium and copper had a significantly higher serum value among those who reported using OCs. Vitamin B12 was found to have a significantly lower mean serum value for those on the pill. OC use as well as serum laboratory levels may be influenced by many additional factors, however our confounding factors in this study showed no significant difference. Additional research with further screening questions in regards to supplement, diet and birth control use would be beneficial to further understand OC interactions with nutrition-related serum levels.

Key Words: Oral Contraceptives, NHANES, Micronutrients, Serum Values

Chapter I: Introduction

Background

Unintended pregnancies account for approximately half of all pregnancies in the United States (Centers for Disease Control and Prevention (CDC), 2015a). It is estimated that the average American woman spends three decades of her life trying to prevent unintended pregnancy (Culwell & Feinglass, 2007). Worldwide, oral contraceptives (OCs) are the third most commonly used birth control with prevalence rates of 30 to 40 percent throughout various areas (United Nations, Department of Economic and Social Affairs, & Population Division, 2011). OCs, often referred to as “the pill”, are defined as oral drugs containing hormones estrogen and progestin which are effective in preventing pregnancy when taken correctly (CDC, 2016e). In the United States, OCs are estimated to be currently used by 16% or 6 million women ages 15-44 years (CDC, 2015b; Daniels, Daugherty, & Jones, 2014; Guttmacher Institute, 2016). With about 1 out of 4 women ages 15 to 24 years using the pill, it is the leading contraceptive method for US women ages 15 to 24 (Daniels et al., 2014).

Since a large number of young women are taking OCs as a leading form of birth control, health effects and outcomes are crucial to continually monitor and investigate. In the United States, 4 out of 5 women have used OCs in their lifetime (Daniels & Mosher, 2013). In 1982, the percentage of women having ever used an OCs was 76 percent, which increased to 82 percent in 1995 and has remained stable since (Daniels & Mosher, 2013).

Prescription drugs such as OCs may have negative side effects related to levels of micronutrients important for reproductive health. The World Health Organization (WHO) reports OCs on nutrient requirements should receive high attention as it has clinical importance (Palmery, Saraceno, Vaiarelli, & Carlomango, 2013). With half of pregnancies being unintended in the United States (CDC, 2015a), adequate nutrient intake and serum levels are important for all women capable of becoming pregnant. Micronutrients of concern regarding their levels as a result of OCs include folic acid, vitamins B2, B6, B12, C, E, magnesium, selenium, zinc (Palmery et al., 2013), iron, and copper (Anderson, 2010). All are important for reproductive health (Palmery et al., 2013; Anderson, 2010), and some nationally measured through the National Health and Examination Survey (NHANES). To our knowledge, interactions between OCs and micronutrients of concern have not previously been studied on a nationally representative sample of US young adult women using OCs.

When looking at the effect of OCs on micronutrients, additional factors that may contribute to depletion in micronutrient levels among women using OCs such as poverty, access to health care, and poor dietary habits of young women ages 18-24 years, must be considered (Palmery et al., 2013). An age range of 18-24 years has often been used in other national survey studies involving young women and health behaviors (Atkins & Bradford, 2014; Culwell & Feinglass, 2007). Young women, who often have lower consumption of nutrient dense foods, may be at greater nutrition risk when taking OCs. Proportionately, those with less income have higher OC use (Ayoola, Zandee, Johnson, & Pennings, 2014). Those with low income may experience malnourishment as a result of poverty; therefore the investigation of the effect of poverty on the relationship between OCs and micronutrient depletion is of particular importance.

Purpose Question

What is the impact of oral contraceptive use on nutrition-related serum laboratory values among US women ages 18-24 years?

Specific Aims

1. Describe and compare nutrition-related laboratory levels for US women using oral contraceptives compared to those not using oral contraceptives.
2. Describe and compare potentially confounding factors of nutrition-related laboratory such as dietary quality, dietary supplements, income, and health insurance for US women using oral contraceptives compared to those not using oral contraceptives.

Hypothesis

Due to interactions between oral contraceptives and nutrition-related laboratory values described in smaller studies, it is hypothesized that oral contraceptive use will be associated with abnormal nutrition-related serum laboratory values at the US population level.

Significance of Study

Research considering micronutrient status combined with current OC use among young women ages 18-24 years has not previously been done in a national, population-representative sample (Daniels et al., 2014). The use of NHANES data provides a unique opportunity for such a study, as OC use, serum micronutrients, dietary habits, and income are collected. The impact of such research investigating the effects of OCs on micronutrients could result in improvements to diet, supplementation, and contraceptive use recommendations for young women. As the average woman prevents unintended pregnancy for three decades of her lifetime (Culwell & Feinglass, 2007), micronutrient deficiencies could greatly impact quality of life due to years of possible negative nutrition medication interactions. Overall, national analysis of OCs and effects on nutrition-related laboratory values has potential for setting national best practice improvements, policy, and further research.

Career Significance

Through the investigation of OC effects on blood micronutrients in young women using NHANES data, I will gain important quantitative analytic skills by using national survey data, weighting the data to account for complex sampling design, applying statistical methods learned in graduate coursework by comparing and assessing multiple factors such as income and dietary markers, and gaining insight to National Center for Health Statistics (NCHS) survey techniques related to nutrition and contraceptives. Improving all of these skills will bolster my skills in being able to conduct nutritional epidemiologic studies. As a dietitian with interest in public health, understanding how to investigate the many factors in women's lives that can impact nutrition such as birth control, poverty, and dietary quality will help me interpret and incorporate evidence-based nutrition into practice. Increased skills researching health and family-planning disparities in the United States will improve my ability to provide empathetic, tailored nutrition services and education for all women.

Chapter II: Literature Review

OCs are the most common and popular form of hormonal birth control among all women and teens (CDC, 2015a). Among the majority of medications, many medication interactions exist, altering biomarkers and micronutrient serum levels. Research on OCs and micronutrients dates back to the 1960's (Adlercreutz et al., 1968), shortly after the first OC was approved by the Food Drug Administration (Nikolchev, 2010). Changes in micronutrients levels have potential to adversely influence physiological functions and alter growth and development. Some factors affecting birth control choices include income and health insurance (Ayoola et al., 2014; Culwell & Feinglass, 2007).

Oral Contraceptives and Micronutrients

With young women taking OCs as a leading form of birth control over decades, the effects of OCs on the body is important to understand, especially for young women and reproductive health. Micronutrients previously studied and important for reproductive health include folic acid, vitamins B2, B6, B12, C, E, magnesium, selenium, zinc (Palmery et al., 2013), iron, and copper (Anderson, 2010). However, due to the available NHANES micronutrient data from 2011-2012, for this study micronutrients to be assessed include folate, vitamin B12, iron, zinc, copper, and selenium (CDC, 2014a). This literature focuses a brief review of literature on each respective micronutrient.

