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Guadalupe Rivera

# The Association Between Birth Control Use and Metabolic Profiles of Women Residing in the United States (NHANES 2015-2016)

By

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_____

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# The Association Between Birth Control Use and Metabolic Profiles of Women Residing in the United States (NHANES 2015-2016)

By

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2022

Thesis Committee Chair: Dr. Shivani A. Patel, PhD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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**Abstract**

The Association Between Birth Control Use and Metabolic Profiles of Women Residing in the United States (NHANES 2015-2016)

By Guadalupe Rivera

**Introduction**: With the increased use of hormonal contraceptives among women in the United States, alongside the linkage between reproductive hormones and metabolic disease, it is important to understand if the use of birth control impacts metabolic profiles in women. While there is previous research on the effects of birth control history in menopausal women, there is less research in women who are of reproductive age. The objective of this research is to conduct cross-sectional descriptive analysis of five metabolic outcomes according to women's history of birth control usage.

**Methods**: Data were from the nationally representative National Health and Nutrition Examination Survey (NHANES) 2015-2016. The study population comprised non-pregnant women aged 20-44 years in the United States. We compared metabolic measures between those who have ever used birth control and those who have not. Differences by birth control history in total cholesterol, systolic blood pressure, Body Mass Index (BMI), waist circumference, and glycohemoglobin levels were modeled using linear and quantile regression.

**Results**: A total 694 women with mean age 32.5 were included in the analysis; 66.57% reported a minority race and ethnicity background. 67.44% reported history of birth control use. In adjusted regression models, women who had used birth control had, on average, a 3.17 mmHg (95%CI) higher systolic blood pressure compared to those who had never used birth control. There were no other statistically significant differences in metabolic measures between women who had ever or never used birth control.

**Discussion**: In a diverse group of US women, we found that women with a history of birth control had higher systolic blood pressure. Findings motivate further research on the role of birth control in hypertension development and the appropriateness of birth control among women at high risk for hypertension.

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## Introduction

In 2019, 61.4% (74,635) of women in the United States used contraceptives. Out of the 61.4% that use contraceptives, 13.7% used the pill, 2.3% used injectables, 2.7% used implants, and 8.3% used the intra-uterine device (IUD) (United Nations, 2019). Previous research demonstrates that birth control can affect women's metabolic risk factors, such as blood pressure and blood glucose, while some other studies find no impact on women's metabolic profiles (Dinger et. al 2009), (Contraception, 2017). With an increasing number of women turning to birth control, it is important to know if the use of birth control impacts metabolic profiles in women. While there is research on the metabolic risk factors, birth control for women in menopause, as well as female hormone use, there is a need for research on women who are premenopausal and the association of birth control and metabolic risk factors, before, during, and after use.

According to the WHO, leading metabolic risk factors for non-communicable disease include raised blood pressure, overweight/obesity, hyperglycemia, and hyperlipidemia. The leading metabolic risk factor is elevated blood pressure with 19% of global deaths are attributed, and the rest follow closely behind (*Non Communicable Diseases*, n.d.). Metabolic risk factors impact women's menstrual cycle, hormonal balance, including risks for chronic diseases like diabetes and raised blood pressure. It is important to note that an individual's metabolic profile affects the risk of chronic diseases and endocrine disorders like PCOS and endometriosis.

Using data from the 2015-16 NHANES survey, the objective of this research was to conduct an analysis of metabolic profiles according to women's history of birth control usage. We hypothesized that metabolic profiles are different between women who have ever used birth control and women who have not.

## Literature Review

### *Birth Control Use in the United States*

According to the CDC, between 2015 and 2017, 64.9% of 72.2 million women aged 15-49 in the United States were currently using contraceptives and nearly all women will use contraception sometime in their life (Daniels & Abma, 2023). From an analysis done using 2006-2010 data from the National Survey of Family Growth (NFSG) looking at women aged 15-44 years of age, 67% Non-Hispanic White Women, 59.9% of non-Hispanic Black Women, and 64.0% Hispanic women use contraception. The most common contraceptive methods are female sterilization, oral contraceptive pill, long-acting reversible contraceptives (LARCs) which includes contraceptive implants and intrauterine devices, and male condom. Studies show that contraceptive use increases with age, with 37.2% among women 15-19, and 73.7% among women aged 40-49% use birth control (Daniels & Abma, 2023).

