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Framing Conversations Around Fertility: Experiences of People with Cystic Fibrosis, Their Parents, and Their Clinical Teams

THESIS

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in Genetic Counseling

By

Nicole Charlotte Nevitt

Thesis Committee:

Professor Eliezer Nussbaum, Chair

Associate Clinical Professor Kathryn Singh

Assistant Clinical Professor Meghan Gillespie

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ABSTRACT OF THE THESIS

Framing Conversations Around Fertility: Experiences of People with Cystic Fibrosis, Their Parents, and Their Clinical Teams

By

Nicole Charlotte Nevitt

Master of Science in Genetic Counseling

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Professor Eliezer Nussbaum, Chair

Cystic fibrosis (CF) is an autosomal recessive genetic condition caused by biallelic pathogenic variants in the *CFTR* gene. The condition is characterized by thick mucus that progressively causes damage to the respiratory and digestive systems. CF also affects fertility in both males and females. Approximately 95% of males with CF experience infertility, largely due to complete or partial congenital bilateral absence of the vas deferens (CBAVD), and even those with biallelic CFTR gene variants without clinical CF features can have CBAVD. CBAVD prevents mature sperm from leaving the body, rendering these males infertile by natural conception methods. However, assisted reproductive technology can help them achieve fertility. About 35% of females with CF face infertility due to altered cervical mucus, ovulation issues, or nutritional problems. Those with significant lung disease must also weigh the medical risks of pregnancy. With highly effective modulator therapy, pregnancy rates in the CF population have

risen dramatically, but there remains a knowledge gap regarding individual fertility capabilities, likely due to inadequate fertility education. Currently, no guidelines exist on discussing fertility with people with CF (pwCF), and it is unclear how well available resources are utilized.

An anonymous survey was distributed to pwCF, parents of pwCF, and healthcare providers from CF care centers via Exchange Forums through the CF Foundation, on social media platforms including Facebook, Reddit, Instagram, and LinkedIn, and online support group forums including CysticFibrosis.com and HealingWell.com. Participants were at least 18 years old, could read/write in English, and lived in the United States (US). Participants completed a fertility knowledge assessment and were asked to describe their experience with fertility discussions as part of their CF care, as well as how they hope fertility will be discussed in the future.

A total of 116 pwCF and 24 parents from 27 states participated, along with 111 providers from all US regions. Responses to short answer questions revealed a strong desire for improved fertility care practices from all groups. Only about half of pwCF indicated satisfaction with their fertility care. Nearly two thirds of pwCF and parents reported fertility conversations were initiated by pwCF or parents rather than providers. Although various care team members engaged in fertility discussions, approximately one in six pwCF stated that no one had discussed fertility with them. Pulmonologists, specialty physicians, and genetic counselors were identified by all groups as best suited for fertility discussions. Most pwCF and parents preferred fertility conversations to occur during teenage years, contrasting with their reported experiences of discussions happening mostly after transitioning to adult care. Provider responses on current practices varied, but a consensus leaned towards discussing fertility during teenage and transition years.

This study highlights a gap between current practices and the expectations of pwCF, parents, and providers regarding CF fertility care. All groups emphasized the importance of this issue and expressed a strong motivation to improve fertility care for pwCF and their families.

I INTRODUCTION

1.1 Overview of cystic fibrosis

Cystic fibrosis (CF) is an autosomal recessive genetic condition characterized by thick mucus that progressively causes damage to the respiratory and digestive systems. Symptoms can extend beyond these primary systems and include frequent lung infections, persistent coughing, wheezing or shortness of breath, pancreatic insufficiency with associated digestive complications and poor growth and weight gain, salty skin, nasal polyps, chronic sinus infections, digital clubbing, infertility, and CF-related diabetes (Savant et al., 2023).

Currently there are almost 40,000 individuals with CF in the United States (U.S.), and approximately 1,000 new cases are diagnosed each year (CF Foundation, 2023). According to a study published in 2022, there are an estimated 146,428 individuals living with CF worldwide (Guo et al, 2022). More than half of individuals with CF are over the age of 18, a proportion which is almost double what it was in 1986 (CF Foundation, 2023). According to the CF Foundation's Registry Summary, the median survival rate as of 2021 is approximately 53 years. This is a significant increase from 38 years in 2009 and 32 years in 1999, and even more so since the discovery of the disease in the 1950's when people with CF did not survive long enough to attend elementary school (CF Foundation, 2023). This is due in large part to earlier detection and evolving treatments that have extended the life expectancy estimate for those living with CF.

CF has a well-established clinical care network that is credentialed through the CF Foundation, with over 130 care centers and over 50 affiliated programs across the U.S. that have received accreditation by meeting a range of criteria. Required members of a CF care team include pulmonologists, nurses, dieticians, social workers, respiratory therapists, and program

coordinators. Additional recommended members include pharmacists, mental health coordinators, physical therapists, and research coordinators. Other specialists that may be on a CF care team are gastroenterologists, genetic counselors, endocrinologists, otolaryngologists, transplant technicians, obstetricians/gynecologists, urologists, psychiatrists, primary care doctors, and palliative care providers. For those with CF, the recommendation is that they are seen at a minimum of every 3 months with modifications based on clinical needs. There is a range of guidelines for CF care centers established by the CF Foundation. Guideline topics include palliative care, CFTR modulator therapy, age-specific guidelines, diagnosis care, infection prevention and control, nutrition and GI care, CF-Related conditions, and respiratory care. Fertility and pregnancy are only minimally covered in the Adult Clinical Care guidelines and there are no guidelines that address when fertility implications of CF should be discussed, how they should be approached, or by who on a CF care team.

1.2 Genetics of cystic fibrosis

CF is caused by biallelic pathogenic variants in the Cystic Fibrosis Transmembrane Regulator (*CFTR*) gene. The *CFTR* gene encodes the instructions for a transmembrane protein that functions as an ion channel on the epithelium of exocrine glands which is crucial both to maintain mucous viscosity and for the normal function of organs such as the lungs and pancreas (National Library of Medicine (US), 2022). An ion channel allows molecules to passively move through a membrane along an electrically charged energy gradient. CFTR is an ATP gated ion channel that involves moving chloride ions from inside the cell to the outside of the cell (Hwang & Kirk, 2013). Chloride ions leaving the cell attract water to the cell's surface allowing cilia to properly move mucus. When the CFTR ion channel is dysfunctional, chloride ions are trapped in

the cell. Without chloride ions leaving the cell, water is not attracted to the area, leaving membranes dehydrated and impairing the cilia's ability to transport mucus. (CF Foundation, 2023). Additionally, when CFTR is not functioning properly, the resulting lack of bicarbonate secretion hinders normal processes and leads directly to the clinical symptoms and signs of CF, especially those in the pancreas and GI systems (Borowitz, 2015).

There are about 20,000 genes that make up our genetic material, and we have two copies of most of our genes - one we inherit from our mother, and the other we inherit from our father. CF is caused by biallelic pathogenic variants in the *CFTR* gene. This means that both copies of the CFTR gene have pathogenic variants in them. These biallelic variants can be in the homozygous state, meaning that they are the same variant as in someone with double F508del variants, or a person could be a compound heterozygote; a compound heterozygote has different pathogenic variants in each of their two copies of the CFTR gene.

While variants can arise new in a child, or occur *de novo*, it is more likely that pathogenic variants were inherited from two carrier parents. For autosomal recessive conditions like CF, when someone has one *CFTR* copy with a pathogenic variant, and one normal copy they are called a 'carrier'. Carriers are not affected with CF, but they can pass on their *CFTR* variant to their children. Each time two CF carriers have a child together, there is a 25% chance (1 in 4) of having a child with CF, a 50% chance (1 in 2) that a child will be a carrier but will not have CF, and lastly, there is a 25 % chance (1 in 4) that a child will not be a carrier of the gene and will not have CF. People with CF (pwCF) will pass one CFTR variant to each of their children. If someone with CF has a child with a CF carrier, there is a 50% chance (1 in 2) a child will have CF, and a 50 % chance (1 in 2) a child will be a carrier but will not have CF. If two pwCF (have children together, there is a 100% chance that each of their children will also have CF.

There are currently 2,111 different *CFTR* variants reported in the SickKids Cystic Fibrosis Mutation Database, although not all of them are CF-causing. While many different *CFTR* variants have been identified, there is a smaller group of about 100 variants that are most frequently identified in pwCF. The most common CF-causing variant is the deletion of phenylalanine at the 508th amino acid in the CFTR gene (F508del, c.1521_1523delCTT, p. Phe508del) for which approximately 85% of Caucasian patients with CF carry at least one copy of (De Boeck, 2014).

There are different classes of CFTR variants that correlate generally to severity of phenotype in an affected individual, but there is some overlap with the classes. Class I variants cause a near absence of the CFTR protein. Class II variants cause defective processing and trafficking of CFTR protein. Class III variants allow for CFTR protein to be produced, however; defective gating disturbs the channel opening. Class IV variants cause impaired conductance of the CFTR channel. With Class V variants there is normal CFTR protein, but a reduced amount of it. Class VI mutations produce an unstable CFTR protein that is prematurely degraded by the lysosomes. There are some arguments for a seventh class of CFTR variant that involves large deletions and frameshift mutations (Bieniek, et al, 2021), but these would otherwise be considered class I.

