

Polycystic Ovarian Syndrome (PCOS), Type 2 Diabetes Risk Factors
and Environmental Influences on PCOS

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Abstract

Polycystic Ovarian Syndrome (PCOS) is an endocrine condition that affects nearly 4-21% percent of women of reproductive age (Azziz, Carmina, Dewailly, Diamanti-Kandarakis, Escobar-Morreale, Futterweit, Janssen, Legro, Norman, Taylor, & Witchel, 2006). Symptoms of the syndrome include insulin resistance (IR), infertility, hirsutism, and obesity (Sivanandy, Zuuren, & Aird, 2018). The etiology and cause of the condition remain largely unknown (Roe & Dokras, 2011). The purpose of this study is to examine possible connections between PCOS and Type 2 Diabetes (T2D) by investigating behavioral, obesogenic, and other risk factors associated with T2D. This study also investigates environmental and behavioral exposures experienced by individuals in their daily lives, as well as if these environmental factors correlated with adverse effects on the PCOS condition. Little is known about the environment and its affect, if any, on women diagnosed with PCOS. Two research questions were posed for this study: first, if there is a relationship between PCOS and T2D and second, if there are environmental factors that have any adverse effects on the PCOS condition. The study design was cross-sectional and observational in nature, using a survey administered via social media. Risk factors for T2D include obesity and a higher body mass index (BMI). The results of this study found a statistical association between some areas related to T2D risk factors and an increased likelihood for a self-reported diagnosis of PCOS. On the other hand, this study found no statistical association between environmental factors and adverse effects on the PCOS condition. The public health and future implications of the study are vast. Future analysis could include clinical studies on A1C levels of women with PCOS. This could further define the association between IR and PCOS.

Keywords: PCOS, Insulin Resistance (IR), Type II Diabetes (T2D), Environment

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List of Acronyms

American Diabetes Association	ADA
Bisphenol A	BPA
Body Mass Index	BMI
Diethylstilbestrol	DES
Endocrine Disrupting Chemicals	EDC
Endocrine Disruptors	ED
Insulin Resistance	IR
Polycystic Ovarian Syndrome	PCOS
Principal Investigator	PI
Quality of Life	QOL
Type 2 Diabetes	T2D

Review of the Literature

Introduction

Polycystic Ovarian Syndrome (PCOS) is an endocrine condition that affects at least 4-21% of women of reproductive age (Azziz, Carmina, Dewailly, Diamanti-Kandarakis, Escobar-Morreale, Futterweit, Janssen, Legro, Norman, Taylor, & Witchel, 2006; National Institute of Health [NIH], 2018), and extends throughout the lifespan of individuals due to its endocrine nature. The syndrome results from the increased production of androgens. This overproduction of androgens results in hyperandrogenism and improper ovulation known as anovulation (NIH, 2018; Stracquadanio & Ciotta, 2015). Women with the syndrome suffer from a variety of symptoms, including hirsutism (excessive male pattern body hair), acne, mood swings, obesity, infertility, insulin resistance, irregular periods, skin tags, acanthosis nigricans (patches of thickened skin and/or darkened/hyperpigmented skin around the groin and neck), and androgenetic alopecia (female pattern hair loss) (Sivanandy, Zuuren, & Aird, 2018).

The condition was originally known as the Stein-Leventhal Syndrome, which was introduced as a condition that is now extremely widespread and impacts between 5-15% of women (Azziz & Adashi, 2016). A pair of medical doctors, Drs. Irving Stein and Michael Leventhal, were interested in women's health and began a study of seven women who had enlarged ovaries and various symptoms similar to symptoms now understood to align with PCOS. In 1934, they presented in New Orleans, Louisiana, on the seven cases of enlarged polycystic ovaries and menstrual disturbances and were the first to report more than one case rather than distinct or separate cases (Azziz & Adashi, 2016). Furthermore, the study and subsequent report was significant because it monitored a cohort of participants with similar symptoms and determined a specific connection (Azziz & Adashi, 2016). Prior to their

presentation there was no scientific evidence of a syndrome such as PCOS. While there is evidence of documentation of PCOS dating back to the 17th century (Sampson), it was understood that the condition was considered a “medical oddity” (Azziz & Adashi, 2016), and cases were isolated to one or two individuals. Other important research was being done in the 1930’s regarding androgens and androgen excess disorders when it was discovered that androgens are produced in the ovaries and that women produce both male and female hormones (Azziz & Adashi, 2016). The reports, presented by Drs. Stein and Leventhal, in combination with the hormone investigations at work at the time, were foundational to the research now being done regarding women’s health.

The diagnostic criteria for PCOS varies; however, there are a few general requirements which identify the condition. PCOS is an endocrine condition characterized by anovulation and high androgens; however, there is no formal definition for the condition and therefore, there is no strict standard for diagnosing PCOS (NIH, 2017; Bazarganipour, Ziaei, Montazeri, Faghihzadeh, & Frozanfard, 2012). This variance of diagnostic criteria results in the wide array of women diagnosed with the condition, and the large gaps in percentages of women affected by the condition, ranging from 4-21% (Azziz et. al., 2006; NIH, 2018). The international recommendation is to follow the Rotterdam Criteria for diagnosis due to its specificity (Teede, Misso, Costello, Dokras, Laven, Moran, Piltonen, & Norman, 2018). The Rotterdam Criteria, which is the most stringent and the international standard for PCOS diagnosis, states that women need to have two of the three clinical experiences: (1) polycystic ovaries (seen via ultrasound), (2) hyperandrogenism (high androgens), and (3) menstrual irregularities, such as the absence of vaginal bleeding for up to six months or an extended duration – greater than 35 days – between vaginal bleeding (Bazarganipour et al., 2012). Challenges also exist regarding the diagnosis and

manifestation of the condition due to the spectrum of ways in which the disorder presents itself and the fact that many individuals likely go undiagnosed (Shorakae, Boyle, & Teede, 2014).

There is no clear etiology for PCOS (Roe & Dokras, 2011), nor is the cause of the condition fully understood. It is thought that the syndrome results from an interaction between several factors such as environment, genetics, metabolism, and fetal exposure (Levine, Fedorowicz, & Ehrlich, 2018; Dumesic, Oberfield, Stener-Victorin, Marshall, Laven, & Legro, 2015). Furthermore, it is theorized that the environment interacts with genes, resulting in PCOS, insulin resistance (IR), obesity, and other similar conditions (Nappi, Barrea, Somma, Savanelli, Muscogiuri, Orio, & Savastano, 2016). IR and other metabolic deviations often accompany PCOS and can result in complications such as obesity and Type 2 Diabetes (T2D) (Broskey, Tam, Sutton, Altazan, Burton, Ravussin, & Redman, 2018). Other risk factors associated with PCOS include: obstructive sleep apnea, metabolic syndrome, heart disease, high blood pressure, stroke, endometrial complications, gestational diabetes, and infertility (NIH, 2017; Centers for Disease Control [CDC], 2018).

PCOS is an endocrine disorder with excess androgens as the hallmark of the condition. While IR is not necessary for diagnosis it often accompanies the condition and occurs in between 50-80% of women afflicted with the ailment (Deeks, Teede, & Moran, 2010). Other metabolic features and risk factors associated with PCOS include metabolic syndrome, prediabetes, T2D, and gestational diabetes (Teede et al., 2018). Functions governed by the endocrine system, which is affected by PCOS, include developmental growth, reproduction, metabolism, glucose regulation, and electrolyte balances (Sherwood, 2006). The body's endocrine system is also responsible for the regulation and maintenance of areas such as blood glucose levels, electrolyte

balance, and mineral levels (The Endocrine System, 2009). Thus, when a woman presents with PCOS, a chronic condition affecting the endocrine system, this homeostasis is unbalanced.

Type 2 Diabetes

According to the CDC, there are several risk factors associated with the potential development of T2D. These can include being overweight, experiencing gestational diabetes, giving birth to a baby greater than nine pounds (CDC, 2017), and, for women with PCOS the increased risk for IR. Insulin resistance is the body's inability to process or use insulin effectively, thus resulting in increased blood glucose levels in the blood stream (NIH, 2018), which is a common accompaniment to the PCOS condition. Lifestyle factors such as lack of physical activity, nutrition, and an increased body mass index (BMI) can also contribute to IR and the risk of T2D (NIH, 2018). In a study by Broskey, Tam, Sutton, Altazan, Burton, Ravussin, and Redman (2018) it was found that women with PCOS have similar metabolic responses to glucose as women with T2D. Additionally, the CDC and American Diabetes Association (ADA) have stated that PCOS is linked to the potential risk of developing T2D. Thus, there is a possible correlation between PCOS and the development of T2D.