Social determinants of health such as race, ethnicity, and healthcare are essential when looking into the association between birth control and metabolic risk factors, given that race is a determinant of access to healthcare. In the United States, it is required that women see a medical professional to obtain a highly effective, reversible birth control method or the prescription for the method. Women without health insurance are less likely to be able to see a doctor, much less receive a prescription, or pay to see a doctor and for the prescription. Historically, this affects minority groups, therefore race is also a factor that comes into play when looking at overall birth control use for women in the United States. In the NFSG study, they found that White women have the most frequent use of any reversible method, with a higher proportion of white women have used the pill compared with all other racial and ethnic groups (Daniels & Abma, 2023). Black women and Hispanic women were found to have the highest proportion of those who had ever used a hormonal method. Across the board, birth control pills are the highest form of

contraceptive use, regardless of education, with more than 77% of women with no high school diploma using it, and more than 84% for all other categories of education. In another study that looked at current use of OCs in 1,940 young African American and White women between 18 to 30 years of age in the CARDIA study, they found that current OC users were younger, with a lower mean BMI, lower waist-to-hip ratios, lower current smoking rates, and more years of education (Kim et al., 2002). This study did not consider other minorities, such as Hispanics and Asians and did not include all women of reproductive age.

Although many women use oral contraceptives, many women discontinue their use for several reasons, indicating that there might be an association between birth control use and women's health to be explored. Contraceptives that contain estrogen and/or progestins can be used to treat women with variety of conditions, such as endometriosis, uterine fibroids, heavy menstrual bleeding, acne, and migraines (Schrager et al., 2020). Yet, according to the NFSG dataset report, women discontinue using the pill for various reasons. One reason women may switch to a new method of contraception is if they are dissatisfied with their current method. From the 45,021 women in the study that discontinued using the pill, 30.4% used and discontinued it due to dissatisfaction, 62.9% experienced side effects, 11.8% were worried that they might have side effects, and 11.5% did not like the changes they experienced in their menstrual cycle. Some effects can be physiological or psychological, with some side effects found to be increases stress hormone profiles and risk of thrombosis. Some side effects that are reported include mood changes, nausea, headaches, and breast tenderness (Littlejohn, 2013). The discontinued use of birth control pills may be an indicator of health issues that come with the use of birth control, and it may be worth looking to see how women's bodies respond to birth control use.

Additionally, health risks that occur after getting the pill is another area to be considered. From

the review of the literature, it seems that there are little to no scientific studies on symptoms women experience after stopping contraceptive birth control use.

## Pathways linking contraceptive use to metabolic health

### *Weight and Body Mass Index*

In research, oral contraceptive use has not been found to affect weight or BMI, yet, some women reported to stop taking the pill is because they believe weight gain is a common side effect of oral contraceptives (OC) ("Contraception," 2017). Researchers from the Cochrane Collaboration did a review, searching for studies on hormonal contraceptives where weight was recorded. They did not find studies that showed a clear link between hormonal contraception and weight gain ("Contraception," 2017). A secondary analysis from a prospective randomized trail conducted in 2014 on the effect of OC use on weight change that included obese women with a follow-up of three months found that OCs are not associated with short term weight or body composition change in obese women (Mayeda et al., 2014). The study included 226 women (128 normal and 98 obese women), with BMI for normal women defined as 19.0-24.9, and BMI for obese women defined between 30.0 – 39.9. Yet, the findings from the study are limited by the duration of follow up, and the lack of a placebo group. Additionally, it could be possible that changes may have been observed over a longer period of follow-up. Their study included Hispanics, Non-Hispanic black, Non-Hispanic White, and Non-Hispanic Asian, and considered education, previous pregnancies, previous birth, use of OC at enrollment, cigarette use, and oral contraceptive use. Another study, a prospective cohort study of 59,510 OC users in Europe, found in an analysis of OC effectiveness with 112,659 women years of exposure and 545 unplanned pregnancies, little variation in effectiveness by BMI/weight (Dinger et al., 2009). Aside from age and parity, this study did not include other sociodemographic factors.

*Birth Control Use and Glycohemoglobin*

With women are at a higher risk of developing diabetes, assessing the association between birth control use and glycohemoglobin may demonstrate give insights on how birth control may affect glycohemoglobin in women. In a cross-sectional study of 33 healthy women, where 15 women used a combined oral contraceptive pill and 18 utilized the progesterone oral pill, it was found that the percentage of HbA1c remains unchanged for progesterone users, while in combined OC users, the values increased from 5.9% to a mean of 8.7% after 3-6 months after administration. This may be due to the estrogen in the pill, which can induce insulin resistance.

