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Disparities in Seeking and Receiving Fertility Counseling and Treatment

By

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Doctor of Philosophy

Epidemiology

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Disparities in Seeking and Receiving Fertility Counseling and Treatment

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M.P.H., University of South Florida, 2007
B.S., University of South Florida, 2004

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Abstract

Disparities in Seeking and Receiving Fertility Counseling and Treatment

By Helen Belinda Chin

In the United States an estimated 6 million women have impaired fecundity. The inability to have a baby affects the quality of life of women who desire children. Further, infertility is a disease of the reproductive system. Fertility counseling, preservation, and treatment can help some women who cannot conceive naturally to have a child; however, there is sometimes disparate access to this type of care. This dissertation examined disparities in seeking and receiving fertility counseling and treatment among participants of the FUCHSIA Women's Study, a population-based cohort study of reproductive-age women.

In study one, we assessed the persistence of a black white racial disparity after accounting for intermediate variables of the association between race and seeking medical help for becoming pregnant. Compared with white women, black women were less likely to visit a doctor for fertility care, even though they were also less likely to have a child at the time of the study interview.

Study two examined geographic differences in visiting a doctor for help becoming pregnant. To compare the results from the FUCHSIA Women's Study with a national sample, this association was also assessed among participants of the National Survey for Family Growth (NSFG). Among women who reported infertility, living in a suburban or small metropolitan county was associated with a greater likelihood of accessing fertility care compared with living in an urbanized or small town/rural county in both the FUCHSIA Women's Study and NSFG.

Despite universal recommendations to inform reproductive-age women diagnosed with cancer about how cancer treatment could affect fertility, many women do not receive this information. Study three identified factors associated with not receiving fertility counseling at the time of cancer diagnosis. Overall, 41% of women reported receiving no information on how cancer treatment could affect their ability to become pregnant. Less educated women or women with children were less likely to receive counseling compared with nulliparous or more educated women.

Collectively, these studies demonstrate disparities in the receipt of fertility counseling and care among certain groups of women. Improving access to fertility care among these groups, may help more women meet their reproductive goals.

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CHAPTER 1: Introduction and Overview

BACKGROUND AND PUBLIC HEALTH IMPORTANCE

In the United States it is estimated that over 6 million women of reproductive age experienced impaired fecundity or the inability to carry a baby to term between the years 2006-2010 [1]. An estimated 1.5 million married or cohabitating women experienced infertility or the inability to become pregnant, during this same time period. Infertility and impaired fecundity are a significant public health issue. These conditions affect women across different education, income, race and ethnic groups [2]. The inability to conceive and carry a baby to term affects the quality of life of women who desire to have children. However, infertility is not only a quality of life issue for women who want to have a child or more children. The American Society for Reproductive Medicine (ASRM), World Health Organization, and International Committee for Monitoring Assisted Reproductive Technology classify infertility as a disease of the reproductive system [3, 4].

Roughly 17% of women 25-44 years old in the US have ever used an infertility service to help them become pregnant [5]. Most women received advice or counseling when they visited a healthcare provider for help getting pregnant. Fewer women used infertility treatments and these ranged from medications to in vitro fertilization. For some women, accessing medical care for infertility counseling and treatment can help them meet their reproductive goals; however, women do not uniformly seek medical care to address these needs.

Some medical conditions and treatments can affect fertility. Young adult women who are diagnosed with cancer are a particularly vulnerable to experience fertility problems directly from their cancer diagnosis or as a result of exposure to potentially gonadotoxic chemotherapy and radiation treatments. This potential damage to fertility is of concern to female cancer patients who want to have children in the future and sometimes influences treatment decisions [6, 7]. The ASRM and the American Society of Clinical Oncology (ASCO) recommend that all women of reproductive age who are diagnosed with cancer receive information about how cancer treatment could affect their fertility and the availability of fertility preservation options [8-10]. Despite this universal recommendation, almost half of reproductive-aged women diagnosed with cancer report not receiving this information from their doctor [6, 11]. Even among doctors who refer patients to fertility specialists, referral patterns vary in terms of frequency and patient characteristics used to determine the need for counseling about fertility preservation [12-14].

STUDY MOTIVATION

There is variation in help-seeking behaviors for infertility treatment among different groups of women. Differences by race, income, and education, among other factors have been documented in the literature, but have not been fully explained [15-17]. Studies of these differences are often small and limited to clinic populations, where all women included have already decided to seek help for their fertility problems. Moreover, much of the literature describing patterns of infertility service use focuses on in vitro fertilization [18, 19]. Less is known about differences among women in their overall use

of medical care for infertility, which includes in vitro fertilization, but also counseling and less invasive procedures such as use of medications.

Infertility treatment has become more successful and more widely used in recent decades [1, 20]. However, increase in the use of these procedures has been disproportionate among specific groups of women within races, socioeconomic groups, and cultural groups [16, 21-23]. Furthermore, African American and Hispanic women are more likely to wait longer to seek care after they experience infertility compared with white women [21, 22, 24]. The first study aim will address racial disparities in seeking any type of help for becoming pregnant.

In addition to disparities by demographic characteristics, differences in physical access to medical care for help getting pregnant can influence use. For example, most women living in areas of the country that are highly urbanized are within 60 minutes of a fertility clinic, while women living in more sparsely populated areas have less access [19]. To address issues with physical access to any type of medical care for help getting pregnant, the second study aim will examine differences in visiting a doctor for help getting pregnant by the level of urbanicity of a woman's place of residence.

Further, gaps in knowledge exist with regard to fertility preservation counseling and utilization among cancer survivors. There are many studies that are limited to certain types of cancers while other cancers are understudied. In addition, even though there have been advances in fertility preservation research, there is a lag in utilization [25].

The final study aim will determine which characteristics make cancer patients less likely to receive fertility counseling at the time of their cancer diagnosis.

Much of the published literature on fertility treatment and preservation is in clinic populations and captures only those women who are already seeking treatment. All proposed study aims will utilize a population-based sample and will be able to characterize both women who do and do not seek fertility counseling and treatment.

STUDY POPULATION

The study aims will be addressed using data from the Furthering Understanding of Cancer Health and Survivorship in Adult (FUCHSIA) Women's Study. The FUCHSIA Women's Study is a population-based cohort study in Georgia of fertility in reproductive-aged female cancer survivors (n=1282) and a group of comparison women (n=1073). Women included in this study were 22-45 years old, and completed an hour long telephone interview which collected information on cancer diagnosis and treatment, menstrual function, desire for children, infertility, pregnancy, reproductive surgeries, infertility treatment, fertility preservation, hormone medications, medical conditions, and lifestyle.

The second data source used for this dissertation is the National Survey for Family Growth (NSFG). The NSFG is a US based survey that is conducted in a nationally representative sample of individuals by the National Center for Health Statistics at the Center for Disease Control and Prevention. The NSFG was first conducted in 1973 to gather information on marriage, divorce, contraception, infertility, and the health of women and infants [26]. The survey is conducted in cycles with the last cycle of completed interviews taking place between 2006 and 2010 [26]. During the 2006-2010 cycle, a national sample of 22,682 men and women between the ages of 15-44 years were

interviewed [26]. There were approximately 10,000 interviews among men and 12,000 among women [26]. For this dissertation, we will be using information from the sections of the interview on use of infertility services and reproductive health in women to compare estimates of a disparity in infertility service use among women in FUCHSIA to a nationally representative sample.

STUDY AIMS

The overarching goal of this dissertation is to characterize disparities in receiving information about fertility treatment and preservation options. The primary objective of *Study Aim 1* is to assess the persistence of racial disparities after accounting for intermediate variables of the association between race and seeking medical help for becoming pregnant. We will also explore differences by race in the length of time women wait from when they first experience infertility to the time they visit a doctor for help becoming pregnant.

In *Study Aim 2* we seek to determine if a geographic disparity exists in visiting a doctor for help becoming pregnant among a population-based sample of reproductive-aged women in Georgia. We will assess the overall association between the level of urbanization of the county where a woman lives and visiting a doctor using data from the FUCHSIA Women's Study and NSFG data to compare our estimates in Georgia to a national sample. Using the FUCHSIA Women's Study data we will also describe differences in the type of provider and infertility service utilized.

Study Aim 3 is to identify and compare factors associated with not receiving information about how cancer treatment could affect future fertility among a cohort of women diagnosed with cancer during their reproductive years. We will also describe

which characteristics make women more or less likely to receive a referral to a fertility specialist at the time of diagnosis.

Aims 1 and 2 of the proposed study will help to identify racial and geographic disparities in seeking medical care for help getting pregnant. *Aim 3* will determine which women are being missed by the universal recommendation that all women diagnosed with cancer during their reproductive years be counseling on how treatment could affect their future fertility. Characterization of disparities in who seeks medical care for infertility can identify areas where general practitioners and community organizations can intervene to provide information on infertility services to women who may currently be unaware of the full range of counseling and treatment options available. Identifying factors that influence whether or not a cancer patient receives critical information on how treatment could affect future fertility can help inform oncologists and other medical providers of missed opportunities to provide this type of counseling.

CHAPTER 2: Background and Literature Review

INFERTILIY

Causes.

Clinical infertility is the failure to conceive after 12 months of trying [27]. There are many causes of female infertility. Some infertility may be caused by a single factor while others may be multifactorial. Some common causes of infertility related to reproductive conditions include polycystic ovary syndrome, endometriosis, and fibroids [28]. These conditions can cause hormonal and physiologic changes that can prevent pregnancy [28]. Infections can also cause infertility. Certain sexually transmitted infections such as chlamydia and pelvic inflammatory disease can cause damage to the fallopian tubes [29]. Scarring or inflammation of the fallopian tubes can prevent fertilization [30]. There are also genetic disorders that cause infertility such as Turner's syndrome, where a woman only has one X chromosome, and is sterile [28]. Environmental factors can also influence ovarian function and in turn fertility [31, 32]. Obesity, excessive exercise, or insufficient caloric intake can also affect reproductive function [28].

Prevalence.

The National Survey for Family Growth (NSFG) reports statistics on impaired fecundity among all reproductive aged women and infertility among married women of reproductive age in the United States [1]. From 2006-2010 there were over 6 million women of reproductive age in the US who reported having impaired fecundity [1]. During this same time period, it is estimated that 1.5 million married women of

reproductive age experienced infertility [33]. This represents a significant public health problem since infertility is both a disease of the reproductive system and a quality of life issue [3]. There are differences in the rates of infertility among women of different races. The NSFG reports that 5.5% of white non-Hispanic women were infertile, while 7.2% of black non-Hispanic women were infertile [33]. Additionally, while there has been a decrease in the rates of infertility among white women in recent decades there has been an increase in rates of infertility among black women [15, 34]. In models adjusted for demographic factors non-Hispanic black women were about 1.8 times more likely to report infertility compared with white women [33]. Biological and sociocultural factors contribute to this disparity, such as differences in 1) prevalence of sexually transmitted infections that can cause infertility, 2) marital status, where married women may detect problems with fertility earlier, and 3) maternal age, with women starting a family at older ages experiencing more infertility [15].

Measures.

There are many ways to evaluate female fertility. One way is to track a woman's menstrual cycle. The length and consistency of menstrual cycles can provide information about a woman's reproductive function [28]. Changes in menstrual cycle patterns may indicate changes in fertility and the absence of a menstrual cycle may signify the absence of ovulation [28, 35]. Using the characteristics of a woman's menstrual cycle can provide important information on her reproductive function and fertility status.

Another way is by asking women if they have ever experienced a period of infertility. This can be defined differently depending on the age of the women. Among

women who are early in their reproductive years, asking whether or not they have experienced a period 12 months or longer when they were having regular sexual intercourse with a male partner without using birth control and did not get pregnant can be an appropriate measure [28]. This measure uses the clinical definition of infertility, which is failing to conceive after 1 year of trying. Among women who are of advanced maternal age or as a measure of subfertility among all reproductive aged women, it may be more appropriate to ask the same question, but over a period of 6 rather than 12 months [28]. These measures of infertility are very broad however, and do not distinguish between male versus female factors of infertility.

Female fertility can also be measured clinically. Biomarkers such as anti-Müllerian hormone (AMH) measure ovarian reserve. Tests for infertility using AMH as a marker test specifically for problems with the ovaries. AMH is a glycoprotein produced in females by the granulosa cells of the preantral and small antral follicles in the ovary [36]. AMH declines naturally with age as ovarian reserve decreases, but it may also decrease due to exogenous factors that affect ovarian reserve. AMH is a better marker of ovarian reserve than other markers of fertility, such as follicle-stimulating hormone (FSH), because AMH is relatively stable throughout the menstrual cycle and does not change meaningfully with the use of oral contraceptives [37]. In addition, AMH begins to decline naturally when women are in their twenties, unlike other markers of fertility that do not change until women already have impaired fertility [38-40]. Further, declining AMH has been used to predict the onset of menopause [41]. Although AMH is arguably the best clinical marker of female fertility, there are no commonly accepted clinical cut points, and it measures quantity of antral follicles, but not quality [42, 43].

INFERTILIY TREATMENT

Treatment.

Fertility treatment can assist some women who are diagnosed with infertility get pregnant [22]. Fertility treatments include medications or procedures such as ovarian stimulating medication, intrauterine insemination, and in vitro fertilization (IVF) [44]. Fertility treatments have become more successful and more widely used in recent years [1, 20]. Each fertility treatment may be differentially successful based on factors such as the woman's age, cycle day 3 luteinizing hormone (LH)/ follicle-stimulating hormone (FSH) ratio, etiology of infertility, and parity [24, 45]. It is important for women to be aware of the different treatments that are available to help them become pregnant and to receive information on the appropriateness of each of the treatments for their specific cause of infertility. However, these treatments remain differentially utilized as a result of a number of factors including that some women do not know they exist [21, 22].

CANCER AND INFERTILITY

Cancer during the reproductive years.

Many women of reproductive age are diagnosed with cancer each year. According to the Surveillance, Epidemiology, and End Results (SEER) statistics for 2010 the age adjusted incidence rate of cancer in women between the ages of 20-49 was 187 per 100,000 [46]. Over the past few decades, there have been great improvements in how cancer is treated. With this improvement in cancer treatment a greater need to address survivorship issues has developed. It has been well documented that cancer studies have reported decreased fertility in women treated with chemotherapy, especially alkylating

agents [47, 48]. Since there is limited evidence on how cancer treatment affects future fertility in reproductive aged women diagnosed with cancer, it is difficult for physicians to advise their patients. It is also difficult to decide which treatment regimen is most appropriate for women who want to have children in the future when there is a choice of treatment options.

There have been many studies done in populations of childhood cancer survivors examining how treatment affects their future fertility [48-53]. These studies show that young girls treated for cancer suffer damage to their ovarian function. Later in life childhood survivors are more likely experience premature ovarian failure. In addition, childhood survivors who experienced normal menstrual function were more likely to have reduced ovarian reserve. There are also numerous registry-based studies conducted in Scandinavian countries [54-56]. These studies show that women diagnosed with cancer are more likely to be nulliparous and among those who did have children, more likely to have fewer children compared with their siblings. However, there are fewer studies of how cancer treatment affects the reproductive potential of women who are diagnosed with cancer during their reproductive years, although this body of literature is growing.

In addition to questions about which cancer treatment options are best for women who want to preserve their fertility, there is also conflicting advice given to women who have been diagnosed with cancer about when and if they should attempt pregnancy after cancer treatment. Specifically women with hormone responsive cancers have been advised not to become pregnant or use hormones necessary for fertility preservation and IVF [57]. However, there have been several recent studies that find women who have

hormone responsive cancers do not have increased risk of cancer recurrence if they get pregnant [58-60].

FERTILIY PRESERVATION

Fertility preservation methods.

Women who are diagnosed with certain conditions which require potentially gonadotoxic treatment are at risk for infertility. For women who are fertile at the time of treatment, fertility preservation may be an option that allows for future pregnancies [61]. Fertility preservation methods include procedures such as egg, embryo, and ovarian tissue freezing [62]. Recently, egg freezing was reclassified so that it is no longer considered an experimental treatment, showing the advances in this area of medicine [63].

There are several fertility preservation options available [62, 64]. Embryo and oocyte preservation are the established methods of fertility preservation. These procedures require ovarian stimulation and retrieval of mature eggs for freezing eggs or for fertilization and freezing embryos. Embryo and egg freezing are the most successful forms of fertility preservation, but have a time commitment attached to them to stimulate the ovaries and harvest mature eggs [64]. There are also newly emerging experimental methods that can decrease or eliminate the waiting time to harvest eggs for preservation. These methods do not rely on the natural timing of a woman's menstrual cycle and so can be started immediately [65]. Random start ovarian stimulation can begin at any time in the menstrual cycle decreasing the amount of time needed from the traditional 2-6 weeks to within 2-3 weeks [66, 67]. The shorter delay of cancer treatment is important for

women who are concerned about their future fertility, but do not want to postpone cancer treatment or can only postpone for a short period of time [68-70].

Immature oocyte and ovarian tissue cryopreservation do not require stimulating ovulation and therefore can be performed immediately, but these procedures are still experimental. Harvesting these immature eggs eliminates waiting time for fertility preservation because eggs can be harvested and frozen in the state of maturity at which they exist at the time of diagnosis [71]. The immature eggs are frozen and then later matured in vitro IVF [71]. A few dozen births have been reported in the literature after using ovarian tissue cryopreservation and only one birth in a cancer survivor after cryopreserving immature oocytes [72, 73]. Additionally, with ovarian tissue cryopreservation there is some concern about transplanting cancer cells back into patients using frozen ovarian tissue [74]. For women who need to have pelvic radiation, moving the ovaries out of the field of radiation is another option, but there is limited data on the efficacy of this procedure in preserving fertility, but it may offer partial protection of the ovaries and has been associated with better hormone function [75].

Although fertility preservation is becoming more common, it is still rare [61, 76]. The ASRM and the ASCO recommend that fertility preservation be discussed with patients of reproductive age who are diagnosed with cancer as early as possible [8, 10]. The value of early referral for fertility preservation in cancer patients is multifold. Early referral allows for earlier initiation of cryopreservation cycles and in some cases multiple cycles. Undergoing multiple cycles increases the number of eggs that can be retrieved and used for fertility treatment in the future [65]. In addition, early referral allows some

women to take advantage of a window of opportunity between early treatment that does not affect fertility (e.g., some surgeries) and the start of potentially gonadotoxic treatment regimens such as chemotherapy or radiation. In a study of breast cancer patients, women who were referred pre-surgery were able to start their chemotherapy regimens sooner than those who were referred to an infertility specialist for fertility preservation after surgery [65]. This earlier start to chemotherapy may benefit the patient and yield better outcomes for their cancer diagnosis [65].

Fertility counseling at time of diagnosis.

Loss of fertility has been reported to be almost as important to reproductive aged women diagnosed with cancer as concerns about survival [6, 77]. Although communication of the potential risks of cancer treatment on future fertility is a significant concern to many women, the quality of such conversations with their doctors is variable. ASRM and ASCO recommend doctors have these discussions with all their patients of reproductive age [8-10]. In a survey of oncologists however, only 14% reported always, or almost always giving educational materials about fertility preservation to their patients [12]. Among physicians who gave educational materials to their patients, only 27% thought that these materials were relevant to the patient's cancer diagnosis [12].

In a study of patient satisfaction with the discussion of how cancer treatment could affect their reproductive health, over half of the women reported the conversation lasted between 1 and 10 minutes [78]. Conversations that lasted greater than 10 minutes were most likely to occur in gynecologic cancer practices [78]. Additionally, only 14% of women reported being encouraged to talk to a fertility specialist regarding fertility

preservation options [78]. Women who have more information about their options regarding fertility preservation and the effects of cancer treatment on fertility report less decisional conflict and regret regarding fertility related issues [78, 79]. Usually, the discussion about how cancer treatment could affect fertility and reproductive health is physician initiated, highlighting the importance of the physician's role in communicating this information [78].

DISPARITIES IN HEALTH

Health outcomes and access to care.

Health disparities have been described in many different ways. Healthy People 2020 defines a health disparity as "a particular type of health difference that is closely linked with social, economic, and/or environmental disadvantage" [80]. These disadvantaged groups experience adverse health outcomes systematically based on group membership [80, 81]. Two of the factors contributing to health disparities are differential access to and utilization of the medical system [23, 82]. There are many reasons for differences in the use of medical services by various groups. Some of the reasons documented in the literature that span across many health conditions include lack of awareness about treatments and services, lack of access to these services, and lack of trust of the medical system as a result of perceived discrimination in the past as well as historical injustices [23]. In studies of access to healthcare, African American and Hispanic individuals report more difficulty accessing care compared to white individuals [83]. Identifying factors that cause disparities in access to healthcare information is important, especially because it can be modified through communication. Identifying

groups that are underutilizing a medical service because of lack of information can highlight an area where change can be made by physicians and other health care professionals to improve both the quantity and quality of health information provided to these groups. Critical gaps exist in understanding disparities in accessibility to and utilization of fertility treatment and preservation.

Health seeking models.

Health behavior and health seeking models have been used to explain differences in utilization of health services across different health outcomes [23]. The general hypothesis of the Health Belief Model is that 2 things affect whether a behavior will occur: 1) a certain value placed by an individual on a particular goal and 2) the individual's estimate of the likelihood that a given action will achieve that goal [84]. In the context of infertility, the driving factors leading to seeking help for infertility could be 1) the desire to become pregnant and 2) the belief that seeking fertility counseling will result in an increased chance of becoming pregnant. The Health Belief Model is multidimensional and is comprised of perceived susceptibility and perceived severity of the health outcomes, as well as perceived benefits and perceived barriers of getting medical attention for the health outcome. The susceptibility of an individual to infertility and the severity of the condition are difficult to recognize. Unlike acute health outcomes, such as a heart attack, infertility does not present itself as the appearance of new and undesired symptoms, but rather is characterized by an absence [23]. This characteristic of infertility makes health seeking behavior for its treatment more complex than acute diseases.