Folic Acid

Folic acid, also known as vitamin B9, is a water-soluble vitamin often fortified in food sources. A lack of folic acid through dietary intake may lead to folate deficiency. Folic acid is responsible for DNA synthesis and cell division within the body, especially in cells that experience rapid growth, such as red blood cells. A lack of red blood cells is referred to as anemia. Adequate folate is especially important in early pregnancy for neural tube and brain growth, which occurs in the first four weeks of pregnancy, making folate a high priority micronutrient for women who may become pregnant. Inadequate folate may lead to neural tube defects (NTDs), brain malformation, heart defects, and orofacial clefts in the lip and palate. NTDs are the most common malformation that can occur during pregnancy, however, supplemental folic acid prevents many NTD's (Palmery et al., 2013). Research on folate deficiency and OCs began early in the 1960's. According to an article reviewing several studies, OCs have been found to negatively impact folate serum levels, however, neutral findings were also found (Palmery et al., 2013). It is believed that OCs may play a negative role on absorption, excretion, and metabolism of folate in the body. In contrast, another recent study looking at young women ages 18-35 years found elevated folate levels among those taking OCs without dietary supplementation (Fayet-Moore, Petocz, & Samman, 2014). Overall, it is suggested that women looking to become pregnant should supplement with folic acid (Palmery et al., 2013). In fact, on today's market, an approved folate-fortified OC is available in efforts to increase folate levels in reproductive-aged women who may become pregnant. The folate-fortified birth control pill has been found to increase folate levels to healthy recommended ranges (Castaño, Aydemir, Sampson-Landers, & Lynen, 2014).

Vitamin B12

Also known as cobalamin, vitamin B12 is responsible for DNA synthesis and energy production, similar to other B vitamins. The human body greatly relies on animal food sources of vitamin B12 or supplementation. If deficient, side effects may manifest themselves through the nervous system as cells cannot complete cell divisions correctly. Similar to folic acid, NTDs may also occur in infants when women are deficient in vitamin B12. Several studies found in a systematic review demonstrate low blood levels of vitamin B12 in OC users (Palmery et al., 2013) as well as among young women specifically (Fayet-Moore et al., 2014). However, another study found that vitamin B12 and folate may not be significantly altered, and more research is needed to draw stronger conclusions (Wilson, Bivins, Russell, & Bailey, 2011).

Iron

Iron is associated with red blood cells and carrying oxygen throughout the body. Menstrual cycles for over 3 three years have been associated with lower iron stores in young women (Sekhar, Murray-Kolb, Kunselman, Weisman, & Paul, 2017). With women using hormonal contraceptives, lighter menstrual cycles result in less blood loss and therefore, less iron loss. Unlike the other vitamins and mineral discussed, separate recommended dietary allowances (RDAs) have been discussed for women taking and not taking OCs. For women in childbearing years not taking OCs, the RDA is 18 milligrams per day, where for women taking OCs, the RDA is 10.9 milligrams per day. It is encouraged that women do not decrease foods rich in iron or multivitamins while taking an OC (Anderson, 2010). Low iron stores result in iron deficiency, which may or may not manifest itself as anemia. Deficient iron stores are linked to low birth weight pregnancies, altered cognitive function and behavior alterations for both women and infants (Fayet-Moore et al., 2014; Lozoff, 2007; Murray-Kolb & Beard, 2007; Murray-Kolb & Beard, 2009).

Selenium

Not as widely discussed and found in mostly animal sources and plants, selenium is responsible for antioxidant enzymes and largely in thyroid function and associated hormones.

OCs may inhibit selenium absorption. It is thought selenium absorption may be decreased with OC use with both statistically significant as well as statistically not significant findings (Palmery et al., 2013). Similar results are supported by the same study looking at other micronutrients in young women ages 18-35 years (Fayet-Moore et al., 2014). More research is needed to draw stronger conclusions. Lack of adequate dietary selenium has been associated with higher risk of cancer, cardiovascular disease, thyroid disease, and negative reproductive outcomes (Fayet-Moore et al., 2014). Additionally, it is of particular importance for young women as selenium has been thought to protect against breast cancer (Palmery et al., 2013).

Zinc

Zinc is an important essential mineral, especially in reproduction for both males and females, as it is involved with DNA and RNA metabolism, gene expression, and enzyme activity. Changes in zinc excretion from tissues or zinc absorption may be concern in women taking OCs as low zinc levels have been found (Fallah, 2009, Palmery et al., 2013). For OC users, increased zinc levels have been reported suggesting zinc may redistribute itself in the blood when taking the pill (Anderson, 2010). Because zinc and iron are often found together in many protein food sources, body deficiencies often coexist (Fayet-Moore et al., 2014). RDAs for zinc have not been altered for women using OCs at this time.

Copper

Copper and vitamin C are closely linked due to metabolic interactions and are commonly discussed together in research. Due to this association, copper is found to be increased instead of decreased among women using OCs (Anderson, 2010; Babić et al., 2013; Berg, Kohlmeier, & Brenner, 1998). Because of increased copper levels, one of the proteins that carries copper in the blood actually destroys vitamin C, resulting in lower vitamin C levels (Anderson, 2010). Vitamin C, also water soluble, is involved with essential metabolic functions, the formation of collagen and tissues, maintaining minerals such as iron and copper, and acting as an antioxidant, neutralizing free radicals within the body. Deficiencies may lead to clinical issues related to tissues such as poor wound healing, scurvy, and connective tissues disorders (Palmery et al., 2013). Lower vitamin C levels have been found through plasma and cellular components, such as white-blood cells, in women who take OCs (Fayet-Moore et al., 2014). At this time, there is not strong enough evidence to support changing needed vitamin C levels beyond the already suggested RDAs for women on the pill (Anderson, 2010). Copper also plays a role in iron status being associated with iron anemia and metabolism (Fayet-Moore et al., 2014).

Summary of Micronutrients

The table below reviews research discussed related to each specific micronutrient of concern.

Table 1: Comparison of Oral Contraceptive Effects of Micronutrient Levels

Micronutrient	Elevated Levels	Lower Levels	Small or No Difference
Folate	(Fayet-Moore, Petocz, & Samman, 2014)	(Palmery et al., 2013)	(Palmery et al., 2013) (Wilson, Bivins, Russell, & Bailey, 2011).
Vitamin B12		(Fayet-Moore, Petocz, & Samman, 2014) (Palmery et al., 2013)	(Wilson, Bivins, Russell, & Bailey, 2011).
Iron		(Fayet-Moore, Petocz, & Samman, 2014)	
Zinc	(Anderson, 2010)	(Palmery et al., 2013) (Fallah, Sani, & Firoozrai, 2009)	(Fayet-Moore, Petocz, & Samman, 2014)
Copper	(Anderson, 2010) (Babić et al., 2013) (Berg, Kohlmeier, & Brenner, 1998)		

Selenium		(Fallah, Sani, & Firoozrai, 2009) (Fayet-Moore, Petocz, & Samman, 2014) (Palmery et al., 2013)	(Palmery et al., 2013)
Note. Included articles and studies assess women of all ages.			