Since IR is the body's inability to properly metabolize insulin (McEwen & Hartmann, 2018), it often results in "increased circulating insulin levels" in the bloodstream and impacts the body's ability to regulate overall glucose levels (Diamanti-Kandarakis & Dunaif, 2010). Furthermore, the interaction between insulin and the ovaries may correlate with androgen production. Therefore, insulin affects not only the regulation of blood sugar but also the hyperandrogenism experienced by women with PCOS as well as the ovulation process (Diamanti-Kandarakis & Dunaif, 2010).

Upwards of 35% of women present with Impaired Glucose Tolerance (IGT) (Salley, Wickham, Cheang, Essah, Karyane, & Nestler, 2007) which can be assessed in various ways. Some of these ways are an oral glucose tolerance test (OGTT), fasting glucose test (FGT), blood A1C levels, or the euglycemic glucose clamp technique (ADA, 2016; Diamanti-Kandarakis & Dunaif, 2010). The screening allows physicians to understand “how your body processes glucose” and can be an important indicator for the potential development of T2D (ADA, 2016). IR is considered a metabolic burden by the Androgen Excess Society (AES) and therefore is of greater concern for women with PCOS and can manifest regardless of weight (Salley et. al., 2007). While the presence of IR is not necessary for the diagnosis of PCOS, it is generally understood that women with PCOS will also present with IR (Legro, Kuneslman, Dodson, & Dunaif, 1999).

Several studies have been conducted to examine the development of T2D in women with PCOS. In a study by Legro, Kuneslman, Dodson, and Dunaif (1999) which assessed “the prevalence of glucose intolerance” with the purpose of determining an increased risk of IGT and T2D, it was found that 38.6% of the women with PCOS, had either IGT or T2D. A 2004 study looked at women in the Mediterranean and found that 2.5% ($n=3$) of participants had T2D and 15.7% ($n=19$) qualified as IGT in a study of 121 participants (Gambineri, Pelusi, Manicardi, Vicennati, Cacciari, Morselli-Labate, Pagotto, & Pasquali, 2004). A study in Italy which compared women with PCOS to population data, found that after a 10-year timespan an increase of 16.9%, from a 2.2% baseline, of women with PCOS has T2D (Gambineri, Patton, Altieri, Pagotto, Pizzi, Manzoli, & Pasquali, 2012). While this study used population as a proxy for a control group, it nevertheless demonstrates the relevance and increasing risk of T2D for women

with PCOS (Gambineri et al., 2012). Overall, these studies point out the potential link between PCOS and T2D.

Environmental Factors

It is thought that various elements affect women with PCOS, including heredity, individual biology, and the environment in which a person interacts. Environmental contributors are vast, and they include industrial chemicals, plasticizers, pollutants, and pesticides (Palioura & Diamanti-Kandarakis, 2016). Exposure to these chemicals, known as Endocrine Disruptors (EDs) or Endocrine Disrupting Chemicals (EDCs), have the potential to interact with hormones and either lead to or exacerbate PCOS symptoms. The NIH (2010) describes EDs as compounds or substances that “may mimic or interfere with the function of hormones in the body” which could result in adverse health responses impacting both humans and wildlife. In short, an ED either prohibits or somehow interferes with the natural mechanisms of the endocrine system.

There are numerous natural and synthetic EDCs that impact the health and wellbeing of populations such as pesticides, chemicals, and those products which come in contact with the foods that are ingested by humans. Some familiar disruptors are Bisphenol A (BPA), dichloro-diphenyl-trichloroethane (DDT), and lead, which have been discontinued in consumer products after evidence of negative health impacts emerged (Kabir, Rahman, & Rahman, 2015). However, the residual effects of these chemicals in the environment continue to impact the population (Kabir et al., 2015).

Environmental health is a relatively new field. Some concerns related to environmental health came into view in the 1950s and documented evidence began to be published in the 1990's (Kabir et. al., 2015; Schug, Johnson, Birnbaum, Colborn, Guillette, Crews, Collings, Soto, vom Sall, McLachlan, Sonnenschein, & Heindel, 2016). Evidence of the health impact of

EDs was established in the 1950's when pregnant women, after being prescribed diethylstilbestrol (DES) presented with rare vaginal cancers (Kabir et. al., 2015; NIH, 2010). Several EDCs have undergone many studies, including dioxins, BPA and DDT, while others remain to be detected and researched further.

In short, the population is exposed to innumerable EDCs on a daily basis through such avenues as inhalation of contaminated air and dust, topical exposure through products placed on the skin, in household applications such as fire retardants used on furniture and ingested through foods which have been stored in plastic containers. The population as a whole is exposed to a multitude of EDCs on a regular basis, and it is impossible to discern to what degree and in which situations exposure occurs (Kabir, et. al., 2015; Vandenberg, Hauser, Marcus, Olea, & Welshons, 2007; Diamanti-Kandarakis, Burguignon, Giudice, Hauser, Prins, Soto, Soeller, & Gore, 2009). Consequently, EDCs are a broad mixture of chemicals, personal products, and applications in agriculture or industry which impact the overall health and wellbeing of the population to an unknown degree (Kabir et. al., 2015).

One of the challenges of ED/EDCs in the environment – global, national, and local – are the unknowns regarding dose and time/length of exposure to the ED/EDC. For example, prior to the cessation of lead-based paint in 1978 (EPA, 2017) individuals were exposed to lead toxins in their homes, and those who continue to live in older homes are at-risk of continued exposure to unsealed lead. EDCs have the potential to remain in the environment well after their introduction to water, soil, or air and persist for an unknown period of time (Kabir et. al., 2015). It is important to examine several areas concerning the dose and length of exposure, such as an individual's age when exposed, the amount of time since exposure, potential EDC mixtures,

dose-response elements, transgenerational effects and the concentrations of specific EDCs (Kabir et al., 2015; Diamanti-Kandarakis et al., 2009; Schug et al., 2016).

An individual's age when exposed is relevant to the overall discussion of EDCs because younger individuals who are exposed at an early age (in utero, during infancy, and early childhood) are more susceptible to negative health effects from EDCs later in life; and with PCOS specifically, it is thought that early exposure to EDCs may affect adolescent females as they approach puberty and menstruation due to the puberty-endocrine connection of the condition (Kabir et al., 2015). Adults and developing children are impacted by EDCs very differently. It is important to be aware of the different impact the environment has on developing fetuses and children as compared to adults. The transgenerational impacts of EDCs may also contribute to the increase in the diagnosis of PCOS as the consequences of exposure to EDCs impact the overall health of individuals as well as the wellbeing of their children/grandchildren (Schug et al., 2016; Diamanti-Kandarakis et al., 2009). While it has been stated that PCOS is not fully understood with regard to its cause or pathogenesis, it is thought, that EDs contribute in part to the manifestation of the condition.

We come in contact with multiple mixtures of EDCs in our daily life, and BPA in particular seems to impact women with PCOS. Knowing the full effect of EDCs in the environment is unidentifiable, and it is sufficient for the purposes of this study to recognize that BPA acts, along with other chemicals and environmental exposures, as an ED. BPA is a plasticizer, and it is often used in products that come in contact with food, such as, bottles (i.e. baby bottles), plastic containers, and the lining of canned goods. It can also be found in dental fillings, landfill leachates, and air and dust particles. Some concerns with BPA are that it can leach into the foods from the containers in which they have been stored (Vandenberg et al.,

2007). Furthermore, the heating of BPAs can impact the migration of the chemical to foods either through the temperature or length of time applied (Vandenberg et. al., 2007).