Measuring health disparities.

Fertility treatment.

As fertility treatment becomes more common and more successful in helping women become pregnant, a new area for disparity has emerged [45]. Some women are able to utilize available treatments to help them become pregnant, whereas others are not as a result of factors such as cost, discomfort with infertility treatments, or access to fertility care [24, 45]. Quantifying this disparity is difficult, however, because help seeking behavior by women who are infertile is different from many other health problems in that not all who experience the condition need medical attention. Some women who are infertile will have already completed their family while others do not want to have any children. Help seeking behavior for infertility care therefore is limited to those women who have not completed their desired family size and are comfortable with the use of assisted reproductive technology to become pregnant. Only about half of couples who experience clinical infertility (1 year of trying without a pregnancy) seek help for getting pregnant [85].

Although there are many factors that may prohibit women from utilizing fertility treatments (e.g., insurance coverage, cost, comfort with treatment methods), all women should be able to receive information on these treatments. Yet, disparities remain in who goes to a doctor for help becoming pregnant [21, 24]. Studies have reported that African American women are less likely to use medical treatment for their infertility compared to white women [5, 24]. Among women who do seek medical help to become pregnant, African American women wait longer to seek care after difficulty becoming pregnant

compared with white women [22, 24, 86]. This delay in seeking help for becoming pregnant may affect the success and availability of certain infertility treatments. Even in places where there is mandated coverage for infertility treatment, women accessing these services have higher education and income and are more likely to be white compared to those who do not [16]. Thus, even when the burden of the cost of these treatments is reduced, disparities remain in who accesses them [16, 87]. Some of this lack of utilization may also come from cultural norms that attach stigma to infertility or from lack of information on the types of treatments available [21]. Both of these barriers to treatment can be addressed by 1) identifying which groups of women are not receiving the information they need to make informed decisions about their fertility, 2) determining the reasons why these women are not receiving this important information, and 3) increasing providers' awareness that these women need more information about infertility and fertility treatment options. Using data from the FUCHSIA Women's Study, we will be able to describe the characteristics of women who are not visiting a doctor to receive information on fertility treatment. Identifying these characteristics in women can be used to target interventions and recommendations more precisely and help these women overcome information-based obstacles to treatment. This is an advantage over prior clinic-based studies that were limited to women seeking care [22, 88].

Assisted reproductive technology outcomes.

There are differences in the pregnancy outcomes among black and white women who use assisted reproductive technology. For example, African American women have less success with ART compared to white women [24, 86, 87]. There have been some

studies that report no difference in pregnancy outcomes after IVF, but these studies have been small overall and small numbers of African American women were included [89, 90]. Since African American women underutilize ART services, these results have limited generalizability [91]. In a large clinic-based study that utilized data from the Society for Assisted Reproductive Technology Clinic Outcome Reporting System database, authors found significant disparities by race and ethnicity in ART outcomes [86]. Adjusting for maternal age, number of embryos transferred, male factor infertility, and several female reproductive conditions that can cause infertility, compared to white women, Asian, black, and Hispanic women were 10%, 38%, and 13% less likely to have a live birth after ART, respectively [86].

Fertility preservation methods.

Advances in fertility preservation methods have opened this option up to more women [9]. Women who were not candidates previously because of lack of a male partner and unwillingness to use donated sperm can now freeze eggs instead of embryos [8]. Female cancer patients who could not pursue fertility preservation because the time to stimulate the ovaries to harvest mature eggs can now take advantage of expedited stimulation protocols, which result in shorter times to harvest eggs [66]. Yet, fertility preservation is still a rarely used medical procedure with only about 4% of female cancer patients pursuing this type of treatment [25].

Despite the recommendations for universal fertility counseling by ASRM and ASCO, disparities exist in who receives information on fertility preservation methods [13, 25]. A recent review reported that among men and women diagnosed with cancer

between 34% and 72% recall being counseled on how their disease and treatment would affect their fertility [11]. In a national survey of oncologists, only about half consistently refer patients who are diagnosed during their reproductive years to a reproductive endocrinologist or infertility specialist [92]. Among physicians who do not routinely refer, characteristics of the patient can influence the decision to refer. Studies exploring these differences have been limited to women diagnosed with cancer types that are most likely to receive treatment shown to adversely affect fertility. These studies found associations between age, race, parity, and education and receipt of fertility counseling [13, 25]. These studies suggest that oncologists are using certain patient characteristics to decide which cancer patients receive fertility counseling.

STUDY POPULATIONS

The Furthering Understanding of Cancer, Health, and Survivorship (FUCHSIA) Women's Study is a population-based cohort study of women of reproductive age who have been treated for cancer compared with women of the same age who have never experienced cancer treatment. Cancer survivors in the FUCHSIA Women's Study were identified through the Georgia Cancer Registry. Cancer survivors were eligible to participate in the study if they were: female, diagnosed between the ages of 20-35 years, diagnosed with any malignant cancer or in situ breast cancer, able to complete the telephone interview in English, and 22-45 years old at the time of the interview. Comparison women, who were never diagnosed with cancer, were recruited from a purchased list frequency matched on the distribution of age and area of residence of the cancer survivors. There were a total of 1282 cancer survivors and 1071 comparison women who completed the telephone interview.

The FUCHSIA Women's Study used a computer-assisted telephone interview to collect information on study participants [93]. The interview took approximately 1 hour to complete. It collected detailed information on various health topics including menstrual function, desire for children, infertility, pregnancy, reproductive surgeries, hormone medications, medical conditions and lifestyle.

The National Survey for Family Growth is a US based survey that is conducted in a nationally representative sample of individuals by the National Center for Health Statistics at the Centers for Disease Control and Prevention. The NSFG was first conducted in 1973 to gather information on marriage, divorce, contraception, infertility, and the health of women and infants [26]. The survey is conducted in cycles with the last cycle of completed interviews taking place between 2006 and 2010 [26]. During the 2006-2010 cycle, a national sample of 22,682 men and women between the ages of 15-44 years were interviewed [26]. There were approximately 10,000 interviews among men and 12,000 among women [26].

CONTRIBUTIONS

This dissertation will contribute to the existing literature in several ways. The FUCHSIA Women's Study is a population-based study and represents a diverse group of women. The study population is reflective of the demographic make-up of Georgia and so includes a high proportion of black participants, who are a traditionally underrepresented group. Women also participated from all across the state, so there is representation from women living in areas with differing levels of urbanization. Data from these participants can help shed light on the characteristics of women who do not

receive the fertility counseling and care they may desire. Currently, the literature on disparities in fertility care seeking is dominated by clinic-based studies, so results from the FUCHSIA Women's Study will add a large population-based study to the clinic-based literature. Our studies focus on describing the characteristics of women who do and do not seek or receive medical care for help getting pregnant and can describe overall disparities, not just disparities among help seekers, which is the population clinic-based studies are limited to examining. In addition to disparities in the use of fertility care in the general population, we will be able to address disparities in fertility-related care among reproductive age cancer survivors. We will use the NSFG to compare the results from the FUCHSIA Women's Study to a nationally representative sample.

Using the cancer survivors in the FUCHSIA Women's Study we will examine disparities in the receipt of critical information on the effects of cancer treatment on fertility and fertility preservation options among the cancer survivors in our study. There are gaps in the literature with regard to fertility preservation counseling and utilization among cancer survivors. Many studies limit inclusion into the study based on certain types of cancers while other types of cancers are understudied [25]. In addition, several studies in this area of research are fertility clinic-based. These studies only include women who have sought help for their infertility and do not provide any information about infertile women from a population level [22, 23, 86, 88].

Fertility treatment and preservation methods are procedures that have the potential to improve the quality of life of women who face infertility. While fertility treatment and preservation methods can help to treat or prevent infertility in some women, information

on these methods is not universally available [25, 92]. All women who want or may want to have children should be given the opportunity to receive information about fertility treatment and preservation methods; however there is sometimes a lack of access to fertility counseling which contributes to disparities in treatment utilization. Using data from the FUCHSIA Women's Study and NSFG, we will be able to identify women who are underserved in the areas of fertility counseling, treatment, and preservation.

CHAPTER 3: Racial Disparities in Seeking Care for Help Getting Pregnant

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Abbreviations: ART: assisted reproductive technology; CI: confidence interval; DAG: directed acyclic graph; FUCHSIA Women's Study: Furthering Understanding of Cancer, Health, and Survivorship in Adult Women's Study; HR: hazard ratio; IVF: in vitro fertilization; RR: risk ratio; STI: sexually transmitted infection; US: United States

Running Head: Racial Disparities in Infertility Care

ABSTRACT

Fertility counseling and treatment can help women achieve their desired family size, however, disparities exist in the utilization of this care. This study examines the persistence of a racial disparity in visiting a doctor for help getting pregnant by estimating the direct effect of this association using data from the FUCHSIA Women's Study, a population-based cohort study. This cohort included 1073 reproductive age women (22-45 years) with 28% reporting infertility. We fit log binomial models to quantify the magnitude of the racial difference in reported care seeking after adjustment for hypothesized mediators using inverse probability weighting. Compared with white women, black women were less likely to visit a doctor in the total population [adjusted risk ratio (aRR) = 0.57, 95% confidence interval (CI): 0.41, 0.80] and in the subgroup of women with infertility [aRR = 0.75, 95% CI: 0.56, 0.99]. In addition, black women waited twice as long on average before seeking help compared with white women. There were notable racial differences in visiting a doctor for help getting pregnant in this study although reports of infertility were similar by race. These differences may be mitigated through improved communication about the range of counseling and treatment options available.

Keywords: care seeking; disparities; infertility; race

INTRODUCTION

Infertility and impaired fecundity affect millions of women in the United States. Estimates of the prevalence of infertility range from 6%-15% among women of reproductive age [33, 94]. The burden of infertility and impaired fecundity affects women across demographic groups and exists unnoticed among women not actively trying to get pregnant [2, 95]. This inability to conceive or carry a baby to term affects the quality of life of women. Infertility, however, is not just a quality of life issue, the American Society for Reproductive Medicine (ASRM), World Health Organization, and International Committee for Monitoring Assisted Reproductive Technology classify infertility as a disease of the reproductive system [3, 4]. National organizations have been established to provide support for those suffering from infertility and education to the public at large [96]. Recently, focus has been directed towards addressing the causes of infertility from a broader societal perspective [97]. The Centers for Disease Control and Prevention developed a National Action Plan to address the detection, prevention, and management of infertility at the population level [98].

In the most recent cycle of the National Survey for Family Growth, 12% of female participants, representing 7.4 million women in the US, reported ever using medical services for infertility. These services ranged from advice, to provision of medications, to in vitro fertilization (IVF) [5, 44]. Counseling provides information to optimize chances of natural conception, as well as guidance about more involved procedures. For example, controlled ovarian hyperstimulation with injectable gonadotropins and timed intercourse or intrauterine insemination are often successful in younger women, but are also associated with a higher risk of multiple gestations [99,

100]. Whereas IVF, which is more invasive and expensive, when performed using single embryo transfer, has a higher ongoing pregnancy rate and lower risk of multiple gestations compared with other less invasive treatments [101, 102]. This information is essential to making informed decisions about medical care for getting pregnant.

Healthy People 2020 describes health disparities as not only differences in a health-related outcome, but differences that systematically and adversely affect disadvantaged populations [80, 81]. The social construct of race which represents a combination of factors including, appearance, culture, and social factors has been used as the basis for discrimination and perpetuating disadvantage [103]. In the US, black race is associated with a history of unequal treatment, exposure to racism, deprived neighborhoods, and lack of socioeconomic opportunity. These exposures have led to racial disparities in health and health related outcomes [104-106]. According to the National Survey for Family Growth, among married women, black women are more likely to report infertility compared with white women. Further, racial disparities exist in the utilization of infertility treatments with non-Hispanic white women most likely to receive treatment [5, 33]. As fertility counseling and treatment become more common and more successful in helping women become pregnant, a new area for disparity has emerged [45].

Gaps remain in understanding disparities in the accessibility to and utilization of infertility counseling and treatment. The preponderance of the literature is in clinic-based studies and only provides information on the subgroup of help-seeking women with infertility. Even among women who do seek medical help to become pregnant, studies have found that black women wait longer to seek care after difficulty becoming pregnant

compared with white women [22, 24]. Infertility treatment may be cost prohibitive for some women, however, even in states where there are mandates that insurance coverage include infertility treatment, disparities by race and education persist [16, 107].

The primary objective of this paper is to assess the persistence of racial disparities after accounting for known mediating pathways of the association between race and seeking medical help for becoming pregnant. We also explore differences by race in the length of time women wait from when they first experience infertility to the time they visit a doctor for help becoming pregnant.

METHODS

We used data from the Furthering Understanding of Cancer Health and Survivorship in Adult (FUCHSIA) Women's Study. The FUCHSIA Women's Study is a population-based cohort study examining how cancer treatment during the reproductive years affects future fertility. It compares the reproductive experiences of female cancer survivors to a group of comparison women who never had cancer treatment. Comparison women were frequency matched on age and place of residence to the cancer survivors. Analyses for this paper utilize comparison women only because women who have been treated for cancer may have different access to and motivations for seeking medical care for help becoming pregnant compared with the general population, even if they did not receive treatment believed to impair fertility. Women were eligible to participate if they were 22-45 years old at recruitment, had a working telephone, and spoke English. Women were recruited to participate in the study independent of their fertility status, which allows us to examine infertility service use in the overall population and characterize participants who did and did not seek help for becoming pregnant. Women

consented to participate and completed the study interview by telephone. The study was approved by the Emory University and Georgia Department of Public Health Institutional Review Boards.

Defining race and racial disparities in health are challenging [108]. In this study, the exposure was designated as self-reported black race compared with self-reported white race. We used self-reported race to represent the composite of factors that make up the experience of being black in the US to estimate disparities attributable to this complex measure. The outcome was whether or not women accessed care for help getting pregnant regardless of whether they used treatment or not. It was determined by the question "Have you ever visited a doctor or health professional for help becoming pregnant?" We also collected information on periods of possible impaired fertility through the question "Has there ever been a period of time during which you had unprotected sex with a male partner for 6 months or longer but you did not get pregnant? Only count periods of time when you had sex at least 3 times per month." Participants who answered 'yes' to this question were classified as sub-fertile. Follow-up questions captured the total number of months of impaired fertility, age when it happened, whether the woman was actively trying to get pregnant at the time, if spontaneous conception occurred, and any recurrences. We used the age and total months of impaired fertility to define infertility. Women reporting a period of time lasting 12 months or longer between the ages of 20-34 years or a period of 6 months or longer at age 35 years or older when they had unprotected intercourse but did not get pregnant were classified as infertile. These determinations correspond to the ASRM definition of infertility, although their definition also includes that unprotected intercourse must be appropriately timed [109].

Interviewers collected information from women on their general health and reproductive experiences, as well as demographic and lifestyle characteristics. We asked women for their race, current level of education, total household income in the previous 12 months, and address at the time of the interview. We asked participants how many children they desired and how many children they had given birth to at the time of the interview. To gauge women's feelings about invasive infertility procedures, women were asked about their comfort with intrauterine insemination and IVF using a 5 point Likert type scale. Women also answered questions about diagnosis with reproductive conditions including polycystic ovary syndrome, fibroids, or endometriosis and about sexually transmitted infections (STIs) including chlamydia, gonorrhea, or pelvic inflammatory disease.

Many of the participant characteristics collected in the interview were considered mediators of the association between race and visiting a doctor for help getting pregnant in our directed acyclic graph (DAG) (*Figure 3-1*). Our main objective was to quantify the racial disparity that remains if the distribution of these sociodemographic factors were balanced between black and white women. To do this, we controlled for measured variables on all indirect paths between the social construct of race and visiting a doctor for help getting pregnant in a weighted analysis. Weights were created using the inverse probability of the participants' self-reported race based on their education, income, place of residence, comfort with assisted reproductive technology (ART), and history of reproductive conditions and STIs. The weights created a pseudo-population where hypothesized mediators were balanced between black and white women. For analyses conducted in the subgroup of women who reported infertility, age at infertility and

actively trying to get pregnant were also included in the estimation of the weights. Weights were scaled to represent the observed sample size. Values in the tails of the distribution (at the 5st and 95th percentile) were truncated to reduce the influence of extremely large or small weights in the analysis [110].

We fit generalized linear models with a log binomial distribution to estimate the total and direct effect of the social construct of race on visiting a doctor for help getting pregnant. To compare the results from our weighted analysis to traditional multivariable methods we fit a modified Poisson model with robust variances, because the log binomial model did not converge [111]. Assuming that the DAG depicts the true causal relationships, differences in the coefficients from the models with versus without adjustment for mediating variables represents the proportion of the total effect mediated by the specified paths [112].

To address possible differences by race in the time waited before visiting a doctor for help getting pregnant, we fit Cox proportional hazard models to estimate hazard ratios for visiting a doctor among women with infertility. The start time in these models was defined as the age at which women reported their first infertile period and the event time was the age at first doctor's visit. Women who did not visit a doctor were censored at age of hysterectomy, menopause, spontaneous conception, or interview. Survival models were adjusted for the same set of mediators as models in the main analysis using multivariable and weighted models. SAS 9.3 was used for all statistical analyses.

RESULTS

The FUCHSIA Women's Study comparison group included 1,073 women. Of these women, 309 were black (29%), 712 were white (66%) and 52 reported another race

(5%). Our analyses were restricted to women who reported black or white race. Characteristics of the sample by race are presented in *Table 3-1*. Median age at interview was 38 years for both black and white women. Black women in the study population had comparable education levels to white women, but lower household incomes. Most study participants resided in a large metropolitan area, with more white women reporting rural residence. The prevalence of STIs was higher among black women compared with white women (25% vs 5%) as well as the prevalence of fibroids (30% vs. 9%), while other reproductive conditions were more similarly distributed. Childlessness differed between the groups with 73% of black women and 84% of white women giving birth to at least one child at the time of the interview. Meeting reproductive goals also differed by race with over half of black women reporting they currently had fewer children than they desired compared with 39% of white women. The characteristics among the subgroup of women who experienced infertility were similar to the full sample (data not shown).

Of the 978 women who answered the question about experiencing impaired fertility, 44% reported a sub-fertile period, with similar reporting by race (*Table 3-2*). When using the stricter definition of infertility, the percentage dropped to 30% for black women and 28% for white women. Among the infertile, 67% of black women and 76% of white women reported primary infertility, or infertility before ever giving birth. Although report of this more restrictive period of infertility was similar by race, there were large differences in who was actively trying to get pregnant among this group. Thirty-two percent of black women and 67% of white women reported they were trying to conceive at the time of infertility.

Estimates of the total effect of the social construct of race on visiting a doctor for help getting pregnant showed that black women were less likely to have a visit [risk ratio (RR) = 0.42, 95% confidence interval (CI): 0.28, 0.64] (*Table 3-3*). This association remained in the subset of women who experienced infertility [RR = 0.48, 95% CI: 0.32, 0.71]. Estimates of the direct effect of race on visiting a doctor for help getting pregnant in the full sample using the weighted model was RR = 0.57, 95% CI: 0.41, 0.80. Among the subgroup of women who reported infertility, the weighted RR was 0.75, 95% CI: 0.56, 0.99. In multivariable models including the full set of mediators, the results were similar. The difference in the coefficients from the unadjusted and adjusted models represents 35% of the total effect explained by mediating paths in the full sample and 61% in the subgroup of women with infertility.

The distribution of ages at reported infertility cluster in the 20's for both black and white women with an overall median age of 26 years [interquartile range (IQR): 23-30]. Age at visiting a doctor for help getting pregnant among women with infertility is shifted towards the 30's with an overall median age of 29 years [IQR: 26-32]. Among women who visited a doctor after they reported infertility, white women waited a median of 1 year [IQR: 0-2] and black women waited 2 years [IQR: 0-4]. The unadjusted Kaplan-Meier plots show black women are less likely to have visited a doctor by the study interview (*Figure 3-2*). The maximum time women waited from first infertile period to visit was 12 years for both black and white women, however at this time 47% of white women and only 22% of black women had visited a doctor for help. The unadjusted hazard ratio (HR) for the association between race and visiting a doctor for help getting pregnant was 0.37, 95% CI: 0.22, 0.60 (*Table 3-4*). Adjusted models controlled for the

same mediators as the main models, restricted to infertile women. Using traditional adjustment, the estimated association moves towards the null [HR = 0.68, 95% CI: 0.39, 1.16], but the reduced likelihood of visiting a doctor remained. In the weighted model, the estimate was of a consistent magnitude as the fully adjusted model [HR = 0.70, 95% CI: 0.48, 1.03].

DISCUSSION

There were substantial racial differences in visiting a doctor for help getting pregnant in this study even though reports of impaired fertility were similar across race groups. To examine racial disparities in this paper, we used black race as the exposure in our analyses, recognizing that race is an amalgam of many different components. We were focused on aspects of the experience of black race in the context of the US as a result of cultural beliefs, experiences with discrimination, poor access to healthcare and economic opportunity among other factors. Our goal was to estimate the racial disparity that remained after accounting for a set of identified mediating paths from the social construct of race to visiting a doctor for help getting pregnant. We controlled for hypothesized mediators of this association, including sociocultural factors such as comfort with using assisted reproductive technologies, which other studies report differ by race [21, 22].

In the main analysis, we included all women regardless of their infertility status to get a picture of the overall disparity in infertility service use. In our study, 9% of women who reported visiting a doctor for help getting pregnant never reported experiencing infertility. We addressed those most likely to need medical help for getting pregnant in the analyses restricted to infertile women. In mediator-adjusted models, hypothesized

intermediate pathways were only able to partially explain the difference by race in visiting a doctor for help getting pregnant. Adjusted estimates from the survival analysis were consistent and showed that not only do black women visit the doctor for help getting pregnant less often than white women, they also wait longer after experiencing infertility. The fact that racial disparities persist despite control for mediating paths suggests that additional components that contribute to the social construct of race are influencing this association.