Dietary Quality

Women who take OCs may experience inadequate nutrition further contributing to the depletion of micronutrients (Palmery et al., 2013), particularly young women. Young women generally lack a diet rich in fruits, vegetables, and grains, particularly whole grains, which are rich sources of the nutrients of concern regarding OCs. Additionally, these diets are often higher in fats, sodium, and sugar (California Department of Public Health, 2012). According to the CDC, 80 percent of older adolescents do not eat fruit and vegetables 5 or more times per day (CDC, 2008). Fruit, vegetable, and grain foods contain many micronutrients, such as folate and iron, which are nutrients of concern for young women who may become pregnant (California Department of Public Health, 2012). Overall, adolescent girls often lack adequate intakes of calcium, iron, zinc, folate, and vitamins A, E, and B6 (Story & Hermanson, 2000). Further, barriers exist for consuming a diet higher in essential nutrients such as folate, vitamin B12, selenium, zinc, iron, and copper, as unhealthy options are cheaper in comparison to healthier choices. Low availability of fruits and vegetables, lack of healthy habit role modeling from parents, disordered eating tendencies, and lack of knowledge of proper nutrition are all barriers to consuming sufficient dietary nutrients (California Department of Public Health, 2012). Related to OCs, a study examined disordered eating of adolescent athlete females with reported athlete triad, in which dietary energy intake, menstrual cycles, and bone density are interrelated and adversely affected. It was found that a higher prevalence of disordered eating existed among adolescent athlete females using OCs. Those using OCs were twice as likely to meet the criteria for disordered eating with an odds ratio of 2.47 (Thein-Nissenbaum, Carr, Hetzel, & Dennison, 2014).

Based on the need for further research of specific micronutrients of concern, it is recommended that young women taking OCs should make efforts to eat a well-balanced diet rich in micronutrients, mostly through higher fruit, vegetable, and whole grain intake. A balanced diet is already a priority with various program interventions available for adolescent and young women. Specific to the nutrients of concern with OCs, again folate, iron, vitamin B12, selenium, zinc, and copper, food sources rich in these nutrients are suggested for increased consumption and shown in the following table. For individuals who are already lacking in the depicted nutrients, OCs may further micronutrient deficiencies in the context of a nutrient-deficient diet (Anderson, 2010), which is common in adolescents (Story & Hermanson, 2000).

Table 2: Food Sources of Micronutrients of Concern

Micronutrient	**Food Sources**
Folate	Green vegetables, leafy greens, legumes and beans, eggs, liver
Iron	Poultry, liver, fish, other meats, whole grains, enriched cereals, dried beans, dark leafy greens
Selenium	Vegetables, seafood and meat sources
Copper	Seafood, oysters, liver, nuts, dried beans, dried fruits
Zinc	Seafood, oysters, nuts, beans, whole grain breads
Vitamin B12	Meat, dairy products, eggs

(Adapted from Anderson, 2010; Palmery, Saraceno, Vaiarelli, & Carlomango, 2013)

Dietary Supplements

Dietary supplements may greatly alter nutrient intake as mineral and vitamin content is often higher than Recommended Dietary Reference Intakes (Gahche, 2011). Through its history, NHANES shows that supplement trends have changed over the years in the United States. From 1988-2006, the percentage of those 20 years of age or older taking one or more supplements increased from 42 percent to 53 percent. Additionally, women were more likely to use a supplement (Gahche, 2011). However looking at another analysis of NHANES data, supplement use was reported to have remained fairly stable at 52 percent from 1999-2012 (Kantor, Rehm, Du, White, & Giovannucci, 2016). Adolescent studies using NHANES data have also found that 27 percent of participants ages 11-19 years reported using dietary supplements. Adolescents who used prescription medications were more likely to report use of a supplement (Gardiner, Buettner, Davis, Phillips, & Kemper, 2008). Overall, dietary supplements are widely used in NHANES participants 18-24 years of age.

Income and Healthcare Coverage

A recent study looking at low-income women from communities that were underserved concerning medical access concluded that for the studied population, of those that used contraceptives, about 63 percent, the contraceptive methods used were less effective in preventing pregnancy, such the pill (Ayoola et al., 2014). Among US respondents who participated in the Behavioral Risk Factor Surveillance System (BRFSS) (BRFSS, 2016), another large representative health survey, results showed that lack of health coverage was associated with reduced use of prescribed contraceptives, like the pill (Culwell & Feinglass, 2007).

It is difficult to determine if OC use among young women will increase as other factors such as Medicaid and health coverage can now cover more effective forms of birth control such as intrauterine devices or the increasing use of emergency pills. Another study looking at BRFSS found that with mandated healthcare coverage, also covering contraceptives, OC use increased by 5 percent (Atkins & Bradford, 2014). In the United States, family planning goals have been discussed in the Health People 2020 initiatives to improve pregnancy planning, spacing, and preventing unintended pregnancies. One objective is to increase intended pregnancies to 56 percent. Preventing unintended pregnancies and better access to more effective forms of contraception that last longer with more consistent use is part of the family planning efforts (CDC, 2015a). Recently in the literature, there has been discussion on OCs converting to over the counter medication, which could increase OC use, however, cost remains a concern (Dennis & Grossman, 2012; Baum et al., 2016).

Existing Literature Gaps

Many gaps exist specifically with observing possible nutritional implications and effects of OCs on adolescent and young women. Part of this may be due to the factor that OC use among young women is still fairly new in regards to cultural acceptance. While no data are available showing morbidity and mortality rates related to OCs and their possible effect on nutritional status, OCs do show a benefit in reducing infant mortality rates (World Health Organization, 2015). The United States has an infant mortality rate of 596.1 deaths per 100,000 (CDC, 2016b) and a pregnancy mortality rate of 17.8 deaths per 100,000 (CDC, 2016d). As stated earlier, nearly half of all pregnancies in the United States are unintended, with cause being related to incorrect or inconsistent use of birth control (CDC, 2015a). Limitations and gaps in the research also include observing dietary quality or nutritional laboratory value status among young women and teens taking OCs from a national survey. NHANES represents the general US population of women and allows for multiple variables to be assessed through the use of respondent sequence numbers, linking all responses per individual. Additionally, the probability sampling of

NHANES may allow for stronger conclusions relatable to the American population. Further research is needed to determine association, risk, and level of significance of oral contraceptive effects on micronutrient levels in young women ages 18-24.

Chapter III: Methodology

NHANES

The National Center for Health Statistics working with the CDC has collected household and individual questionnaires, about 5,000 per year, related to health and nutrition, along with a physical examination that includes serum blood collection for laboratory assessments in the United States as part of the NHANES for decades. During certain years, laboratory tests have collected specific micronutrient values including folate, vitamin B12, iron, copper, selenium, and zinc. NHANES data collection from 2011-2012 is the latest survey year that collected micronutrients of interest for exploring the relationship between OCs and micronutrients (CDC, 2014a). In addition, information related to OC use and micronutrients such as dietary factors, ration of income to poverty, and health insurance is also collected (CDC, 2016c).