1.3 Testing and Diagnosis

Sweat chloride testing is a diagnostic assay for CF. Sweat chloride tests measure levels of sodium and chloride in an individual's sweat. PwCF have elevated levels of sodium chloride in their sweat due to the improper function of the CFTR ion channels in their skin cells (Noone & Knowles, 2001). Sweat chloride measurements greater than 60 mmol/L are abnormal,

30-59 mmol/L are intermediate, and 29 or lower means CF is unlikely. If a measurement is abnormal or intermediate, *CFTR* genetic testing should be performed for molecular confirmation.

More than 75% of pwCF are diagnosed by age 2 years (CF Foundation, 2023), with the vast majority now detected in infancy by newborn screening. As of 2010 all 50 states and Washington, DC include CF as part of newborn screening (NBS). In the U.S. each state follows their own protocol for screening for CF, with some states using only immunoreactive trypsinogen (IRT), and others including IRT plus DNA testing (by panel of common CF-causing variants and/or CFTR gene sequencing).

IRT is a protein secreted by the pancreas. Improper function of the CFTR protein leads to stunting of the exocrine ducts of the pancreas, and in turn, a buildup of the IRT enzyme (Price, 2006). An IRT test is a biochemical assay that measures the level of IRT in the blood. Importantly, an increased level of IRT can indicate a diagnosis of CF, but not every newborn with an elevated IRT has CF and additional confirmatory testing is indicated when an infant has an elevated IRT.

After a positive newborn screen, the next test in the diagnostic algorithm is a sweat chloride test and, if positive, *CFTR* genetic testing is next if it was not performed through the initial newborn screen. If two pathogenic variants are identified, it is a confirmed case of CF. If one pathogenic variant is identified, then sweat chloride should be repeated and expanded DNA analysis offered. From here the case could become confirmed as CF if another variant is identified or remain inconclusive and require additional testing if no additional variant is identified. Those with normal sweat chloride and no symptoms are very unlikely to have CF. If a baby has a normal sweat chloride but has symptoms strongly suggestive of CF, a repeat sweat test and CFTR analysis should be performed.

With the implementation of newborn screening in the United States, there has been an increasing number of ambiguous cases, which fall under the umbrella of CFTR Related Metabolic Syndrome (CRMS) which is also known as Cystic Fibrosis Screen Positive Inconclusive Diagnosis (CFSPID). These are infants with abnormal NBS tests but inconclusive sweat tests and/or DNA test results (Munck et al, 2020).

A diagnosis, or suspected diagnosis, from birth is crucial as it carries the benefits of improved long-term lung function and nutrition when there is access to clinical care prior to symptom onset (Borowitz, et al., 2009). With variant-specific therapies becoming available at earlier ages, timely molecular confirmation of disease will become increasingly important.

1.4 CFTR-related disorders

CFTR-related disorders (CFTR RD) are a spectrum of nonlethal conditions caused by variants in the *CFTR* gene. People with these conditions have biallelic *CFTR* variants, but do not meet clinical diagnostic criteria for CF. There are three main clinical phenotypes of people with *CFTR*-related disorders: congenital bilateral absence of the vas deferens (CBAVD) due to CFTR dysfunction, acute recurrent or chronic pancreatitis due to CFTR dysfunction, and disseminate bronchiectasis due to CFTR dysfunction. A proportion of men with 'isolated' CBAVD also have recurrent sinusitis, bronchitis, or rhinosinusitis (Bombieri et al, 2011). While some individuals with CFTR RD are identified early in life due to either newborn screening or mild symptoms in childhood, others are not diagnosed until later in life until they present with infertility or another related symptom.

1.5 Cystic fibrosis prognosis and treatment

CF was previously considered a childhood-fatal condition, but now pwCF live well into adulthood. This is due to a variety of advances in treatments, and early diagnosis. Some treatments that have made major contributions to this increase in life expectancy in those with CF include respiratory therapy, chest physical therapy, vest therapy, mucolytics, antibiotics, anti-inflammatories, lung transplantation, and most recently, CFTR modulator therapies. CFTR modulator therapies are drugs that target an individual's specific CFTR ion channel defect to allow for returned function. The first modulator was FDA approved in 2021, and there are currently four on the market: Kalydeco® (ivacaftor), Orkambi® (lumacaftor + ivacaftor), Symdeco® (tezacaftor+ivacaftor), and Trikafta® (elexacaftor + tezacaftor + ivacaftor) (Goetz & Savant, 2021). These novel therapies have changed the natural history of CF because of the profound impact they have had on symptom management. In turn, this has resulted in longer life expectancy, improved quality of life, and increased fertility for pwCF.

These novel drug treatments are not available to everyone with CF. These therapies target specific mechanisms of disease, and so they are only available to those with specific variants. An estimated 90% of adults with CF qualify for modulator therapies (Despotes & Donaldson, 2022). While they help restore partial function to the CFTR channel and can massively improve symptomatology, they cannot undo previous damage done to the body, nor completely restore the channel’s function and, importantly, are not a cure for CF. Gene therapies could be an option in the future, however, they are still in the research stages.

Gene therapy is a treatment that supplements or alters a gene(s) to treat or cure disease. In the case of CF, a gene therapy would aim to insert a functional *CFTR* gene into someone's cells. There are two kinds of gene therapy: non-integrating and integrating. In non-integrating gene

therapy, the new functional *CFTR* gene remains separate from an individual's genome in the cell, and therefore is not permanent. Integrating gene therapy embeds the new functional *CFTR* gene into the individual's genome, making the treatment permanent. One kind of integrating gene therapy called CAR-T therapy has already been approved to treat some patients with leukemia and lymphoma, and similar therapies are being tested in the lab for CF. Currently there is enrollment for a clinical trial testing the safety and tolerability of 4D-710, a gene therapy, in adults who do not qualify or do not tolerate modulator therapies (ClinicalTrials.gov, 2023). More clinical trials and treatments will continue to develop and become available in research and clinical settings.

1.6 Fertility and Cystic Fibrosis

Biallelic disease-causing variants in the *CFTR* gene can cause fertility complications for both men and women with CF. Prior research has shown that not only is there a gap in knowledge for individuals' own fertility capabilities, but the mode of fertility education in this population is in some places non-existent, and in others inadequate (Sawyer, et al, 2009). Prior to the implementation of highly effective modulator therapies, reaching reproductive age with adequate health to pursue pregnancy or family planning was not a possibility for many pwCF. Now, with many pwCF well managed with highly effective modulators therapies, many more pwCF are living long enough and are healthy enough to now pursue family life and children of their own. Currently, there are no guidelines on how and when fertility should be discussed with people with CF, and while there are resources available, it is unclear how well they are utilized.

How does cystic fibrosis affect male fertility?

Male individuals with CF can experience infertility, either due to complete or partial congenital bilateral absence of the vas deferens (CBAVD) in about 95% of affected males (de Souza, 2018) or mucus blockage of the mature vas deferens (Naz Khan et al, 2022). Those with CFTR RD harbor biallelic *CFTR* gene variants but may present with only CBAVD and not have clinical features of CF. Whether CBAVD is a primary effect of the CF as a condition and the vas deferens never forms, or that thickened mucus blocks ducts that have previously formed causing recession of the vas deferens was previously not understood (Heaton & Pryor, 1990). More recently, it has been delineated that the mechanism that causes CBAVD is indeed mucus blockage leading to deterioration (Cuppens and Cassiman, 2004). This deterioration is thought to happen after 18 weeks, and likely in the third trimester (Gaillard et al, 1997). Because the vas deferens is the pathway that sperm use to travel out of the testes, CBAVD or a mucus blockage in the vas deferens prevents mature sperm from leaving the body, and therefore leaves men infertile by natural conception methods. Because spermatogenesis still occurs in the testicles, fertility can be achieved using assisted reproductive technology (ART) (Radpour, et al, 2008). ART that is suitable for aiding CF-related fertility implications in males include testicular biopsy and extraction of sperm followed by in vitro fertilization (IVF) or intrauterine injection (IUI). Other possibilities include using donor sperm, a donor embryo and adoption.

How does cystic fibrosis affect female fertility?

Females with CF have less of an impact on fertility than males with CF, but there is a greater incidence of subfertility in women with CF than in the general populations with rates of 35% and 10%, respectively (Hughan et al, 2019). Fertility issues in women with CF have been

attributed to differences in cervical mucus, including mucus plug formation, as well as disruptions to body homeostasis in ovulation and nutrition. Complexities of fertility for women with CF also include the contraindication for carrying a pregnancy for those with significant lung manifestations, not to mention the potential teratogenic effects from CF treatments (Ahmad, et al, 2013). Additionally, having pancreatic insufficiency increases the likelihood of fertility-related problems in women with CF. Pancreatic insufficiency also increases the likelihood of CF-related diabetes. Women with CF-related diabetes are more likely to require a cesarean section and have more frequent CF exacerbations during pregnancy, in addition to the multiple fetal risks faced by poorly controlled maternal diabetes (Davern et al, 2022). It is important that women with CF have good glucose control prior to becoming pregnant.