Sociocultural factors that were unmeasured in our study may explain some of the racial disparity we found. In our study we controlled for discomfort with ART, which only partially captures the stigmatization that may surround infertility for some women. In a fertility clinic-based study, black women were more likely to report that they were concerned about social stigmatization and disappointing a spouse because of their infertility [21]. Furthermore, black women were more likely to self-refer for care compared with white women, however we did not see this greater likelihood of self-referral in our study. The remaining racial disparity we observed could also be the result of unmeasured confounding. We did not hypothesize any factors in our DAG that would cause both race and visiting a doctor for help getting pregnant. All of the covariates considered were mediators of this association. It is possible that there were factors that were not identified that confound the association between some of the mediators considered and the outcome, which could be distorting the estimate of disparities we observed.

In our study, black women were less likely to be married or report they were trying to get pregnant during an infertile period compared with white women. However,

women who are not married or cohabitating may still want to have a child and women not actively trying may want children in the future. The broad definition of infertility we used enabled us to capture potential fertility problems in these women. While all women classified as having infertility in our study do not represent unmet need (e.g., women who do not desire children or have completed their family size) and some may be the result of mistimed intercourse, it is important to identify all women who are at possible risk of needing infertility services. Since fertility as well as the potential success of infertility treatments decline with age, there is a benefit to discussing infertility treatment options with younger women [113, 114]. For example, with IVF, the success rate of fresh non-donor cycles has been reported to be 40% in women 35 years and younger and only 1% in women 44 years and older [113]. Despite our broad inclusion criteria, models restricting to women who reported primary infertility and wanting to have at least one child still showed a racial disparity.

The FUCHSIA Women's Study was well suited to examine disparities by race. Women who participated in our study reflect the demographic composition of Georgia women of reproductive age (20-44 years), which is 34% black [115]. Therefore, black women, a traditionally underrepresented group, had good representation in this study. Categories of education, place of residence, and household income were also well represented. In addition, women were recruited to participate in the study independently of their fertility status. This is in contrast to clinic-based studies that can only describe disparities among women who visit a fertility clinic for help getting pregnant, giving our study the advantage of being able to compare women who did and did not visit a doctor for help getting pregnant.

We recruited women using a purchased marketing list which may have lacked information on some women we wanted to participate in our study. This may have been a source of selection bias, but comparison women were similar to cancer survivors on many factors including race. Another potential limitation is that the data are restricted to self-reported information on fertility discussions with healthcare providers without verification of these visits with medical records. However, we expect women are able to remember a self-initiated visit to the doctor for help getting pregnant and found in our pilot studies that women are able to consistently report information about their fertility and infertility treatments received [93].

Our study showed that even with control for an extensive list of hypothesized mediators a black/white racial disparity persisted. It is possible that stigma around infertility, which was unmeasured in our study, may be contributing to this disparity by limiting the sources of informal information and advice black women have access to in their social network. Better targeting of online resources, which have been suggested to be a preferred method of receiving information on stigmatized illnesses, could improve access to information on infertility and treatment [116]. Accessing information online is associated with women feeling more comfortable discussing infertility issues with their healthcare provider [117]. Initiation of conversations about available counseling and treatment options by a primary healthcare provider could also improve the exchange of information. This may decrease feelings of discomfort in visiting a specialist or using ART. Further, additional targeted outreach by organizations already in existence to fight stigma and improve knowledge about fertility problems, as well as support those suffering from infertility could be beneficial [96]. Provision of information on the wide

range of counseling and treatment options from different sources may decrease discomfort with infertility services, in turn reducing the disparity in their use, and help a greater number of women meet their reproductive goals.

Table 3-1. Demographic and Reproductive Characteristic of Participants in the FUCHSIA Women's Study by Race

Characteristic	Total women, no. n = 1,021	Black n = 309 %	White n = 712 %	*P* value[a]
Age at interview (years)				
22-29	64	7.1	5.9	0.74
30-39	552	53.1	54.5	
40-45	405	39.8	39.6	
Education				
Less than high school/ high school grad	50	6.5	4.2	0.06
Some college or technical school	238	24.3	22.9	
College graduate	381	31.7	39.8	
Some graduate school/ graduate degree	351	37.5	33.1	
Missing	1			
Income				
Less than or equal to $50k	279	41.6	21.8	<.0001
$50k - 100k	386	40.0	37.8	
$100k+	338	18.4	40.4	
Missing	4			
Place of residence				
Non-metropolitan	117	6.2	13.8	0.0001
Small metropolitan	158	12.3	16.9	
Large metropolitan	746	81.6	69.4	
Ever given birth				
Yes	822	72.5	84.0	<.0001
No	199	27.5	16.0	
Fewer kids than desired at interview[b]				
Yes	431	51.2	38.8	0.0003
No	583	48.8	61.2	
Missing	7			
Comfortable with assisted reproductive technology[c]				
Strongly agree	101	6.9	11.3	0.09
Agree	229	20.0	23.8	
Neither agree nor disagree	113	11.5	11.0	
Disagree	289	32.1	27.0	
Strongly disagree	280	29.5	26.9	
Missing	9			
Polycystic ovary syndrome				
Yes	80	5.5	8.9	0.07
No	937	94.5	91.1	
Missing	4			
Endometriosis				

Yes	91	7.5	9.6	0.28
No	927	92.5	90.4	
Missing	3			
Fibroids				
Yes	155	30.4	8.7	<.0001
No	861	69.6	91.3	
Missing	5			
Chlamydia				
Yes	94	21.0	4.1	<.0001
No	927	79.0	95.9	
Gonorrhea				
Yes	27	5.5	1.4	0.0002
No	994	94.5	98.6	
Pelvic inflammatory disease				
Yes	25	4.9	1.4	0.001
No	996	95.2	98.6	

[a] P-values were calculated using a chi square statistic.

[b] Fewer kids defined by subtracting the number of children a woman desired from the number of children she had at the time of the interview.

[c] Based on the question: "I would be/would have been comfortable with the idea of using assisted reproductive technology, such as in vitro fertilization or artificial insemination, to help me get pregnant."

Table 3-2. Proportion of Women in the FUCHSIA Women's Study Reporting Subfertility and Infertility[a]

Characteristic	Total women, no. n = 978	Black n = 292 %	White n = 686 %	*P* value[b]
Subfertility[c]				
Yes	432	45.6	43.6	0.57
No	546	54.5	56.4	
Infertility[d]				
Yes	278	29.8	27.8	0.54
No	700	70.2	72.2	
Actively trying[e]				
Yes	156	32.2	67.0	<.0001
No	122	67.8	33.0	

[a]Twenty-six white women and 17 black women had missing values for the question asking about impaired fertility.

[b] P-values were calculated using a chi square statistic.

[c]Subfertility: A period of time lasting at least 6 months when a women was having regular unprotected intercourse, but did not get pregnant.

[d]Infertility: A period of time lasting at least 6 months at or after age 35 years or at least 12 months between the ages 20-34 years when a woman was having regular unprotected intercourse, but did not get pregnant.

[e]Actively trying to get pregnant among those with infertility during the reported infertile period.

Table 3-3. Crude and Adjusted Risk Ratios of the Association Between Race and Visiting a Doctor for Help Getting Pregnant in the FUCHSIA Women's Study

	Women visiting a doctor, no.	Total women, no.	Unadjusted		Adjusted[a]		Weighted[b]	
			RR	95% CI	RR	95% CI	RR	95% CI
All women								
White	136	712	1.00	reference	1.00	reference	1.00	reference
Black	25	309	0.42	0.28, 0.64	0.54	0.35, 0.81	0.57	0.41, 0.80
Infertile women[c]								
White	97	191	1.00	reference	1.00	reference	1.00	reference
Black	21	87	0.48	0.32, 0.71	0.76	0.52, 1.11	0.75	0.56, 0.99

Abbreviations: RR: risk ratio; 95% CI: 95% confidence interval

[a]Adjusted: traditional adjustment for education, income, place of residence, comfort with ART, reproductive conditions, and sexually transmitted infections (models with the infertile group of women also included age at start of infertility and whether or not women were actively trying to get pregnant at the time they reported infertility); adjusted models use modified Poisson model because the log binomial model failed to converge

[b]Weighted: data were weighted by the inverse probability of being exposed (black race); probabilities were calculated as a function of the mediators from the adjusted models

[c]Infertile women: Women who reported a period of time lasting at least 6 months at or after age 35 years or at least 12 months between the ages 20-34 years when a woman was having regular unprotected intercourse, but did not get pregnant.

Table 3-4. Crude and Adjusted Hazard Ratios of the Association Between Race and Visiting a Doctor for Help Getting Pregnant in the FUCHSIA Women's Study

	Women visiting a doctor, no.	Total women, no.	Unadjusted		Adjusted[a]		Weighted[b]	
			HR	95% CI	HR	95% CI	HR	95% CI
Infertile women[c]								
White	97	191	1.00	reference	1.00	reference	1.00	reference
Black	21	87	0.37	0.22, 0.60	0.68	0.39, 1.16	0.70	0.48, 1.03

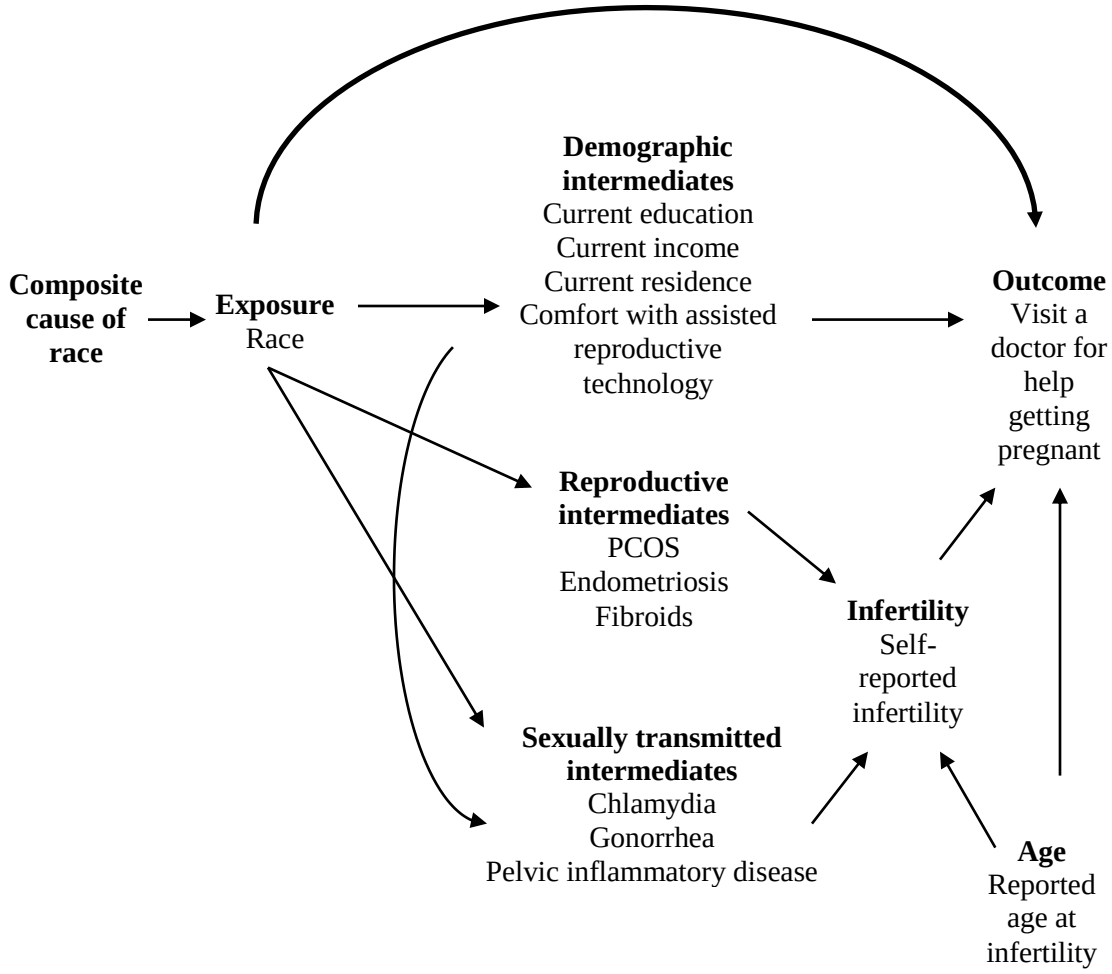
Abbreviations: HR: hazard ratio; 95% CI: 95% confidence interval

[a]Adjusted: traditional adjustment for education, income, place of residence, comfort with ART, reproductive conditions, sexually transmitted infections, age at start of infertility, and whether or not women were actively trying to get pregnant at the time they reported infertility

[b]Weighted: data were weighted by the inverse probability of being exposed (black race); probabilities were calculated as a function of the mediators from the adjusted models

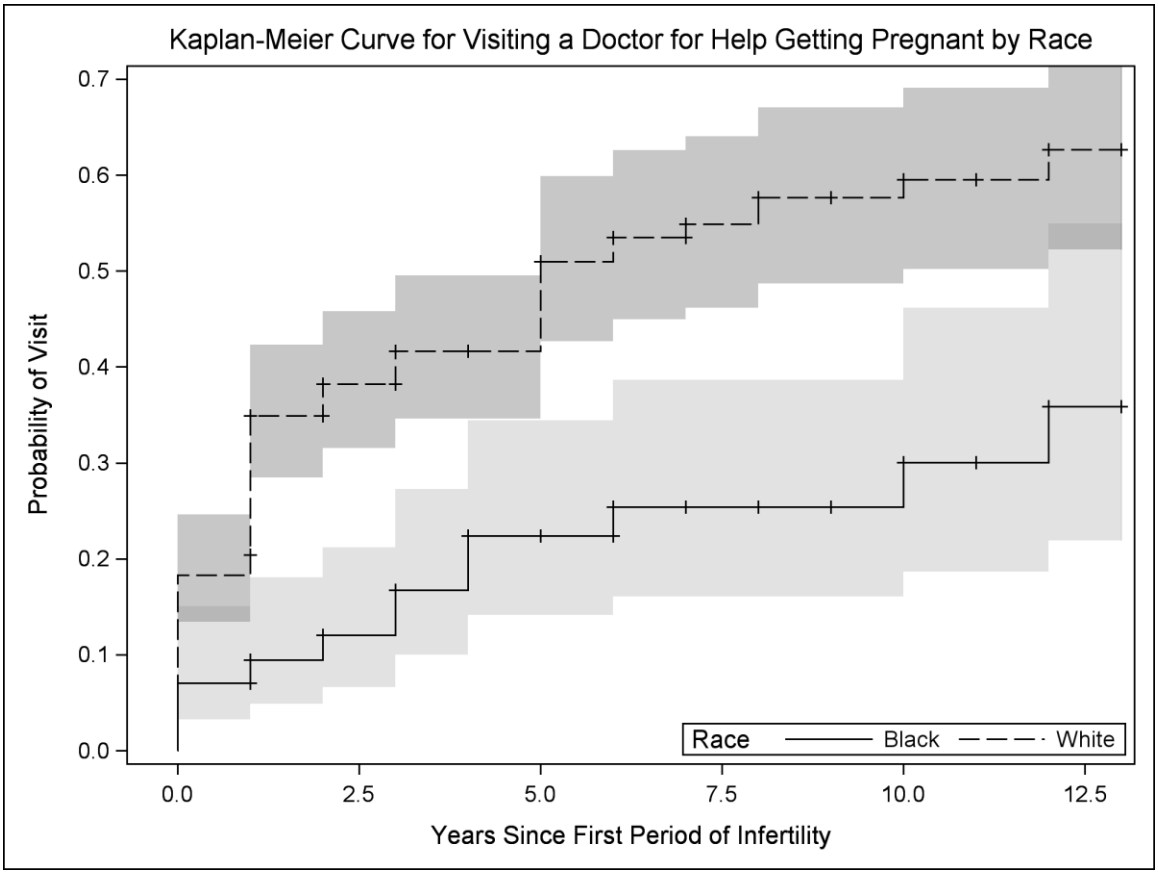
[c]Infertile women: Women who reported a period of time lasting at least 6 months at or after age 35 years or at least 12 months between the ages 20-34 years when a woman was having regular unprotected intercourse, but did not get pregnant.

Figure 3-1. Directed Acyclic Graph of the Relationship Between Race and Visiting a Doctor for Help Getting Pregnant in the FUCHSIA Women's Study[a]



[a]Bold line indicates the direct effect of the exposure on the outcome.

Figure 3-2. Unadjusted Survival Curves for Visiting a Doctor for Help Getting Pregnant by Race in the FUCHSIA Women's Study



CHAPTER 4: Differences in Women's Use of Medical Help for Becoming Pregnant by the Level of Urbanization of County of Residence in Georgia

ABSTRACT

Objective: The goal of this study was to determine if there are differences by geographic type of residence in visiting a doctor for help getting pregnant in a population-based study.

Methods: Using data from the FUCHSIA Women's Study, a cohort study of fertility outcomes in reproductive aged women, we fit log binomial and modified Poisson models to estimate the association between the level of urbanization of the county were a woman lived and seeking help for becoming pregnant. This association was assessed using a two and four category classification scheme.

Results The prevalence of visiting a doctor for help getting pregnant ranged from 13-17% across all geographic groups examined. The greatest differences were seen using the four category classification, where adjusted estimates revealed that women living in suburban counties were most likely to seek medical care for help getting pregnant compared with women living in urbanized counties (adj. PR = 1.16, 95% CI 0.75, 1.80); among women who reported infertility this difference was more pronounced (adj. PR = 1.59, 95% CI 1.00, 2.53). Women who reported infertility and lived in a small metropolitan county were also more likely to seek fertility care (adj. PR = 1.36, 95% CI 0.80, 2.30), while women in rural counties were equally likely to seek fertility care compared with women in urbanized counties (adj. PR = 1.09, 95% CI 0.55, 2.17).

Conclusion Our results suggest that women living in the most rural and most urbanized counties access medical care for help getting pregnant less frequently than women in

suburban and small metropolitan counties. Increased communication about infertility treatment by providers who women see for regular care may help decrease this disparity.

INTRODUCTION

The ability to have a biologic child is important to many women of childbearing age, and experiencing infertility can lead to a decreased quality of life. Infertility counseling and treatment may help some women who are unable to conceive naturally become pregnant. Although medical care for infertility encompasses a wide range of services, much of the literature on tracking infertility service use to date has focused on use of in vitro fertilization (IVF) [18, 19]. Less is known about geographic differences in overall medical care for infertility, which includes IVF, but also includes counseling and less invasive procedures such as use of medications to stimulate ovulation. According to the National Survey for Family Growth (NSFG), 17% of reproductive-aged women in the United States reported ever using an infertility service from 2006-2010 [5]. Among these women, advice and infertility testing were the most commonly reported services used [5].

There has been an overall increase in the use of infertility care since 1982 when the NSFG began collecting this information, yet not all women who need medical help to get pregnant are getting the assistance they need. Underutilization of infertility services may be a result of many factors including discomfort with certain procedures, high cost, and lack of awareness of the range of options available [21, 22, 118]. The Centers for Disease Control and Prevention (CDC) recently released a National Public Health Action Plan to address the detection, prevention, and management of infertility; one of its objectives is to eliminate disparities in access to treatment for infertility [98]. Where a woman lives may be a factor contributing to these disparities.

There are several documented barriers to access to medical care in rural areas. These areas often have fewer healthcare providers per population served compared with

urban areas. This limits the number of providers to choose from and types of doctors available for specialized care [119-121]. Rural areas also have low population density, which often results in longer travel times to visit a doctor, increasing the time commitment needed to seek medical care [122]. For example, most women living in areas of the country that are highly urbanized are within 60 minutes of a fertility clinic, while women living in more sparsely populated areas have longer travel times to reach specialized fertility care [19]. Further, rural residence is also associated with lack of insurance or insurance instability which may limit women's ability to seek care. Even with insurance, many treatments are not covered [107, 123, 124]. At the population level, insurance coverage affects women's use of fertility counseling and treatment. In states where there is mandated insurance coverage for infertility care, rates of use of assisted reproductive technology (ART) have increased more rapidly than in states without mandates. However, in some subgroups, including black women, women with less education, and women with lower income, ART use remains low [107, 125]. The combination of both physical and financial barriers make accessing medical care in some rural and remote areas challenging.

Little is known about differences by geographic type of residence and seeking medical advice and treatment for infertility. In this paper, we seek to determine if a geographic disparity exists in visiting a doctor for help becoming pregnant among a population-based sample of reproductive-aged women in Georgia. The objectives of this study are to assess the overall association between the level of urbanization of the county where a woman lives and seeking fertility care or counseling and to describe differences in the type of provider accessed and infertility service utilized.

METHODS

We used data from the Furthering Understanding of Cancer Health and Survivorship in Adult (FUCHSIA) Women's Study to address our study objectives. The FUCHSIA Women's Study is a population-based cohort study to examine how cancer treatment affects the fertility of female cancer survivors who were diagnosed during their reproductive years. Women who never had cancer were recruited as a comparison group frequency matched on age and place of residence to the cancer survivors. For this paper we restricted the analysis to comparison women only, because women who have been treated for cancer, in general, have increased contact with medical care compared with the rest of the population, which may also facilitate engaging with the medical system to address infertility. Further, treatment for cancer may have included receiving information on or referrals for fertility preservation and treatment. Women were eligible to participate if they were 22-45 years old at recruitment, had a working telephone, and spoke English. They were recruited independent of their fertility status. Women consented to participate and completed the study interview by telephone. The study was approved by the Emory University and Georgia Department of Public Health Institutional Review Boards.