As for data collection procedures for NHANES, a complex, multistage probability design is used to locate participants. Four stages were used in the following order:

1. Selection of primary sampling units (PSUs), which are counties or small groups of contiguous counties.
2. Selection of segments within PSUs that constitute a block or group of blocks containing a cluster of households.
3. Selection of specific households within segments.
4. Selection of individuals within a household.

   Between 2011-2012, 13,431 individuals were selected from 30 locations. Of those selected, 9,756 participated in the interview and 9,338 participated in the MEC health examination (CDC, 2014c).

Measures

This study considers only young women using a form of OC in comparison to those who are not using OCs, it is important to note that through the use of a questionnaire, 177 women ages 18-24 reported currently using the pill and 711 reported not currently being on the pill. Missing responses total 2,410 for current birth control pill use. A survey question regarding women not currently on any form of birth control was not included (NHANES, 2013a).

Laboratory values for this study include folate, vitamin B12, iron, selenium, zinc, and copper. Various exclusions and eligibility factors are identified for each lab value. All laboratory data were collected within a MEC facility, allowing for identical conditions between all MEC facilities collecting, processing, storing, and shipping test tubes (CDC, 2015c).

For the confounding factors of dietary quality and supplement use, ratio of family income to poverty, and health insurance, NHANES measures all through the use of survey questionnaires. Dietary quality was measured by total dietary intake for both the first and second day of interviews (CDC, 2014b). Additionally, total micronutrient intake from dietary supplements in a 24-hour period was measured for both the first and second interviews (CDC, 2014b). All participants were eligible to report income with survey questions available regarding monthly family income and monthly poverty level (NHANES, 2015a). Family income was then divided by poverty guidelines for that survey year to determine the ratio (NHANES, 2015b). Participants were asked if they were covered by health insurance such as Medicaid, private insurance, or any form of health coverage (NHANES, 2013b).

The table below lists variables, confounding factors, eligibly criteria, and the specific question asked by NHANES interviews and questionnaires with available responses.

Table 3: NHANES Variables and Criteria		
Variable	**Eligibility and Exclusion Criteria**	**Question Asked and Response Options**
Oral contraceptive use (NHANES, 2013a)	Females 12 years and older were eligible.	Question: Are you taking birth control pills now? Response options: Yes, No, Refused, Don't know, Missing
Folate (NHANES, 2014a)	Participant's ages 1 and older, not meeting any exclusion criteria set by NHANES were eligible for data collection.	Laboratory Draw, Serum folate measured in both ng/mL.
Vitamin B12 (NHANES, 2014b)	Those who were ages 20 and older, not meeting any exclusion criteria set by NHANES were eligible.	Laboratory Draw, Vitamin B12 measured in both pg/mL.
Iron (NHANES, 2014c)	Participants 12 years of age and older were tested.	Laboratory Draw, Refrigerated iron measured in both µg/dL and µmol/L.
Selenium, Zinc, Copper (NHANES, 2014d)	Values were measured of one-third of the study samples for those 6 years of age or older. Additionally, 2011-2012 was the first NHANES data collection set for selenium, zinc, and copper.	Laboratory Draw, Serum selenium measured in µg/L, serum zinc measured in µg/dL, and serum copper measured in both µg/dL.
Dietary Intake (CDC, 2014b)	All participants of all ages were eligible.	For each respondent, total energy and nutrient intakes calculated from all food and beverages consumed in a 24-hour period for both interview days were collected. Intake Measurements: Food Folate (mcg) Vitamin B12 (mcg) Iron (mg) Zinc (mg) Copper (mg) Selenium (mcg)
Supplement Use (CDC, 2014b)	All participants of all ages were eligible.	For each respondent, intake of nutrients due to dietary supplements consumed in a 24-hour period prior to the interviews were calculated. Intake Measurements: Folate, DFE (mcg) Vitamin B12 (mcg) Iron (mg) Zinc (mg) Copper (mg) Selenium (mcg)
Ratio of family income to poverty (NHANES, 2015b)	Females of all ages were eligible.	Monthly family income (reported as a range value in dollars) Was measured based on the following response options. Family income was then divided by poverty guidelines for that survey year. Range Responses: $0 - $399 $400 - $799 $800 - $1249 $1250 - $1649 $1650 - $2099 $2100 - $2899 $2900 - $3749 $3750 - $4599 $4600 - $5399 $5400 - $6249 $6250 - $8399 $8400 and over Refused Don't know Missing

Health Insurance (NHANES, 2013b)	Females of all ages were eligible.	Question: Are you covered by health insurance or some other kind of health care plan? Responses: Yes, No, Refused, Don't know, Missing

Impact of OCs

This study is a quantitative cross-sectional study through the use of NHANES data to determine associations between OCs and abnormal serum laboratory values using data from 2011-2012. Eligible participants from NHANES include young women, ages 18-24, currently using an OC and those not currently using OCs. Serum laboratory values compared include folate, vitamin B12, serum iron, selenium, zinc, and copper. All of which have serum values available from NHANES. Confounding factors include dietary quality including dietary supplement use, income, and health insurance. Specifically, the following SPSS labels to include per micronutrient and factor are as follows:

- Folate Form, Serum- Serum Folate nmol/L
- Vitamin B12- Vitamin B12 pmol/L
- Standard Biochemistry Profile- Iron refrigerated µmol/L
- Copper, Selenium, and Zinc- Serum Copper µmol/L, Serum Selenium µmol/L, Serum Zinc µmol/L
- Dietary Interview- Total Nutrient Intake First Day and Second Day- Food Folate mcg, Vitamin B12 mcg, Iron mg, Zinc mg, Copper mg, Selenium mcg
- Income- Ratio of Family to Income Poverty
- Health Insurance- Covered by Health Insurance
- Dietary Supplement Use 24-Hour- Total Dietary Supplement First Day and Second Day- Folate DFE mcg, Vitamin B12 mcg, Iron mg, Zinc mg, Copper mg, Selenium mcg

Data analysis

To account for the complex sampling design, all data analysis was performed in Stata version 13 that generated weighted estimates using the complex samples command. We compared lab values and other potential confounding factors between those using OCs and those who are not using OCs with chi-square tests and independent t-tests. Significance for these tests was set at $\alpha<0.05$.

Ethical Considerations

Because of the nature of this study using de-identified secondary data, privacy of NHANES participants is kept as NHANES has assigned a respondent sequence number for each participant. Other ethical issues, including informed consent, have previously been considered for NHANES by the institutional review board (IRB) of the National Center for Health Statistics (CDC, 2012). Idaho State University determined this secondary analysis of NHANES to be exempt.

Chapter IV: Results

Sample size included 57 women who reported using OCs out of a total sample size of 345 women. Average age for respondents was similar between both groups (20.99 vs. 21.13).