It is important to mention that, according to the CDC, women who experience metabolic and endocrine disorders, like polycystic ovarian syndrome (PCOS) are at a higher risk of developing metabolic risks like diabetes and gestational diabetes (CDC, 2020). Given that both PCOS and Type 2 diabetes have the same risk factors such as hypertension, obesity, and dyslipidemia, there might be an explained correlation of Type 2 diabetes and PCOS, which is highly prevalent with Type 2 diabetes (Livshits & Seidman, 2009). The first course of action for women experiencing endocrine disorders tends to be birth control prescription, and diabetes medication, alongside nutrition and health recommendations (NICHD, 2017). This is important to explore given that there is overwhelming evidence on how diabetes is more difficult and deadlier for women, with the lifetime risk of diabetes being higher in women, and HbA1c levels are one way to measure and assess diabetes.

*Hypertension*

Cardiovascular disease (CVD) remains one of the most common causes of mortality worldwide and is an area of interest to accurately assess the prevalence of key cardio metabolic risk factors (Palmer & Toth, 2019). Hypertension, defined as an elevated blood pressure greater than 140/90 mmHG, and is a major risk factor for CVD and the leading cause of death among

women in the U.S (Hage et al., 2013). One form of hypertension that occurs exclusively in women is oral contraceptive use. Combined estrogen and progestin oral contraceptive pills (OCPs) are associated with small but significant increases in blood pressure and risk in cardiovascular events in the general women population. A study done on 68,297 female nurses between the ages of 25-42 years of age concluded that current users had a significant, moderately increases risk of hypertension, but the risk decreased after the cessation of oral contraceptives (L. Chasan-Taber, & Willet, W.C., 1996). The risk increases significantly with age, cigarette smoking, duration of OCP use, and obesity. As the general women population is increasing contraceptive use, knowing the effects on women of reproductive age is important to be able to help policy and clinical recommendations.

*Hyperlipidemia*

Hyperlipidemia involves elevated levels of any or all lipids, including cholesterol, in the blood. According to the CDC, between 2017 to 2020, 10 % of adults age 20 or older had high total cholesterol levels of 240 mg/dL or more (CDC, 2023). Women experience hormonal changes throughout life, including those associated with menarche, pregnancy, and menopause that can alter serum lipoprotein levels. In the United States, there are 10.7% of Non-Hispanic White females, 10.0% of Hispanic females, 9.3% of Non-Hispanic Black females, and 8.7% of Non-Hispanic Asian adults with high total cholesterol levels (CDC, 2023).

While studies have been done on hyperlipidemia management in women menopausal and post-menopausal women with female hormone replacement therapy, there are not a lot of studies on premenopausal women and the use of birth control (Phan & Toth, 2014). A study on a sample of 233 pre-menopausal women between the ages of 20 and 54, excluding for diabetics, observed that for women taking oral contraceptives, there were changes in their circulating phospholipid levels, as well as elevated triglycerides (Hertel et al., 2017). Looking at levels for women who

have taken birth control can give increased insights on the effects of birth control on metabolic risk factors on women of reproductive age.

*Birth Control Use and Metabolic Outcomes*

A study using NHANES III (1999-2006) data found that there is a persistent increase of metabolic syndrome among adults 20 and older living in the United States, stating that is a serious public health concern because it raises the likelihood of increased prevalence of type 2 diabetes (Mozumdar & Liguori, 2010). In woman, they found the prevalence of four of the five metabolic abnormalities they analyzed increased significantly between the surveys for women. These metabolic abnormalities include abdominal obesity, hypertriglyceridemia, high blood pressure, and high fasting glucose. The concern is an increase in metabolic syndrome especially in certain ethnic groups and younger women, as it can consequently lead to an increase in diabetes, its comorbidities, amongst other chronic diseases given their increased risk levels. Although research has been done on the use of birth control and hypertension, the study was conducted on a group of majority white nurses, and since they all fall under the same demographics, the study does not consider the factors of access to health insurance, race, ethnicity, income, and education. This study attempts to do so using NHANES data on a nationally representative population.

*Scientific Premise*

These metabolic outcomes are all deeply intertwined, and this research is attempting to identify how birth control use associates with the metabolic outcomes of women who currently have or ever have used birth control. There is a large amount of research on menopausal women and birth control and female hormone therapy use to address metabolic issues, but there is not a lot of research done on the association between birth control use and metabolic syndrome for women of reproductive age. As mentioned before, there is little to no research conducted on the

changes that women experience after they get off birth control pills or other methods of contraceptive use, with not a lot of research on what happens when women with previous endocrine or metabolic disorders get off the pill. Additionally, there is conflicting evidence on whether birth control pills do influence metabolic risk factors across all the outcomes. Regarding the outcome for BMI, research that has been conducted on weight gain and birth control tend to be short term, where in fact the long-term association between birth control and changes in weight need to be measured.