1.7 Previous studies of fertility topics in people with CF and related disorders

Prior research has shown that not only is there a gap in knowledge for patients' own fertility capabilities, but the mode of fertility education in this patient population is in some places non-existent, and in others inadequate (Sawyer, et al, 2005; Sawyer, et al, 2009; Kazmerski et al., 2018).

Based on prior research of people living with CF, as well as other studies surrounding perspectives on fertility conversations and education for young adults with Klinefelter syndrome, Turner syndrome, congenital adrenal hyperplasia (CAH), primary ciliary dyskinesia (PCD) (all genetic disorders that impair fertility), and individuals with Differences of Sexual Development (DSD) there is significant evidence that patients often prefer that fertility information be disclosed as early as possible within appropriate limits (Papadakis, 2021). Some feel that this is a conversation that could start in childhood with the support of parents. Direct conversations with

patients about fertility can help shape autonomy and encourage participation in their own care and family planning, but how and when these discussions should be held is not well defined (Sutton et al, 2005). It is time that the content and timing of these conversations be assessed to help clinics facilitate discussions that best suit the needs of the cystic fibrosis population.

1.8 Aims and Hypotheses

This study's aims are to assess baseline knowledge about fertility impact from CF among individuals in the CF community including people with the condition, their parents, and their medical teams; to assess how fertility impact from CF is addressed in the CF population across the US; too identify potential disparities surrounding who has access to fertility counseling; and to create actionable evidence for standardization of fertility education for the CF population. Hypotheses for this study are as follows:

A. There will be variation in fertility discussion across the country including aspects of how old someone was when the concept was introduced, who was part of the conversation, and what resources were explored with the participant.
B. Clinics across the country will have different policies and practices of how and when fertility is discussed with patients and their families.
C. Most pwCF would have preferred initiating fertility conversations at younger rather than older ages.
D. Parents of children with CF will prefer that fertility conversations take place after 18 years of age.
E. Clinics and individuals will agree that there are areas for improvement for fertility discussion in the CF community.

II. METHODS

2.1 IRB protocol

While this study qualified for exempt review, it was ultimately evaluated with the expedited review process (authorized by 45 CFR 46.110 and 21 CFR 56.110) by the Institutional Review Board of the University of California, Irvine (Appendix A). The choice to pursue a more in-depth review process stemmed from the desire to protect study participants and mitigate possible psychological risks due to the sensitive nature of the topic.

2.2 Participants

Participants were required to be 18 years old or older, live in the United States, and be able to read and write in English. Participants had to fall into one of three major groups: a person with cystic fibrosis, a parent of a person with CF, or a health care provider at a CF care center. There was no prospect for direct benefit by the participants, however, participants could benefit through engaging in their own fertility knowledge and care and contribute to actionable evidence towards the need for guidelines regarding fertility care in patients with CF.

2.3 Recruitment

Participants were recruited online through the snowball technique using email and social media platforms including Facebook, LinkedIn, Reddit, and CF-specific forums on CysticFibrosis.com and HealingWell.com. An electronic flier (Appendix B) was distributed on social media both through public posts on the lead researcher's personal Facebook, Instagram, and LinkedIn profiles, and through CF-specific social media pages. Administrators of these pages were contacted before posting and either gave permission for the lead researcher to post or

the administrators posted the flier themselves. The flier and post encouraged individuals to participate and to share the flier with other individuals and groups within the CF community. This flier included the lead researcher's direct contact information for questions or concerns, asking that formal channels be used for questions/concerns rather than messaging directly through social media. The flier was also sent directly to the NSGC's CF Special Interest Group, and genetic counselors within this group were also asked to distribute the flier independently. The survey was also sent to several mailing lists through the CF Foundation. These include Assoc. Director, Director/Co-director, Dietitian/Nutritionist, Genetic Counselor, Mental Health Coordinator, Nurse, Nurse Practitioner, Patient Family Liaison, Physical Therapist, Physician, Physician Assistant, Program Coordinator, Psychiatrist, Psychologist, Respiratory Therapist, and Social Worker. Additionally, it was shared via the CFF's CF Exchange (Listservs) including Nurse Practitioners & Physician Assistants, Child Life, Program Coordinators (includes Nurses), Genetic Counseling & CFTR Genetics, Learning & Leadership, Patient and Family Advisory (PFA), Physical Therapists, Psychologists, Psychiatrists, and Mental Health Coordinators, Respiratory Therapists, Social Workers, and Dietitians.

2.4 Survey

Protection of participant privacy

There was no identifiable or HIPAA protected information collected in this survey, nonetheless participant privacy was a priority during the survey design, collection, and analysis processes. All participation was entirely voluntary, and participants were able to exit the survey at any time if any potential emotional stressors arose from answering questions.

Potential psychological risks to participants included distress resulting from thinking and discussing the topic of fertility. Although information about infertility related to a diagnosis of CF is readily available on the internet, a study participant could theoretically have learned about their own potential infertility for the first time by participating in this study. To address this, links to the CFF.org pages addressing fertility were provided in the consent section and in the beginning of the question block about participants' experience with fertility discussions to ensure that participants had reputable information at their disposal. Participants were also able to exit the survey at any time. Participants' IP addresses were not tracked. All data collected was stored securely and confidentially on a password protected account on Qualtrics, and on a password-protected and firewall-protected laptop.

Informed consent

Informed consent was obtained using an IRB-approved study information page that was the initial page of the online survey (Appendix C). Individuals gave consent as a research participant by choosing "Yes" to indicate their consent to the terms at the bottom of the page. This information page included a description of the risks and benefits of participating, along with information about a lottery for one of five $20 Amazon gift cards, the methods in which the research data was to be collected and stored and contact information for the lead researcher and the University of California Irvine's Office of Research.

The extent of participation was a one-time anonymous survey accessed online via Qualtrics. Participants were required to answer all of the knowledge questions in order for their data to be used for analyses. There were three major tracks of the survey depending on the participant's relationship to CF. Participants who themselves have CF had 40 questions.

Participants who identified as having a child with CF had 48 questions. Participants who were healthcare providers in CF clinics had 19 questions. The entire survey can be viewed in Appendix D.

The survey was published on 11/25/2022. The survey closed on 3/22/2023. On 12/14/2022 it came to the team's attention that the survey consent page was shown twice for the CF provider group. The survey had to be edited and re-published at this point to remove the survey consent from the end of the survey. Two surveys were manually pushed through to complete status due to this error.

2.5 Data analysis

Data analysis was performed with SPSS and Microsoft Excel. Primary data cleaning included removing all responses that did not complete the knowledge assessment. For questions that 'Other' responses were possible with an open-text option, responses that fit into one of the original answer choices were re-coded where appropriate. In some cases, where there were multiple respondents typing in the same response, a new category was added, and they were coded accordingly. Chi-square analysis was used to test for any associations that existed between categorical variables and against expected distributions. ANOVA analysis was used to compare variance across means (continuous variables) when comparing three or more groups. P-values of <0.05 were considered statistically significant.

2.6 Knowledge assessment scoring

The knowledge assessment included six questions and was presented to all participants, regardless of their relationship to cystic fibrosis. Participants received one point for picking the

right answer, as well as one point for each wrong answer they did not select, such that the total possible score was 20 points A scoring guide can be found in Appendix E.

II RESULTS

3.1 Demographics and Participant Characteristics

There were 275 responses to the survey, of which 251 were determined complete enough to be included in the study. On average, participants took 20.84 minutes to complete the survey. Of the 251 participants 116 were pwCF, 24 were parents of pwCF, and 111 were providers in CF care centers (Table 1). Among pwCF, 55.7% were female and 44.3% were male. When we asked the parents of children with CF what the sex of their child was 31.6% responded female and 68.4% responded male. PwCF ranged in age from 20-81 with the average age of the group being 34.35 years. The average age of the children of the parents surveyed was 13.71 years.

Respondents came from all regions of the US. In the pwCF group, the most strongly represented areas were Midwest and Northeast regions, and the least represented were the Rocky Mountain and Southwest regions. Most children represented by the parent group were in the Pacific and Southeast regions, and least represented in the Rocky Mountain and Northeast areas. Providers were more evenly distributed, but less represented in the Rocky Mountain region as well. For additional information about the demographics of the populations see Table 1.