Micronutrient Serum Lab Values

Differences in mean serum lab values of women using OCs compared to those not using OCs were significant for half of the micronutrients tested (3 of 6, see Table 4). Those with significant mean serum value differences included vitamin B12 (339.87 vs. 416.01 pmol/L, p=0.0083), selenium (1.72 vs. 1.60 µmol/L, p=0.0038), and copper (25.36 vs. 17.51 µmol/L, p=0.0002) for those using OCs compared to those not using OCs, respectively. Mean serum lab values with no significant differences included folate (41.77 vs. 43.08 nmol/L, p=0.7989), iron (15.19 vs. 13.28 µmol/L, p=0.1694), zinc (11.69 vs. 12.24 µmol/L, p=0.4393) for those using OCs compared to those not using OCs, respectively.

For both contraceptive use groups, vitamin B12, iron, selenium, zinc and copper mean lab values were within normal range when considering serum levels in the clinical setting. However, folate values were elevated for both groups (22.18 vs. 21.35 ng/mL) with normal range being 1.8-9.0 ng/mL (American Board of Internal Medicine, 2018).

Other Factors

Potentially confounding factors included health insurance, income to poverty ratio, dietary nutrient intake, and dietary supplement use. Marginally significant difference was observed among those who reported having health insurance between young women that use oral contraceptive and those that do not use (90.6% vs. 73.9%, respectively, p=0.059). Mean poverty to income ratio values were not found to be significant between oral contraceptive use groups (p=0.569).

Total nutrient intake for all nutrients on both days of data collection showed no significant difference between oral contraceptive groups for all micronutrient measures. No estimates yielded for 24-hour dietary supplements use as sample sizes were insufficient for both days of data collection.

Table 4: Comparison of Micronutrient Lab Values and Other Factors According to Oral Contraceptive Use Among Young US Women Ages 18-24			
Variable, unit, (sample size of participants who reported using OCs, sample size of participants who reported not using OCs)	**Participants who reported using OCs** (weighted average, 95% confidence intervals)	**Participants who reported not using OCs** (weighted average, 95% confidence intervals)	**P-Value**
Serum Labs			
Folate, nmol/L (n=319)	41.77 (33.65-49.90)	43.08 (39.65-46.52)	0.7989
VitaminB12, pmol/L (n=197)	339.87 (278.14-401.60)	416.01 (388.06-443.97)	0.0083*
Iron, µmol/L (n=324)	15.19 (12.89-17.50)	13.28 (11.85-14.72)	0.1694
Selenium, µmol/L (n=115)	1.72 (166-1.78)	1.60 (1.52-1.68)	0.0038*
Zinc, µmol/L (n=115)	11.69 (10.53-12.84)	12.24 (11.31-13.17)	0.4393
Copper, µmol/L (n=115)	25.36 (21.81-28.92)	17.51 (16.22-18-81)	0.0002*
Confounding Factors			
Covered by Health Insurance? (n=343) (weighted percent)			0.059
Yes	90.6%	73.9%	
No	9.4%	26.1%	
Income to poverty ratio (n=316) (weighted percent)			0.569
At or below the federal poverty level	39.1%	44.4%	
Above the poverty level	60.9%	55.6%	
Total Nutrient Intake- Day 1			
Folate, mcg (n=340)	359.10 (308.11-410.09)	398.94 (348.46-449.41)	0.1917
Vitamin B12, mcg (n= 340)	3.66 (2.61-4.70)	4.21 (3.69-4.75)	0.2034
Iron, mg (n=340)	12.57(10.55-14.59)	13.70(12.33-15.06)	0.2704
Selenium, mcg (n=340)	94.37 (78.56-110.17)	97.52 (90.31-104.73)	0.7194
Zinc, mg (n=340)	8.55 (7.22-9.88)	9.47 (8.73-10.21)	0.2066
Copper, mg (n=340)	1.11 (0.85-1.36)	1.06 (0.97-1.15)	0.7199
Total Nutrient Intake- Day 2			
Folate, mcg (n=311)	356.98 (291.68-422.29)	366.73 (314.63-418.83)	0.8387

Vitamin B12, mcg (n=311)	3.49 (2.69-4.28)	4.68 (3.62-5.75)	0.1535
Iron, mg (n=311)	14.18 (11.95-16.41)	13.85 (12.04-15.66)	0.8493
Selenium, mcg (n=311)	82.25 (68.66-95.84)	95.77 (82.83-108.70)	0.1681
Zinc, mg (n=311)	8.97 (7.69-10.25)	8.90 (7.91-10.07)	0.9859
Copper, mg (n=311)	1.00 (0.87-1.12)	0.96 (0.85-1.07)	0.6620
24-Hour Dietary Supplement Use-Day 1			
Folate, mcg (n=33)	954.89	865.10	
Vitamin B12, mcg (n=33)	95.92	30.73	
Iron, mg (n=32)	23.44	29.62	
Selenium, mcg (n=18)	35.06	40.59	
Zinc, mg (n=28)	18.03	16.91	
Copper, mg (n=19)	1.92	1.85	
24-Hour Dietary Supplement Use-Day 2			
Folate, mcg (n=32)	968.32	956.76	
Vitamin B12, mcg (n=34)	361.25	41.16	
Iron, mg (n=32)	24.51	30.01	
Selenium, mcg (n=18)	44.23	58.85	
Zinc, mg (n=27)	17.64	17.99	
Copper, mg (n=19)	0.96	2.11	

*$p \leq 0.05$
+ Sample size of each test is indicated as there was a variation in respondents that received dietary supplements

Chapter V: Discussion

Abnormal serum levels of micronutrients were hypothesized to be found among women using OCs in comparison to those not using OCs. Half of evaluated serum lab values showed significant differences in this study, however the magnitude of the difference between for contraceptive use categories were in the normal range. Elevated folate levels were reported overall for this age group with no differences according to contraceptive use.

Mean serum vitamin B12 was found to be significantly lower among women using OCs compared to women not using OCs. This is supportive of research available finding women using OCs and just young women alone may have lower or no difference in mean serum lab values of vitamin B12 (Fayet-Moore, Petocz, & Samman, 2014; Wilson et al., 2011). Differences in our vitamin B12 findings may be due to physiological interactions of OCs. Previous research finding vitamin B12 levels to be lower in OC users speculated that vitamin B12 may not be deficient but may be redistributed in the body as a result of hormonal interactions. This study also controlled for dietary and supplemental factors (Wilson et al., 2011). For this study, both of our observed means were within a normal clinical practice range. While no significant differences were found with dietary intake of vitamin B12, research does address that young women in general may often be lacking in dietary sources of vitamin B12 depending on personal dietary and trending habits, such as those following vegetarian or plant based diets (Fayet, Flood, Petocz, & Samman, 2014). Further questions in regards to individual dietary practices may be beneficial in identifying further subgroups of young women who may be at greater risk when using OCs.

Serum selenium had higher averages among women using OCs compared to those not using OCs. This is contrary to our hypothesis of anticipating lower levels as also found by previous research also measuring serum selenium (Fallah, Sani, & Firoozrai, 2009; Fayet-Moore, Petocz, & Samman, 2014; Palmery et al., 2013). Lower levels may be due to physiological interactions. This study may be one of the first to identify higher levels of selenium in OC users. Mean serum levels found are within normal clinical ranges. Dietary and supplement intake of selenium may be factors, however we did not see evidence of significant higher intake of selenium from dietary intake. However, for both days and groups, average selenium intake is higher than the RDA. Average selenium intake from supplements is within the RDA for both groups, however due to a small sample size, we were unable to assess significance of differences in supplement intake in this study. Combining both dietary and supplement intake averages, total selenium intake from all sources would be above the RDA of 55 mcg (National Institutes of Health, 2018a).