Evidence of the connection of BPA and PCOS is strong. Multiple studies have found elevated levels of BPA in bodily serums (urine, amniotic fluids, umbilical cord blood, and follicular fluids) in women with PCOS (Vandenberg et. al., 2007; Rochester, 2013). These elevated levels are hypothesized to be linked to the higher testosterone and androgen levels experienced by women with PCOS as compared to their non-PCOS effected counterparts (Vandenberg et al., 2007). BPA is known to be an estrogenic compound, which can negatively impact the biological atmosphere of the female reproductive system (Tsutsumi, 2005) and could negatively affect androgen receptors and ovarian function (Gregoraszcuk, & Ptak, 2013). In four separate studies, it has been reported that increased levels of BPA have been found in bodily fluids such as blood and urine in women with PCOS (Konieczna, Rachon, Owczarek, Kubica, Kowalewska, Kudlak, Wasick, & Namiesnik, 2018; Kandaracki, Chatzigeorgiou, Livadas, Palioura, Economou, Koutsilieris, Palimeri, Panidis, Diamanti-Kandarakis, 2011; Rashidi, Amanlou, Lak, Ghazizadeh, Haghollahi, Bagheri, & Eslami, 2017; Akin, Kendirci, Narin, Kurtoglu, Saraymen, Kondolot, Kocak, & Elmali, 2014).

The developmental origins of adult disease and/or the developmental origins of health and disease are often called the “Barker Hypothesis.” The Barker Hypothesis states that adult diseases potentially originate from fetal exposure in utero, which could lead to adverse health conditions later in life (Li & Huang, 2006; Homburg, Gudi, Shah, & Layton, 2017; Morrison, Botting, Darby, David, Dyson, Gatford, Gray, Herrera, Hirst, Kim, Kind, Krause, Matthews, Palliser, Regnault, Richardson, Sasaki, Thomposon, & Berry, 2018; De Boo & Harding, 2006). PCOS could in fact be considered a condition where the Barker Hypothesis is applicable because

there is emerging data showing the link between exposure to high androgens during pregnancy (and/or in early childhood) and their impact on the reproductive system and a predisposition to the development of PCOS (Xu, Kwon, Abbott, Geller, Dumesic, Azziz, Guo, & Goodarzi, 2011). Research done on rats and Rhesus Monkeys, found that exposure to androgens in utero manifested into PCOS-like symptoms later in adolescence and adulthood (Fernandes, Bourguignon, Lux-Lantos, & Libertun, 2010; Xu et al., 2011). Such studies allow “us to study intrauterine androgen influences of fetus and infants, which is difficult to study in humans” (Xu et al., 2011, e27286).

While study on humans is limited and ethically difficult, one study assessed androgen exposure through the regulation of sebum oils found on the skin of infants and their mothers (Homburg et al., 2017). The sebaceous glands and oils excreted from these glands are indicators of androgen prominence (and can play a role in acne incidents in later years) because they emit various hormones, including testosterone, estrogen, and insulin (Zouboulis, Picardo, Ju, Kurokawa, Torocsik, Biro, & Schneider, 2016). The study looking at sebum oils on infants found that maternal sebum oils were high at birth and diminished within the first four weeks of the infant’s life, indicating that exposure to androgens does in fact occur in utero and is lessened after birth (Homburg et al., 2017). Ultimately, the information regarding prenatal exposure to androgens and the link to the potential development of PCOS is varying and insufficient (Xu et al., 2011).

Pollution found in water could also be considered an ED/EDC. The NIH (2018) defines water pollution as “any contamination of water with chemicals or other foreign substances that are detrimental to human, plant, or animal health.” Just as in the overall environment, toxins found in water have the potential to come from various sources such as agricultural runoff or

waste from food and sewage processing locations. Water may also carry heavy metals (i.e., lead or mercury), pesticides, bacteria, oil, and pharmaceuticals (NIH, 2018; Snyder, Westerhoff, Yoon, & Sedlak, 2003). Additionally, EDCs/EDCs in water have the potential to impact individuals, habitats, and ecosystems if left unchecked and are found frequently in water supplies both nationally and internationally (Leusch, Neale, Arnal, Aneck-Hahn, Balaguer, Bruchet, Escher, Esperanza, Grimaldi, Leroy, Scheurer, Schlichting, Schriks, & Hebert, 2017; Falconer, Chapman, Moore, & Ranmuthugala, 2006; Snyder, et. al., 2003). There is sufficient documentation regarding the existence of EDCs in water supplies; however, research specific to EDCs in water and PCOS is limited.

Additionally, smoking is known to lead to an abundance of diseases and negative health outcomes within the population and is the “leading cause of preventable disease” (CDC, 2017). Annually, thousands of individuals experience cancers, (i.e. lung and throat), heart disease, respiratory complications such as asthma or chronic obstructive pulmonary disease, and death related to smoking (CDC, 2017). Nicotine also impacts the endocrine system in several ways and can impact hormone receptors with negative results. Specifically in women, nicotine affects testosterone and can adversely impact menstruation and ovulation which can further exacerbate PCOS (Tweed, Hsia, Lutfy, & Friedman, 2012). Cigarette smoking also impacts insulin which for women with PCOS has the potential to aggravate IR (Tweed, et. al., 2012). Therefore, nicotine can be classified as an EDC and thus can negatively impact women with PCOS.

Purpose of the Study

The purpose of this study was twofold. First, it examined PCOS and T2D risk factors, and investigated if there are contributing factors to the potential development of T2D for women with PCOS. Second, it analyzed environmental factors that may contribute to the PCOS

condition with a focus on the things we encounter in our everyday lives such as cooking techniques, familial influences, and water sources.

Research Questions

There were two research questions posed for the current study.

1) Is there a correlation between women with PCOS and a greater risk for developing T2D?

2) Are there environmental factors, such as exposure to various pollutants and EDs/EDCs, early exposure to androgens, and tobacco use, that exacerbate women with PCOS?

Hypothesis

The hypotheses associated with these research questions were:

H₁: PCOS is associated with a greater risk for developing T2D.

H₂: There are environmental factors, such as fetal exposure, pollutants, food choices, smoking, and other behaviors, that have an adverse effect on the PCOS condition.

Methods

Study Design

This study used a cross-sectional design and was observational in nature. It was intended to investigate women with Polycystic Ovarian Syndrome (PCOS) and how it relates to women's health through the examination of T2D risk factors and environmental exposures.

Participants

The target population for this study was women who have been diagnosed with PCOS. The ages of the participants ranged from 18 to 70 years old to account for the endocrine nature of the condition spanning from puberty, reproductive age, and menopause. The selection process for participants was made using the social media platform Facebook. The Principal Investigator (PI) cooperated with various PCOS and community forums on Facebook to administer the survey. The Facebook groups in which the survey was posted were: PCOS – Polycystic Ovary Syndrome, PCOS, Catholic Women with PCOS, Christian Women with PCOS, and What's UP Corona. With the exception of the Corona page, all forums are international in character. Permission to post the survey on these pages was obtained from the PCOS – Polycystic Ovary Syndrome, Christian Women with PCOS, and What's UP Corona groups. The Catholic Women and PCOS groups were open forums with no admin/moderator permissions needed to post. The survey was also posted on the PI's social media page and a college social group – Sacrifice of Love: Past, Present, and Future! – from which the survey was shared by other individuals.

The number of individuals needed to obtain the proper power was 220, which was calculated using G*Power software (Faul, 2014). For purposes of this study, individuals who answered "No" to the informed consent question, "Do you live in the United States?" and "Have you been diagnosed with PCOS?" were disregarded in the data analysis. Also, minors were

eliminated from the analysis of the data. The geographical target population for this study was women who live in the United States.

Survey Instrument

The apparatus used to collect data for this study was a voluntary survey presented to participants via social media, i.e. Facebook. Participants answered “Yes” or “No” to the informed consent section, which was required prior to starting the survey (see Appendices A and B for Informed Consent and PCOS Instrument). The questions used for the study survey were derived from the National Health and Nutrition Examination Survey (NHANES), Health Related Quality of Life Questionnaire for Polycystic Ovary Syndrome (PCOSQ-50), and the Coronary Artery Risk Development in Young Adults (CARDIA) study. Questions were also developed from initial research regarding prenatal and parental exposures. Responses were obtained from survey questions which included yes/no, fill-in, and Likert scale answers. Survey questions varied to include questions relating to T2D risk factors and daily environmental exposures. The survey itself was administered using Esri/ArcGIS software known as Survey123 (Esri, 2018), through a subscription obtained by the PI. Participant data was received anonymously and remained confidential on a password protected computer.