Demographics				
	PwCF (N=116)	Parents (N=24)	Children of Parents (N=19)	Providers (N=111)
Age (mean) N=113	34.35	*	13.71	*
Sex	N=115		N=19	
Female	64 (55.7%)	*	6 (31.6%)	*
Male	51 (44.3%)	*	13 (68.4%)	*
Gender	N=115		N=19	
Female	64 (55.7%)	*	6 (31.6%)	*
Male	50 (43.5%)	*	12 (63.2%)	*
Non-binary	1 (0.9%)	*	1 (5.3%)	*
Parental Role		N=24		
Biological Mother	*	15 (62.5%)	*	*
Biological Father	*	6 (25.0%)	*	*
Adoptive Mother	*	0	*	*
Adoptive Father	*	1 (4.2%)	*	*
Guardian	*	2 (8.3%)	*	*
Ethnicity	N=115	N=24		
American Indian or Alaska Native	5 (4.3%)	1 (4.2%)	*	*
Asian	6 (5.2%)	0	*	*
Black or African American	2 (1.7%)	2 (8.3%)	*	*
Native Hawaiian or Pacific Islander	0	1 (4.2%)	*	*
Hispanic	3 (2.6%)	0	*	*
White	99 (86.1%)	19 (79.2%)	*	*
other	0	1 (4.2%)	*	*
Education	N=115	N=24		
Some high school	2 (1.7%)	0	*	*
High school graduate	16 (13.9%)	3 (12.5%)	*	*
Some college	23 (20.0%)	3 (12.5%)	*	*
College degree	42 (36.5%)	12 (50.0%)	*	*
Some graduate level	9 (7.8%)	2 (8.3%)	*	*
Graduate degree	23 (20.0%)	4 (16.7%)	*	*
Region of US	N=112		N=19	N=104
Midwest	37 (33.0%)	*	2 (10.5%)	30 (28.8%)
Northeast	24 (21.4%)	*	1 (5.3%)	22 (21.8%)
Pacific	11 (9.8%)	*	6 (31.6%)	17 (16.3%)
Rocky Mountain	1 (0.9%)	*	0	3 (2.9%)
Southeast	22 (19.6%)	*	8 (42.1%)	19 (18.3%)
Southwest	6 (5.4%)	*	2 (5.4%)	13 (12.5%)

Table 1. **Demographic characteristics of the study population.**

* Indicates that this answer option was not offered to this group The ‘Children of Parent’ group represents the children with CF of the parent group surveyed. These responses were provided by the parents.

Providers varied across multiple clinical roles and represented both adult and pediatric clinics. See Table 2 for more details.

Provider Clinical Roles and Clinic Population				
	Adult Clinic	Pediatric Clinic	Both Adult and Pediatric Clinic	**Total**
Clinical Role				
Dietician	2	2	1	**5**
Genetic Counselor	0	2	3	**5**
Nurse	8	7	5	**20**
Nurse Practitioner	3	2	3	**8**
Physician	16	14	2	**32**
Social Worker	6	7	4	**17**
Pharmacist	2	3	0	**5**
Respiratory Therapist	1	1	2	**4**
Other	1	2	5	**8**
Total	**39**	**40**	**25**	**104**

Table 2. **Provider Clinical Roles and Clinic Population**

[Answers included in 'Other' were Physician Assistant, Mental Health Coordinator, Physical Therapist, and Research Coordinator.]

We asked pwCF and parents how they or their children were diagnosed with CF (Table 3). Among pwCF the majority (52.6%) were diagnosed in childhood because of symptoms, 14.9% were diagnosed via newborn screening, 14.0% were diagnosed in adulthood because of symptoms, and 6.1% were diagnosed in adulthood due to infertility. Comparably, 40% of parents reported that their children were diagnosed via newborn screening, 45% were diagnosed in childhood because of symptoms, and 15.0% were diagnosed in adulthood because of symptoms.

How were you diagnosed with CF?		
	PwCF (N=114)	Children of Parents (N=19)
Prenatally	3 (2.6%)	*
Newborn Screening	17 (14.9%)	8 (40.0%)
Childhood because of symptoms	60 (52.6%)	9 (45.0%)
Adulthood because of symptoms	16 (14.0%)	3 (15%)
Adulthoood because of infertility	7 (6.1%)	0
In adulthood by routine carrier screening	5 (4.4%)	0
Due to a family history	4 (3.5%)	*

Table 3. **Method of CF Diagnosis**

* Indicates that this answer option was not offered to this group. The 'Children of Parent' group represents the children with CF of the parent group surveyed. These responses were provided by the parents.

3.2 Knowledge Assessment

The total possible knowledge score was 20 points. There was a significant difference seen in scores between groups with the highest scores among providers in CF Care Centers (average score of 17.0 or 85.0%), followed by pwCF (average of 15.8 points or 79.0%), followed by parents of pwCF (average score of 14.1 or 70.6%) ($p < 0.001$) (Table 4). A perfect score was earned by one provider and two pwCF, but concerningly 10 providers and 21 pwCF had a score of 70% or lower. Almost three quarters of the combined groups earned a score of 80% or higher.

Knowledge Exam Score							
	Average Score	Average Score (%)	Minimum Score(%)	Maximum Score (%)	St. Error	Significance	F; df
PwCF	15.8	79.0%	30%	100%	2.82	<0.001	15.150; 2
Parents	14.1	70.6%	35%	95%	2.83		
Providers	17.0	85.0%	55%	100%	1.67		

Table 4. **Knowledge Exam Scores Across Groups.**

3.3 Fertility Discussion Experience- PwCF and Parents

Participants were asked who had discussed fertility with them with the option to select all that apply from a list of options. PwCF most commonly chose pulmonologist or other CF doctor (57%), obstetrics gynecology urologist or reproductive endocrinologist (48%), or genetic counselor (36%). Parents of children with CF reported that most commonly the pulmonologist or CF doctor (32%), primary care physician (27%), or friend/mentor (27%), had discussed fertility with them. This differs from who parents reported had discussed fertility with their child. In the children or parents surveyed group, the most common selections were no one (27%), pulmonologist or other CF doctor (23%), and parents (23%). Strikingly, 14% of pwCF and 18% of parents of pwCF reported that no one had discussed fertility with them (Figure 1).

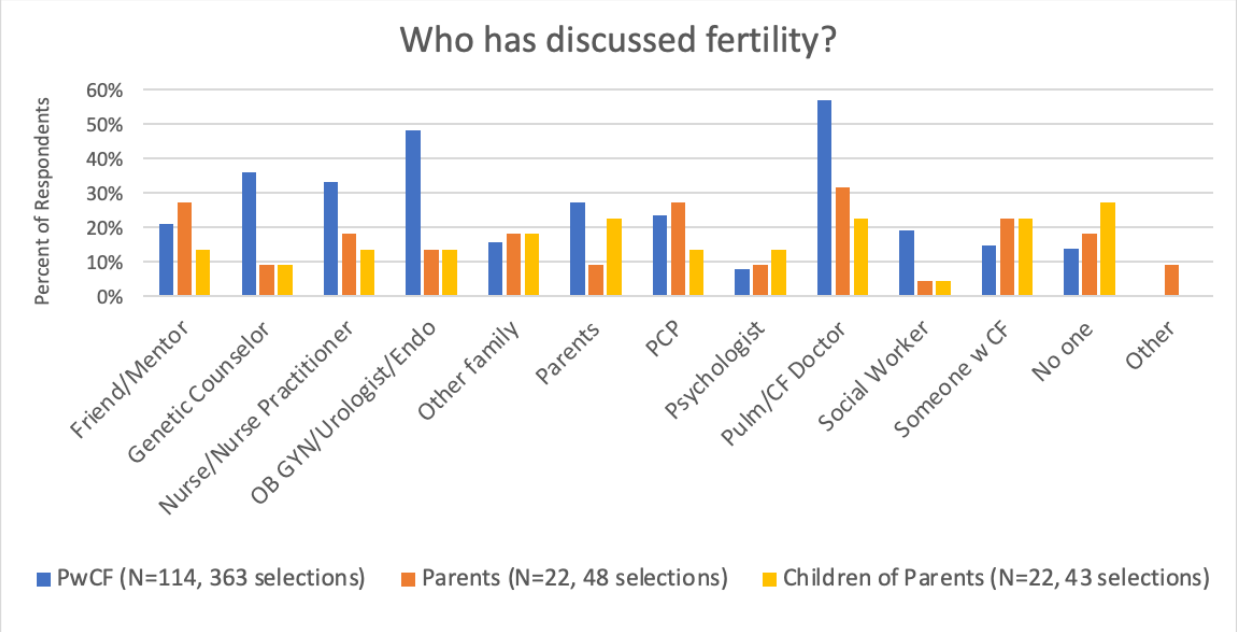

Figure 1. **Support Members Involved in Fertility Discussions for PwCF, Parents, and Children of Parents.**

Respondents could select all that applied. [Endo=Endocrinologist; OB GYN= obstetrics gynecologist; PCP= primary care physician; Pulm=Pulmonologist]. The 'Children of Parent' group represents the children with CF of

the parent group surveyed. These responses were provided by the parents. Responses for "other" included reading about fertility and discussing with the child's surgeon.

Fourteen percent of pwCF reported that no one on their care team had discussed fertility with them. Looking more closely at those who indicated that no one discussed fertility with them; these individuals, the average age of these individuals was 41 years, ranging from 20 to 66 years (Table 5). This group consisted of 44% females and 56% males, all of whom were of white ethnicity. Nearly half of the pwCF who indicated no fertility discussions turned to internet sites other than CFF.org for their research, and one-third indicated that they used no resources at all.