This thesis aims to explore the association of birth control and metabolic profiles in the United States using NHANES data, considering demographics like race and ethnicity, education, income, and access to healthcare. By looking into the differences of birth control on women's metabolic profiles, it can give us a clearer picture on the difference in outcomes that women experience when on the pill and can offer a pathway to increase research areas to investigate what women experience once they get off the birth control pill.

## Methods

### *Study population*

Data for this study come from participants in the National Health and Nutrition Examination Survey (NHANES) from the years 2015-2016. NHANES is a cross-sectional study that is nationally representative of the US population. For the survey, the interviews were collected in-person in households, and the questionnaires were answered by participants at the mobile examination centers (MEC), using the Audio Computer Assisted Self-Interview (ACASI) system, as well as by trained interviewers using the Computed Assisted Personal Interview (CAPI) system. Recruitment and follow-up events took place from January 2015 to December

2016. Eligibility for post-MEC data collection depended on the participant's age, gender, and whether they had completed the required components. For this analysis, the data is IRB exempt given that NHANES are a publicly available dataset.

The target population of interest was women between the ages of 20-44 years of age residing in the United States. The issue of interest is these of birth control and its association with metabolic profiles of women. For the analysis, women of reproductive age between 20 – 44 years of age were included. The WHO defines women of reproductive age as being between 20-49 years of age. Other studies that included women of reproductive age and birth control defined reproductive age as between 20 – 44 years of age. (Nguyen et al. 2017). Pregnant status at the time of examination was used to determine if the female participant was or was not pregnant at the time of the examination, and pregnant women were excluded from the study.

As seen in Figure 1, the total source population assessed for eligibility was 9,191 participants. Out of those participants, 4,112 males, 3,791 women who were not between the ages of 20-44 years of age, 70 women who were pregnant, and 336 participants who did not participate in the birth control survey data were excluded. 960 female participants who fit the criteria were eligible for the analysis. The eligible sample (N = 960) is defined as individuals who were included in the criteria are females, between the ages of 20-44, not missing data for the birth control variable, and not pregnant at the time of the examination. Out of the individuals who fit the criteria for the analysis, women who did not participate in the examination or had missing data for average systolic blood pressure, Body Mass Index (BMI), waist circumference, cholesterol levels, and glycohemoglobin were included in the analytical sample (N = 874).

*Study measures*

In this analysis, never or ever birth control use from the survey data is used to identify participants who had ever taken any form of birth control pills for any reason. It is used to differentiate between those who have never taken birth control pills and those who ever have taken birth control pills. The National Cholesterol Education Program Adult Treatment Panel III guidelines defines outcomes of included in metabolic syndrome as three or more of the following: waist circumference, triglyceride levels, HDL-C, blood pressure, and fasting glucose (Palmer & Toth, 2019). Due to limitations in the data set, the sample size and time of the analysis, the five metabolic processes measured in this study include average systolic blood pressure, Body Mass Index (BMI), waist circumference, total cholesterol, and glycohemoglobin (A1c).

BMI was measured using kilograms/meters$^2$ as a continuous variable. Waist circumference (cm) was included as another outcome, as it is an indicator of adipose tissue, which correlates with an increased risk of cardiometabolic disease and other chronic diseases. Total cholesterol, measured in milligrams/deciliters is the sum of an individual's HDL cholesterol, LDL cholesterol, and 20% of their triglyceride levels. Glycohemoglobin measures the average glucose levels in an individual's body over the past two or three months from when the test was conducted. Glycohemoglobin will be used as a continuous variable to see overall A1c levels for those who have not or have ever used any kind of birth control. Average systolic blood pressure is defined as the average of the first three numbers when taking blood pressure. For the analysis, missing blood pressure variables were created to do a missing analysis to see which individuals were missing the first, second, or third reading for their systolic blood pressure. If they were missing the first, second, or third reading, the fourth reading was used in replacement for the missing reading. After inputting the fourth reading for the missing readings,

168 individuals had all four readings, 3588 had the first three readings, and 1,323 individuals were missing either the first, second, third or all readings.