Demographic questions of participants included age, ethnicity, marital status, and whether they lived in the United States. Example questions are: “What is your age?”, “What is your birthdate?”, “What is the highest grade/level of school you have completed or the highest degree you have received?”, and “What is your ethnicity?”. Many of the questions were multiple choice, with answers pertaining specifically to the question. Pertinent answers to the school level question were: High school diploma or equivalent (GED), Associate’s degree (community college), Bachelor’s degree, Master’s degree, Post-Graduate or professional degree (Ph.D., MD.,

DDS., etc.), other, and less than high school graduate. The possible answers for the marital status question were married, widowed, never married/single, living with a partner, and dating (boyfriend/girlfriend). The question regarding ethnicity allowed for participants to check a box entitled: White/Caucasian, Hispanic/Latino, Black/African American, Native American/American Indian, Asian/Pacific Islander, and other. The “other” option gave participants the opportunity to write in an ethnicity.

According to the CDC (2017), risk factors for T2D include high BMI, obesity, and giving birth to a child at or above nine pounds. Survey questions which address T2D risk factors include: the weight and height of an individual, if a child was born weighing over nine or more pounds, if participants take diabetic medications, and if they worry they are at-risk for developing prediabetes or T2D. Example questions for this area of the study included: “Are you currently taking diabetic medications to lower your blood sugar (these are sometimes called oral agents)?” and “If you have children, have any of your deliveries resulted in a baby that weighed nine (9) pounds or more at birth?”. Answers for these questions were “Yes,” or “No,” or “I do not have children.”

The survey also included questions specific to obesity and its relationship with health. These questions were: “In the past four weeks: how often have you felt concerned about being overweight?”, “In the past four weeks: how often have you felt the need to decrease your weight to control your PCOS status?”, and “In the past four weeks: how often have you felt concerned about regaining weight shortly after any weight loss?”. Answers for these questions were “Never – Rarely – Sometimes – Often – Always” on a Likert scale. Lastly, a question asked the participants if they were obese or overweight as children, with the answer options being “Yes” or “No.”

BMI results were determined using the height (in inches) and weight reported by participants then calculated using the CDC's BMI Calculator. Participants were also categorized into weight categories: underweight, normal, overweight, and obese. A BMI below 18.5 is considered underweight, a BMI between 18.5-24.9 is considered a normal/healthy weight, a BMI between 25.0 and 29.9 is overweight, and a BMI 30.0 and above is obese (CDC, 2017). The formula for calculating BMI is: $[\text{weight (lb.)} / \text{height (in.)}]^2 \times 703 = \text{BMI}$.

Questions were also posed to address the environmental aspects of an individual's built environment as well as behaviors associated with health and the environment. These questions related to eating habits such as if and how often participants eat at fast food restaurants, the type of water used in their homes, and if they have ever used tobacco products. Examples of these questions are: "Do you eat at fast food restaurants (i.e. McDonalds, Taco Bell, etc.)?", "How frequently do you eat at fast food restaurants?", "What is the main source of water (tap or drinking) in your home?", and "Have you ever used tobacco products such as cigarettes, cigars, e-cigarettes, chewing tobacco, etc.?". Answers for these questions were "Yes" or "No," "0-2 times per week," "3-5 times per week," "6 or more times per week," "community/municipal water," "a well or rain cistern," "unknown," and "Yes" or "No" respectively. Participants were also asked how they usually cook their food, with the ability to check all responses that applied: grill, stovetop, microwave, bake, slow cooker, and other. They were also given the opportunity to write a cooking application in the "other" category (i.e., fry).

Ethical Considerations

This study was approved on October 23, 2018 by the Institutional Review Board (IRB). The IRB# is: 031-1819-EXP (see Appendix C).

Dependent and Independent Variables

The dependent variable (DV) for the basis of this study was women who self-reported a diagnosis of PCOS. This dichotomous DV stands as the common denominator for both research questions and was the basis on which data was analyzed.

There are several independent variables (IVs) associated with this study. As per the hypothesis of this study, the IV has various facets to account for T2D risks and environmental factors. Survey questions posted to participants regarding T2D were related to BMI, medications, infant weight at delivery, and health beliefs and behaviors. Similarly, those questions regarding the environmental aspects of the IV included familial exposure, location/zip code exposure, fast food eating habits, cooking behaviors/methods, and the participants' tobacco use.

Procedure

Informed consent, which was a required question, was received from participants at the start of the survey. Participants were notified that their participation was completely voluntary, and they could choose to skip questions or stop at any time throughout the survey. After answering the required informed consent with a “Yes” or “No” response, participants were able to move on to the remainder of the survey. The survey was administered via social media forums, specifically Facebook groups. When introducing themselves to various Facebook groups, the PI used verbiage such as: *Hello, my name is Becky. I'm a student finishing up my Master's degree and I'm working on my thesis in Public Health on PCOS. If you are able to help with my survey and data to further what we know about the condition I would be grateful. Thank you, Becky.*

The survey was posted once to each of the following Facebook groups: PCOS – Polycystic Ovary Syndrome, Christian Women with PCOS, What's UP Corona, PCOS, Catholic

Women with PCOS, and Sacrifice of Love: Past, Present, Future!. The three groups requiring administrator approval were: Christian Women with PCOS, What's UP Corona and PCOS – Polycystic Ovary Syndrome to which the PI was able to post as a “Share Monday Announcement.” Two groups were open forums, and the PI sought to inform group leaders before posting although approval was not required. The open groups were: PCOS and Catholic Women with PCOS. Additionally, the PI posted the survey on her personal page as well as a collegiate group (Sacrifice of Love: Past, Present, Future!) from which it was shared by others. Therefore, recruitment of participants occurred once in various locations. The survey was first posted on Tuesday, December 4, 2018 on the PI's Facebook page and was last posted on January 29, 2019 to three Facebook groups: PCOS, Catholic Women with PCOS, and What's UP Corona. Thus, the duration of time used to collect data was a total of eight weeks.

Data from the survey was exported and downloaded from Survey123 to Excel on a personal computer. From there it was imported from Excel into IBM SPSS software. The data from the survey also went through a recoding process once it was imported into SPSS. This process called for several steps, because the data needed to be transformed from “choice0, choice1, etc.” to numerical data. The data was recoded accordingly.

Participants were asked in which zip code they lived as well as the zip code where they worked. Analysis of this information was done using US Census data from 2010. The participants' zip codes were entered into the Census on the *American Fact Finder* website (United States Census Bureau, 2010). SPSS columns were titled “Pop_City” and “Pop_Work,” and the zip code where people lived was input into the census website and rounded to the nearest thousandth, hundredth, or tenth as appropriate. For example, the population from zip code: 91739 was entered into the search bar, the information returned as 34,794, which was then

rounded to 35,000. This process was repeated for the population where participants worked. Incomplete zip codes (less than 5 numbers) were not analyzed. The PI used the range options in SPSS using the “Range, LOWEST through value” as 29,000, “Range from 30000 through 59000,” and “Range, value through HIGHEST” starting at 60,000. In the data view, the value labels were labeled 1.00 = low density, 2.00 = medium density, and 3.00 = high density.

Throughout the PCOS data set, missing data was coded as 999. Answers such as “Unknown” or “No Opinion” were also coded as missing. Also, a demographic age outlier (225 years) was excluded from the final analysis.

Participants who answered “No” to informed consent and any minors who answered the survey were eliminated from analysis. In addition, participants who answered “No” to having been diagnosed with PCOS were not included in the data analysis. The removal of these participants’ accounts for the specific requirements of both the IRB and the DV of the study.

Results

Participant Demographics

The target population of this study was women diagnosed with PCOS and those surveyed self-reported a diagnosis of PCOS. The total participants in the current study was 392 individuals, with 96.4% ($n=378$) stating they had been diagnosed with PCOS. The remaining 3.5% ($n=14$) did not report being diagnosed with PCOS. About one in ten (1:10) women are diagnosed with PCOS nationally (Office of Women's Health, 2019).