Of those who indicated that no one had discussed fertility with them:	
Age	N=16
Average Age	41
Minimum Age	20
Maximum Age	66
Sex	N=16
Female	7 (43.8%)
Male	9 (56.3%)
Ethnicity	N=15
White	15 (100%)
How were you diagnosed with CF	N=16
Newborn screening	1 (6.3%)
In childhood because of symptoms	11 (68.8%)
In adulthood because of symptoms	3 (18.8%)
In adulthood by routine carrier screening	1 (6.3%)
Resources Utilized in Fertility Research	N=16
Discussions with medical team	1 (6.3%)
Discussions with others with CF	1 (6.3%)
CFF.org	2 (12.5%)
Other internet sites	7 (43.8%)
Other	2 (12.5%)
None	5 (31.3%)

Table 5. **Characteristics of PwCF Who Indicated No One Discussed Fertility with Them**

Respondents that selected "other" did not use the open-text option.

We asked participants who had initiated conversations surrounding fertility care in CF via a select all that apply question (Table 6). Two thirds of pwCF respondents indicated that they had initiated conversations, about half indicated that providers had initiated these conversations, and 20% said a parent initiated. A different distribution was seen in the parent group, where nearly two thirds of conversations were initiated by providers and nearly half were initiated by parents.

Who intitiated fertility conversations?		
	PwCF (N=89, 129 selections)	Parents(N=14, 18 selections)
Patient initiated	58 (65.2%)	3 (21.4%)
Parent initiated	18 (20.2%)	6 (42.9%)
Provider initiated	48 (53.9%)	9 (64.3%)
Other	5 (5.6%)	0

Table 6. **Initiation of Fertility Conversations in PwCF and Parents.**

Respondents could select all that applied. "Other" answers are listed in Appendix F

When asked how many fertility conversations were had, over half of pwCF indicated that they had no fertility related conversations as part of pediatric care. Close to one third of pwCF reported that they had 1-2 conversations with their pediatric care team, and a minority had discussions at more than three visits. Discussions were significantly more prevalent in adult care centers ($p<0.001$). Many pwCF (44.6%) reported that they had 1-2 fertility conversations in the adult clinic and 48.9% reported 3 or more conversations (Table 7).

In how many visits was fertility discussed?		
Pediatric visits	PwCF (N=91)	Parents (N=22)
None	48 (52.7%)	8 (36.4%)
1-2 visits	28 (30.8%)	6 (27.3%)
3-4 visits	11 (12.1%)	4 (18.2%)
Many visits	4 (4.4%)	4 (18.2%)
Adult visits	N=92	
None	6 (6.5%)	*
1-2 visits	41 (44.6%)	*
3-4 visits	25 (27.2%)	*
Many visits	20 (21.7%)	*

Table 7. **Frequency of Fertility Conversations in PwCF and Parents.**

For pwCF, discussions were more prevalent in adult care centers as compared to pediatric care centers ($p<0.001$)

3.4 Fertility Discussion Experience- Providers in the Clinic

Data was collected from providers about the circumstances in which fertility is discussed in their clinics (Table 8). Providers were asked with whom and at what ages do you discuss fertility and were able to select all that applied to their clinic. Providers most commonly selected 'Patient when they are considering family planning' (72.3%), 'patient during transition to adult care' (70.3%), and 'patient in teens' (53.5%). As far as timing and frequency of fertility discussions, clinicians reported that they discuss fertility most commonly when questions are brought to the team (84.6%), when discussing a new diagnosis of CF (55.8%), and every few years at follow up visits (31.7%) (Table 9).

With whom and at what ages do you discuss fertilty?				
	Adult (N=39, 100 selections)	Pediatric (N=39, 148 selections)	Both Adult and Pediatric (N=23, 88 selections)	**Total Providers (N=101, 336 selections)**
Parents in infancy	1 (2.6%)	18 (46.2%)	8 (34.8%)	**27 (26.7%)**
Parents in childhood	1 (2.6%)	12 (30.8%)	5 (21.7%)	**18 (17.8%)**
Parents in teens	2 (5.1%)	19 (48.7%)	8 (34.8%)	**29 (28.7%)**
Patient in childhood	0	1 (2.6%)	0	**1 (1.0%)**
Patient in teens	6 (15.4%)	32 (82.1%)	16 (69.6%)	**54 (53.5%)**
Patient during transition to adult care	28 (71.8%)	28 (71.8%)	15 (65.2%)	**71 (70.3%)**
Patient when they turn 18	16 (41.0%)	15 (38.5%)	13 (56.5%)	**44 (43.6%)**
Patient when they are considering family planning	37 (94.9%)	17 (43.6%)	19 (82.6%)	**73 (72.3%)**
Other	9 (23.1%)	6 (15.4%)	4 (82.6%)	**19 (18.8%)**

Table 8. **Fertility Conversation Timing by Providers.**

Respondents could select all that applied. Responses for 'other' are detailed in Appendix G

When is CF-related fertility discussed in your clinic?				
	Adult (N=39, 93 selections)	Pediatric (N=40, 84 selections)	Both Adult and Pediatric (N=25, 51 selections)	**Total Providers (N=104, 252 selections)**
New diagnosis of CF	24 (61.5%)	23 (57.5%)	11 (44.0%)	**58 (55.8%)**
At every follow up visit	4 (10.3%)	0	1 (4.0%)	**5 (4.8%)**
At least annually during follow up visits	19 (48.7%)	2 (5.0%)	6 (24.0%)	**27 (26.0%)**
Every few years at follow up visits	5 (12.8%)	18 (45.0%)	10 (40.0%)	**33 (31.7%)**
If questions are brought to the team	35 (89.7%)	33 (82.5%)	20 (80.0%)	**88 (84.6%)**
Other	6 (15.4%)	8 (20%)	3 (12.0%)	**17 (16.3%)**

Table 9. **Fertility Conversation Initiation by Providers.**

Respondents could select all that applied. Responses for 'other' are detailed in Appendix H

When asked who discusses fertility with their patients, clinicians reported that pulmonologists (91%), nurses (40%), nurse practitioners (39%), social workers (36%), and genetic counselors (21%), were most commonly holding fertility discussions (Figure 2). Eleven percent of clinicians selected 'other', and typed in the answers 'pharmacist, mental health counselor, any team member, referral to high risk OBGYN, and unsure'. Since it was possible that people in more than one role are discussing fertility, providers were able to select all that applied.

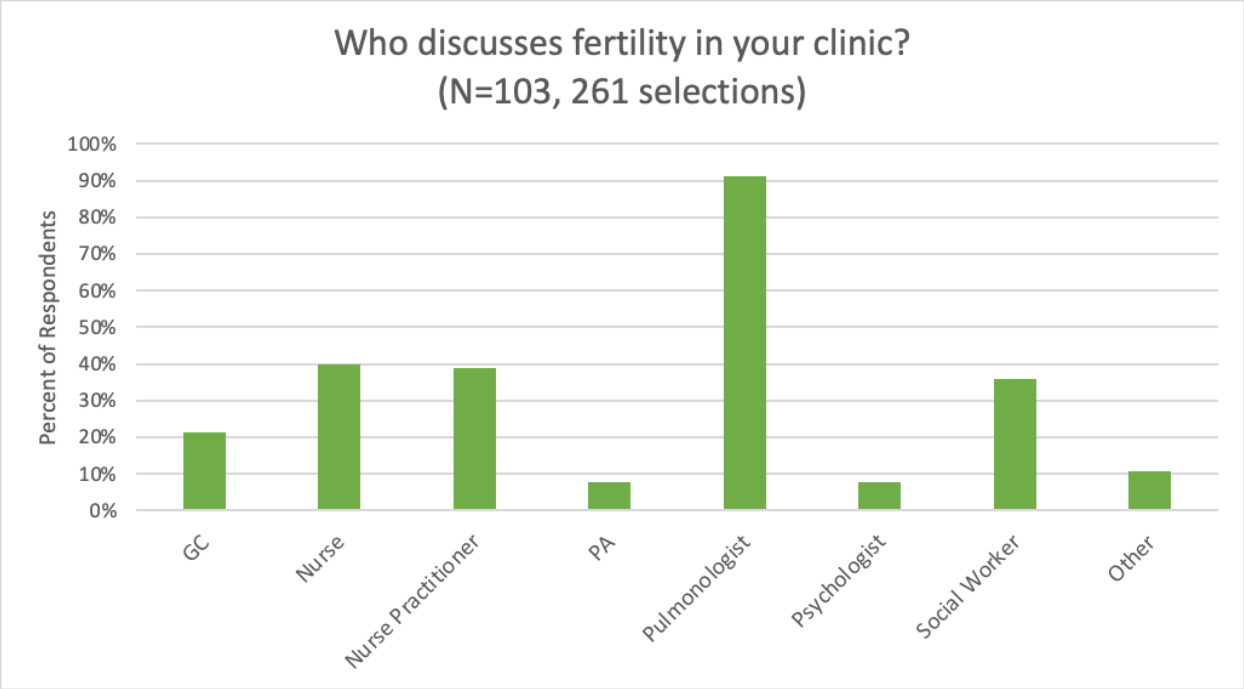

Figure 2. **Care Team Members Involved in Fertility Discussions.**

Respondents could select all that applied. [GC= Genetic Counselor; PA= Physician Assistant]

"Other" answers included pharmacist, mental health counselor, any team member, referral to high risk OBGYN, and unsure.