Serum copper also had higher averages among women using OCs compared to those not using OCs. Available research does support that higher copper levels are seen with women using OCs (Anderson, 2010; Babić et al., 2013; Berg, Kohlmeier, & Brenner, 1998). Levels of elevated copper are also due to physiological interactions and may vary depending on differing hormonal components of the type of pill used (Berg, Kohlmeier, & Brenner, 1998). There is not an available RDA to compare copper results to as copper is self regulated by the body and deficiencies and toxicities are rare in the United States (National Institutes of Health, 2017). Overall, our finding with copper are supported by previous research.

While average folate serum levels were not different by OC use status among young adult women, means were significantly above the clinical normal range values for both groups. Folate has received much attention in women's health especially with its role and importance in early pregnancy stages for both intended and unintended pregnancies. Research supports that dietary folate efforts in the United States have helped to increase serum folate levels in the US population (Fayet-Moore, Petocz, & Samman, 2014). While some previously done research shows decreased levels of serum folate when using OCs, the authors recognize that questionable compliance with OC regimens and dietary intake were limitations (Palmery et al., 2013). Reviewing supplement intake of folate in this study, in comparison to the RDA for women (400 mcg/day (National Institutes of Health, 2018b)), average folate intake for average reported 24-hour supplement intake was above the RDA (respectively 954 vs. 865 mcg and 968 vs. 956 mcg). High intake of folate from food sources is not found to be harmful, however folate from supplements and fortified foods is recommended to not exceed recommended Upper Limit (UL) which is 1,000 mcg daily for adults (National Institutes of Health, 2018b). Similar to other evaluated serum labs in this study, it may be beneficial to further understand supplement use among young women as prenatal vitamins and vitamins targeted towards women also often contain folate. Additionally, some newer forms of OCs are fortified with folate. Qualitative data understanding which participants may or may not have been using fortified versions of the pill may be useful in recognizing additional folate coming from OC use.

While we saw no significant differences in iron, sources do state that higher body iron levels are found in women using OCs vs. non-users. Elevated body iron among those using OCs is supported through research indicating that reduced menstrual blood loss due to OC use may attenuate the impact of menstruation on iron status (Frassinelli-Gundersonson, Margen, & Brown, 1985; Anderson, 2010). Additionally, NHANES survey guidance does outline OCs as an interfering substance, stating “ingestion of oral contraceptives will elevate iron” (NHANES, 2011-2012). However, other research has found iron status to be significantly decreased among university-aged women with no exclusion criteria given for women using OCs, however other measures of iron status were measured including hemoglobin, ferritin and transferrin (Fayet-Moore, Petocz, & Samman, 2014). It is important to note that serum iron is not the preferred measure of iron status, however in combination with other iron status indicators it can be used in analysis of iron disorders as a result of physiological function. Other studies analyzing iron status often use ferritin, which was not available in the NHANES 2011-2012 data set for assessment. Further analysis looking at more reliable and precise indicators of iron status should be assessed and included in NHANES data on a reoccurring basis.

For all micronutrients of concern, further research evaluating supplement intake and its role with serum values should be assessed. Due to a small sample size for supplemental intake, tests of significance were a limitation in our study. With NHANES, reported supplement intake was measured for day one in-person at the MEC, surveying supplement use within the last 24-hours. Supplements reported were then analyzed to identify the specific levels of micronutrients contained. It is important to note that day two of 24-hour supplement use was collected 3-10 days after day one of data collected. Further analysis looking at longer periods of supplement use with simultaneous use of OCs along with other confounding factors reviewed in this study may be beneficial for better understanding supplement use in young women of childbearing age. Qualitative data on reason for supplement use and type of supplement use may be beneficial in better understanding women's supplement use among those using birth control.

As stated earlier, nearly half of all pregnancies in the United States are unintended, with cause being related to incorrect or inconsistent use of birth control (CDC, 2015a). Informational data such as consistency of taking the pill and type of OC used is not asked. The 2011-2012 data set only includes one question identifying women who were using OCs as birth control. While there are respondents stating they were not currently taking a form of OC, other birth control methods were not assessed. Other hormonal pills used for other purposes were addressed in NHANES, however birth control pills were not included in this category (NHANES, 2013a) and were not assessed in this study. Having this information available may have made it possible to increased sample size for our study group along with being able to assess effects of other forms of birth control on serum micronutrient levels.

Additionally, many limitations exist when looking at nutrition related studies. Through the collection of food frequency questionnaires and 24-hour food recalls, both used by NHANES, dietary intake estimates may not be a true representation of usual diet. Food frequency questionnaires are the most widely used method for dietary intake in epidemiological studies (Willett, 2013, p. 86). However, gaps may be missed as they rely on usual habits of dietary intake and not exact measurements. Additionally, NHANES also uses 24-hour food recalls for the Total Nutrient Intake Files. While 24-hour food recalls are a more accurate assessment of recent nutrition intake, 24-hour food recalls do not represent long-term intakes. To say if these limitations either increase or decrease micronutrients, variation would greatly depend on either under or over reporting of dietary intake. Participants misreporting usual or recent dietary intake is another major concern when using 24-hour food recalls. Additionally, dietary supplements may alter micronutrient intakes and/or affect blood serum values. However, 24-hour recalls do tend to be more accurate than food frequency questionnaires as participants are more likely to recall their food intake and supplement use over shorter periods of time.

Beneficial to the study, NHANES represents the general US population of women and allows for multiple variables to be assessed through the use of respondent sequence numbers, linking all responses per individual. Additionally, the probability sampling of NHANES may allow for stronger conclusions relatable to the American population along with reputable and validated serum laboratory values. Further research is needed to determine association, risk, and level of significance of oral contraceptive effects on micronutrient levels in young women with the addition of other confounding factors.

As half of our evaluated micronutrients of concern had significant difference in serum values, further research is still needed to draw stronger conclusions about interfering factors. Additional questions in regard to OC use may be beneficial to include in NHANES data. As new forms of birth control emerge, understanding interactions of different types of birth control is also important, especially as some types are more reliable in preventing pregnancy compared to OCs. Serum values and physiological indicators that correlate with identified micronutrients of concern may also help in analyzing OC interactions. Understanding dietary and supplement use of young women could better be evaluated through the use of qualitative data. This may additionally help us identify subgroups of young women who may be at greater risk of OC interactions. As for clinical and nutrient recommendations, assessing the individual is still best practice as all factors affecting health should be considered.