The variable was used to identify participants whose sex is female assigned at birth. Out of the 9971 participants who had both interview and MEC data, 5079 participants were female (4892 were male). Income is measured as the total household income reported in U.S. dollars and is separated into 4 categories: Under $20,000 per year, between $20,000 and $74,999, between $75,000 and $99,999, and $100,000 and above. The status of health insurance at the time of examination includes individuals covered by any kind of health insurance or healthcare plan. This can include health insurance obtained through employment or from government programs like Medicare and Medicaid. Healthcare insurance coverage is considered a confounder in this analysis, as access to healthcare impacts access to birth control.

*Statistical analysis*

This analysis investigates the question of differences in metabolic profiles of women by history of birth control use (those who have never used birth control [reference], versus those who have ever used birth control). The 5 outcomes for metabolic profiles (glycohemoglobin levels, average systolic blood pressure, Body Mass Index (BMI), waist circumference, and total cholesterol) were analyzed to verify if they fit the linear regression assumptions to complete a linear regression analysis with the outcomes and the independent variable, birth control use. Total cholesterol, average systolic blood pressure and BMI fit the assumptions, but glycohemoglobin and waist circumference did not fit the normality assumptions. Therefore, for those two outcomes, median regression was conducted. The unadjusted mean difference and the adjusted mean difference for each outcome was found via linear regression and median

regression conducted using R software and included survey weights, cluster, and stratum indicators to account for the survey design.

## Results

Table 1 shows the characteristics of the 694 women included in this analysis. This sample consists of women between the ages of 20 to 44 years of age, with mean age 32.4 years. Out of the 694 women identified in Figure 1, 67.44% have history of contraceptive use, and 32.56% have never used contraceptives. Demographically, 29.54% of women are Hispanic, 33.43% are Non-Hispanic White, 19.74% are Non-Hispanic Black, and 17.29% identified as another race. 11.53% of women have less than a high school degree, 16.28% have a high school degree, 39.34% have some college education, and 32.85% of women are college graduates or above. Only 1.30% of the women in the sample have an income less than $20,000 and 62.59% of the women have an income between $20,000 and $74,999. 15.27% of women have an income between $75,000 and $99,999, and 32.85% of women have an income greater than $100,000. Out of the 694 women, 80.36% of them were covered by health insurance, and 19.74% were not covered by health insurance at the time of examination.

### *Distribution of metabolic parameters*

Table 2 displays the means and medians of metabolic parameters by contraceptive use. In women who have ever used contraceptives, total cholesterol was 180.98 [174.02, 185.62] and for those who have ever used birth control, total cholesterol was 176.72 [174.02, 181.75]. For systolic blood pressure and birth control, the average blood pressure for those who have ever used birth control is 114.00 [113.00, 115.00] and 112.00 [110.00, 114.00] for those who have never used birth control. For A1c levels, women who have ever used contraceptives have on average a median of 5.30 [5.20, 5.40] glycohemoglobin. Women have never used contraceptives

have on average a median of 5.46 [5.40, 5.60] glycohemoglobin. For BMI, the median BMI for women who have ever used contraceptives is 29.00 [28.00, 30.00], as well as for women who have never used contraceptives [28.00, 31.00]. For waist circumference, the average waist circumference in centimeters for women who have ever used birth control is 95.00 [93.00, 97.00], and the average waist circumference for those who have never used birth control is 96.00 [92.00, 100.00].

*Unadjusted Regression Models*

Table 2 displays the unadjusted and adjusted linear regression models estimating differences in the five outcomes, according to history of contraceptive use. Women who have never used contraceptives were the reference group for all models. The unadjusted mean difference in cholesterol was 4.25 [-3.48, 11.60], suggesting that women who have ever used birth control have on average, a 4.25-unit difference in total cholesterol than those who have never used birth control. The unadjusted mean difference in systolic blood pressure indicates that on average, there is a 1.70 [-0.67, 4.00] unit difference between those who have ever used and those who have never used birth control. The unadjusted median difference of –0.16 [–0.28, –0.04] suggests that there is a 0.16-unit difference in A1c levels between those who have ever used birth control and those who have never used birth control. The unadjusted median difference in BMI is –0.21 [–1.90, 1.50], suggesting that there is a 0.21 difference between those who have never used birth control and those who have ever used birth control. The mean difference of –0.56 [-4.20, 3.10] in waist circumference indicates that there is a 0.56 unit different between those who have ever used birth control and those who have never used birth control.