Geographic type of residence was defined based on the 2013 National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme [126]. This classification scheme categorizes counties into one of six groups based on level of urbanization. Four of these groups fall under metropolitan: large central, for counties with at least 1 million residents that also contain the largest principal city of the metropolitan statistical area (MSA), have their entire population contained in the largest principal city of the MSA, or have at least 250,000 people in any principal city in the MSA; large fringe, for counties

that have at least 1 million residents, but do not meet the additional criteria for large central; medium, for counties in an MSA with populations between 250,000 and 999,999 residents; and small, for counties in an MSA that have less than 250,000 residents. The remaining two groups are non-metropolitan. Micropolitan counties fall in a micropolitan statistical area (between 10,000 and 49,999 residents) and noncore counties are those that are smaller than a micropolitan area.

For this study, participants address at the time of the interview was used to construct the exposure variable describing the level of urbanization of participants' residence. The 6 level NCHS scheme was collapsed into larger groups to create two new classification schemes (*Figure 4-1*). The first scheme used a four category classification, where the first two categories were maintained from the original scheme (large central and large fringe), but are referred to in this paper as urbanized and suburban counties, respectively. The third category combined medium and small metropolitan counties into one group, small metropolitan. The fourth category encompassed all non-metropolitan counties to form a small town/rural category. The second scheme collapsed the four categories further into two groups. The first group, large metropolitan, was created by combining urbanized and suburban counties. The second group, small/non-metropolitan, was created by combining the small metropolitan and small town/rural groups. The outcome for this study was defined directly from a question on the interview which asked "Have you ever visited a doctor or health professional for help becoming pregnant?" This question was asked of all participants regardless of marital status or reported infertility.

The interview also contained questions that allowed us to capture information on the characteristics of the study participants, to include race, current level of education,

and total household income in the previous 12 months. Information on type of health insurance at the time of the interview was used as a proxy of health insurance status at the time women may have wanted to visit a doctor for help getting pregnant. In addition, women were asked if they knew whether their insurance included full or partial coverage for fertility treatment. Women reported if they had any experience with infertility and the ages at which it occurred. Infertility was defined as reporting a period of time lasting 12 months or longer between the ages of 20-34 years or a period of 6 months or longer at age 35 years or older when they had unprotected intercourse at least 3 times per month, but did not get pregnant. This definition is similar to that of the American Society for Reproductive Medicine, although their definition also includes that unprotected intercourse must be appropriately timed [109]. To capture some of the cultural aspects that may be affecting women's decision-making, women were asked their feelings about adoption, use of invasive infertility treatments, and importance of having a biologic child using a 5 point Likert-type scale.

Data Analysis

SAS 9.4 (Cary, NC) was used for all statistical analyses. We examined participant characteristics by county geographic category and by visiting a doctor for help getting pregnant. Among those with the outcome, we also described type of doctor visited and type of infertility service used. Log binomial models were fit to estimate a prevalence ratio (PR) for visiting a doctor for help getting pregnant for each of the county of residence classification schemes. Modified Poisson regression with robust variances was used in cases where the log binomial model did not converge [111]. Models were fit for both the total population and restricted to the subgroup of women who reported ever

experiencing infertility, to assess the association between level of urbanization of county of residence and visiting a doctor for fertility counseling and treatment among those most likely to need help. Visiting a doctor for help getting pregnant among women living in small and non-metropolitan counties was compared with women living in a large metropolitan county. Similarly, the prevalence of visiting a doctor among participants from suburban, small metropolitan, and small town/rural counties were each compared with visiting a doctor among participants from an urbanized county.

Based on the literature and a causal diagram created for this study, we determined important covariates of the association between place of residence and visiting a doctor for help getting pregnant. The first set of models controlled for race (black, white, other race), education (college or greater, less than college degree) and income (less than $50k, $50-100k, $100k+). These demographic factors were hypothesized as confounders of the association being evaluated. In the second set of models, we additionally controlled for women's comfort with ART and adoption, how important it was to have a biologic child, insurance status (private, public, self, none), and among the subgroup who reported a period of infertility, age at infertility. Information on comfort with ART and adoption as well as the importance of having a biologic child were collected on a Likert type scale, but responses were dichotomized for inclusion in models. These additional variables were hypothesized as important covariates of the association between type of place of residence and visiting a doctor for help getting pregnant, but not as traditional confounders, so were included in a separate model.

RESULTS

For this study 1073 comparison women from the FUCHSIA Women's study were included in the analysis. The characteristics of the sample by four category place of residence are presented in Table 4-1. The age at interview was similar by type of metropolitan residence (median age between 38-39 years). We had good representation by race in the overall study population although when we stratified by our exposure we found less diversity in the small town/rural and small metropolitan counties, which is consistent with state demographics [127]. Participants from urbanized counties were most likely to have at least a college degree and had the highest household incomes of the four metropolitan categories. Small town/rural and small metropolitan counties had the most uninsured and publicly insured women. The majority of women across all four categories did not know if their insurance policy covered fertility treatment (small town/rural: 72.6%, small metropolitan: 65.5%, suburban: 70.0%, urbanized: 71.5%). Participants from small town/rural counties reported experiencing infertility the most (36.8%) and participants from suburban counties reported infertility the least (20.6%). Age at infertility ranged from 25 to 28 years old across the four groups. Compared with women living in urbanized counties, women from small town/rural counties reported less comfort with assisted reproductive technology (ART), but greater comfort with adoption (*Figure 4-2*). The importance of having a biologic child was similar across all four geographic categories, with most women reporting that this was very important to them.

Table 4-2 presents the characteristics of doctor visits for fertility counseling and treatment. The crude proportion of women visiting a doctor for help getting pregnant ranged from 13% in the small town/rural counties to 17% in the suburban counties. Among women who visited a doctor for help getting pregnant, women in small

town/rural counties reported doing so at the youngest ages (median 27 years, interquartile range (IQR) 24, 30), while women from urbanized counties reported the oldest ages (median 30.5 years, IQR: 27, 34.5). Many women saw more than one type of healthcare provider. For most women this included visiting their obstetrician/ gynecologist. Women living in small metropolitan counties were the most likely of the four groups to report visiting their general practitioner for help (20%). Sixty percent of women from urbanized counties reported visiting a fertility specialist compared with 33% in small town/rural counties. Residents of urbanized and suburban counties also reported more use of alternative medicine with 14% reporting a visit to an acupuncturist or naturopath compared with 5% among small town/rural and small metropolitan residents. Type of treatment received also differed by level of county urbanization. Women from small town/rural and small metropolitan counties were more likely than those from urbanized or suburban counties to receive medications, but less likely to receive testing alone or IVF. Participants who lived in small town/rural and urbanized counties reported surgery more than the other two groups. Women who reported receiving the most invasive treatment procedure, IVF, differed by type of county of residence with 20% of women from urbanized, 15.2% from suburban, 12.5% from small metropolitan, and no women from small town/rural counties reporting receipt of this treatment modality. Receipt of counseling only and insemination was similar across groups.

In the full sample, using the two category classification scheme, the unadjusted models showed women from small and non-metropolitan counties were less likely to visit a doctor for help getting pregnant compared with large metropolitan county residents, prevalence ratio (PR) = 0.82, 95% confidence interval (CI): 0.59, 1.14 (*Table 4-3*).

Adjustment for demographic factors (*Model 1*) attenuated the association, adjusted (adj.) PR = 0.91, 95% CI 0.65, 1.28. The addition of variables measuring comfort with ART and adoption, importance of a biologic child, and insurance status to the model resulted in the estimate shifting closer to the null, adj. PR = 0.95, 95% CI: 0.67, 1.33 (*Model 2*). In unadjusted models restricted to women who experienced infertility, there was a similar, yet slightly more pronounced reduced likelihood of seeking fertility care or counseling among women from small and non-metropolitan counties compared with women from a large metropolitan county (PR = 0.73, 95% CI: 0.53, 1.02). Adjusting for demographic factors reduced the magnitude of the association (adj. PR = 0.80, 95% CI: 0.58, 1.09). Like results from *Model 2* in the full sample, including additional covariates in the model with infertile women only did not meaningfully change the estimate from the model fit with demographic factors alone.

Table 4-4 shows the results for the four category county level of urbanization classification scheme. Unadjusted estimates show women residing in small town/rural counties were less likely (PR = 0.89, 95% CI 0.48, 1.65) and women living in a suburban county were more likely (PR = 1.15, 95% CI: 0.74, 1.78) to visit a doctor compared with women living in an urbanized county. The prevalence ratio comparing women from a small metropolitan county to women from an urbanized county was null (PR = 0.94, 95% CI: 0.54, 1.63). In adjusted estimates the prevalence of seeking fertility care among women from small metropolitan and small town/rural counties were similar to that of urbanized counties. However, women living in suburban counties remained slightly more likely to visit a doctor compared with women from urbanized counties in all adjusted analyses.

Restricting to the infertile sample, there was a similar crude association across the four categories of county level of urbanization, with small town/rural county residents being less likely and suburban county residents being more likely to visit a doctor for help getting pregnant (PR = 0.76, 95% CI: 0.38, 1.54 and PR = 1.30, 95% CI: 0.77, 2.17, respectively). The unadjusted estimate comparing small metropolitan county residents to women living in an urbanized county was null (PR = 1.06, 95% CI: 0.57, 1.94). Again, after adjusting for covariates, the increased likelihood of visiting a doctor for help getting pregnant among women from a suburban county compared with an urbanized one persisted (*Model 1*, adj. PR = 1.49, 95% CI: 0.93, 2.40 and *Model 2*, adj. PR = 1.59, 95% CI: 1.00, 2.53). Unlike models fit with the entire population however, women from a small metropolitan county showed an increased likelihood of visiting a doctor similar to that of the suburban residing participants (*Model 1*, adj. PR = 1.30, 95% CI: 0.74, 2.27 and *Model 2*, adj. PR = 1.36, 95% CI: 0.80, 2.30). Adjusted estimates comparing small town/rural residents with urbanized county residents were null.

DISCUSSION

This large population based study provides critical information about the relationship between women's access to fertility-related counseling and treatment and the level of urbanization of the county where they live. The proportion of women in our study who reported ever visiting a doctor for help getting pregnant ranged from 13-17% which is consistent with the national average of 15% among 22-44 year old female participants in the 2006-2010 NSFG. Differences in seeking fertility counseling and care were detected only among the infertile sample of women when using the two category classification of type of residence. Living in a small and non-metropolitan county was

associated with being slightly less likely to visit a doctor for help getting pregnant compared with living in a large metropolitan county. However, using the finer four category coding of the exposure, we were able to see differences masked in by the two category classification scheme. Among the full sample and women with infertility, living in a suburban county was associated with a greater likelihood of visiting a doctor for help getting pregnant. The most notable differences were again among the women who reported experiencing infertility. After accounting for differences in the distribution of participant characteristics by type of residence, women from small town counties became similar to the women from suburban counties in their use of medical care for help getting pregnant and small town/rural residents became more similar to urbanized county residents.

Some of the variables we controlled for in the analysis, specifically the demographic factors included in *Model 1*, we hypothesized may be confounders of the association between place of residence and visiting a doctor for help getting pregnant. There were additional variables that were not identified in the conceptual model for this study as confounders, but were considered important covariates and may be mediators of the association being evaluated. For example, they type of county where a woman lives might influence how she feels about having a child or more children, which in turn might affect her use of medical care to become pregnant. We used *Model 2* to assess the magnitude of the association between type of place of residence and visiting a doctor for help getting pregnant holding these potential mediators constant. Results from these models using the four category scheme for type of place of residence among the full sample did not differ from results from the confounder only adjusted models. In models

that were restricted to the subgroup of infertile women, however, there was a stronger association present after adjusting for potential mediators compared with adjusting for hypothesized confounders alone indicating that not controlling for these factors may be masking some of the effect.

Comfort with ART and adoption and the importance of having a biologic child, which were used as indicators of cultural concerns, showed differences between geographic groups. Moving from the least urbanized to most urbanized counties, there was a trend of increasing comfort with ART and decreasing comfort with adoption. When women were asked how important it was that they have a biologic child, however, the majority of women regardless of type of county of residence reported that this was very important to them. Discomfort with invasive procedures, which may be a partly due to lack of knowledge of these treatments, and limited access to certain specialists may constrain the range of treatment options women receive for help getting pregnant. Women living in small town/rural counties and small metropolitan counties were most likely to report receiving medications as part of their treatment, which may be a reflection of the type of healthcare provider they are seeing for care. Women living in these two types of places of residence all reported seeing their obstetrician/gynecologist for fertility care, who may have prescribed them with medications, since IVF would require referral to a fertility specialist and visiting an ART clinic.

A strength in our study was that women were recruited to participate independently of their fertility status, allowing for a comparison between women who did and did not visit a doctor for help getting pregnant. This is an advantage over fertility

clinic-based studies which are only able to describe women who seek help. All women interviewed were asked whether or not they ever visited a doctor for help getting pregnant, regardless of their marital or infertility status. Of those visiting a doctor for help getting pregnant, close to 10% never reported experiencing a period of infertility. Because the interview was extensively detailed, we were able to capture information not commonly collected in studies such as women's feelings about ART and adoption, as well as how important having a biologic child was to them. This information was used to describe some of the cultural and environmental factors that may differ by type of county of residence.

The sample size overall for this study was large, but once women were divided into four categories based on their type of place of residence, the sample size for each of these groups became small. The small sample within each category of our exposure variable caused many of our estimates to be imprecise; however, we focused on an issue that has been sparsely addressed in the literature. Studies looking at geographic disparities in use of medical help have focused on other health outcomes or access to only specialized care for becoming pregnant [19, 128-130]. Another limitation was that we were constrained to women's place of residence at the time of the interview, which on average, was 9 years after the age at visiting a doctor for help getting pregnant. On the population level, there has been an approximately 3.5% increase in the urban population in the state of Georgia between 2000 and 2010 [131, 132]. This shift in population towards urbanized counties means some women may be misclassified. Even among women who did move they may have moved from the same type of county as their current residence or visited a doctor after moving, and so would still be correctly

classified. Lastly, there may be unmeasured or unidentified confounding in our study. The second set of models controlled for both hypothesized confounders and potential mediators of the association between type of geographic place of residence and visiting a doctor for help getting pregnant. Confounders of the mediator and the outcome that were not included in our model may be distorting the estimate of differences in use of fertility care by type of place of residence we observed.

This study adds to the literature on disparities in access to care for help getting pregnant. The population based aspect of our study aligns with the CDC's National Action Plan focused on addressing infertility and its treatment at the population level [98]. Suburban county residents were consistently the most likely to visit a doctor for fertility counseling and treatment of the four categories of county level of urbanization. Our results suggest that there may be limited differences in seeking medical care for help getting pregnant among small metropolitan county residents compared with suburban residents, after controlling for differences in the characteristics of women in these populations. This study also confirms urban/rural differences in access to healthcare with fewer women who live in small town/rural counties are accessing care for help getting pregnant compared to women living in other types of counties. In our study, a greater proportion of women from small town/rural counties reported experiencing infertility, suggesting that the differences in utilization of fertility care may represent a geographic disparity in access to care. Lastly, this study highlights a differences in a little explored comparison between residents within large metropolitan counties, with the urbanized counties being less likely to access infertility care compared with suburban residents.

Although increasing the number of fertility specialists in small town/rural counties may not be possible, efforts can be made to increase the provision of information about infertility care by general practitioners and obstetrician/gynecologists, from whom our study shows women living in small town/rural counties are most likely to seek fertility care or counseling. This strategy is also applicable to practitioners in urbanized counties where fertility specialists may be available, but inaccessible for reasons other than physical access. An improved effort to communicate with patients about their reproductive goals and medical options available to meet these goals by less specialized healthcare providers may increase the use of medical care for help getting pregnant allowing more women to achieve their desired family size.

Table 4-1. Characteristics of Participants by Four Category County Level of Urbanization

	Type of county				
	Small town/rural (n = 113)	Small metropolitan (n = 171)	Suburban (n = 655)	Urbanized (n = 134)	Total (n = 1073)
	n (%)	n (%)	n (%)	n (%)	n (%)
Age at CATI (years)					
22-29	12 (10.6)	14 (8.2)	36 (5.5)	10 (7.5)	72 (6.7)
30-39	66(58.4)	87 (50.9)	355 (54.2)	68 (50.8)	576 (53.7)
40-45	35 (31.0)	70 (40.9)	264 (40.3)	56 (41.8)	425 (39.6)
Race					
White	94 (83.2)	121 (70.8)	419 (64.5)	78 (59.1)	712 (66.8)
Black	16 (14.2)	40 (23.4)	203 (31.2)	50 (37.9)	309 (29.0)
Other	3 (2.7)	10 (5.9)	28 (4.3)	4 (3.0)	45 (4.2)
Missing	0	0	5	2	7
Education					
High school and less	10 (8.9)	13 (7.6)	26 (4.0)	3 (2.3)	52 (4.9)
Some college	43 (38.1)	50 (29.2)	151 (23.1)	13 (9.8)	257 (24.0)
College graduate	30 (26.6)	55 (32.2)	250 (38.2)	61 (45.9)	396 (36.9)
Graduate school	30 (26.6)	53 (31.0)	228 (34.8)	56 (42.1)	367 (34.2)
Missing	0	0	0	1	1
Income					
Less than $50k	56 (50.9)	60 (35.5)	159 (24.7)	24 (18.5)	299 (28.4)
$50k - 100k	40 (36.4)	69 (40.8)	252 (39.1)	41 (31.5)	402 (38.2)
$100k+	14 (12.7)	40 (23.7)	233 (36.2)	65 (50.0)	352 (33.4)
Missing	3	2	11	4	20
Insurance					
Private	84 (74.3)	127 (74.3)	534 (81.7)	109 (82.0)	854 (79.7)
Public	7 (6.2)	12 (7.0)	16 (2.5)	2 (1.5)	37 (3.5)
Self-insured	4 (3.5)	9 (5.3)	44 (6.7)	11 (8.3)	68 (6.4)
None	18 (15.9)	23 (13.5)	60 (9.2)	11 (8.3)	112 (10.5)
Missing	0	0	1	1	2
Experienced infertility					
Yes	39 (36.8)	46 (27.7)	177 (28.3)	27 (20.6)	289 (28.1)
No	67 (63.2)	120 (72.3)	449 (71.7)	104 (79.4)	740 (71.9)
Missing	7	5	29	3	44
Age at infertility					
Median years (IQR)	25 (22, 29)	26 (24, 29)	27 (23, 30)	28 (26, 31)	27 (23, 30)

Table 4-2. Characteristics for Doctor Visits for Women Seeking Help in Getting Pregnant by Four Category County Level of Urbanization

	Type of county				
	Small town/ rural (n = 15)	**Small metropolitan (n = 24)**	**Suburban (n = 112)**	**Urbanized (n = 20)**	**Total (n = 171)**
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Visited a doctor for help getting pregnant					
Yes	15 (13.3)	24 (14.0)	112 (17.1)	20 (14.9)	171 (15.9)
No	98 (86.7)	147 (86.0)	543 (82.9)	114 (85.1)	902 (84.1)
Age at visit[a]					
Median (IQR)	27 (24, 30)	29.5 (27, 32)	30 (27, 34)	30.5 (27, 35)	30 (27, 33)
Type of doctor[b]					
General practitioner	1 (6.7)	5 (20.8)	14 (12.5)	2 (10.0)	22 (12.9)
Obstetrician/ gynecologist	15 (100.0)	24 (100.0)	99 (88.4)	16 (80.0)	154 (90.1)
Fertility specialist	5 (33.3)	11 (45.8)	53 (47.3)	12 (60.0)	81 (47.4)
Acupuncturist/ naturopath	1 (6.7)	1 (4.2)	15 (13.4)	3 (15.0)	20 (11.7)
Other	0 (0.0)	0 (0.0)	3 (2.7)	0 (0.0)	3 (1.8)
Type of treatment[c]					
None	2 (13.3)	3 (12.5)	16 (14.3)	3 (15.0)	24 (14.0)
Testing only	1 (6.7)	4 (16.7)	27 (24.1)	6 (30.0)	38 (22.2)
Surgery	4 (26.7)	2 (8.3)	21 (18.8)	5 (25.0)	32 (18.7)
Medications	10 (66.7)	16 (66.7)	56 (50.0)	8 (40.0)	90 (52.6)
Insemination	3 (20.0)	4 (16.7)	26 (23.2)	5 (25.0)	38 (22.2)
IVF[d]	0 (0.0)	3 (12.5)	17 (15.2)	4 (20.0)	24 (14.0)

[a]Two women were missing age at visit.
[b]Women could report visiting more than one doctor.
[c]No treatment and testing only were mutually exclusive with the other categories of treatment, but women could report more than one treatment that involved surgery, medications, insemination, or IVF.
[d]in vitro fertilization (IVF) attempt, not success

Table 4-3. Crude and Adjusted Odds Ratios of the Association between Small Metropolitan and Non-metropolitan vs. Large Metropolitan County Residence and Visiting a Doctor for Help Getting Pregnant

	Visited a doctor for help getting pregnant								
	Unadjusted			Model 1[a]			Model 2[b]		
All Women	**PR**	**95%CI**		**PR**	**95%CI**		**PR**	**95%CI**	
Large metropolitan	1.00	reference		1.00	reference		1.00	reference	
Small and non-metropolitan	0.82	0.59	1.14	0.91	0.65	1.28	0.95	0.68	1.33
Infertile women[c]									
Large metropolitan	1.00	reference		1.00	reference		1.00	reference	
Small and non-metropolitan	0.73	0.53	1.02	0.80	0.58	1.09	0.83	0.60	1.14

[a] Adjusted for: education (less than college degree vs. college degree or greater), income (less than $50k, $50-100k, $100k+), race (black, white, other)

[b]Adjusted for: covariates in model 1 + comfort with assisted reproductive technology (yes/no), comfort with adoption (yes/no), biologic child (important/unimportant), insurance status (private, public, self, none); models among infertile women also include age at infertility (20's, 30's, 40's)

[c]Model 2 for infertile women uses modified Poisson model (all other models use log binomial regression)

Table 4-4. Crude and Adjusted Odds ratios of the Association Between Four Category County Level of Urbanization and Visiting a Doctor for Help Getting Pregnant