The demographics of the sample population in this study is as follows (Table 1). The mean age of the population was 31.51, with the youngest participant(s) being 17 (minors were excluded from data analysis). The oldest participant was age 70, making the range 53 years. Regarding marital status, the majority of the population, 61.5%, reported being married ($n=243$). The second leading group, 14.9%, stated they had never married/were single ($n=59$). Similarly, 11.4% of participants ($n=45$) expressed that they were living with a partner at the time of the study, while 10.1% of the participants ($n=40$) reported they were dating at the time of the study.

The primary ethnicity of the participants (Table 1) was White/Caucasian, 84.1% ($n=332$), and those of Hispanic/Latino ethnicity were the second highest population at 11.1% ($n=44$). Those of Black/African American background were 4.6% ($n=18$) of the sample, and Asian/Pacific Islanders were 4.3% ($n=17$) of the sample.

The education level of participants ranged from less than high school to post-graduate degrees; however, the majority of the participants, 38.5%, reported receiving a Bachelor's degree ($n=152$). Additionally, 19.7% of the participants reported having received a high school education or equivalent (i.e. GED) ($n=78$) and 18.2% of the population surveyed had an Associate's degree ($n=72$). Of the participants, 14.2% ($n=56$) reported having a Master's degree,

and 3.8% ($n=15$) had received a Post-Graduate degree or other professional degree (i.e. Ph.D., DDS).

PCOS and Type 2 Diabetes

The current study aimed to answer two research questions. The first question was: “*Do women with PCOS have a greater risk for developing T2D?*” A Chi-Square Test of Independence was used to analyze the relationship between self-reported PCOS diagnosis, and several risk factors used to assess T2D among the participants. It was hypothesized that women with PCOS have a greater likelihood of developing T2D than their female counterparts who do not have PCOS with PCOS being the outcome variable.

Several variables were found to be significantly related to a participant’s self-reported PCOS diagnosis (Table 2). First, participants reporting being concerned with regaining weight after weight loss was found to be significantly associated with PCOS, ($X^2(2)=7.08, p < 0.05$). Second, participants reporting feeling the need to decrease their weight in order to control their PCOS condition was found to be significantly associated with PCOS ($X^2(1)=9.37, p < 0.05$). Specifically, those who reported having a higher need to lose weight were 6.02 times more likely to report being diagnosed with PCOS than those who reported having a lesser need to lose weight ($OR:6.02, 95\% CIs [1.65, 21.93]$). Additionally, participants’ perception of their current weight (e.g. high weight, healthy weight, or low weight) was found to be significantly associated with self-reported PCOS ($X^2(2)=19.48, p < 0.05$). Furthermore, participants’ self-perceived risk for prediabetes and T2D was significantly associated with PCOS ($X^2(1)=7.13, p<.05$). Specifically, those who reported that they felt at risk for prediabetes or T2D were 4.57 times more likely to report being diagnosed with PCOS than those who reported not feeling at risk for prediabetes or T2D ($OR: 4.57, 95\% CIs [1.36, 15.4]$). Lastly, BMI was found to be significantly

associated with self-reported PCOS ($X^2(1)=7.63, p < 0.05$). Specifically, those who reported being overweight were 4.21 times more likely to report being diagnosed with PCOS than those who reported being underweight (OR: 4.21, 95% CIs [1.4, 12.64]). Among the above T2D risk factors, the results demonstrate that various risk factors for T2D were significantly associated with higher rates of women reporting a PCOS diagnosis.

In addition to the results above, several variables were found not to be significantly associated with self-reported PCOS diagnosis. They were: participants who delivered an infant weighing nine pounds or more at birth ($X^2(1)=0.47, p > 0.05$), participants feeling concerned about being overweight ($X^2(1)=1.34, p > 0.05$), participants currently taking diabetic medications to lower blood sugar levels ($X^2(1)=3.57, p > 0.05$), and if the participant had been overweight as a child ($X^2(1)=0.081, p > 0.05$). These reported results are not statistically significant and therefore do not support the possibility of a significant relationship with risk for T2D and self-reported PCOS.

PCOS and the Environment

The second research question was: *“Do environmental factors have an adverse effect on the PCOS condition?”* A Chi-Square Test of Independence was used to analyze the relationship between self-reported PCOS diagnosis and environmental factors experienced by participants. It was hypothesized that environmental factors have an adverse effect on the condition. The environmental factors analyzed in the current study were: zip codes of where the participant’s both lived and worked, if anyone in the participants’ families (aunt, grandmother, sister, etc.) had ever been diagnosed with PCOS, if the participants’ mothers have/had PCOS, if their biological mother had PCOS during pregnancy, birth control use, fear of cancer, if participants eat at fast food restaurants (i.e. McDonalds, Taco Bell, etc.), the frequency with which the participants

reported eating at fast food restaurants (e.g. 0-2 times per week, 3-5 times per week, and 6 or more times per week), the main source of water in the participants' homes (e.g. community/municipal or well/rain cistern), if they cook with natural gas, and if they have ever used tobacco products. A total of twelve factors were analyzed. The results of the Chi-Square Test of Independence found no statistical association between environmental factors and PCOS (Table 3).

Discussion

PCOS is an endocrine condition which affects upwards of five million women in the United States (CDC, 2018) and includes various manifestations and symptoms (NIH, 2017). Areas of concern for women include, but are not limited to, obesity, IR, T2D, hirsutism, and infertility (NIH, 2017). The condition is characterized by anovulation (absence or improper ovulation), increased levels of androgens (male hormones in the body) and ovarian cysts (NIH, 2017). While it is not uncommon for women of reproductive age to experience ovarian cysts (Office of Women's Health [OWH], 2019), it is the addition of the hormonal characteristics that result in a diagnosis of the condition known as PCOS.

Some of the health complications that can be associated with PCOS include diabetes and gestational diabetes, IR, obesity, and high blood pressure (CDC, 2018). Both the CDC and ADA have stated that having PCOS is itself a risk factor for the development of T2D (Gambineri, et al., 2012; CDC, 2018). It is a syndrome in which various symptoms and manifestations affect each woman with the condition differently and has the potential to greatly impact their quality of life and overall health (OWH, 2019). This particular study investigated women who self-reported being diagnosed with PCOS and the relationship and connection of PCOS to both T2D risk factors and environmental factors.

PCOS and Type 2 Diabetes

This particular study looked at risk factors related to T2D, such as obesity, infants born at or above nine pounds, and BMI and their connection to PCOS. The majority of women who participated stated obesity was a major concern with several statistically significant findings pointing to obesity as a strong predictor for a PCOS outcome. Furthermore, though IR is not used for the diagnosis of PCOS, it is an indicator for T2D as well as PCOS (NIH, 2018). Women were

asked if they feel they could be at risk for prediabetes or T2D and if they are taking medications to help lower their blood sugar. The results of the current study found that women with PCOS had the awareness that they could develop prediabetes or T2D. Specifically, those who reported that they felt at-risk for T2D were 4.57 times more likely to report being diagnosed with PCOS than those who reported not feeling at-risk for T2D. This finding relates to current research, which states that insulin resistance (a risk factor for T2D) and PCOS are linked (NIH, 2018) and that in 50-80% of those with PCOS possibly experience IR (Deeks et al, 2010). However, the findings of this study indicated there was no statistical association between those taking diabetic medication and the diagnosis of PCOS. Regardless, while this particular study did not find a link between those taking diabetic medications to control blood sugars, and PCOS, it did find a link between the perceived risk for developing prediabetes/T2D and PCOS.

The first variable found to have a significant relationship with PCOS diagnosis was: “How often have you felt concerned about regaining weight shortly after any weight loss?”. It is important to note that PCOS is a condition that has the potential to result in weight gain and/or obesity (though lean or low BMI is not unexpected among women with PCOS). Additionally, excess weight may exacerbate the PCOS condition (Mayo Clinic, 2017), and weight management is important for numerous reasons as a form of disease prevention. Overweight and obese individuals are at an increased risk for many diseases, including hypertension (high blood pressure), heart disease, sleep apnea, and a lowered quality of life (CDC, 2015). Furthermore, obesity is a known risk factor for T2D, and therefore the concern for individuals with PCOS who are experiencing weight gain could be associated with an increased risk for T2D.