*Models Adjusted for Demographics*

The adjusted difference in total cholesterol between women who have used birth control and those who have not is 0.08 [-5.61, 5.77]. For the adjusted model with average systolic blood pressure with demographics, the mean adjusted difference was 3.17[1.21, 5.13]. After conducting the adjusted quantile regression with demographics for A1c, the median adjusted difference is -0.01[-0.07, 0.04]. After conducting the adjusted quantile regression at the median for BMI, the adjusted median difference is -0.38 [2.17, 1.81]. Given that the confidence interval includes zero, there is no statistically significant difference in BMI between women who have ever used birth control and women who have never used birth control. The mean adjusted difference for the adjusted model for waist circumference was 0.61[-2.27, 3.50].

**Discussion**

Since the approval of the first oral contraceptive in the 1960s, more than 72 million women in the United States have used contraception. With the rise of metabolic disorders, such as diabetes, hypertension, and hyperlipidemia, and a high percentage of women using oral contraceptives, investigating the associations of birth control is essential to understanding women's health. The findings from the regression analysis revealed that there is no significant cross-sectional difference in for women who have ever taken birth control and women who have never taken birth control in terms of total cholesterol, BMI, waist circumference, and glycohemoglobin. However, a statistically significant 3 mmHg difference in average systolic blood pressure was observed in women who have taken birth control compared to women who have never taken birth control.

One potential explanation for the higher systolic blood pressure in women who have taken birth control may be the effect of estrogen-containing contraceptives, which can increase blood pressure. This elevation in blood pressure could lead to an increased risk of stroke and

heart attack, especially in women with pre-existing hypertension. Conversely, reasons as to why there were no differences in other metabolic processes may be attributed to birth control's role in regulating hormone levels in some women, thus aiding in weight management, and maintaining normal BMI and waist circumference (NICHD, 2017).

*Relation of findings to the Literature*

This study contributes to the literature by exploring the association between birth control and women's metabolic profiles in the United States, focusing on women of reproductive age from diverse racial and ethnic backgrounds while adjusting for demographics, including healthcare status. While some previous studies focus primarily on menopausal women, this research fills a gap in understanding metabolic syndrome in women of reproductive age, given the widespread use of contraceptives in this population.

In relation to other studies exploring the association between metabolic profiles and birth control use, this analysis explored diverse populations, including Hispanic and Asian women. The CARDIA study, which primarily included African women between the ages of 20 – 44 years of age, found that current oral contraceptive users were younger, with a lower mean BMI, lower waist-to-hip ratios, lower current smoking rates, and more years of education. This is a demonstration of the potential selection into the exposure. The CARDIA study did not include Hispanic or Asian women in their study (Kim et al., 2002). Another study done on 68,287 predominantly white female nurses included women between the ages of 24-42 years of age and concluded that users had significant increased risk of hypertension (L. Chasan-Taber, & Willet, W.C., 1996). With 59.9% of Black Women, and 64.0% of Hispanic women using contraception in the United States, it is important to include women of different races and ethnicities or adjust for race in the analysis. This study's inclusion criteria encompassed women from various racial

and ethnic backgrounds, providing a more comprehensive perspective on the association between birth control and metabolic profiles.

*Strengths and Weaknesses of the study*

One strength this analysis had in comparison to other studies is that it included women from different race and ethnicities, socioeconomic background, and education. Another study looking at 233 pre-menopausal women observed changes in phospholipid levels (Hertel et al., 2017). A weakness from the present analysis is that only total cholesterol was taken into consideration, and not LDL, HDL, or fasting triglyceride levels. Taking these levels might give further insight on the cholesterol quality of women who have ever used birth control or have never used birth control.

A significant limitation of this study is the NHANES data's inability to differentiate between different types of birth control pills, grouping them all into one category. There are different types of birth control (estrogen and progesterone, estrogen only, progesterone only). With the different hormone present in each pill, this limitation hinders the analysis of how different types of birth control may affect metabolic outcomes differently. Additionally, self-reported data from the reproductive health questionnaires and insurance introduces the possibility of recall bias. In addition, birth control pills are often used to control hormonal issues, which can help improve metabolic outcomes while women are on the birth control pill. This leads to a reverse causation bias, which cannot be addressed in a cross-sectional study. A way to address this in the future is to use data that allows for an analysis on women's metabolic outcomes during and after the use of the birth control pill.

Due to limitations in sample size, there are other covariates such as physical activity, alcohol use, and smoking, that were considered but not able to include. To be able to do a deeper analysis, perhaps using several years of data may help. Given that metabolic syndrome contains risk factors that are all interrelated, it is possible that with a larger sample size and additional data, there might be the potential to consider covariates like self-reported diabetes, self-reported hypertension, alcohol use, smoking use, and sedentary levels.