	Visited a doctor for help getting pregnant								
	Unadjusted			Model 1[a]			Model 2[b]		
All Women	**PR**	**95%CI**		**PR**	**95%CI**		**PR**	**95%CI**	
Urbanized	1.00	reference		1.00	reference		1.00	reference	
Suburban	1.15	0.74	1.78	1.16	0.75	1.80	1.14	0.74	1.75
Small metropolitan	0.94	0.54	1.63	1.05	0.60	1.81	1.04	0.60	1.80
Small town/rural	0.89	0.48	1.65	1.02	0.54	1.94	1.10	0.57	2.10
Infertile women[c]									
Urbanized	1.00	reference		1.00	reference		1.00	reference	
Suburban	1.30	0.77	2.17	1.49	0.93	2.40	1.59	1.00	2.53
Small metropolitan	1.06	0.57	1.94	1.30	0.74	2.27	1.36	0.80	2.30
Small town/rural	0.76	0.38	1.54	0.90	0.45	1.78	1.09	0.55	2.17

[a] Adjusted for: education (less than college degree vs. college degree or greater), income (less than $50k, $50-100k, $100k+), race (black, white, other)

[b]Adjusted for: covariates in model 1 + comfort with assisted reproductive technology (yes/no), comfort with adoption (yes/no), biologic child (important/unimportant), insurance status (private, public, self, none); models among infertile women also include age at infertility (20's, 30's, 40's)

[c]Model 2 for infertile women uses modified Poisson model (all other models use log binomial regression)

Figure 4-1. Four and Two Category Classification of Counties of Residence for FUCHSIA Participants Based on the NCHS Urban/Rural Classification Scheme

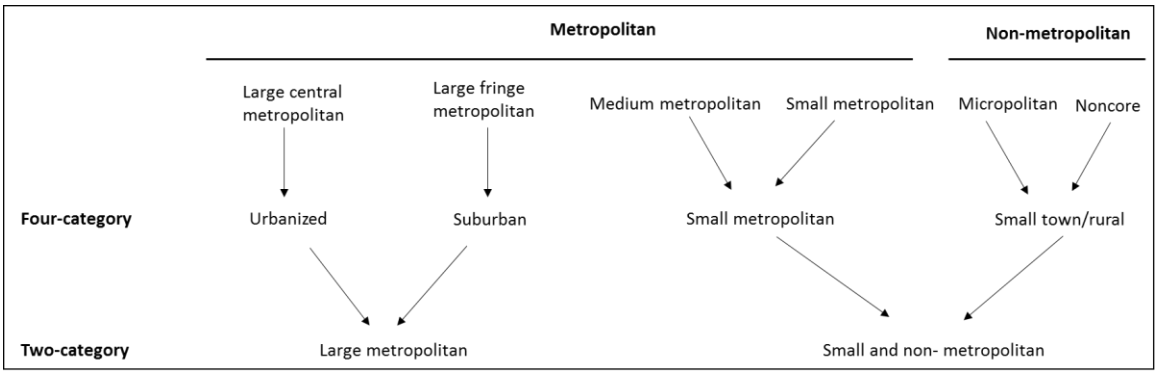
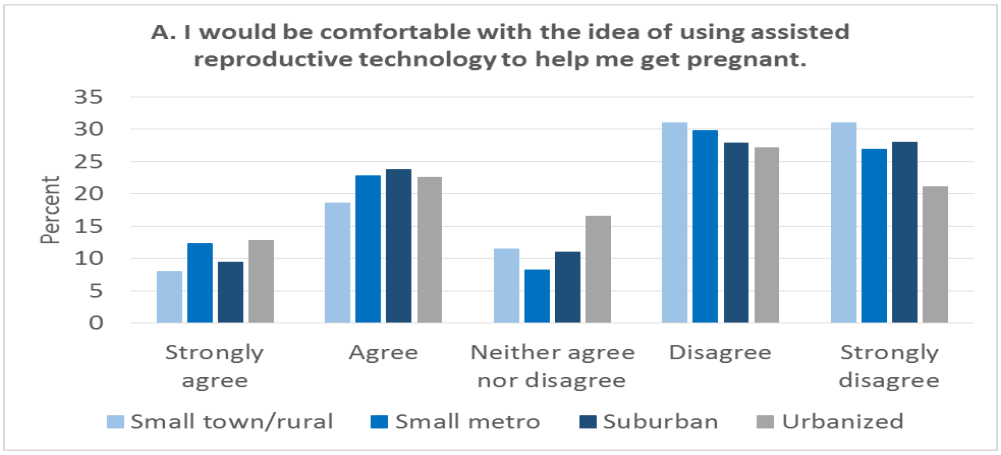
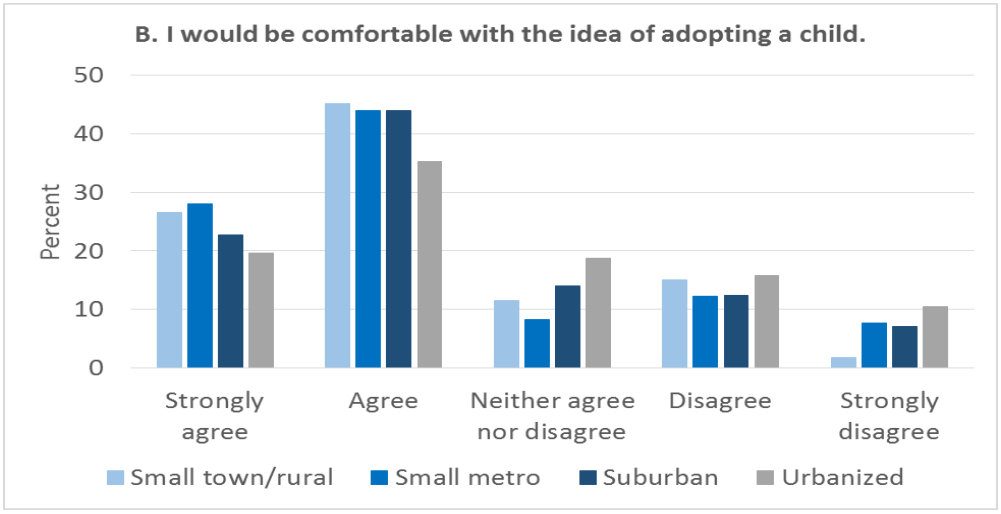
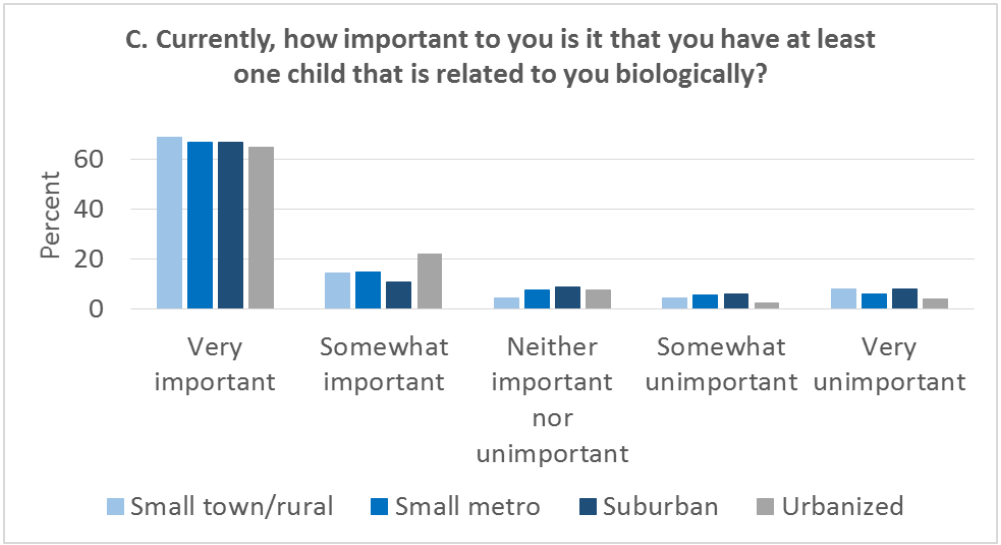


Figure 4-2. (A-C). Feelings about Biologic Children, Assisted Reproductive Technology, and Adoption by Four Category County Level of Urbanization







CHAPTER 5: Assessing Urban-Rural Differences in Women's Use of Medical Help for Becoming Pregnant Using the National Survey for Family Growth

INTRODUCTION

The National Survey for Family Growth (NSFG) is a US based survey that is conducted in a nationally representative sample of individuals by the National Center for Health Statistics at the Center for Disease Control and Prevention. The NSFG was first conducted in 1973 to gather information on marriage, divorce, contraception, infertility, and the health of women and infants [26]. The survey is conducted in cycles with the last cycle of completed interviews taking place between 2006 and 2010 [26].

The National Survey for Family Growth (NSFG) reports statistics on impaired fecundity among all reproductive aged women and infertility among married women of reproductive age in the United States [1]. Impaired fecundity refers to a physical difficulty either getting pregnant or carrying a pregnancy to live birth. Infertility is defined as lack of pregnancy after 12 months of trying to get pregnant. The NSFG estimates that from 2006-2010 there were over 6 million women of reproductive age who reported having impaired fecundity [1]. During this same time period, it is estimated that 1.5 million married women of reproductive age experienced infertility [33]. This represents a significant public health problem since infertility is both a disease of the reproductive system and a quality of life issue [3].

Disparities in the prevalence of infertility and use of medical care for infertility have been assessed among women in the NSFG. Compared with white women, non-Hispanic black women were about 1.8 times more likely to have infertility [33]. Additionally, unmarried, less educated, younger, and minority women were less likely to use an infertility service for help getting pregnant [5]. Disparities in seeking medical care

for help getting pregnant by geographic type of residence has not been explored in this dataset.

In *Chapter 4*, the overall association between the level of urbanization where a woman lives and seeking fertility care or counseling was assessed. This analysis was replicated in the 2006-2010 cycle of the NSFG to compare estimates obtained in the FUCHSIA Women's Study with national estimates.

METHODS

During the 2006-2010 cycle of the NSFG, a national sample of 22,682 men and women between the ages of 15-44 years were interviewed [26]. This study utilized women between the ages of 22 and 44 years who completed the survey. Data from these participants were obtained from the publicly available dataset from the National Center for Health Statistics.

Type of place of residence was defined based on the participants address at the time of the survey and the population based on the 2000 US Census. NSFG classifies type of place of residence as metropolitan statistical area (MSA) – central city, MSA – other, and not MSA. For this study, we collapsed these categories into a 2 level variable to examine women living in a metropolitan area (MSA) compared with women living in a non-metropolitan area. The three level original variable was also used in analysis, with MSA – central city referred to as urbanized, MSA – other referred to as suburban and small metropolitan, and not MSA referred to as small town/rural.

The outcome was defined based on the question "(During any of your relationships,) (have/did) you (or your husband/or your husband or partner at the time)

ever been to a doctor or other medical care provider to talk about ways to help you become pregnant?"

Information on characteristics of the participants included in our study was also obtained from the survey. Women who had fertility problems were identified as either sub-fecund or infertile. Sub-fecundity was measured in all participants and defined as a participant's inability to conceive or carry a baby to term. Infertility was measured only among participants who were married or cohabitating and was defined as 12 months of intercourse without contraception without getting pregnant. Based on the literature and a causal diagram for our study question, we determined race, education, and income were important confounders of the association between type of place of residence and visiting a doctor for help getting pregnant.

Analyses were conducted using SAS-callable SUDAAN 11.0.1, and SAS 9.4 survey procedures. To account for the sampling strategy used to select participants in the overall survey, weights provided by the NSFG were incorporated in all analyses. Descriptive statistics of participant characteristics by type of geographic category were generated. Logistic regression models were fit to estimate a prevalence ratio (PR) for visiting a doctor for help getting pregnant for each of the geographic type of residence classification schemes.

Models were fit for the 1) total population, 2) subgroup of women who reported being sub-fecund, and 3) subgroup of women who reported being infertile. Subgroup analyses were conducted among women with sub-fecundity or infertility to assess the association between level of urbanization of county of residence and visiting a doctor to talk about ways to help women get pregnant among those most likely to need help.

Visiting a doctor for help getting pregnant among women living in metropolitan area was compared with women living in a non-metropolitan area. Similarly, the prevalence of visiting a doctor among participants from suburban and small metropolitan and small town/rural areas were each compared with visiting a doctor among participants from an urbanized area.

RESULTS

There were the 9,161 women included in our analysis with good representation across the demographic factors of interest (*Table 5-1*). Urbanized areas had the most racial diversity, small town and rural areas had the most women without at least some college education, and suburban and small metropolitan areas had the highest incomes and largest proportion of women privately insured. Table 5-2 shows the proportion of women who reported being sub-fecund or infertile. Reports of sub-fecundity were similar across types of place of residence, while reports of infertility were highest in urbanized counties.

Results from models comparing women living in a non-metropolitan area to women living in a metropolitan area showed null results for visiting a doctor for help getting pregnant overall and in subgroup analyses (*Table 5-3*). Using the three category classification there were differences between groups (*Table 5-4*). Women from suburban and small metropolitan areas as well as women from small town and rural areas were more likely to visit a doctor for help getting pregnant compared with women from urbanized areas (adjusted prevalence ratio, adj. PR = 1.30, 95% CI: 1.06, 1.60 and adj. PR = 1.24, 95% CI: 0.98, 1.57, respectively). In adjusted analyses for the subgroup of women who reported sub-fertility, these association became null. However, when

restricted to women reporting infertility, women living in a suburban or small metropolitan area again had an increased likelihood receiving fertility care compared with women from urbanized areas (adj. PR = 1.26, 95% CI: 0.92, 1.72). Women from small town and rural areas were similar in their use of fertility care to women in urbanized areas.

DISCUSSION

Women in certain geographic areas are accessing care for help getting pregnant differently from others. In the NSFG, results from analyses in the subgroup of women with infertility were consistent with results from the FUCHSIA Women's Study (*Chapter 4*). Women from suburban and small metropolitan areas were most likely to visit a doctor for help getting pregnant compared with women from urbanized areas. Women from small town/rural counties had a similar prevalence of visiting a doctor compared with women from urbanized counties. Among the full sample however, both women from suburban/ small metropolitan and women from small town/ rural areas were more likely to visit a doctor for help getting pregnant compared with women living in an urbanized area. We did not observe this increased likelihood of visiting a doctor for help getting pregnant among women living in small town/rural areas in the FUCHSIA Women's Study. This may be due to differences in the study populations being assessed; the FUCHSIA Women's Study is contained within the state of Georgia, while the NSFG is US wide.

A limitation of this study includes the broad categories of type of place of residence in the publicly available dataset. Women from across the country were classified into only three groups which were likely heterogeneous. We were unable to

distinguish women living in different states or different regions of the country. Women living in urban or rural locations in one part of the country may share a different set of characteristics compared with women living in another part of the country.

A strength of using the NSFG data is the large sample size and representativeness of women across the US. This study population includes women from various education levels, places of residence, and household income categories.

This study adds to the literature on disparities using NSFG data. Geographic differences in visiting a doctor for help getting pregnant among women in NSFG suggests that disparities in accessing fertility care may be nationwide. Improved communication with women by their regular doctor as well as advocacy and support groups can improve women's knowledge of the many options available for medical help getting pregnant, which may increase use of infertility services in places it is currently less common.

Table 5-1. Characteristics of Female Participants 22-44 Years of Age in the National Survey For Family Growth 2006-2010 Cycle

	Type of place of residence							
	Small town & Rural		Suburban & Small metropolitan		Urbanized		Total	
	(n = 1355)		(n = 3922)		(n = 3891)		(n = 9161)	
	n[a]	%[b]	n[a]	%[b]	n[a]	%[b]	n[a]	%[b]
Age at Interview								
22-29	528	35.3	1369	30.5	1740	43.7	3637	35.7
30-39	545	39.8	1759	45.6	1541	37.7	3845	41.9
40-44	280	24.9	790	23.9	609	18.6	1679	22.4
Missing	2		4		1			
Race								
Black	183	8.3	611	10.1	1148	24.4	1942	14.4
White	1032	79.2	2333	69.9	1860	54.3	5225	66.7
Other race	140	12.5	978	20.0	883	21.3	2001	18.9
Education								
High school and less	680	49.3	1566	36.3	1694	36.8	3940	39.0
Some college	402	30.0	1183	29.6	1109	27.5	2694	29.0
College graduate	207	15.2	837	24.5	798	26.7	1842	23.4
Graduate school	66	5.5	336	9.6	290	9.0	692	8.6
Income								
Less than $50k	935	65.6	2264	50.0	2825	64.1	6024	57.6
$50k - 75k	258	19.9	751	20.8	582	17.1	1591	19.4
$75k+	162	14.5	907	29.2	484	18.8	1553	22.9
Insurance								
Private	745	56.8	2424	68.0	1997	58.9	5166	62.8
Public	260	15.9	659	12.5	994	20.2	1913	15.7
Other/none[c]	350	27.3	839	19.5	900	20.9	2089	21.5

[a]Actual number of participants interviewed.
[b]Weighted percents.
[c]Currently covered only by a single-service plan, only by the Indian Health Service, or currently not covered by health insurance

Table 5-2. Women Reporting Subfecundity and Infertility Among Participants 22-44 Years of Age in the 2006-2010 National Survey for Family Growth

	Type of place of residence							
	Small town & Rural		Suburban & Small metropolitan		Urbanized		Total	
	(n = 1355)		(n = 3922)		(n = 3891)		(n = 9161)	
	n[a]	%[b]	n[a]	%[b]	n[a]	%[b]	n[a]	%[b]
Subfecund[c]								
Yes	141	10.5	420	10.5	419	10.5	980	10.5
No	1214	89.5	3502	89.5	3472	89.5	8188	89.5
Infertile[d]								
Yes	43	4.7	165	5.7	125	7.3	333	6.0
No	793	95.3	2180	94.3	1746	92.7	4719	94.0

[a]Actual number of participants interviewed.
[b]Weighted percents.
[c]Subfecund defined as difficulty conceiving or delivering a(nother) baby or 36 months with the same partner without using contraception and no months of non-intercourse and not getting pregnant.
[d]Infertile was measured only in married or cohabitating women as 12 or more months of intercourse without pregnancy and without contraception.

Table 5-3. Crude and Adjusted Prevalence Ratios of the Association Between Metropolitan and Non-metropolitan Residence and Visiting a Doctor for Help Getting Pregnant Among Participants 22-44 Years of Age in the 2006-2010 National Survey for Family Growth

	Visited a doctor for help getting pregnant					
	Unadjusted			Adjusted[a]		
All Women	**PR**	**95%CI**		**PR**	**95%CI**	
Metropolitan	1.00	reference		1.00	reference	
Non-metropolitan	0.95	0.76	1.18	1.04	0.85	1.27
Subfecund women[b]						
Metropolitan	1.00	reference		1.00	reference	
Non-metropolitan	0.93	0.67	1.30	1.02	0.76	1.39
Infertile women[c]						
Metropolitan	1.00	reference		1.00	reference	
Non-metropolitan	0.95	0.57	1.59	0.96	0.63	1.47

[a] Adjusted for confounders: education (less than college degree vs college degree or greater), income (less than $50k, $50-75k, $75k+), race (black, white, other) [b]Subfecund defined as difficulty conceiving or delivering a(nother) baby or 36 months with the same partner without using contraception and no months of non-intercourse and not getting pregnant.
[c]Infertile was measured only in married or cohabitating women as 12 or more months of intercourse without pregnancy and without contraception.

Table 5-4: Crude and Adjusted Prevalence Ratios of the Association Between Three Level Type of Place of Residence and Visiting a Doctor for Help Getting Pregnant Among Participants 22-44 Years of Age in the 2006-2010 National Survey for Family Growth

	Visited a doctor for help getting pregnant					
	Unadjusted			Adjusted[a]		
All Women	**PR**	**95%CI**		**PR**	**95%CI**	
Urbanized	1.00	reference		1.00	reference	
Suburban/small metropolitan	1.48	1.21	1.80	1.30	1.06	1.60
Small town/rural	1.22	0.96	1.55	1.24	0.98	1.57
Subfertile women[b]						
Urbanized	1.00	reference		1.00	reference	
Suburban/small metropolitan	1.22	0.94	1.57	1.05	0.83	1.34
Small town/rural	1.05	0.73	1.53	1.06	0.76	1.48
Infertile women[c]						
Urbanized	1.00	reference		1.00	reference	
Suburban/small metropolitan	1.41	0.99	2.01	1.26	0.92	1.72
Small town/rural	1.18	0.67	2.09	1.12	0.70	1.78

[a] Adjusted for confounders: education (less than college degree vs college degree or greater), income (less than $50k, $50-100k, $100k+), race (black, white, other)
[b]Subfecund defined as difficulty conceiving or delivering a(nother) baby or 36 months with the same partner without using contraception and no months of non-intercourse and not getting pregnant.
[c]Infertile was measured only in married or cohabitating women as 12 or more months of intercourse without pregnancy and without contraception.

CHAPTER 6: Characteristics Associated with the Receipt of Fertility Counseling Among a Cohort of Female Cancer Survivors

ABSTRACT

Objective: The goal of this study was to assess which characteristics are associated with receipt of fertility counseling among a cohort of young women diagnosed with cancer.

Methods: Using a large population-based registry sample we examined differences in fertility counseling by overall sociodemographic factors, factors that might influence a patient initiated discussion, and factors that might influence a healthcare provider initiated discussion. Counseling by cancer type was also assessed. Logistic regression models were fit and results from bivariate and multivariable models were used to determine the most influential variables associated with the likelihood of receiving counseling.