The next variable examined in this study was: “How often do you feel the need to decrease your weight to control your PCOS condition?” This variable was found to be

statistically significant and results specifically found that those who feel they need to decrease their weight are 6.02 times more likely to be diagnosed with PCOS. These findings further support the association between obesity and PCOS. An additional variable looked at self-perceived weight (e.g. did the participant consider their weight to be low, healthy, or high), and 298 participants answered “Yes” to both feeling their weight was high and having been diagnosed with PCOS (Table 2).

BMI information was calculated for participants because a higher BMI is a risk factor for PCOS and T2D (NIH, 2016), and the majority of participants ($n=292$) reported having a high BMI (25.0 or greater). The OR for BMI was 4.21, and therefore individuals with a BMI over 25 were 4.21 times more likely to be diagnosed with PCOS than those with a lower or healthy BMI. Thus, all variables concerning the weight of the participant point to the concern that a higher body weight is associated with a higher likelihood of being diagnosed with PCOS

Finally, participants were asked if they feel they could be at-risk for prediabetes or diabetes. This was the most specific T2D question in this study. Results found that those who reported feeling at-risk for prediabetes/diabetes were 4.57 times more likely to be diagnosed with PCOS. This finding aligns with the current research that there may be a connection between PCOS and T2D (CDC, 2018; ADA, 2014). PCOS and T2D are both considered metabolic conditions because individuals with either a possibility of experiencing insulin resistance, which is the body’s inability to use insulin efficiently (NIH, 2018.). The findings from this study help to confirm the connection between T2D risk factors, specifically regarding one’s weight, and PCOS. Obesity remains a national concern, and upwards of 34% of adults experience negative health affects related to obesity, including prediabetes and T2D (Michell, Catenzcci, Wyatt, & Hill, 2011). This finding supports the awareness that women with PCOS appear cognizant of

weight management concerns, and therefore education and interventions are appropriate to help improve the overall health of the target population. Furthermore, hormones have a definite impact on the health of an individual, and women with PCOS are no exception. Educating and informing women with PCOS about the reproductive and insulin hormones active in their bodies would be beneficial, not only to the weight conversation, but also to the overall health of women experiencing PCOS as a chronic condition.

Questions that were found to be insignificant in the relationship between T2D and PCOS were “How often have you felt concerned about being overweight (e.g. low concern, healthy concern, and high concern [with zero responses])?”, “Are you currently taking diabetic medication to lower your blood sugar?”, “Were you overweight as a child?”, and “Have any of your deliveries resulted in a baby that weighed nine pounds or more?” While these four questions are relevant to the general conversation relating to T2D risk factors and the population, for those surveyed in the current study, no statistical association was found between risk factors and a PCOS diagnosis. Overall, obesity, weight loss, and beliefs about prediabetes/T2D are indicators for the likely diagnosis of PCOS. Women with PCOS undergo a whole variety of signs and symptoms and are not limited to weight and weight management, but also include overall quality of life.

PCOS and Environmental Factors

The current study also looked at environmental factors and whether or not there was any association with women diagnosed with PCOS. This study found no statistical significance associated with the mostly behavioral questions posed to participants. While not statistically significant, it remains important to investigate and discuss these findings. In this particular study the areas addressed included: cooking practices (i.e. bake/cook using gas), fast food eating

habits, familial exposure, water sources, and population density in the areas where individuals live and work. Overall, these findings align with the literature in that the cause and etiology for PCOS is still largely unknown (Roe & Dokras, 2011).

It has been theorized that PCOS is a possible outcome of familial exposure, specifically while in the womb (Kabir et al, 2015). Addressing the transgenerational aspects of PCOS is difficult at best, and the current study also desires to explore the connection to overall familial exposure. Ultimately, the survey responses to the questions presented found no statistical significance regarding mothers, both biological and non-biological, and the association with PCOS.

Behavioral questions were also asked of participants regarding fast food habits and frequency of eating at fast food restaurants, tobacco use, if they use natural gas to cook, and if they currently use birth control. These behaviors, while insignificant in findings, are elements of the environment in which one lives, works, and plays. Analysis of the responses, though, they did not point to a connection between the environment, a self-declared diagnosis of PCOS, and adverse effects upon the condition.

Potential Endocrine Disruptors (EDs) were observed in the current study, specifically the use of tobacco products and if well/cistern water is used in the homes of women with PCOS. The majority of individuals stated they have not used tobacco products ($n=262$); therefore tobacco use was not found to have a negative impact on the PCOS condition.

As discussed in the literature review, water pollution may also be considered an environmental hazard and impact not only the health of women with PCOS but also the population as a whole. Well water and cistern use do not encounter the same policies and testing regulations as community or municipal water sources (EPA, 2017) and therefore have the

potential to carry various contaminants. In this study, regarding the use of well/cistern versus community/municipal water as tap or drinking water in individual's homes, no association was found between the water used in one's home and any adverse effects on one's health, namely the PCOS condition.

Population density is important to consider in relation to the health of the population. The observed population in the current study was divided into three elements: low, medium, and high density in both the city in which participants lived and worked. Thus six areas of density were examined. Again, no link was found between population density and PCOS.

Finally, it is valuable to speak about birth control/contraceptives and the observed use of this medication in the population assessed. Birth control is a common treatment for PCOS due to its ability to regulate hormones and help with other unwelcome symptoms of PCOS (PCOS Awareness Association, 2017). By definition, birth control is considered an endocrine disruptor (ED) because it disrupts the natural hormones experienced by individuals. In this case, women with PCOS have higher androgens (male hormones) and birth control is a Food and Drug Administration regulated treatment used to help balance these hormones. This study found no statistical connection between the use of birth control and any adverse effects on women with PCOS.

In conclusion, the findings of this study are consistent with the literature regarding both T2D and environmental factors. The literature expresses that there is a link between PCOS and T2D, especially where IR and obesity are concerned. While this study did not examine IR specifically, it speaks to the concern and feelings women who self-reported PCOS have toward weight gain and weight management. Therefore, this study affirms and aligns with the literature regarding higher BMI as a risk factor for T2D. Similarly, this study also parallels the current

literature which states that there is still more to learn regarding the environment, endocrine disruptors/endocrine disrupting chemicals and any adverse effects they may have on PCOS. Many behavioral, environmental, and biological aspects have the potential to affect the overall health of women living with PCOS as a chronic health condition, and several areas can be addressed to help positively impact the overall health and wellbeing of those who live with chronic illness.

Public Health Implications

The impact of the current study is considerable and helps address the concerns women with PCOS may have regarding their health, endocrine health, T2D, and the environment. Several areas surfaced during the analysis and discussion of T2D risk factors and their relationship to PCOS. Women with PCOS seem to be aware of their weight, especially when it comes to regulating their PCOS condition. This means that employing educational efforts upon diagnosis helps women more fully understand the endocrine nature of the condition, the potential challenges and positive aspects of the condition, and coping strategies for living with chronic illness.

Communication with women with PCOS should remain open, especially where T2D risk factors are concerned. As the current study found, some elements of T2D risk factors and PCOS are linked, and women should be made aware of the endocrine and metabolic/IR nature of the condition as well as the possible impact on blood glucose levels. Additionally, it has been proposed that women with PCOS should have their A1C levels screened periodically to document their overall health (Veltman-Verhulst, et al., 2013, Lanzo, Monge, & Trent, 2015). This is certainly an important and invaluable consideration when discussing the relationship between PCOS and T2D.

Weight management and weight loss can be extremely difficult for women with PCOS. Behavioral modifications should be encouraged for women within this target population. Women should be made aware of the negative impact that being overweight or obese has on their health and they should be informed about the importance of living an active, healthy lifestyle as well as encouraged to adopt lifestyle behavior changes. Likewise, an intervention addressing lifestyle changes, coping strategies for living with a chronic condition, and providing individuals with a variety of tools to help live a healthy lifestyle might greatly improve the quality of life experienced by individuals diagnosed with either T2D and/or PCOS.

It remains unknown if or how the environment affects women's health, particularly PCOS. The environment has an important role on an individual's lifestyle and health outcomes, and the environmental exposures experienced from where individuals live, work, and play have the potential to impact their overall health. While some EDs/EDCs are known to be linked to PCOS (i.e. BPA), others need further investigation. Nevertheless, due to the regular and daily environmental exposures experienced by the population, EDs/EDCs is a growing area of interest and study for public health and other professionals.