*Recommendations and Next Steps*

As the general women population is increasing contraceptive use, knowing the association between hormonal contraceptives and metabolic health in women of reproductive age is important to be able to help policy and clinical recommendations. Recommendations for clinicians is to be mindful of the potential impact of birth control on blood pressure, particularly in women with existing hypertension. Age, blood pressure control, and other risks for heart disease should be carefully considered when recommending birth control methods, especially for women over 35 years old, where estrogen-containing contraceptives may pose greater risks (MD, 2020). Women with high blood pressure may need to carefully consider potential risks before initiating birth control.

Moving forward, conducting a sensitivity analysis that includes women with diagnosed metabolic disorders, such as diabetes, gestational diabetes, hypertension, obesity, and hyperlipidemia would enhance the study's quality. There is not a lot of research or data on the associations of birth control once women choose to get off the birth control pill. Additionally, investigating women's metabolic profiles before and after birth control use and comparing them could provide insights into the long-term effects of contraceptives on metabolic health. The comparison of women's metabolic profiles before and after birth control use would be a stronger

analysis than this current one given that some women start using the birth control pill to control hormonal issues like PCOS, which leads to a reverse causation bias. With the increase in metabolic disorders, additional next steps in research would be to look at women with a previous metabolic disorder and disease, and see how their metabolic processes are affected before, during, and after birth control use. Additional considerations that should be included in research are women's experiences in birth control use, and their symptoms (physical or physiological). Changes in symptoms may be reflective mental or neurological effects of the pill as well. Future research should also incorporate measures such as LDL, HDL, and fasting glucose to gain a more comprehensive understanding of cholesterol quality and overall metabolic health in women using birth control.

**Conclusion**

In a diverse sample of reproductive age US women, there were no significant differences between never-users and ever-users of birth control in 4 out of the 5 metabolic parameters examined. However, a there was a difference regarding systolic blood pressure, where women who have ever used birth control pills 3.17 units higher in women who have ever used birth control compared to never-users. This analysis, alongside a review of existing literature, underscores the need for longitudinal prospective cohort studies. Such studies would explain the impacts of birth control on metabolic pathways, including potential associations with diabetes and heart disease. Moreover, there is a pressing need for longitudinal investigations that include women with obesity. Given the widespread adoption of contraceptive methods, particularly the birth control pill, and the increase in metabolic risks in women, understanding the ramifications of pill usage is important for prioritizing women's health. Furthermore, comprehensive research accounting for various types of birth control is crucial, given estrogen and progesterone's

regulatory roles in key physiological processes such as menarche, insulin regulation, glycemic control, lipid metabolism, and others. Such research efforts can yield more definitive and actionable insights.