Results: Overall, approximately 40% of cancer survivors in our study reported that they did not receive fertility counseling at the time of their cancer diagnosis. Women were less likely to be counseled if they had no college education (OR = 0.52, 95% CI: 0.27, 1.01). Women who were nulliparous at diagnosis were more likely to be counseled (OR = 1.92, 95% CI: 1.31, 2.82). Among the variables assess directly related to cancer diagnosis, receipt of chemotherapy compared with no chemotherapy and diagnosis with a reproductive cancer compared with "other" cancers were associated with being counseled (OR = 4.33, 95% CI: 2.93, 6.41 and OR = 8.52, 95% CI: 3.98, 18.24, respectively).

Conclusion: For women diagnosed with cancer, treatment that improves survival is a priority, but addressing survivorship issues is also important. Providing fertility counseling at diagnosis allows women to assess how cancer treatment might affect their

fertility, and for some women, provides the opportunity to use fertility preservation for the chance of children after cancer.

INTRODUCTION

Many women of reproductive age are diagnosed with cancer each year. According to the Surveillance, Epidemiology, and End Results (SEER) statistics for 2010 the age adjusted incidence rate of cancer in women between the ages of 20-49 was 187 per 100,000 [46]. Advances in cancer treatment over the past few decades have led to improved outcomes after cancer diagnosis. With increased survival after cancer, there is a greater need to address survivorship issues, especially regarding fertility in young female cancer survivors.

Women who are diagnosed with cancer are often treated with potentially gonadotoxic treatments which may put them at risk for infertility by affecting the reproductive system and reducing ovarian function. [48, 133, 134]. Chemotherapy with alkylating agents and radiation to the pelvis, abdomen, brain, or total body can compromise future fertility [64]. Registry-based studies have found decreased rates of childbearing and increased probabilities of childlessness among female cancer survivors [54-56].

Since many cancer treatments have the potential to affect future fertility, there are universal recommendations that all cancer patients receive information about how cancer treatment could affect fertility and about fertility preservation options. Since 2005, the American Society for Reproductive Medicine (ASRM) and the American Society of Clinical Oncology (ASCO) have recommended doctors have these discussions with all their patients of reproductive age as early as possible [8-10]. These recommendations extend to providing women who express an interest in fertility preservation or are

ambivalent towards this option with a referral to a fertility specialist for further discussion [8].

In a survey of oncologists however, only 14% reported always, or almost always giving educational materials about fertility preservation to their patients [12]. When patients were asked about their experiences with fertility counseling at cancer diagnosis, only 14% of women reported being encouraged to talk to a fertility specialist [78]. Most of the time, the discussion about how cancer treatment could affect fertility and reproductive health is physician initiated, highlighting the importance of oncologists communicating this information [78]. Women diagnosed with certain cancers, such as those that are hormone dependent, may especially need fertility counseling because they may experience decreased ovarian reserve even before cancer treatment begins [135, 136].

Patient characteristics can affect whether or not they receive counseling. The physician's perception of a patient's ability to afford fertility treatment or desire to have a child or more children can influence their decision to provide fertility counseling. Women with lower education, older age at diagnosis, and women who had children before diagnosis have been found to be less likely to be counseled about the fertility-related issues that could arise due to cancer treatment [25]. In studies of referral to a specialist for a fertility preservation consultation, authors found white, younger, and nulliparous women were more likely to receive a referral [13, 137]. Cancer type also influenced receipt of referral, with breast cancer and lymphoma survivors most likely to

be referred. Cancer stage can also impact referral patterns, with poorer prognosis associated with a lower likelihood of referral [14].

The current literature provides some information about which women are receiving fertility counseling from the healthcare providers treating their cancer; yet gaps in identifying the factors most strongly associated with getting counseled remain. Some of the literature is among non-US populations where the healthcare system may not be comparable. Other studies suffer from small sample size and lack of diversity across demographic factors. Additionally, most studies restrict to a few cancer types, so some cancer types are not represented in the literature.

Loss of fertility has been reported to be almost as important to reproductive aged women diagnosed with cancer as concerns about survival [6, 77]. Women report better quality of life and less distress if they received fertility counseling [138, 139]. An appreciation for fertility counseling at diagnosis was found regardless of whether a woman used a fertility preservation method or not [140]. Even among women for whom fertility preservation is not an option, fertility counseling provides an opportunity to process the potential loss of fertility after cancer treatment [11].

In this study we assessed which characteristics of young women diagnosed with cancer are associated with receiving fertility counseling. Using a large population-based registry sample, we examined differences in counseling by overall sociodemographic factors, factors that might influence a patient initiated discussion, and factors that might influence a healthcare provider initiated discussion. We also looked differences in the proportion of women counseled by cancer type.

METHODS

The Furthering Understanding of Cancer Health and Survivorship in Adult (FUCHSIA) Women's Study is a population-based cohort study designed to examine how cancer treatment during the reproductive years affects future fertility. Women were eligible to participate in the main study if they were diagnosed with an invasive cancer (excluding non-melanoma skin cancer) or ductal carcinoma in situ, were at least 2 years post diagnosis at recruitment, were of reproductive age (22-45 years old) at recruitment, had a working telephone, and spoke English. Additionally, for this study, women who had a hysterectomy or both ovaries removed at the time of cancer diagnosis were excluded. These further exclusions limited the study population to only women who could become pregnant at the time of the cancer diagnosis.

Eligible cancer survivors were identified and contacted by the Georgia Cancer Registry (GCR) who shared information about the FUCHSIA Women's Study with potential participants. Women who agreed that the study could contact them were invited to complete a computer-assisted telephone interview. The interview collected information about cancer diagnoses and treatments, medical conditions, experience with infertility, pregnancy history, desire for children, reproductive goals, and demographic and lifestyle factors [93]. In addition to information collected via interview, we obtained data on age at diagnosis, cancer type, stage, and first course of treatment from the GCR. Women consented to participate in the study orally at the time of the interview. The Emory University and the Georgia Department of Health Institutional Review Boards approved this study.

The outcome for this study was defined based on the question "Did you talk to a doctor or other health professional about how this cancer treatment could affect your ability to become pregnant?" Follow up questions collected information on who initiated the discussion and if they were referred to a fertility specialist to discuss fertility preservation. We used these questions to identify women being counseled and referred to specialists in accordance with the ASRM and ASCO guidelines.

Three categories of factors that might influence whether or not a woman received fertility counseling at the time of diagnosis were assessed. There was some overlap across categories as depicted in Figure 6-1. First, we examined sociodemographic characteristics that might affect a woman's inclination and ability to pursue fertility preservation. These factors included race, education, income, and insurance status, as well as age, relationship status, and place of residence at the time of diagnosis. Education, income, and insurance status assessed at the time of the interview served as proxies for these factors at the time of diagnosis.

Second, we looked at factors that might influence a woman's decision to initiate a discussion with her doctor about how treatment could affect her future fertility at the time of cancer diagnosis. These factors included parity, desire for future children, and comfort with assisted reproductive technology. It was hypothesized that women with prior obstetric or gynecologic problems might be more likely to initiate a conversation. Reproductive conditions considered included fibroids, endometriosis, polycystic ovary syndrome, amenorrhea, and surgery to the uterus, ovaries, or fallopian tubes. Sexually transmitted infections examined included chlamydia, gonorrhea, pelvic inflammatory disease, human papilloma virus, and herpes. Pregnancy at the time of diagnosis and

history of miscarriage, stillbirth, induced abortion, ectopic pregnancy, low birth weight or preterm birth were also assessed.

Lastly, factors that might affect a healthcare providers initiating fertility counseling with a patient were examined. Patient characteristics that may influence physician initiated counseling included comorbidities (hypertension, diabetes), smoking status, and obesity. Characteristics of the cancer diagnosis, such as treatment modality and type might also influence the oncologist providing counseling. Treatment with chemotherapy and radiation was obtained through self-report in the interview. Cancer type was obtained from the GCR and grouped as breast, reproductive (uterine, cervical, and ovarian), Hodgkin's lymphoma, non-Hodgkin's lymphoma, brain, thyroid, and other cancer types. Cancers were grouped in this way because of their effects on the reproductive system directly, through radiation to the pelvic region, or by disrupting hormone function.

Statistical Analysis

Descriptive statistics were generated for all of the sociodemographic, patient, and physician factors by whether or not women were counseled. Patients who went on to receive a referral were also characterized. We fit descriptive models to assess which factors were most strongly associated with receiving fertility counseling at the time of cancer diagnosis, starting with bivariate logistic models for each of the factors hypothesized to influence receipt of counseling. Next, fully adjusted multivariable models were fit for each of the three categories of factors.

All of the factors hypothesized were considered important predictors of the outcome conceptually. However, results from the bivariate and fully adjusted

multivariable models were used to determine the most influential variables in determining the likelihood of receiving counseling. Three considerations were taken into account during variable selection: magnitude of effect, precision of the estimate, and statistical significance of the estimate at $p<0.10$.

In our study, women diagnosed with melanoma and thyroid cancer were recruited from the major metropolitan center of the state, because women with these cancers are least likely to receive chemotherapy and radiation as part of their cancer treatment. Women diagnosed with other cancer types were recruited statewide. Because of this recruitment design thyroid and melanoma survivors have a different demographic representation from the other survivors recruited from the entire state. Therefore, we performed secondary analyses in which thyroid and melanoma survivors were excluded.

RESULTS

There were a total of 1,282 cancer survivors in the FUCHSIA Women's Study. We excluded women who had a hysterectomy or both ovaries removed before cancer diagnosis (n = 153) and women who had missing information on the outcome (n = 13) leaving 1,116 women in the analysis. For the analyses that excluded cancer survivors with a diagnosis of thyroid cancer (n = 123) and melanoma (n = 102) the sample size was 892 women. Overall, 59% of women in our study were counseled on how cancer treatment could affect their ability to become pregnant. Approximately 40% of discussions were initiated by the oncologist and the same proportion by the patient.

Demographic characteristics of participants stratified by counseling are presented in Table 6-1. Women were well distributed across the sociodemographic characteristics examined. Among nulliparous women 64% were counseled compared with 54% of

women who had at least one child and 65% women who reported having fewer children than desired were counseled compared with 52% who did not report wanting more children at the time of the interview (*Figure 6-2*). Among the physician influencing characteristics examined, approximately half of study participants were diagnosed between the ages of 30-35 years old and most survivors were diagnosed after 2000. The largest cancer group were breast cancer survivors (n=393), and the most likely cancer type to be counseled was Hodgkin lymphoma (*Figure 6-3*).

The unadjusted estimates for each of the characteristics examined are presented in Supplemental Tables 6-(A-C). Among the sociodemographic characteristics, higher education, private insurance, being married or living with a partner at the time of diagnosis, and living in a small metropolitan area were all associated with receiving counseling. Among the patient characteristics, reproductive history, certain STIs, and reproductive surgeries also influenced counseling. Women were more likely to receive counseling if they were nulliparous compared with women who had a child (OR = 1.56, 95% CI: 1.23, 1.98) or had a human papilloma virus (HPV) infection compared with those who did not (OR= 1.61, 95% CI: 1.05, 2.47). Women were less likely to receive counseling if they had surgery on their fallopian tubes, which was most commonly for birth control, compared with women who did not (OR = 0.47, 95% CI: 0.31, 0.73), had a preterm birth compared with women who did not (OR= 0.59, 95% CI: 0.42, 0.85), or had a low birth weight birth compared to those who did not (OR= 0.64, 95% CI: 0.41, 1.02).

Among characteristics that might influence a physician to counsel, treatment modality and cancer type were associated with receipt of fertility counseling. Crude

estimates for chemotherapy and radiation show that women who received these treatments were more likely to receive counseling, especially those who receive chemotherapy (OR = 3.93, 95% CI: 3.05, 5.06). Year of diagnosis was not associated with receipt of counseling. In analyses excluding women diagnosed with thyroid cancer or melanoma, similar associations were observed across the three categories of variables with slightly stronger associations than the full sample for some variables (*Supplemental Tables 6-(D-F)*).

Adjusted estimates are presented in Table 6-2. Model 1 included all variables identified as important from all three groups of factors considered. Being unmarried and not cohabitating and having surgery on the fallopian tubes remained strongly associated with not receiving fertility counseling (OR = 0.52, 95% CI: 0.37, 0.73 and OR= 0.46, 95% CI: 0.27, 0.78, respectively). Having fewer children than desired (OR = 1.61, 95% CI: 1.19, 2.17), receiving chemotherapy as part of treatment (OR = 4.33, 95% CI: 2.93, 6.41), and diagnosis with a reproductive, breast, Hodgkin lymphoma, and thyroid cancer compared with other cancer types were associated with a greater probability of receiving counseling. Women diagnosed with non-Hodgkin's lymphoma were less likely to receive counseling compared with other cancers. Model 2 includes only those factors that were considered to influence the physician in initiating counseling. In this model education, relationship status, parity, chemotherapy, and cancer type remained strongly associated with receipt of counseling.

Information on stage of cancer was missing for many participants. We examined the association between cancer stage and fertility counseling among breast cancer

survivors, our largest cancer group that also had almost complete information on stage (*Supplemental Table 6-G*). Diagnosis with stage 0 breast cancer (the only cancer type where stage 0 was included) was associated with a decreased probability of counseling and stage 4 cancer an increased probability of counseling compared with stage 1. Counseling among survivors of a stage 2 or 3 cancer was similar to stage 1. Although 59% of cancer survivors (n=660) reported receiving fertility counseling, only 13% of those participants received a referral to a fertility specialist. This included 44 breast cancer survivors, 15 Hodgkin lymphoma survivors, and 26 survivors of all the other cancer types combined.

DISCUSSION

All women should be counseled on how cancer treatment might affect their future fertility. In our study, 40% of cancer survivors reported not receiving information on how cancer treatment could affect their future fertility. Further, only 13% of women who received counseling were referred to a fertility specialist to discuss fertility preservation options. Although many women who received counseling in our study initiated a conversation about their fertility concerns with regard to cancer treatment, the importance of a healthcare provider initiated conversation should not be overlooked. Other studies have found that most women do not bring up their interest in fertility preservation unless prompted [9].

In all analyses, having no college education was associated with a reduced likelihood of fertility counseling. The association between less education and not being counseled highlights an opportunity to improve counseling techniques. Women with a

high school degree or less may not be reporting that they received counseling for many reasons. One reason is that they actually never received any information on how cancer treatment could affect their fertility. An alternative reason is that these women were not counseled appropriately. Women with less education may not be as medically literate about fertility treatment and preservation options available and counseling for these women should be sensitive to this. Relationship status was another factor associated with counseling. Women who were not in a relationship were less likely to be counseled compared with women with a partner. Single women may be less likely to bring up a conversation about fertility preservation because they are not currently planning for a family, but they may still want the opportunity to have children in the future. These cases underscore the importance of a physician initiated discussion.

Several patient factors were associated with receiving counseling. Women who were nulliparous or had a desire for more children at the time of diagnosis were more likely to get counseled about fertility compared with women who had children or did not want any more. Although this is promising, only 65% of women who wanted children in the future were counseled and only 54% of women without children were counseled. Additionally, women who already have children may want more children after cancer, but are less likely to be counseled, which may prevent them from fulfilling their reproductive goals. Women diagnosed with HPV before diagnosis were more likely to receive fertility counseling. It is possible that these women were more aware of fertility issues because of their experience with HPV and were more likely to initiate a conversation. It is also possible that they were more likely to have a healthcare provider initiated conversation because they developed a reproductive cancer, although only 17%

of women diagnosed with HPV later went on to develop cervical cancer. Most of the women who had surgery on their fallopian tubes had their tubes tied as birth control, and they were the least likely to receive fertility counseling. Many of these women may have not been interested in fertility preservation options, but still could benefit from learning about how cancer treatment could affect their reproductive health, including possible early menopause.

Of the physician factors examined, treatment with chemotherapy and certain cancer types were associated with receipt of counseling. Being diagnosed with a reproductive cancer was the most strongly associated with receiving counseling of all the cancer types examined. It may be that in discussing these types of cancers and their treatment a direct connection with fertility is made. Although counseling in this group of cancer survivors is high, close to 20% of women diagnosed with a reproductive cancer reported that they did not receive fertility counseling. Diagnosis with non-Hodgkin lymphoma was associated with a decreased likelihood of receiving counseling compared with women diagnosed with all other cancers. These women are often treated with alkylating agents which are known to affect ovarian function, and could benefit from fertility preservation [141].

Our analyses excluding thyroid and melanoma patients showed stronger associations for some variables we examined, confirming that including these two groups masked some of the associations between the factors we considered and receipt of fertility counseling. When we excluded women diagnosed with melanoma, black women were less likely to receive counseling, however, this association disappeared in adjusted

analyses suggesting that other factors were driving this difference. Also of note was that the association between type of place of residence became weaker, which was expected because thyroid and melanoma cancer survivors were the least likely to receive potentially gonadotoxic treatment and were exclusively recruited by the FUCHSIA Women's Study from the metropolitan area.

A limitation of this study is that our outcome is based on patient recall. Being diagnosed with cancer is a stressful time in a woman's life and information provided by the oncologist at and around the time of diagnosis may not be recalled by survivors. Some groups of women, such as women who completed their family size, less educated women, and women who were using a permanent birth control method, may be less likely to remember receiving counseling because they did not think that information was relevant to them, however we could not measure this. Also unmeasured was the quality of the counseling. Among women who received counseling, some may not have gotten all the information they needed to make informed decisions about fertility preservation. Lastly, some of our demographic variables including education, income, and insurance were measured at the time of the interview. We used current status of these variables as proxies for at the time of diagnosis, but there could be misclassification, especially for women diagnosed many years before the interview.

A strength of this study is that it included all cancers. This enabled us to see differences in receipt of counseling across cancer types. Some cancers were more strongly associated with getting counseled than others. Non-Hodgkin lymphoma survivors were least likely to be counseled. Because our study included women

diagnosed over several decades, we could compare counseling and referral before and after the guidelines for universal counseling by ASRM in 2005 and ASCO in 2006. When we looked at counseling and referral however, we did not see much increase in more recent years. Often the need for fertility counseling is based on whether or not women already had children at the time of cancer diagnosis. In our study we were able to look at the unique outcome of having fewer children than desired which captures women who have not yet reached their desired family size, regardless of parity.

There are many reasons cited as to why some women do not receive fertility counseling. Concerns about delay in treatment and risk of recurrence result in some women not receiving fertility counseling, but many of these concerns are not evidence-based. Early referral and accelerated ovarian stimulation protocols allow some women to take advantage of a window of opportunity between early treatment that does not affect fertility (e.g., some surgeries) and the start of potentially gonadotoxic treatment regimens [65, 142, 143]. However, women need to be counseled and referred to a specialist early and before treatment with potentially gonadotoxic regimens to take advantage of this opportunity. Women with hormone responsive cancers are sometimes advised not to become pregnant because of concern of increased risk of cancer recurrence [57]. However, there have been several recent studies that show no increased risk of recurrence in women who use in vitro fertilization to become pregnant after cancer [58-60, 144]. Lastly, some women are not counseled because they are not candidates for embryo cryopreservation. Until recently, embryo cryopreservation was the only non-experimental fertility preservation option for women, but now oocyte or egg freezing is no longer

considered experimental, so women who do not have partners and do not want to use donor sperm have preservation options available to them [145].

While life-saving cancer treatment is the priority at the time of diagnosis, survivorship issues should not be ignored. In our study, women with less education, who were unmarried, or already had a child were less likely to receive counseling suggesting that these characteristics make the healthcare provider, cancer patient, or both less likely to initiate a discussion about future fertility. An encouraging result from our study was that women with fewer children than desired were more likely to receive counseling than those who did not desire future children, and many of the other factors we examined showed no differences in receipt of counseling. However, the overall proportion of women offered fertility counseling at the time of diagnosis was inadequate at only 59%. For some women a well-coordinated cancer treatment and fertility preservation strategy at the time of diagnosis may allow them to have the children they want in the future without compromising their treatment plan.

Table 6-1. Demographic Characteristics of Cancer Survivors by Whether or Not They Received Fertility Counseling

	Received Fertility Counseling				
	Yes (n=660)		No (n=456)		
	n	%	n	%	p value
Age at diagnosis (years)					
20-24	96	58.9	67	41.1	0.99
25-29	209	58.9	146	41.1	
30-35	355	59.4	243	40.6	
Race					
White	463	59.4	317	40.6	0.81
Black	165	58.1	119	41.9	
Other race	32	62.8	19	37.3	
Missing			1		
Education[a]					
High school or less	26	37.1	44	62.9	<0.01
Some college	175	61.0	112	39.0	
College graduate	247	59.5	168	40.5	
At least some graduate school	212	61.8	131	38.2	
Missing			1		
Income[b]					
Less than or equal to $50k	208	55.2	169	44.8	0.13
$50k - 100k	242	61.7	150	38.3	
$100k+	199	61.0	127	39.0	
Missing	11		10		
Insurance[c]					
Private	516	61.4	325	38.6	0.02
Self	35	61.4	22	38.6	
Public	59	53.2	52	46.9	
None	49	46.7	56	53.3	
Missing	1		1		
Married or cohabitating at time of diagnosis					
Yes	463	62.2	282	37.9	<0.01
No	197	53.1	174	46.9	
Type of place of residence at diagnosis[d]					
Urbanized	100	55.3	81	44.8	0.07
Suburban	367	57.3	273	42.7	
Small metropolitan	131	66.2	67	33.8	

Small town/rural	62	63.9	35	36.1	

[a]Current education at the time of the interview.
[b]Current income at the time of the interview.
[c]Private insurance includes employer, school, military or VA insurance; self includes COBRA, public includes Medicare and Medicaid.
[d] Type of place of residence based on a modified version of the NCHS urban rural categories.