Study Limitations and Strengths

As with any study, various strengths and limitations exist for this one. A particular strength of this study was that survey questions were derived from several national studies which are intended to assess the overall health of the United States. These studies included the National Health and Nutrition Examination Survey (NHANES), The Coronary Artery Risk Development in Young Adults Study (CARDIA), and a quality of life questionnaire specific to PCOS (PCOSQ-50). Questions derived from these surveys were specific to T2D risk factors, such as "Are you currently taking diabetic medication to lower your blood sugar?" and "Have any of

your deliveries resulted in a baby nine (9) pounds or more?” and environmental questions such as: “What is the main source of water used in your home?” and “Have you ever used tobacco products?”. Questions derived from the PCOSQ-50 survey were answered on a Likert scale, and simultaneously addressed quality of life and obesity concerns for women diagnosed with PCOS. Questions such as: “How often have you felt the need to decrease your weight to control your PCOS condition?” and “Have you ever experienced a fear of cancer?” were derived from this study. While the survey used in this study was original, the use of questions and topics from the NHANES, CARDIA, and PCOSQ-50, as well as novel questions, allowed for a unique and well-rounded survey.

The current study helps to fill in some of the gaps in the existing research. Research on the topic of PCOS found that few independent studies on the topic were accessible. The current study is among the limited studies with a focus on environmental exposures and behaviors and their relationship with PCOS. As such, this is possibly the only study with the focus on environmental behaviors and their potential effect on the PCOS condition.

Limitations also exist within the study, specifically within the instrument used. Questions specific to the diagnosis of T2D experienced by participants were not asked (i.e. “Have you been diagnosed with prediabetes or T2D?”). Therefore, assessing T2D as an outcome of the PCOS condition was unattainable. Future studies should include questions more specific to a T2D diagnosis and look more specifically at T2D among women who have PCOS.

Due to the self-report nature of the study, bias exists. Namely, recall bias occurs because the current study asks the participants questions starting with: “In the last four months...” It is possible that participants responded according to their recollection of experiences. Response bias may also be a limitation because of the self-report nature of this study. Lastly, sampling bias is a

limitation for the current study because those with PCOS were actively recruited, while those without PCOS were not, which resulted in a smaller sample for those without PCOS.

While several of the variables were collapsed into two groups to meet the assumptions of the Chi-Square statistical analysis two by two expectations, some variables were not condensed. In some cases, such as population data, it was logical to keep responses as low, medium, and high density. However, other variables could have been collapsed but were not. Thus, odds ratios were not calculated for these variables. Lastly, there were some variables that did not meet the cell count assumption of the Chi-Square test, and therefore the Fisher's exact test was used where the count (number of participants) was less than five.

Future Directions

Within this area of study there are many topics and potential for growth. It is recommended that future studies investigate if women who have been diagnosed with PCOS have a greater likelihood of developing T2D. This could be done by including questions that ask participants if they were diagnosed with T2D as well as looking at blood glucose reports, and/or including A1C levels. A study such as this might require clinical observations to explore a relationship between PCOS and T2D. Future studies might also investigate IR, metabolic syndrome, and T2D and their possible relationship to PCOS. The endocrine nature of these four conditions lend themselves to a strongly developed study.

Another area for future study would be to explore the relationship of women with PCOS and their (female) offspring (children and/or grandchildren) and if there is a familial and/or biological connection impacting a PCOS diagnosis. This study might be longitudinal or retrospective in nature, and the risk of attrition might need to be considered. However, because little is known about the cause and etiology of PCOS, this line of study has merit.

Future studies might also investigate EDs and/or EDCs and their potential effects on the overall health of the population, particularly women with PCOS. As has been expressed, many EDs become a known hazard only after adverse effects upon one's health are seen (i.e. DES, a pharmaceutical which led to unexpected vaginal cancers), and researching ways to mitigate this exposure as a form of prevention has value. EDs are a ubiquitous part of our environment, and therefore cannot be separated from daily experiences. However, there may be ways in which individuals can mitigate exposure to compounds within their environments. An example of such an investigation might include individuals primarily using glass in their homes for food storage, or the removal of parabens and other topical components used by women. A well-developed study might include an investigation of the ingredients used in common household products and the exposure individuals might experience within their everyday lives.

Lastly, an investigation of lifestyle factors and behavioral interventions would be of great interest to the growth of literature where PCOS is concerned. Considerations such as quality of life, nutrition, physical activity, and weight management for women with PCOS are essential. Investigating short- and long-term outcomes resulting from behavior change programs specifically targeting women with PCOS would be a welcome way to further the literature. A study of this kind would also benefit those participating in the intervention and add to the knowledge base of PCOS and behavior change.

Conclusion

PCOS is the foremost endocrinopathy condition experienced by women of reproductive age, affecting between 4-21% of women (Azziz & Adashi, 2016). It is diagnosed clinically when women have two out of three of the following: polycystic ovaries via ultrasound, high androgens, and/or anovulation which is often manifested in irregular menstrual cycles. It is a condition

affecting women of all ages and spans the course of a lifetime. There is no clear etiology or cause for PCOS. Insulin resistance often accompanies PCOS, regardless of obese versus lean body composition, and therefore is considered a metabolic complication for women with PCOS. As such, T2D has been found to be associated with PCOS and therefore women with a PCOS diagnosis should be aware of this connection. Additionally, the environment in which we live, work, and play have an impact on health in many ways, and PCOS is no exception to this possibility. Further research needs to be done regarding how environmental exposures might affect women with PCOS.

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Appendix A: Participant Informed Consent

PURPOSE & PARTICIPATING: My name is Rebecca “Becky” Frost and I am a graduate student at California Baptist University (CBU) doing research on Polycystic Ovarian Syndrome (PCOS) and women’s health concerns. The study being conducted is directed toward women with PCOS and components related to the condition, including environmental factors and potential long-term health risks. The following survey is focused on women living in the United States between the ages of 18-60 years old who have been diagnosed with PCOS. It examines the health behaviors and concerns specific to women with PCOS and will take about 6-7 minutes to complete.

RISK & BENEFIT: Risks associated with the survey are minimal; however, you may experience discomfort upon answering some questions. If unease is experienced, you may either skip the question(s) or stop taking the voluntary survey. If concerns or questions arise, please contact Becky at rebeccag.frost@calbaptist.edu for resources and/or assistance regarding the survey or study.

COMPENSATION: There is no compensation associated with this survey and study.

VOLUNTARY PARTICIPATION: Your participating in the survey is fully voluntary, and you may choose to refuse or discontinue taking the survey at any time.

CONFIDENTIAL: The survey is anonymous, and records of data collected will remain secure on a password protected computer.

CONTACT INFORMATION: The principal Investigator (PI), Rebecca “Becky” Frost, is a graduate student at CBU. She can be contacted at (909) 239-1027 or rebeccag.frost@calbaptist.edu. The faculty advisor for this study is Melissa Wigginton, DrPH and can be contacted at mwigginton@calbaptist.edu or by phone at (951) 552-8537. For further

information regarding the nature of the study, you may contact Erin Smith, Ph.D. with CBU's Institutional Review Board (IRB) at (951) 552-8626, or esmith@calbaptist.edu.

AGREEMENT: I agree to participate in the PCOS study being conducted and I understand that participation is voluntary.

Appendix B: PCOS Survey

What is your age?

What is your birthdate (month/day/year)?

What is the highest grade/level of school you have completed or the highest degree you have received?

High school diploma or equivalent (GED)

Associates degree (community college)

Bachelor's degree

Master's degree

Post graduate or professional degree (Ph.D., MD., DDS., etc.)

Other

Less than high school graduate

What is your marital status?

Married

Widowed

Never married/single

Living with a partner

Dating (boyfriend/girlfriend)

What is your ethnicity (please check all that apply)?

White/Caucasian

Hispanic/Latino

Black/African American

Native American/American Indian

Asian/Pacific Islander

Other

Do you live in the United States?

Yes

No

What zip code do you live in?

What zip code do you work in?

Have you ever been diagnosed with Polycystic Ovarian Syndrome (PCOS)?

Yes

No

Has anyone in your family (mom, grandmother, aunt, sister, etc.) ever been diagnosed with PCOS?