References

Adlercreutz, H., Eisalo, A., Heino, A., Luukkainen, T., Penttil, I., & Saukkonen, H. (1968). Investigations on the Effect of an Oral Contraceptive and its Components on Liver Function, Serum Proteins, Copper, Coeruloplasmin and γ -Glutamyl Peptidase in Postmenopausal Women. *Scandinavian Journal Of Gastroenterology*, *3*(3), 273. doi:10.3109/00365526809180601

American Board of Internal Medicine. (2018). ABIM Laboratory Test Reference Ranges-January 2018. Retrieved from http://www.abim.org/~/media/ABIM%20Public/Files/pdf/exam/laboratory-reference-ranges.pdf.

Anderson, J. (2010). Nutrition and oral contraceptives. Retrieved from http://extension.colostate.edu/topic-areas/nutrition-food-safety-health/nutrition-and-oral-contraceptives-9-323/.

Atkins, D. N., & Bradford, W. D. (2014). Changes in state prescription contraceptive mandates for insurers: the effect on women's contraceptive use. *Perspectives On Sexual And Reproductive Health*, *46*(1), 23-29. doi:10.1363/46e0314

Ayoola, A. B., Zandee, G. L., Johnson, E., & Pennings, K. (2014). Contraceptive Use among Low-Income Women Living in Medically Underserved Neighborhoods. *JOGNN: Journal Of Obstetric, Gynecologic & Neonatal Nursing*, *43*(4), 455-464 10p. doi:10.1111/1552-6909.12462

Babić, Ž., Tariba, B., Kovačić, J., Pizent, A., Varnai, V. M., & Macan, J. (2013). Relevance of serum copper elevation induced by oral contraceptives: a meta-analysis. *Contraception*, *87*(6), 790-800. doi:10.1016/j.contraception.2012.10.006

Baum, S., Burns, B., Davis, L., Yeung, M., Scott, C., Grindlay, K., & Grossman, D. (2016). Perspectives among a diverse sample of women on the possibility of obtaining oral contraceptives over the counter: A qualitative study. *Women's Health Issues*, *26*(2), 147-152. doi:10.1016/j.whi.2015.08.007

Behavioral Risk Factor Surveillance System. (2016). About BRFSS. https://www.cdc.gov/brfss/about/index.htm.

Berg, G., Kohlmeier, L., & Brenner, H. (1998). Effect of oral contraceptive progestins on serum copper concentration. *European Journal Of Clinical Nutrition*, *52*(10), 711-715.

California Department of Public Health. (2012). Adolescent nutrition. Retrieved from http://www.cdph.ca.gov/programs/NutiritionandPhysicalActivity/Documents/MO-NUPA-AdolescentNutritionHandouts.pdf.

Castaño, P. M., Aydemir, A., Sampson-Landers, C., & Lynen, R. (2014). The folate status of reproductive-aged women in a randomized trial of a folate-fortified oral contraceptive: dietary and blood assessments. *Public Health Nutrition*, *17*(6), 1375-1383 9p. doi:10.1017/S1368980013000864.

Centers for Disease Control and Prevention. (2008). Nutrition and the health of young people. Retrieved from http://www.cdc.gov/HealthyYouth/nutrition/pdf/facts.pdf.

Centers for Disease Control and Prevention. (2012). NCHS research ethics review board (ERB) approval. Retrieved from http://www.cdc.gov/nchs/nhanes/irba98.htm.

Centers for Disease Control and Prevention. (2013). NHANES 2011-2012 reproductive health. Retrieved from http://www.cdc.gov/reproductivehealth/contraception/.

Centers for Disease Control and Prevention. (2014a). NHANES 2011-2012 laboratory data. Retrieved from https://wwwn.cdc.gov/Nchs/Nhanes/Search/DataPage.aspx?Component=Laboratory&CycleBeginYear=2011.

Centers for Disease Control and Prevention. (2014b). NHANES 2011-2012 dietary data. Retrieved from https://wwwn.cdc.gov/Nchs/Nhanes/Search/DataPage.aspx?Component=Dietary&CycleBeginYear=2011.

Centers for Disease Control and Prevention. (2014c). 2011-2012 overview. Retrieved from https://www.cdc.gov/nchs/nhanes/nhanes2011-2012/overview_g.htm.

Centers for Disease Control and Prevention. (2015a). Unintended pregnancy prevention. Retrieved from http://www.cdc.gov/reproductivehealth/unintendedpregnancy/.

Centers for Disease Control and Prevention. (2015b). Contraceptive use. Retrieved from http://www.cdc.gov/nchs/fastats/contraceptive.htm.

Centers for Disease Control and Prevention. (2015c). NHANES 2011-2012 lab data overview. Retrieved from https://www.cdc.gov/nchs/nhanes/nhanes2011-2012/labdoc_g.htm.

Centers for Disease Control and Prevention. (2016a). Contraception. Retrieved from http://www.cdc.gov/reproductivehealth/contraception/.

Centers for Disease Control and Prevention. (2016b). Infant health. Retrieved from http://www.cdc.gov/nchs/fastats/infant-health.htm.

Centers for Disease Control and Prevention. (2016c). Survey Questionnaires. Retrieved from https://www.cdc.gov/nchs/nhanes/nhanes2011-2012/questionnaires11_12.htm.

Centers for Disease Control and Prevention. (2016d). Pregnancy mortality surveillance system. Retrieved from http://www.cdc.gov/reproductivehealth/maternalinfanthealth/pmss.html.

Centers for Disease Control and Prevention. (2016e). Contraception. Retrieved from https://www.cdc.gov/reproductivehealth/contraception/.

Contraception and Adolescents. (2007). *Pediatrics*, *120*(5), 1135. doi:10.1542/peds.2007-2535.

Culwell, K., & Feinglass, J. (2007). The association of health insurance with use of prescription contraceptives. *Perspectives On Sexual & Reproductive Health*, *39*(4), 226-230 5p.

Daniels, K., Daugherty, J., & Jones, J. (2014). Current contraceptive status among women aged 15-44: United States, 2011-2013. *NCHS Data Brief*, (173), 1-8.

Daniels, K., & Mosher, W. D. (2013). Contraceptive methods women have ever used: United States, 1982-2010. *National Health Statistics Reports*, (62), 1-15.

Dennis, A., & Grossman, D. (2012). Barriers to Contraception and Interest In Over-the-Counter Access Among Low-Income Women: A Qualitative Study. *Perspectives On Sexual & Reproductive Health*, *44*(2), 84-91. doi:10.1363/4408412

Fallah, S. Sani, F.V., Firoozrai, M. (2009). Effect of contraceptive pill on the selenium and zinc status of healthy subjects. *Contraception*, *80*(1), 40-43.

Fayet, F., Flood, V., Petocz, P., & Samman, S. (2014). Avoidance of meat and poultry decreases intakes of omega-3 fatty acids, vitamin B12 , selenium and zinc in young women. *Journal*

Of Human Nutrition And Dietetics: The Official Journal Of The British Dietetic Association, *27 Suppl 2*135-142. doi:10.1111/jhn.12092

Fayet-Moore, F., Petocz, P., & Samman, S. (2014). Micronutrient status in female university students: iron, zinc, copper, selenium, vitamin B12 and folate. *Nutrients*, *6*(11), 5103-5116. doi:10.3390/nu6115103

Frassinelli-Gundersonson, EP., Margen, S., Brown, JR. (1985). Iron stores in users of oral contraceptive agents. *American Journal of Clinical Nutrition, 41(4),* 703-12. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/3984924.