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## Tables and Figures

Figure 1. Participant Diagram

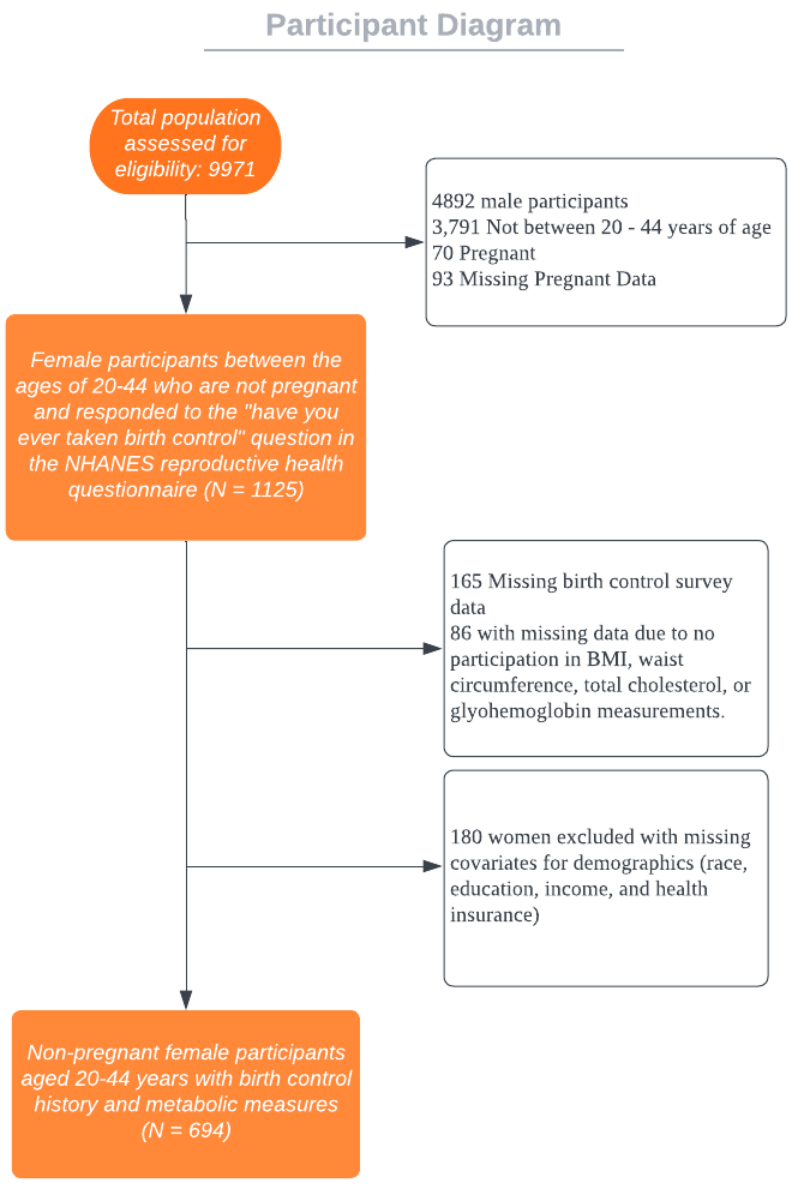

Table 1. Characteristics of Women with Never or Current Contraceptive Use

| Variables | N = 694 | Mean/Prevalence (%), (95% CI) |
|---|---|---|
| History of Contraceptive Use, % | | |
| Never | 226 | 32.56% [29.00, 36.00] |
| Ever | 468 | 67.44% [64.00, 71.00] |
| Age (20-40 years), mean | - | 32.50 [32.00, 33.00] |
| Race, % | | |
| Non-Hispanic White | 232 | 33.43% [30.00, 37.00] |
| Non-Hispanic Black | 137 | 19.74% [17.00, 23.00] |
| Hispanic | 205 | 29.54% [26.00, 33.00] |
| Other/Multiracial | 120 | 17.29 [15.00, 20.00] |
| Education, % | | |
| Less than high school | 80 | 11.53%, [9.30, 14.00] |
| High School Graduate/GED | 113 | 16.28%, [14.00, 19.00] |
| Some college or AA degree | 273 | 39.34% [36.00, 43.00] |
| College graduate or above | 228 | 32.85 [29.00, 37.00] |
| Income, % | | |
| Under $20,000 | 9 | 1.30% [0.63, 2.50] |
| $20,000-$74,999 | 435 | 62.68% [59.00, 66.00] |
| $75,000-$99,999 | 106 | 15.27% [13.00, 18.00] |
| $100,000 and over | 144 | 20.75 [18.00, 24.00] |
| Health Insurance, % | | |
| Yes | 557 | 80.36% [77.00, 83.00] |
| No | 137 | 19.74% [17.00, 23.00] |

Table 2. Differences in metabolic profiles of women by history of contraceptive use.

| | Mean or Median Levels (95%CI or IQR) | | Mean or Median Differences (95%CI); (Ref=never) | |
|---|---|---|---|---|
| | Women who have ever used contraceptives N=468 | Women who have never used contraceptives N=226 | Unadjusted difference* | Adjusted difference* |
| HbA1c, (%)[1] | 5.30 [5.20, 5.40] | 5.46[5.40, 5.60] | -0.16[-0.28, -0.04] | -0.01 [-0.07, 0.04] |
| Total Cholesterol, (mg/dL)[2] | 180.98[174.02, 185.62] | 176.72[174.02, 181.75] | 4.25[-3.48, 11.60] | 0.08 [-5.61, 5.77] |
| Systolic Blood Pressure, (mmHg)[2] | 114.00[113.00, 115.00] | 112.00[100.00,114.00] | 1.70[-0.67, 4.00] | 3.17 [1.21, 5.13] |
| Body Mass Index, ($kg/m^2$)[1] | 29.00[28.00, 30.00] | 29.00[28.00, 31.00] | -0.21[-1.90, 1.50] | -0.38[-2.17, 1.82] |
| Waist circumference, (cm)[2] | 95.00[93.00, 97.00] | 96.00[92.00, 100.00] | -0.56[-4.20, 3.10] | 0.61[-2.27, 3.50] |

*Difference includes mean difference and median difference.

[1] Median IQR reported for unadjusted and adjusted quantile regression.

[2] Mean (95% confidence interval) reported for unadjusted and adjusted linear regression.