Yes

No

Unknown

Does your mother have PCOS?

Yes

No

Unknown

Did your mother (birth/biological) have PCOS during pregnancy?

Yes

No

Unknown

How much do you weigh?

How tall are you (feet/inches)?

Have you ever been pregnant?

Yes

No

If you have children, have any of your deliveries resulted in a baby that weighed nine (9) pounds or more at birth?

Yes

No

I do not have children

What is your belief about the effect of being overweight on a person's health? (Likert Scale)

Harmless – Somewhat Harmless – Neutral – Harmful – Very Harmful

Would you consider yourself? (Likert Scale)

Too Thin – Slim – Normal/Healthy Weight – Obese – Very Obese

Do you feel you could be at risk for diabetes or prediabetes?

Yes

No

Unknown/No Opinion

Are you currently taking diabetic medications to lower your blood sugar (these are sometimes called oral agents)?

Yes

No

Do you use birth control?

Yes

No

In the past four weeks: how often have you felt concerned about being overweight? (Likert scale)

Never—Rarely – Sometimes – Often – Always

In the past four weeks: how often have you felt the need to decrease your weight to control your PCOS status? (Likert scale)

Never – Rarely – Sometimes – Often – Always

In the past four weeks: how often have you felt concerned about regaining weight shortly after any weight loss? (Likert scale)

Never – Rarely – Sometimes – Often – Always

In the past four weeks: have you experienced fear of cancer? (Likert scale)

Never – Rarely – Sometimes – Often – Always

Were you overweight or obese as a child?

Yes

No

Do you eat at fast food restaurants (i.e. McDonalds, Taco Bell, etc.)?

Yes

No

How frequently do you eat at fast food restaurants?

0-2 times per week

3-5 times per week

6 or more times per week

What is the main source of water (tap or drinking) in your home?

Community/Municipal water

A well or rain cistern

Unknown

Do you cook or bake with natural gas?

Yes

No

How do you usually cook your food (check all that apply)?

Grill

Stovetop

Microwave

Bake

Slow Cooker

Other

Have you ever used tobacco products such as cigarettes, cigars, e-cigarettes, chewing tobacco, etc.?

Yes

No

Appendix C: IRB Approval

RE: IRB Review

IRB No.: 031-1819-EXP

Project: Polycystic Ovarian Syndrome (POCS), Environmental Influences and Type 2 Diabetes Risk Factors

Date Complete Application Received: 9/28

Date Final Revision Received: 10/19

Principle Investigator: Rebecca G. Frost

Faculty Advisor: Melissa Wigginton

College/Department: CHS

IRB Determination: Expedited Application Approval – Student research using anonymous survey questionnaires; no minor participants; no more than minimal risk/risk appropriately mitigated; no deception utilized; acceptable consent procedures and documentation; acceptable data protection procedures. Data collection may begin, in accordance with the final submitted documents and approved protocol.

Waiver of Documentation of Consent: Per 45 CFR 46.117, the IRB has approved the request to waive the documentation of informed consent (e.g., no participant signatures will be collected, though participants do receive a copy of the consent information) because the signature of the participant would be the only linking record to the data that may harm the participant if released.

Future Correspondence: All future correspondence about this project must include all PIs, Co-PIs, and Faculty Advisors (as relevant) and reference the assigned IRB number.

Approval Information: Approval is granted for one year from date below. If you would like to continue research activities beyond that date, you are responsible for submitting a Research Renewal Request with enough time for that request to be reviewed and approved *prior* to the expiration of the project. In the case of an unforeseen risk/adverse experience, please report this to the IRB immediately using the appropriate forms. Requests for a change to protocol must be submitted for IRB review and approved prior to implementation. At the completion of the project, you are to submit a Research Closure Form.

Researcher Responsibilities: The researcher is responsible for ensuring that the research is conducted in the manner outlined in the IRB application and that all reporting requirements are met. Please refer to this approval and to the IRB handbook for more information.

Date: October 23, 2018

Appendix D: Tables

Table 1: Demographic Description of Surveyed Participants

Variable	<i>n</i>	%
Ethnicity/Race		
White/Caucasian	332	84.1
Hispanic/Latino	44	11.1
Black/African American	18	4.6
Asian/Pacific Islander	17	4.3
Native American/ American Indian	4	1.0
Other	8	2.0
Marital Status		
Married	243	61.5
Never Married/Single	59	14.9
Living with Partner	45	11.4
Dating	40	10.1
Widowed	1	0.3
Education Level		
Less than High School	5	1.3
High School/GED	78	19.7
Associates	72	18.2
Bachelors	152	38.5
Masters	56	14.2
Post Graduate	15	3.8
Other	14	3.5

Table 2: Chi-Square Table of PCOS Diagnosis and T2D

	<u>Diagnosed with PCOS</u>		X^2	<i>df</i>	<i>p</i>	<i>OR</i>	<i>95% CI</i>
	Yes	No					
BMI							
Underweight	52	6	7.63	1	0.01	4.21	[1.4, 12.64]
Overweight	292	8					
How often have you felt concerned about regaining weight shortly after any weight loss							
Low concern	105	8	7.08	2	0.03		
High concern	209	3					
No concern	61	3					
How often have you felt the need to decrease your weight to control your PCOS condition							
Less Need	142	11	9.37	1	0.00**	6.02	[1.65, 21.93]
More Need	233	3					
How often have you felt concerned about being overweight							
Low concern	132	7	1.34	1	0.25	1.84	[0.63, 5.36]
Healthy	246	7					
High concern (n/a)							
Do you consider your weight							
Low weight	6	0	19.48	2	0.00		
Healthy weight	73	9					
High Weight	298	5					
Do you feel you could be at risk for prediabetes or diabetes							
Yes	282	5	7.13	1	0.01	4.57	[1.36, 15.4]
No	74	6					

Are you currently taking diabetic medication to lower your blood sugar

Yes	116	1	3.57	1	0.07**	5.76	[0.74, 44.52]
No	262	13					

Were you overweight as a child

Yes	144	7	0.81	1	0.37	0.62	[0.21, 1.79]
No	234	7					

Have any of your deliveries resulted in a baby that weighed nine (9) pounds or more

Yes	37	1	0.47	1	0.69	2.06	[0.25, 16.96]
No	144	8					

Note: n = 395

**Fisher's Exact test was used

Table 3: Chi-Square Table of PCOS and Environmental Factors

	<u>Diagnosed with PCOS</u>		X^2	<i>df</i>	<i>p</i>	<i>OR</i>	95% CI
	Yes	No					
Does your mother have PCOS							
Yes	33	0	1.77	1	0.38	1.13	[1.08, 1.18]
No	259	14					
Does your biological mother have PCOS							
Yes	13	0	0.63	1	1.0**	1.05	[1.02, 1.08]
No	247	12					
Does a member of your family have PCOS							
Yes	117	2	2.92	1	0.14	3.5	[0.76, 16.06]
No	184	11					
Do you eat at fast food restaurants							
Yes	248	9	0.01	1	0.91	1.07	[0.35, 3.25]
No	129	5					
How frequently do you eat at fast food restaurants							
0-2 times	337	11	3.13	2	0.21		
3-5 times	31	3					
6 or more times	7	0					
Have you ever used tobacco products							
Yes	116	2	1.73	1	0.25**	2.66	[0.59, 12.06]
No	262	12					
What is the main source of water in your home							
Well/Rain Cistern	29	0	1.29	1	0.62**	1.09	[1.06, 1.13]
Community/ Municipal	313	14					

Have you ever experienced a fear of cancer							
High concern	38	2	0.26	1	0.64**	0.67	[0.15, 3.12]
Low concern	339	12					
Population of the city you live in							
Low density	156	5	2.48	2	0.29		
Medium density	120	5					
High density	17	2					
Population of the city you work in							
Low density	139	7	0.47	2	0.79		
Medium density	111	4					
High density	14	1					
Do you use birth control							
Yes	78	0	3.61	1	0.08**	1.26	[1.2, 1.33]
No	300	14					
Do you cook or bake with natural gas							
Yes	150	5	0.09	1	0.76	1.19	[0.39, 3.62]
No	227	9					

Note: n = 395

**Fisher's Exact test was used