Table 6-2. Adjusted Odds Ratios for Characteristics of Cancer Survivors and Receipt of Fertility Counseling

	Model 1			Model 2		
	aOR	95% CI	p value	aOR	95% CI	p value
Age at diagnosis (years)						
20-24	0.93	0.73, 1.18	0.56	0.95	0.76, 1.18	0.62
25-29	Reference			Reference		
30-35	1.07	0.85, 1.37		1.06	0.85, 1.32	
Race						
White	Reference		0.98	Reference		0.89
Black	1.04	0.72, 1.49		0.99	0.71, 1.39	
Other race	0.99	0.48, 2.05		1.17	0.60, 2.29	
Missing						
Education[a]						
High school or less	0.52	0.27, 1.01	0.20	0.41	0.22, 0.77	**0.05**
Some college	0.95	0.64, 1.41		0.94	0.65, 1.36	
College graduate	Reference			Reference		
At least some graduate school	0.81	0.57, 1.16		0.92	0.66, 1.28	
Missing						
Insurance[b]						
Private	Reference		0.46	Reference		0.58
Self	0.88	0.45, 1.71		0.94	0.50, 1.77	
Public	0.87	0.51, 1.47		0.90	0.55, 1.48	
None	0.65	0.38, 1.11		0.70	0.43, 1.15	
Missing						
Married or cohabitating at time of diagnosis						
Yes	Reference		**<0.01**	Reference		**<0.01**
No	0.52	0.37, 0.73		0.52	0.37, 0.72	
Place of residence at diagnosis[c]						
Large central	0.90	0.60, 1.35	0.52	0.82	0.56, 1.21	0.15
Large fringe	Reference			Reference		
Small metropolitan	1.28	0.84, 1.94		1.41	0.95, 2.10	
Non-metropolitan	1.22	0.70, 2.14		1.30	0.77, 2.18	
Given birth to at least one child at diagnosis						
Yes	Reference		**<0.01**	Reference		**<0.01**
No	1.92	1.31, 2.82		2.53	1.81, 3.54	

Fewer children than desired at time of interview[d]						
Yes	1.61	1.19, 2.17	**<0.01**			
No	Reference					
Missing						
Human Papilloma Virus before diagnosis						
Yes	1.46	0.86, 2.46	0.16			
No	Reference					
Missing						
Surgery on fallopian tubes before diagnosis[e]						
Yes	0.46	0.27, 0.78	**<0.01**			
No	Reference					
Missing						
Low birth weight or preterm birth before dx[f]						
Yes	0.86	0.56, 1.32	0.48			
No	Reference					
Missing						
Chemotherapy[g]						
Yes	4.33	2.93, 6.41	**<0.01**	4.13	2.87, 5.95	**<0.01**
No	Reference			Reference		
Radiation[h]						
Yes	1.13	0.81, 1.58	0.47	1.21	0.88, 1.66	0.24
No	Reference			Reference		
Cancer types						
Reproductive (cervix, ovary, uterus)	8.52	3.98, 18.24	**<0.01**	8.63	4.23, 17.6	**<0.01**
Breast	2.63	1.73, 3.97	**<0.01**	2.49	1.68, 3.68	**<0.01**
Brain	1.45	0.56, 3.73	0.44	1.99	0.82, 4.83	0.13
Hodgkin lymphoma	3.67	1.93, 6.98	**<0.01**	3.50	1.92, 6.40	**<0.01**
Non-hodgkin lymphoma	0.44	0.19, 1.01	**0.05**	0.40	0.18, 0.87	**0.02**
Thyroid	3.81	2.23, 6.53	**<0.01**	3.52	2.12, 5.84	**<0.01**
Other cancer type	Reference			Reference		

[a]Current education at the time of the interview.
[b]Private insurance includes employer, school, military or VA insurance; self includes COBRA, public includes Medicare and Medicaid.
[c]Type of place of residence based on a modified version of the NCHS urban rural categories.
[d]Fewer kids defined by subtracting the number of children a woman had from the number of children she desired at the time of the interview.
[e]Surgery on fallopian tubes includes getting tubes tied for birth control.
[f]Preterm birth defined as a live birth less than 37 weeks. Low birth weight defined as a live birth less than 2500 grams. "No" includes nulliparous women.

[g]Chemotherapy as self-reported in the interview.
[h]Radiation as self-reported in the interview.

Supplemental Table 6-A: Bivariate Associations Between Sociodemographic Characteristics of Cancer Survivors and Receipt of Fertility Counseling (All Cancers)

	Received Fertility Counseling						
	Yes (n=660)		No (n=456)				
	n	%	n	%	OR	95% CI	p value
Age at diagnosis (years)							
20-24	96	58.9	67	41.1	1.00	0.69, 1.46	0.99
25-29	209	58.9	146	41.1	Reference		
30-35	355	59.4	243	40.6	1.02	0.78, 1.33	
Race							
White	463	59.4	317	40.6	Reference		0.81
Black	165	58.1	119	41.9	0.95	0.72, 1.25	
Other race	32	62.8	19	37.3	1.15	0.64, 2.07	
Missing			1				
Education[a]							
High school or less	26	37.1	44	62.9	0.40	0.24, 0.68	**<0.01**
Some college	175	61.0	112	39.0	1.06	0.78, 1.45	
College graduate	247	59.5	168	40.5	Reference		
At least some graduate school	212	61.8	131	38.2	1.10	0.82, 1.48	
Missing			1				
Income[b]							
Less than or equal to $50k	208	55.2	169	44.8	0.79	0.58, 1.06	0.13
$50k - 100k	242	61.7	150	38.3	1.03	0.76, 1.39	
$100k+	199	61.0	127	39.0	Reference		
Missing	11		10				
Insurance[c]							
Private	516	61.4	325	38.6	Reference		
Self	35	61.4	22	38.6	1.00	0.58, 1.74	**0.02**
Public	59	53.2	52	46.9	0.72	0.48, 1.06	
None	49	46.7	56	53.3	0.55	0.37, 0.83	
Missing	1		1				
Married or cohabitating at time of diagnosis							
Yes	463	62.2	282	37.9	Reference		
No	197	53.1	174	46.9	0.69	0.54, 0.89	**<0.01**
Place of residence at diagnosis[d]							
Large central	100	55.3	81	44.8	0.92	0.66, 1.28	**0.08**

Large fringe	367	57.3	273	42.7	Reference	
Small metropolitan	131	66.2	67	33.8	1.45	1.04, 2.03
Non-metropolitan	62	63.9	35	36.1	1.32	0.85, 2.05

[a]Current education at the time of the interview.
[b]Current income at the time of the interview.
[c]Private insurance includes employer, school, military or VA insurance; self includes COBRA, public includes Medicare and Medicaid.
[d]Type of place of residence based on a modified version of the NCHS urban rural categories.

Supplemental Table 6-B: Bivariate Associations Between Characteristics of Cancer Survivors That Might Influence Initiating a Discussion About Fertility Counseling and Receipt of Fertility Counseling (All Cancers)

	Received Fertility Counseling						
	Yes (n=660)		No (n=456)				
	n	%	n	%	OR	95% CI	p value
Given birth to at least one child at diagnosis							
Yes	286	53.6	248	46.4	Reference		
No	374	64.3	208	35.7	1.56	1.23, 1.98	**<0.01**
Fewer children than desired at time of interview[a]							
Yes	396	64.6	217	35.4	1.68	1.32, 2.14	**<0.01**
No	254	52.0	234	48.0	Reference		
Missing	10		5				
Comfortable with ART[b]							
Strongly agree	82	63.1	48	36.9	1.23	0.72, 2.10	0.39
Agree	192	62.5	115	37.5	1.20	0.76, 1.91	
Neither agree nor disagree	57	58.2	41	41.8	Reference		
Disagree	194	57.1	146	42.9	0.96	0.61, 1.51	
Strongly disagree	129	55.6	103	44.4	0.90	0.56, 1.45	
Missing	6		3				
Polycystic ovary syndrome before diagnosis							
Yes	34	65.4	18	34.6	1.33	0.74, 2.38	0.34
No	619	58.7	435	41.3	Reference		
Missing	7		3				
Endometriosis before diagnosis							
Yes	39	52.7	35	47.3	0.76	0.47, 1.22	0.25
No	619	59.5	421	40.5	Reference		
Missing	2						
Fibroids before diagnosis							
Yes	42	61.8	26	38.2	1.13	0.68, 1.87	0.64
No	614	58.9	428	41.1	Reference		
Missing	4		2				
Chlamydia before diagnosis							
Yes	51	54.3	43	45.7	0.80	0.53, 1.23	0.31
No	609	59.7	412	40.4	Reference		

Missing			1				
Gonorrhea before diagnosis							
Yes	12	48.0	13	52.0	0.63	0.29, 1.40	0.26
No	648	59.4	443	40.6	Reference		
Pelvic Inflammatory Disease before diagnosis							
Yes	18	58.1	13	41.9	0.96	0.46, 1.97	0.90
No	641	59.2	442	40.8	Reference		
Missing	1		1				
Human Papilloma Virus before diagnosis							
Yes	74	69.2	33	30.8	1.61	1.05, 2.47	**0.03**
No	585	58.2	420	41.8	Reference		
Missing	1		3				
Herpes before diagnosis							
Yes	26	59.1	18	40.9	1.00	0.54, 1.84	0.99
No	634	59.1	438	40.9	Reference		
Surgery on ovaries before diagnosis							
Yes	38	57.6	28	42.4	0.93	0.56, 1.54	0.77
No	564	59.4	386	40.6	Reference		
Missing	58		42				
Surgery on fallopian tubes before diagnosis[c]							
Yes	38	42.2	52	57.8	0.47	0.31, 0.73	**<0.01**
No	610	60.6	396	39.4	Reference		
Missing	12		8				
Surgery on uterus before diagnosis							
Yes	15	62.5	9	37.5	1.16	0.51, 2.68	0.72
No	637	58.9	445	41.1	Reference		
Missing	8		2				
History of amenorrhea before diagnosis[d]							
Yes	112	63.6	64	36.4	1.24	0.89, 1.74	0.21
No	500	58.5	355	41.5	Reference		
Missing	48		37				
Pregnant at diagnosis							
Yes	30	66.7	15	33.3	1.40	0.74, 2.63	0.30
No	630	58.8	441	41.2	Reference		
Miscarriage before diagnosis							

Yes	112	59.0	78	41.1	0.98	0.71, 1.35	0.91
No	547	59.1	378	40.9	Reference		
Missing	1						
Stillbirth before diagnosis							
Yes	3	60.0	2	40.0	1.04	0.17, 6.24	0.97
No	656	59.1	454	40.9	Reference		
Missing	1						
Abortion before diagnosis							
Yes	91	60.3	60	39.7	1.06	0.75, 1.50	0.76
No	568	58.9	396	41.1	Reference		
Missing	1						
Ectopic pregnancy before diagnosis							
Yes	4	40.0	6	60.0	0.46	0.30, 1.63	0.23
No	655	59.3	450	40.7	Reference		
Missing	1						
Preterm birth before diagnosis[e]							
Yes	71	49.0	74	51.0	0.59	0.42, 0.85	**<0.01**
No	588	60.6	382	39.4	Reference		
Missing	1						
Low birth weight before diagnosis[f]							
Yes	41	49.4	42	50.6	0.64	0.41, 1.02	**0.06**
No	562	59.0	391	41.0	Reference		
Missing	57		23				

[a]Fewer kids defined by subtracting the number of children a woman had from the number of children she desired at the time of the interview.
[b]Based on the question: "I would be/would have been comfortable with the idea of using assisted reproductive technology, such as in vitro fertilization or artificial insemination, to help me get pregnant."
[c]Surgery on fallopian tubes includes getting tubes tied for birth control.
[d]Amenorrhea defined as 3 months or more without a menstrual period since the participants turned 20 years old.
[e]Preterm birth defined as a live birth less than 37 weeks. "No" includes nulliparous women.
[f]Low birth weight defined as a live birth less than 2500 grams. "No" includes nulliparous women.

Supplemental Table 6-C: Bivariate Associations Between Characteristics of Cancer Survivors That Might Influence A Healthcare Provider's Initiation of a Discussion About Fertility Counseling and Receipt of Fertility Counseling (All Cancers)

	Received Fertility Counseling						
	Yes (n=660)		No (n=456)				
	n	%	n	%	OR	95% CI	p value
Chronic hypertension before diagnosis							
Yes	31	62.0	19	38.0	1.13	0.63, 2.03	0.68
No	628	59.0	436	41.0	Reference		
Missing	1		1				
Diabetes before diagnosis							
Yes	11	55.0	9	45.0	0.84	0.35, 2.05	0.70
No	648	59.2	446	40.8	Reference		
Missing	1		1				
Smoker before diagnosis							
Yes	162	61.8	100	38.2	1.16	0.88, 1.55	0.30
No	496	58.2	356	41.8	Reference		
Missing	2						
BMI at diagnosis[a]							
Underweight	25	56.8	19	43.2	0.85	0.46, 1.57	0.51
Normal	400	60.8	258	39.2	Reference		
Overweight	125	55.3	101	44.7	0.80	0.59, 1.08	
Obese	108	58.1	78	41.9	0.89	0.64, 1.24	
Missing	2						
Year of diagnosis							
1990-94	10	66.7	5	33.3	1.24	0.42, 3.67	0.16
1995-99	67	51.9	62	48.1	0.67	0.46, 0.98	
2000-04	228	57.4	169	42.6	0.84	0.64, 1.09	
2005-09	355	61.7	220	38.3	Reference		
Chemotherapy[b]							
Yes	466	72.9	173	27.1	3.93	3.05, 5.06	**<0.01**
No	194	40.7	283	59.3	Reference		
Radiation[c]							
Yes	345	67.4	167	32.6	1.90	1.49, 2.42	**<0.01**
No	315	52.2	289	47.9	Reference		
Cancer types							
Reproductive (cervix, ovary, uterus)	51	81.0	12	19.1	3.10	1.63, 5.88	**<0.01**
Breast	274	69.7	119	30.3	2.01	1.55, 2.61	**<0.01**

Brain	16	57.1	12	42.9	0.92	0.43, 1.96	0.83
Hodgkin lymphoma	97	82.9	20	17.1	3.76	2.28, 1.96	**<0.01**
Non-hodgkin lymphoma	34	61.8	21	38.2	1.13	0.64, 1.97	0.68
Thyroid	66	54.1	56	45.9	0.79	0.54, 1.16	0.23
Other cancer type	122	36.1	216	63.9	Reference		

[a]Body mass index classified as: underweight = <18.5, normal weight = 18.5-24.9, overweight = 25-29.9, and obese =30 or greater.
[b]Chemotherapy as self-reported in the interview.
[c]Radiation as self-reported in the interview.

Supplemental Table 6-D: Bivariate Associations Between Sociodemographic Characteristics of Cancer Survivors and Receipt of Fertility Counseling (Excludes Melanoma and Thyroid Cancer)

	Received Fertility Counseling						
	Yes (n=584)		No (n=308)				
	n	%	n	%	OR	95% CI	p value
Age at diagnosis (years)							
20-24	83	65.4	44	34.7	0.83	0.53, 1.31	0.30
25-29	174	69.3	77	30.7	Reference		
30-35	327	63.6	187	36.4	0.77	0.56, 1.07	
Race							
White	403	68.4	186	31.6	Reference		**0.03**
Black	154	59.0	107	41.0	0.66	0.49, 0.90	
Other race	27	65.9	14	34.2	0.89	0.46, 1.74	
Missing			1				
Education[a]							
High school or less	23	37.1	39	62.9	0.28	0.16, 0.50	**<0.01**
Some college	163	64.4	90	35.6	0.86	0.61, 1.22	
College graduate	214	67.7	102	32.3	Reference		
At least some graduate school	184	70.8	76	29.2	1.15	0.81, 1.65	
Missing			1				
Income[b]							
Less than or equal to $50k	198	59.8	133	40.2	0.60	0.42, 0.86	**0.01**
$50k - 100k	213	67.6	102	32.4	0.84	0.58, 1.22	
$100k+	166	71.2	67	28.8	Reference		
Missing	7		6				
Insurance[c]							
Private	449	68.9	203	31.1	Reference		**<0.01**
Self	32	71.1	13	28.9	1.11	0.57, 2.17	
Public	58	54.2	49	45.8	0.54	0.35, 0.81	
None	44	50.6	43	49.4	0.46	0.29, 0.73	
Missing	1						
Married or cohabitating at time of diagnosis							
Yes	414	67.2	202	32.8	Reference		
No	170	61.6	106	38.4	0.78	0.58, 1.05	0.10
Place of residence at diagnosis[d]							
Large central	81	67.5	39	32.5	1.12	0.73, 1.71	0.94

Large fringe	310	65.0	167	35.0	Reference	
Small metropolitan	131	66.2	67	33.8	1.05	0.74, 1.49
Non-metropolitan	62	63.9	35	36.1	0.95	0.61, 1.50

[a]Current education at the time of the interview.
[b]Current income at the time of the interview.
[c]Private insurance includes employer, school, military or VA insurance; self includes COBRA, public includes Medicare and Medicaid.
[d]Type of place of residence based on a modified version of the NCHS urban rural categories.

Supplemental Table 6-E: Bivariate Associations Between Characteristics of Cancer Survivors That Might Influence Initiating a Discussion About Fertility Counseling and Receipt of Fertility Counseling (Excludes Melanoma and Thyroid Cancer)

	Received Fertility Counseling						
	Yes (n=584)		No (n=308)				
	n	%	n	%	OR	95% CI	p value
Given birth to at least one child at diagnosis							
Yes	263	56.8	200	43.2	Reference		
No	321	74.8	108	25.2	2.26	1.70, 3.01	**<0.01**
Fewer children than desired at time of interview[a]							
Yes	355	72.2	137	27.9	1.96	1.48, 2.60	**<0.01**
No	222	56.9	168	43.1	Reference		
Missing	7		3				
Comfortable with ART[b]							
Strongly agree	73	67.6	35	32.4	1.04	0.56, 1.93	**0.08**
Agree	170	72.0	66	28.0	1.29	0.75, 2.22	
Neither agree nor disagree	54	66.7	27	33.3	Reference		
Disagree	169	61.7	105	38.3	0.80	0.48, 1.36	
Strongly disagree	112	60.5	73	39.5	0.77	0.44, 1.33	
Missing	6		2				
Polycystic ovary syndrome before diagnosis							
Yes	31	68.9	14	31.1	1.18	0.62, 2.25	0.62
No	546	65.2	291	34.8	Reference		
Missing	7		3				
Endometriosis before diagnosis							
Yes	36	57.1	27	42.9	0.69	0.41, 1.15	0.16
No	546	66.0	281	34.0	Reference		
Missing	2						
Fibroids before diagnosis							
Yes	41	67.2	20	32.8	1.09	0.63, 1.89	0.77
No	539	65.3	286	34.7	Reference		
Missing	4		2				
Chlamydia before diagnosis							
Yes	48	56.5	37	43.5	0.65	0.42, 1.03	0.07

No	536	66.5	270	33.5	Reference		
Missing							
Gonorrhea before diagnosis							
Yes	11	47.8	12	52.2	0.47	0.21, 1.09	**0.08**
No	573	65.9	296	34.1	Reference		
Pelvic Inflammatory Disease before diagnosis							
Yes	16	57.1	12	42.9	0.69	0.32, 1.49	0.35
No	567	65.8	295	34.2	Reference		
Missing	1		1				
Human Papilloma Virus before diagnosis							
Yes	63	71.6	25	28.4	1.36	0.84, 2.21	0.21
No	520	64.9	281	35.1	Reference		
Missing	1		2				
Herpes before diagnosis							
Yes	26	63.4	15	36.6	0.91	0.48, 1.75	0.78
No	558	65.6	293	34.4	Reference		
Surgery on ovaries before diagnosis							
Yes	34	63.0	20	37.0	0.86	0.48, 1.52	0.60
No	492	66.5	248	33.5	Reference		
Missing	58		40				
Surgery on fallopian tubes before diagnosis[c]							
Yes	36	44.4	45	55.6	0.38	0.24, 0.61	**<0.01**
No	536	67.7	256	32.3	Reference		
Missing	12		7				
Surgery on uterus before diagnosis							
Yes	14	70.0	6	30.0	1.24	0.47, 3.27	0.66
No	563	65.2	300	34.8	Reference		
Missing	7		2				
History of amenorrhea before diagnosis[d]							
Yes	106	68.0	50	32.1	1.13	0.78, 1.64	0.53
No	436	65.3	232	34.7	Reference		
Missing	42		26				
Pregnant at diagnosis							
Yes	28	73.7	10	26.3	1.50	0.72, 3.13	0.28
No	556	65.1	298	34.9	Reference		

Miscarriage before diagnosis							
Yes	106	63.5	61	36.5	0.90	0.63, 1.28	0.55
No	477	65.9	247	34.1	Reference		
Missing	1						
Stillbirth before diagnosis							
Yes	3	60.0	2	40.0	0.79	0.13, 4.76	0.80
No	580	65.5	306	34.5	Reference		
Missing							
Abortion before diagnosis							
Yes	86	64.2	48	35.8	0.94	0.64, 1.38	0.74
No	497	65.7	260	34.4	Reference		
Missing							
Ectopic pregnancy before diagnosis							
Yes	3	33.3	6	66.7	0.26	0.07, 1.05	**0.06**
No	580	65.8	302	34.2	Reference		
Missing							
Preterm birth before diagnosis[e]							
Yes	67	51.9	62	48.1	0.52	0.35, 0.75	**<0.01**
No	516	67.7	246	32.3	Reference		
Missing							
Low birth weight before diagnosis[f]							
Yes	40	51.3	38	48.7	0.56	0.35, 0.89	**0.01**
No	489	65.5	258	34.5	Reference		
Missing	55		12				

[a]Fewer kids defined by subtracting the number of children a woman had from the number of children she desired at the time of the interview.
[b]Based on the question: "I would be/would have been comfortable with the idea of using assisted reproductive technology, such as in vitro fertilization or artificial insemination, to help me get pregnant."
[c]Surgery on fallopian tubes includes getting tubes tied for birth control.
[d]Amenorrhea defined as 3 months or more without a menstrual period since the participants turned 20 years old.
[e]Preterm birth defined as a live birth less than 37 weeks. "No" includes nulliparous women.
[f]Low birth weight defined as a live birth less than 2500 grams. "No" includes nulliparous women.