Providers were asked about their protocol for connecting their patients with CF to ART services (Table 10). Half of providers indicated that they themselves would provide a direct referral to these services or reproductive specialists. A quarter indicated that their clinics were not involved in referring patients to ART services. Additionally, providers who selected "other" also typed in answers about providing local resource lists or suggesting that patients contact their insurance to inquire about coverage.

What is your protocol for connecting patients with Assisted Reproductive Technologies (ART)		
Refer patient back to primary care	8	8.1%
Provide direct referral to ART provider	52	52.5%
Clinic is not involved in referring patient to ART services	25	25.3%
Other	5	5.1%
I don't know	9	9.1%

Table 10. **Addressing Assisted Reproductive Technologies in Providers.**

"Other" answers included providing local resource lists or suggesting that patients contact their insurance to inquire about coverage.

3.5 Impressions of Fertility Conversations

Providers were asked what resources they provide to their patients, and pwCF and parents were asked what resources they have utilized in their research about CF-related fertility. Many resources were found to be used as part of CF fertility care (Figure 3). The resources reported most commonly among pwCF, parents, and providers were discussions with the medical team and CFF.org. Providers who selected "other" also typed in that they were unsure, genetic counselors, and CFreshc.org. Parents typed in Reddit, and PwCF typed in medical journals, encyclopedia, and adoption groups.

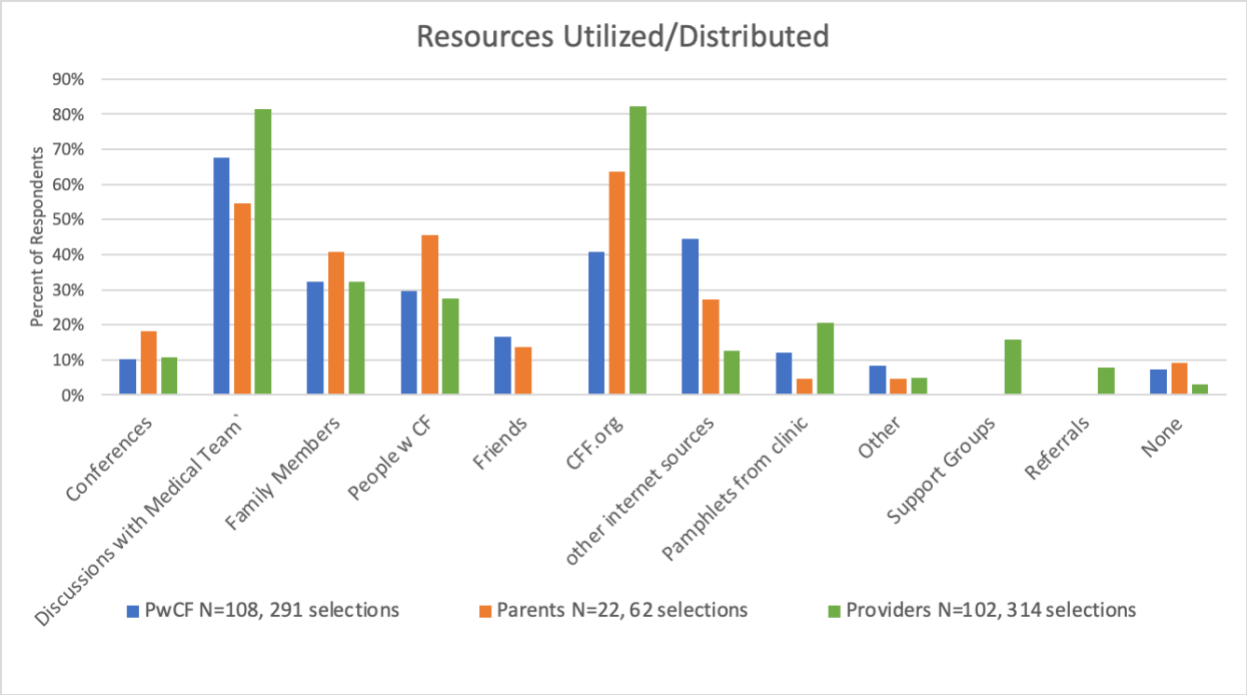

Figure 3. **Fertility-Related Resources Utilized and Distributed by PwCF, Parents, and Providers.**

Respondents could select all that applied. "Other" answers included unsure, genetic counselors, CFreshc.org, Reddit, medical journals, encyclopedia, and adoption groups.

Most pwCF (57%) reported that they were always comfortable with the fertility discussions that took place (Figure 4). However, greater than one third of pwCF also reported feeling only sometimes comfortable or not comfortable. Of the parents surveyed, 43% reported they were always comfortable, but only 21% reported that their children were always comfortable with the discussions. For both them and their children over half of the parents reported that they were only sometimes comfortable or were never comfortable. Level of comfort about fertility discussions did not differ between pwCF and parents (p=0.128). On the other hand, while 58% of pwCF reported that they were never embarrassed or uncomfortable, over one

third reported that they were sometimes or always embarrassed or uncomfortable (Figure 5). In the parent group, 29% reported that they were never uncomfortable or embarrassed and 64% reported that they were sometimes uncomfortable or embarrassed. When answering about their children's experiences, 64% of parents said that their children were sometimes or always embarrassed or uncomfortable. Differences in embarrassment between these three groups were found to be statistically significant ($p<0.001$).

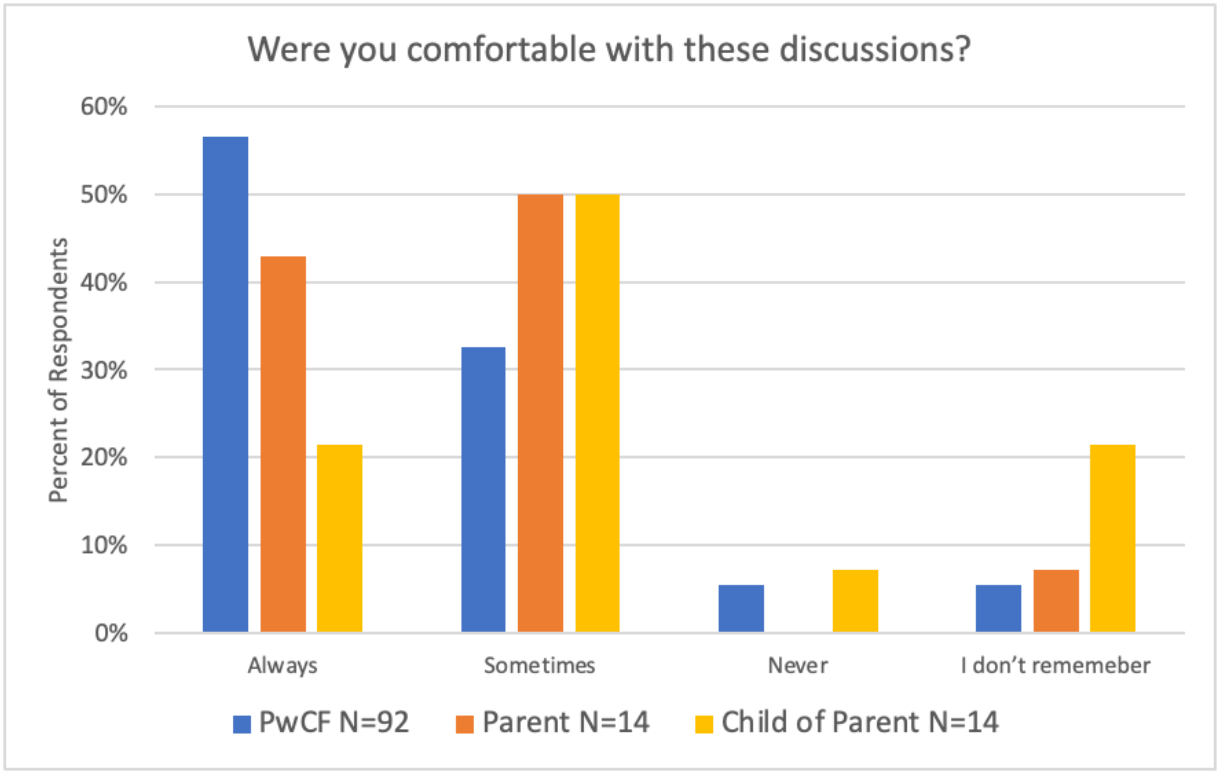

Figure 4. **Comfort in Fertility Discussions in PwCF, Parents, and Children of Parents**

The level of comfort about fertility discussions did not differ across groups ($p=0.128$) The 'Child of Parent' group represents the children with CF of the parent group surveyed. These responses were provided by the parents.