Gahche, J. (2011). *Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994) [electronic resource]*. Hyattsville, MD : U.S. Dept. of Health & Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, [2011].

Gardiner, P., Buettner, C., Davis, R., Phillips, R., & Kemper, K. (2008). Factors and common conditions associated with adolescent dietary supplement use: an analysis of the National Health and Nutrition Examination Survey (NHANES). *BMC Complementary & Alternative Medicine*, *8*8p.

Guttmacher Institute. (2016a). Contraceptive use in the united states. Retrieved from https://www.guttmacher.org/fact-sheet/contraceptive-use-united-states.

Hurwitz, B. E., Henry, N., & Goldberg, R. B. (2009). Long-term oral contraceptive treatment, metabolic syndrome and measures of cardiovascular risk in pre-menopausal women: National Health and Nutrition Examination Survey 1999-2004. *Gynecological Endocrinology*, *25*(7), 441-449. doi:10.1080/09513590902770149

Kantor, E. D., Rehm, C. D., Du, M., White, E., & Giovannucci, E. L. (2016). Trends in Dietary Supplement Use Among US Adults From 1999-2012. *Jama*, *316*(14), 1464-1474. doi:10.1001/jama.2016.14403

Kost, K., Finer, L. B., & Singh, S. (2012). Variation in State Unintended Pregnancy Rates In the United States. *Perspectives On Sexual & Reproductive Health*, *44*(1), 57-64 8p. doi:10.1363/4405712

Lozoff, B. (2007). Iron deficiency and child development. *Food And Nutrition Bulletin*, *28*(4 Suppl), S560-S571.

Martinez, G. M., & Abma, J. C. (2015). Sexual Activity, Contraceptive Use, and Childbearing of Teenagers Aged 15-19 in the United States. *NCHS Data Brief*, (209), 1-8.

Murray-Kolb, L. E., & Beard, J. L. (2007). Iron treatment normalizes cognitive functioning in young women. *The American Journal Of Clinical Nutrition*, *85*, 778-87.

Murray-Kolb, L. E., & Beard, J. L. (2009). Iron deficiency and child and maternal health. *The American Journal Of Clinical Nutrition*, *89*(3), 946S-950S. doi:10.3945/ajcn.2008.26692D

National Health and Examination Survey. (2011-2012). Laboratory Procedure Manual. Iron. Retrieved from https://wwwn.cdc.gov/Nchs/Data/Nhanes/2011-2012/LabMethods/biopro_g_met_iron.pdf.

National Health and Examination Survey. (2013a). Reproductive health. Retrieved from http://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/RHQ_G.htm#RHD442.

National Health and Examination Survey. (2013b). Health insurance. Retrieved from http://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/HIQ_G.htm.

National Health and Examination Survey. (2014a). Folate forms-serum. Retrieved from http://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/FOLFMS_G.htm.

National Health and Examination Survey. (2014b). Vitamin B12. Retrieved from http://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/VITB12_G.htm.

National Health and Examination Survey. (2014c). Standard biochemistry profile. Retrieved from http://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/BIOPRO_G.htm.

National Health and Examination Survey. (2014d). Copper, selenium, and zinc. Retrieved from http://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/CUSEZN_G.htm.

National Health and Examination Survey. (2015a). Income. Retrieved from http://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/INQ_G.htm.

National Health and Examination Survey. (2015b). Demographic variables and sample weights. Retrived from https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/DEMO_G.htm.

National Institutes of Health. (2017). Copper. Retrieved from https://ods.od.nih.gov/News/Copper.aspx.

National Institutes of Health. (2018a). Selenium. Retrieved from https://ods.od.nih.gov/factsheets/Selenium-HealthProfessional/.

National Institutes of Health. (2018b). Folate. Retrieved from https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/.

Nikolchev, A. (2010). A brief history of the birth control pill. Retrieved from http://www.pbs.org/wnet/need-to-know/health/a-brief-history-of-the-birth-control-pill/480/.

Palmery, M., Saraceno, A., Vaiarelli, A., & Carlomango, G. (2013). Oral contraceptives and changes in nutritional requirements. *European Review For Medical & Pharmacological Sciences*, *17*(13), 1804.

Park, B., & Kim, J. (2016). Oral contraceptive Use, Micronutrient Deficiency, and Obesity among Premenopausal Females in Korea: The Necessity of Dietary Supplements and Food Intake Improvement. *Plos ONE*, *11*(6), 1-12. doi:10.1371/journal.pone.0158177

Sekhar, D. L., Murray-Kolb, L. E., Kunselman, A. R., Weisman, C. S., & Paul, I. M. (2017). Association between menarche and iron deficiency in non-anemic young women. *Plos ONE*, *12*(5), 1-11. doi:10.1371/journal.pone.0177183

Story, M., & Hermanson, J. (2000). Nutrition and the Pregnant Adolescent: A practical reference guide. Minneapolis, MN: Center for Leadership, Education, and Training in Maternal and Child Nutrition.

Tepper, N. K., Marchbanks, P. A., & Curtis, K. M. (2014). U.S. Selected Practice Recommendations for Contraceptive Use, 2013. *Journal Of Women's Health (15409996)*, *23*(2), 108-111 4p. doi:10.1089/jwh.2013.4556.

Thein-Nissenbaum, J. M., Carr, K. E., Hetzel, S., & Dennison, E. (2014). Disordered Eating, Menstrual Irregularity, and Musculoskeletal Injury in High School Athletes: A Comparison of Oral Contraceptive Pill Users and Nonusers. *Sports Health: A Multidisciplinary Approach*, *6*(4), 313. doi:10.1177/1941738113498852.

United Nations, Department of Economic and Social Affairs, & Population Division. (2011). World Contraceptive Use 2011. Retrieved from http://www.un.org/esa/population/publications/contraceptive2011/wallchart_front.pdf.

Welti, K., Wildsmith, E., & Manlove, J. (2011). Trends and recent estimates: contraceptive use among U.S. teens and young adults. Retrieved from http://www.childtrends.org/wp-content/uploads/2011/12/Child_Trends-2011_12_01_RB_ContraceptiveUse.pdf.

Willett, W. (2013). *Nutritional epidemiology*. New York : Oxford University Press, 2013.

Wilson, S. C., Bivins, B. N., Russell, K. A., & Bailey, L. B. (2011). Oral contraceptive use: impact on folate, vitamin B_6, and vitamin B_{12} status.*Nutrition Reviews*, *69*(10), 572-583. doi:10.1111/j.1753-4887.2011.00419.x.

World Health Organization. (2015). Family planning/contraception. Retrieved from http://who.int/mediacentre/factsheets/fs351/en/.