Supplemental Table 6-F: Bivariate Associations Between Characteristics of Cancer Survivors That Might Influence A Healthcare Provider's Initiation of a Discussion About Fertility Counseling and Receipt of Fertility Counseling (Excludes Melanoma and Thyroid Cancer)

	Received Fertility Counseling						
	Yes (n=584)		No (n=308)				
	n	%	n	%	OR	95% CI	p value
Chronic hypertension before diagnosis							
Yes	26	57.8	19	42.2	0.71	0.39, 1.30	0.27
No	557	65.9	288	34.1	Reference		
Missing	1		1				
Diabetes before diagnosis							
Yes	11	57.9	8	42.1	0.72	0.29, 1.80	0.48
No	573	65.7	299	34.3	Reference		
Missing			1				
Smoker before diagnosis							
Yes	150	69.1	67	30.9	1.25	0.90, 1.73	0.19
No	433	64.2	241	35.8	Reference		
Missing	1						
BMI at diagnosis[a]							
Underweight	21	67.7	10	32.3	0.98	0.45, 2.13	0.18
Normal	351	68.2	164	31.8	Reference		
Overweight	112	62.2	68	37.8	0.77	0.54, 1.10	
Obese	98	59.8	66	40.2	0.69	0.48, 1.00	
Missing	2						
Year of diagnosis							
1990-94	10	66.7	5	33.3	0.96	0.32, 2.85	0.51
1995-99	57	64.0	32	36.0	0.85	0.53, 1.37	
2000-04	193	62.5	116	37.5	0.80	0.59, 1.07	
2005-09	324	67.6	155	32.4	Reference		
Chemotherapy[b]							
Yes	466	72.9	173	27.1	3.08	2.28, 4.17	**<0.01**
No	118	46.6	135	53.4	Reference		
Radiation[c]							
Yes	301	70.2	128	29.8	1.50	1.13, 1.98	**<0.01**
No	283	61.1	180	38.9	Reference		
Cancer types							
Reproductive (cervix, ovary, uterus)	51	81.0	12	19.1	2.36	1.24, 4.50	**0.01**

Breast	274	69.7	119	30.3	1.40	1.06, 1.86	**0.02**
Brain	16	57.1	12	42.9	0.70	0.32, 1.49	0.35
Hodgkin lymphoma	97	82.9	20	17.1	2.87	1.74, 4.74	**<0.01**
Non-hodgkin lymphoma	34	61.8	21	38.2	0.85	0.48, 1.48	0.56
Other cancer type	112	47.5	124	52.5	Reference		

[a]Body mass index classified as: underweight = <18.5, normal weight = 18.5-24.9, overweight = 25-29.9, and obese =30 or greater.
[b]Chemotherapy as self-reported in the interview.
[c]Radiation as self-reported in the interview.

Supplemental Table 6-G: Receipt of Fertility Counseling by Stage of Cancer Among Breast Cancer Survivors

	Received Fertility Counseling						
	Yes (n=274)		No (n=119)				
	n	%	n	%	OR	95% CI	p value
Cancer stage[a,b]							
Zero[c]	27	56.3	21	43.8	0.56	0.29, 1.07	0.18
One	129	69.7	56	30.3	Reference		
Two	5	71.4	2	28.6	1.09	0.20, 5.76	
Three	91	71.1	37	28.9	1.07	0.65, 1.75	
Four	11	91.7	1	8.3	4.78	0.60, 37.89	
Missing	11		2				

[a]Cancer stage reported by the Georgia Cancer Registry.
[b]Thirteen breast cancer survivors were missing information on stage.
[c]Stage zero includes in situ breast cancer only.

Figure 6-1. Categories of Factors that May Influence Whether or Not a Woman Receives Fertility Counseling at the Time of Cancer Diagnosis.

	SOCIO-DEMOGRAPHIC	PATIENT	PHYSICIAN
Age at diagnosis	☑	☑	☑
Race	☑	☑	☑
Education	☑	☑	☑
Income	☑	☑	☑
Insurance	☑	☑	☑
Married or cohabitating at time of diagnosis	☑	☑	☑
Type of place of residence at diagnosis[a]	☑	☑	☑
Given birth to at least one child at diagnosis		☑	☑
Fewer children than desired at time of interview		☑	
Comfortable with ART[b]		☑	
Reproductive condition before diagnosis[c]		☑	
Reproductive surgery before diagnosis[d]		☑	
Pregnant at diagnosis		☑	☑
Adverse pregnancy outcome before diagnosis[e]		☑	
Adverse birth outcome before diagnosis[f]		☑	
Comorbidities[g]			☑
Smoking history			☑
BMI at diagnosis			☑
Year of diagnosis			☑
Cancer treatment modality[h]			☑
Cancer type			☑

[a]Level of urbanization of the county of residence
[b]Comfort with assisted reproductive technologies such as in vitro fertilization.
[c]Diagnosis with polycystic ovary syndrome, endometriosis, or fibroids.
[d]Surgery on uterus, ovaries, or fallopian tubes.
[e]Miscarriage or stillbirth.
[f]Preterm or low birth weight birth
[g]Chronic hypertension or diabetes.
[h]Chemotherapy and/or radiation.

Figure 6-2. Receipt of Fertility Counseling by Parity and Desire for More Children

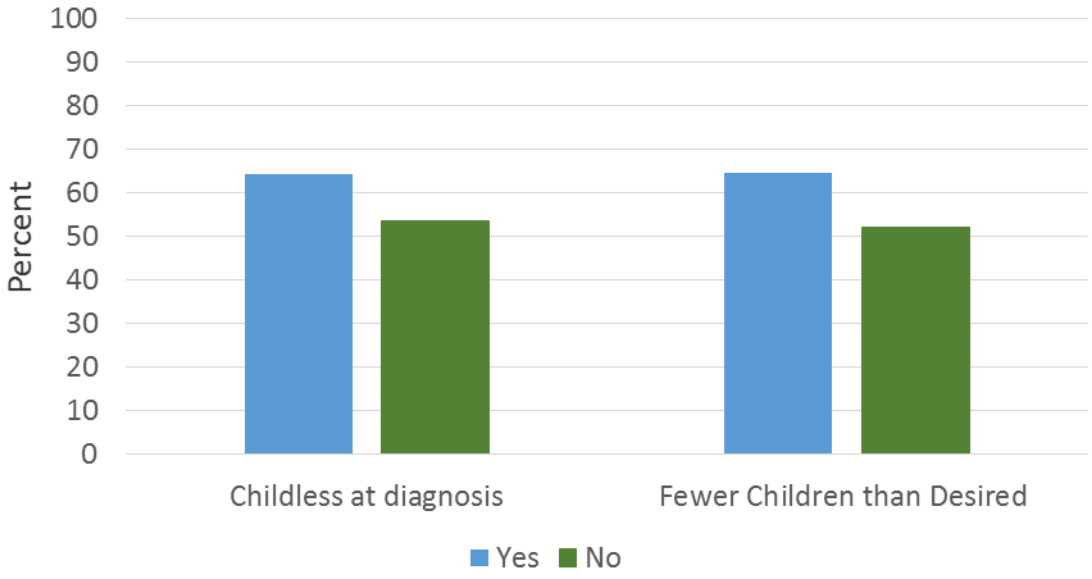
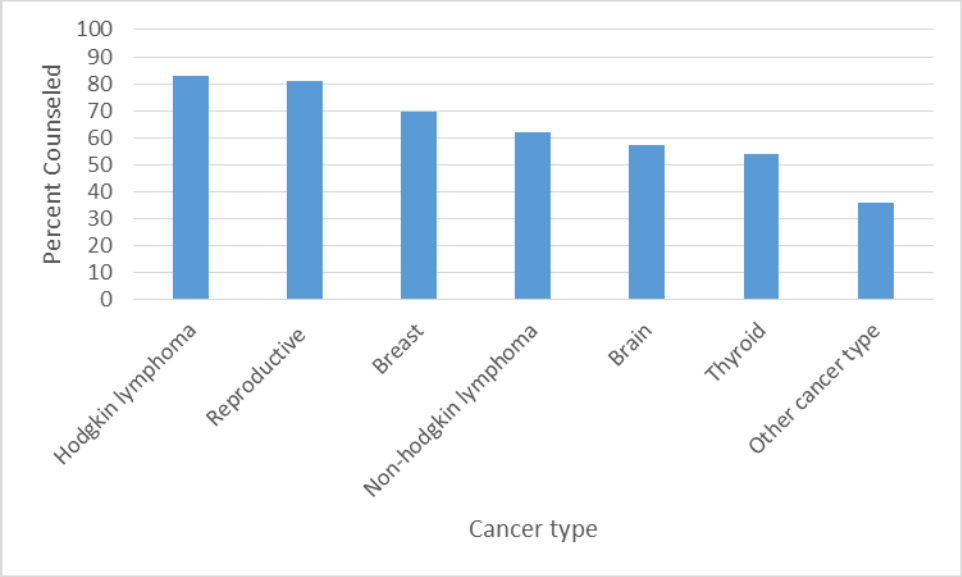


Figure 6-3. Receipt of Fertility Counseling by Cancer Type



CHAPTER 7: Summary of Findings and Future Research

SUMMARY OF FINDINGS

Findings from Aim 1

Aim 1 (Chapter 3) assessed whether a racial disparity existed in visiting a doctor for help getting pregnant. In this study, we found substantial racial differences in visiting a doctor for help getting pregnant, yet similar reporting of impaired fertility in black and white women. Since our paper was focused on how the experience of black race in the US context might affect women's use of medical care for infertility, we estimated the racial disparity that remained after accounting for a set of identified mediating paths from the social construct of race to visiting a doctor for help getting pregnant. These mediator-adjusted models were only able to partially explain the difference by race in visiting a doctor for help getting pregnant. Survival analysis results were consistent in showing a disparity in seeking care for help getting pregnant by race. Black women waited almost twice as long on average compared with white women after experiencing infertility before visiting a doctor for fertility care. Racial disparities persisted despite control for mediating paths or type of analysis used which suggests that additional components that contribute to the social construct of race are influencing the disparity in seeking fertility care.

Findings from Aim 2

Aim 2 (Chapter 4) examined geographic differences in visiting a doctor for help getting pregnant. Results from the four category geographic classification, where we looked at residence in urbanized, suburban, small metropolitan, and small town/rural counties showed differences in visiting a doctor for fertility care by type of county of

residence. The largest differences in seeking fertility care by geographic type of residence were among the women who reported experiencing infertility. Some of this difference could be due to cultural factors that might influence a woman's comfort with assisted reproductive technology and adoption or the importance of having a biologic child. Women from small town/rural counties were least comfortable with assisted reproductive technology and most comfortable with adoption. The opposite trend was seen among women from urbanized counties where women were most comfortable with assisted reproductive technology and least comfortable with adoption. The majority of women regardless of type of county of residence reported that having a biologic child was very important to them.

After controlling for differences in participant characteristics by type of residence, women from small town counties had a similar likelihood of visiting a doctor for help getting pregnant to women from suburban counties. These women were the most likely to seek care. Further, adjusted analyses showed women from small town/rural counties had a similar likelihood of visiting a doctor to women from urbanized counties. These women were the least likely to seek care. Findings from this study suggest a disparity in access to fertility care among small town/rural residents as well as residents of urbanized counties compared with other county types. These findings were consistent with results obtained using the National Survey for Family Growth (Chapter 5).

Findings from Aim 3

Aim 3 (Chapter 6) determined which factors were most strongly associated with receiving fertility counseling at the time of cancer diagnosis. Practice guidelines for

healthcare providers treating cancer patiens state that all women of reproductive age should be counseled on how cancer treatment might affect their future fertility [8]. In our study, 40% of cancer survivors reported not receiving information on how cancer treatment could affect their future fertility. Of the women who received counseling, only 13% were referred to a fertility specialist to discuss fertility preservation options.

We examined three groups of factors that might influence the receipt of counseling. Among the sociodemographic variables assessed having less than some college level education was associated with a reduced likelihood of fertility counseling. Among the patient characteristics that might influence a woman to initiate a discussion about fertility, we found women who were nulliparous or had a desire for more children at the time of diagnosis were more likely to get counseled about fertility compared with women who had children or did not want any (more). When we looked at patient characteristics that might influence a physician's provision of fertility counseling, treatment with chemotherapy and certain cancer types were associated with receipt of counseling. Models including patient characteristics that might influence physicians in providing counseling showed survivors of reproductive cancers were among the most likely to be counseled while survivors of non-Hodgkin lymphoma were least likely to be counseled. However, even among the reproductive cancers, 20% of women diagnosed with ovarian, uterine, or cervical cancer reported not receiving fertility counseling.

Overall Findings

These three studies show that there are certain groups of women who may need fertility counseling and treatment and are not receiving it. Black women, women who live

in an urbanized or small town/rural county, and women with less education were less likely to receive fertility counseling and care. In *Aim 1*, compared with white women, black women in our study were less likely to visit a doctor for help getting pregnant even though they were also less likely to have a child at the time of the interview.

In *Aim 2*, we found that after adjustment for important covariates of the association between type of place of residence and visiting a doctor for help getting pregnant, women living in suburban and small metropolitan areas were most likely to seek this type of care. Women living in urbanized and small town/rural counties were less likely to visit a doctor for fertility care. While unsurprising that women living in less densely populated areas are accessing specialized medical care less frequently than more densely populated areas, it was notable that women living in the most urbanized counties, where there is greater physical access to medical care, were no more likely to access fertility care than women living in the least urbanized.

In *Aim 3*, our results show that despite universal recommendations to provide women of reproductive age with fertility counseling at the time of their cancer diagnosis, close to 41% of women did not report receiving any information on how cancer treatment could affect future fertility. This is alarming because cancer patients are already communicating with a healthcare provider when they need information on possible effects of cancer treatment on fertility and unlike women from the general population, cancer patients should not need to initiate a discussion with a healthcare provider about fertility care. Few variables of the many examined were strongly associated with receiving counseling, indicating that although the provision of counseling overall is

insufficient, there were not disparities in counseling for many of the characteristics we looked at in our study. However, less education, was persistently associated with a reduced likelihood of receiving counseling, which suggests that these women are not being counseled because of their level of education or factors associated with less education, or they were not counseled in a way that was commensurate with their level of understanding.

STRENGTHS AND LIMITATIONS

There were several limitations of the three studies addressing *Aims 1-3* of this dissertation. In studies addressing *Aims 1 and 2*, we utilized the comparison women from the FUCHSIA Women's Study. The recruitment strategy used for these participants may have resulted in selection bias. While, recruitment of the cancer survivors in FUCHSIA was truly population-based, recruitment of comparison women was done using a purchased marketing list which may have lacked information on some women who we wanted to participate in our study. The purchased list was generated to match the distribution of age and location of residence of female cancer survivors 22-45 years old who were recruited by FUCHSIA from all eligible cancer survivors in the state. Despite not being truly population-based, comparison women were similar to cancer survivors on many of the sociodemographic characteristics of interest.

The timing of the measurement of some of the variables was not always ideal. In *Aim 2* we were constrained to women's place of residence at the time of the interview, which on average was 9 years after the age at visiting a doctor for help getting pregnant, so some women may have been misclassified. This may have been mitigated by the fact

that women may not have moved to a different geographic type of county and overall, across the population of the state, there was only a 3.5% increase in the urban population in the state of Georgia between 2000 and 2010 [131, 132].

Some of our demographic variables, education, income, and insurance were measured at the time of the interview. In all three aims, we would have liked to know the values of these variables at the time of the outcome, either visiting a doctor for help getting pregnant (*Aims 1-2*) or receiving fertility counseling at the time of cancer diagnosis (*Aim 3*). Depending on the timing of the interview in relation to the outcome of interest, these may be good proxies of the information we wanted, with longer duration resulting in more uncertainty that the desired measure was being captured. Another limitation across all studies is that the data are restricted to self-reported information on fertility discussions with healthcare providers without verification with medical records. However, we expect women are able to remember a self-initiated visit to the doctor for help getting pregnant (*Aims 1-2*) and found women could consistently report this information in our pilot studies [93]. For *Aim 3*, participants were asked to recall receiving fertility counseling at the time they were diagnosed with cancer. Because this is a uniquely stressful time, information exchanged during this or doctor's visits around this time could have been missed by the participant.

There were also many strengths of these three studies. First, these studies used a population-based sample. Women were recruited to participate independently of their fertility status, allowing for a comparison between women who did and did not visit a doctor for help getting pregnant. This is in contrast to clinic-based studies that can only

describe the characteristics of women who visit a fertility clinic for help getting pregnant. These studies cannot fully capture disparities by race or other sociodemographic factors; they are just able to describe difference in care among help seekers. In addition, all women interviewed in the FUCHSIA Women's Study were asked whether or not they ever visited a doctor for help getting pregnant. This question was asked regardless of a participant's marital or infertility status. Since we did not restrict who we asked this question, we were able to include the full sample in our analyses for *Aims 1 and 2*. This was important because of those visiting a doctor for help getting pregnant, close to 10% never reported experiencing a period of infertility.

The FUCHSIA Women's Study was especially well suited to examine black white racial disparities (*Aim 1*). Black women, who are traditionally underrepresented in research were well represented in the FUCHSIA Women's Study because the study population reflected the demographic composition of women of reproductive age (20-44 years) in Georgia, which is 34% black [115]. Categories of education, type of place of residence, and household income were also well represented allowing us to look at differences in fertility care within these groups. Because the interview was extensively detailed, we could capture information not commonly collected in other studies such as women's feelings about assisted reproductive technology and adoption, as well as how important having a biologic child was to them. This information was used to describe some of the cultural factors that differ by type of county of residence.

Another strength of the FUCHSIA Women's Study is that almost all cancer types were recruited. The study included all invasive cancers except non-melanoma skin cancer, as well as in situ breast cancer. Most studies of cancer survivors limit to a few

cancer types and are limited in their conclusions to those few cancers. The broad inclusion criteria in the FUCHSIA Women's Study allowed us to assess differences in receipt of fertility counseling across most cancer types (*Aim 3*). Because the FUCHSIA Women's Study also included women diagnosed over several decades, we could also compare trends in fertility counseling and referral before and after the guidelines for universal counseling by ASRM and ASCO were released in 2005 and 2006, respectively. Lastly, while some studies have found that parity influences whether or not women get fertility counseling at diagnosis, with women who already have children being less likely to be counseled, parity might not be a good indicator of women's reproductive desires [25]. In *Aim 3* we were able to look at receipt of fertility counseling by the unique outcome of having fewer children than desired which captures women who have not yet reached their desired family size, regardless of parity.

FUTURE RESEARCH

In Aim 1 we found that black women were less likely to visit a doctor for help getting pregnant than white women. We assessed this association using a population-based sample in Georgia. Sociocultural factors were accounted for to the extent available by including women's reported comfort with using assisted reproductive technology and desire for children. In analyses which controlled for these and other mediating variables between race and visiting a doctor for fertility care, a residual disparity remained, suggesting factors not included in our analysis are having an effect on fertility care seeking. Thus, future research into additional sociocultural and demographic factors that might be contributing to these disparities could elucidate ways to improve the dissemination of information on infertility and treatment options, in turn increasing the

utilization of fertility care. These additional factors might include addressing women's feelings around infertility such as stigma, personal sense of failure to conceive a child, and support or discouragement from their family and friends regarding the use of fertility treatment. Additionally, population-based studies of utilization of fertility care are rare and findings from more of these types of studies, that include a women in the general population, could contribute to what has been found among help seeking women in the clinic-based literature. In addition to more research to better explain why racial disparities exist in who visits a doctor for help getting pregnant, better communication about available fertility counseling and treatment options could help address these disparities by decreasing discomfort with using medical help for becoming pregnant.

In Aim 2 we found women living in the most and least urbanized counties were least likely to seek fertility care. In our study, we had limited sample size within each of the four categories of type of place of residence of interest. Analyses conducted using data from NSFG provided a larger sample size which was nationally representative, but was limited by how the geographic categories were classified; they were only provided as a three-level variable and without context to where in the US participants lived. Larger population-based studies in a defined region would provide more precise and interpretable estimates of geographic disparities in visiting a doctor for help getting pregnant. These studies could also provide information on factors driving low use of fertility care in urbanized counties where physical access to care is not the major barrier, but might be caused by financial or sociocultural barriers.

In Aim 3 we found that an unacceptably low proportion of cancer survivors reported that they received information on how cancer treatment could affect their ability to become pregnant. Characteristics of the participants were assessed to find factors associated with receipt of fertility counseling at the time of diagnosis. The only consistent factor that was associated with a lack of counseling was having no college education. Unlike Aims 1 and 2, all women are seeing a healthcare provider at the time they need fertility counseling, so improvements in access to this type of care should be healthcare provider focused. Additional studies assessing oncologist's knowledge about and comfort with fertility counseling could pinpoint some areas for additional education. Awareness by oncologists about the importance of discussing the effects of cancer treatment on fertility among all their patients of reproductive age may improve the frequency with which they offer this type of counseling. The next step would be to find ways to incorporate counseling into routine oncologic care. Potential ideas to do this would be to include it on an already existing checklist used for care or providing a counseling aid with key points for oncologists to address. Surveying oncologists to get their opinions on ways to easily include fertility counseling into care could identify the best way to do this.

There are many ways that can help expand the use of fertility care. Providing women with more information on infertility and treatment options may help increase the utilization of care among the general population. Using regular doctor's visits and already existing organizations that bring awareness to infertility can help facilitate this exchange of information, as well as make specific efforts to reach women who are underrepresented in the utilization of fertility care. This could increase the overall comfort women have with seeking care for help getting pregnant. Additionally, it could

help more cancer patients receive fertility counseling, because awareness of fertility issues may prompt them to initiate a fertility discussion with their oncologist at the time of cancer diagnosis and make them more comfortable visiting a fertility specialist to discuss fertility preservation options. Giving women comprehensive information on their options for medical help to become pregnant can allow them to make informed decisions about how to achieve their reproductive goals.

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