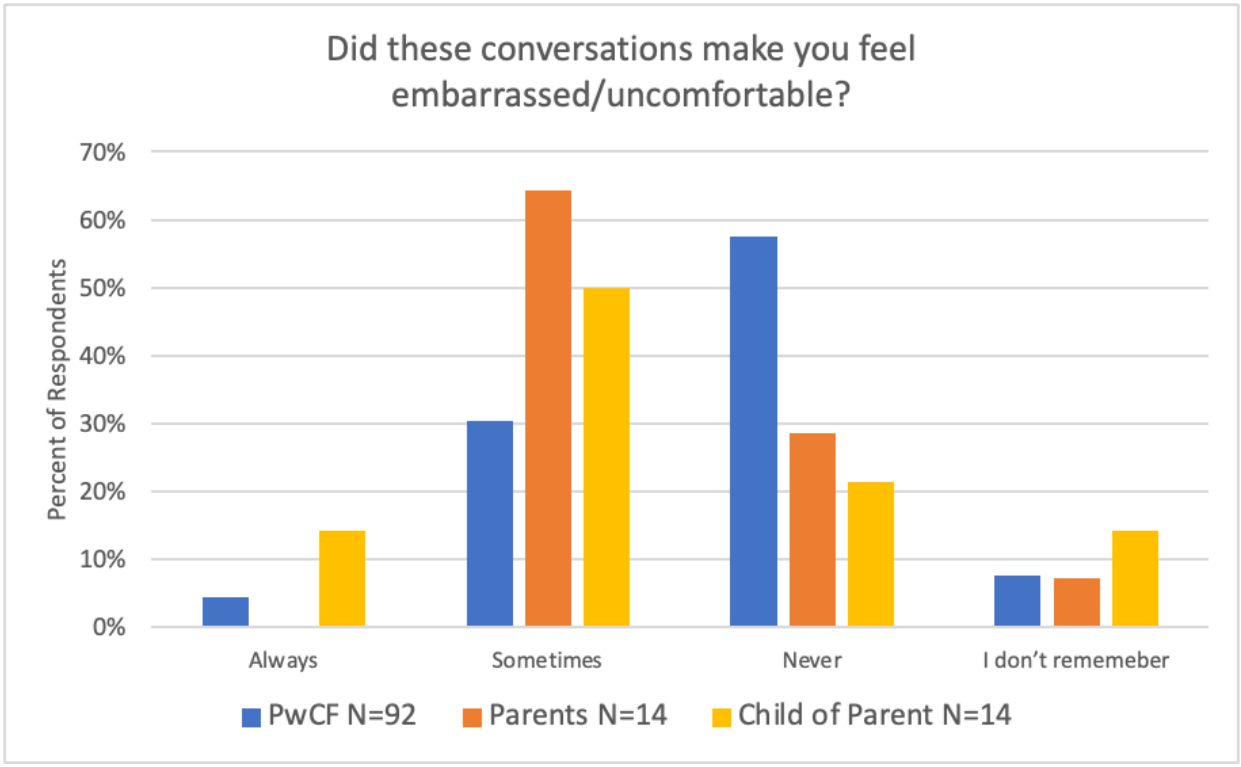

Figure 5. **Embarrassment from Fertility Discussions in PwCF, Parents, and Children of Parents**

Differences in embarrassment between these groups were found to be statistically significant ($p<0.001$) The 'Child of Parent' group represents the children with CF of the parent group surveyed. These responses were provided by the parents.

When asked how much time was spent on fertility discussions, the majority of pwCF and parents of pwCF felt that the amount of time was sufficient, however, many pwCF (29%) reported that it was too little time; very few reported too much time was spent (Figure 6). Parents generally felt that the right amount of time was spent on fertility discussions, and some felt it was too much time. The difference between the pwCF and parent responses was not significant ($p=0.064$). When asked if they felt that the people leading the conversations on fertility were

knowledgeable, half of both the pwCF and parent groups felt like the people were always knowledgeable (p=0.847). On the other hand, the remaining half of each group reported that they were only sometimes or never knowledgeable (Figure 7).

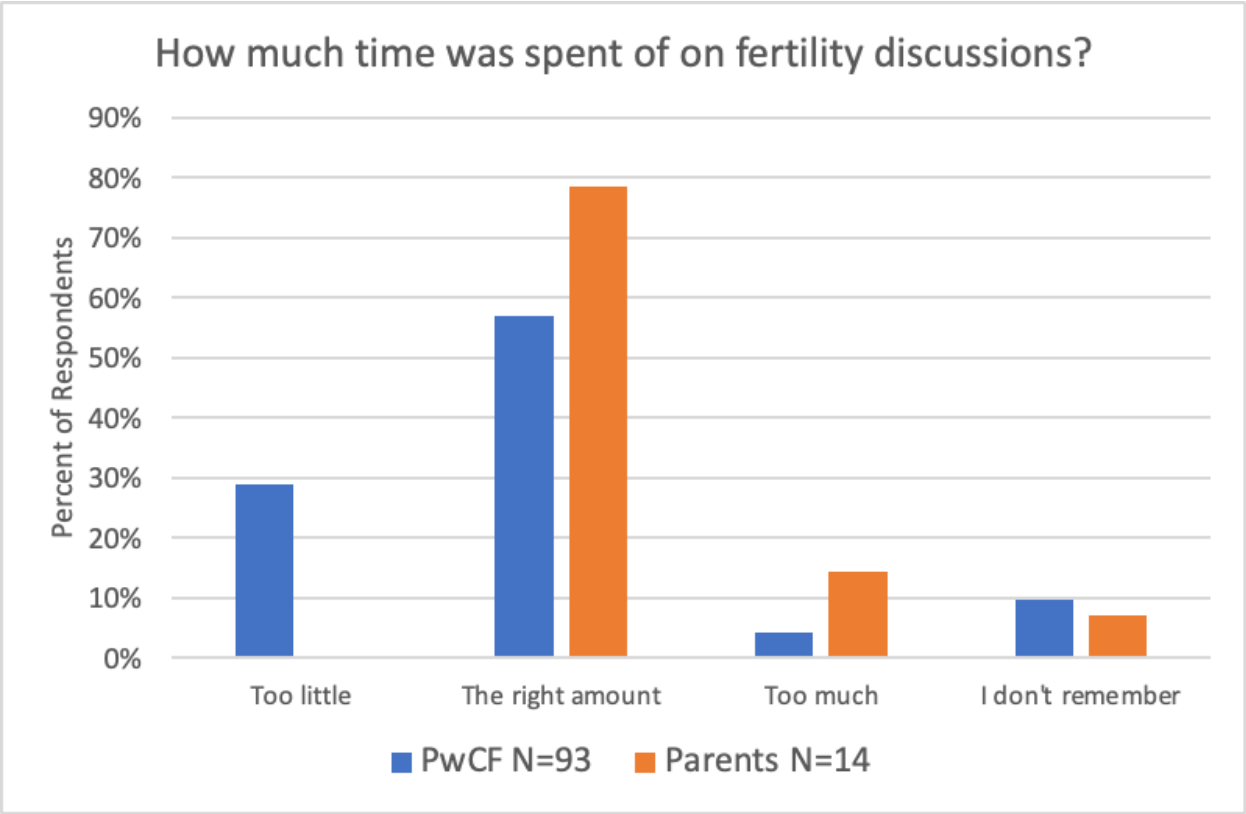

Figure 6. **Assessment of Time Spent of Fertility Conversations in PwCF and Parents**

There was not a statistically significant difference of distribution of responses (p=0.064).

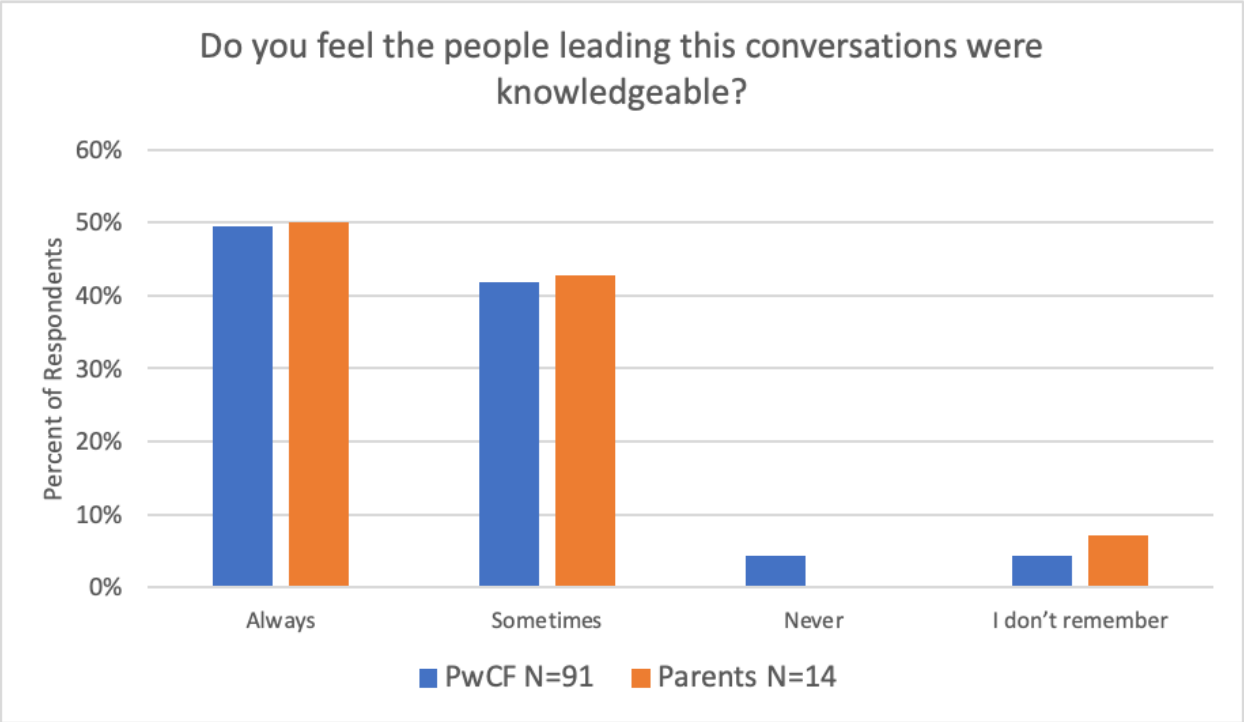

Figure 7. **Impression of Provider Knowledgeability in PwCF and Parents.**

The difference between pwCF and parents was not significant (p=0.847)

In terms of satisfaction, 57% of pwCF felt satisfied with how fertility conversations had gone; however, nearly half were not fully satisfied. Parents were more likely to feel satisfied, with 92% reporting satisfaction (p=0.046) (Figure 8). We asked pwCF and parents if they felt like they had appropriate opportunities to ask fertility related questions (Figure 9). Most parents and pwCF indicated that they had adequate opportunities, but 29% of pwCF and 16% of parents felt like they had not (p=0.241).

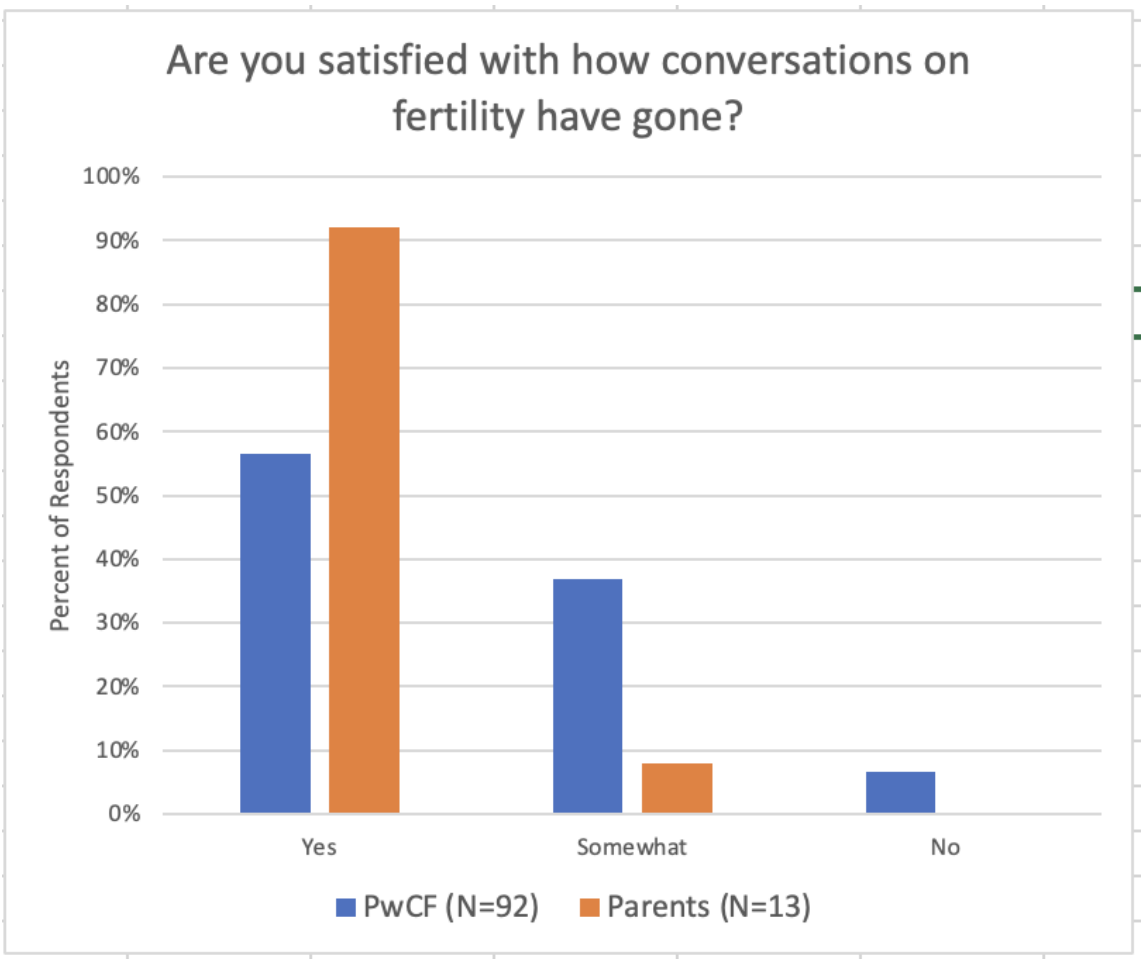

Figure 8. **Satisfaction with Fertility Discussions in PwCF and Parents**

The distribution of satisfaction was statistically significant (p=0.046)

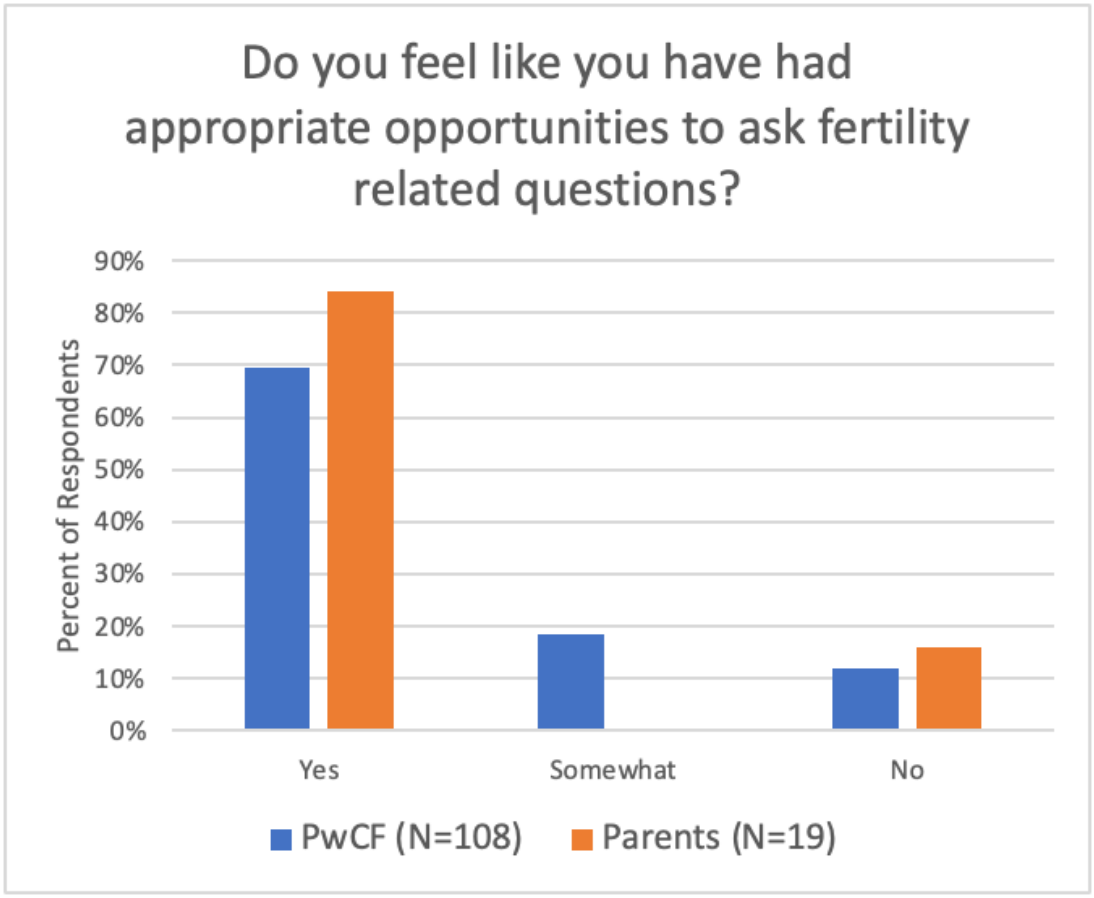

Figure 9. **Assessment of Question Opportunity in PwCF and Parents.**

The difference between pwCF and parents was not significant (p=0.241)

3.6 Hopes for Future Discussions

When asked who would be most appropriate to discuss fertility, pwCF most commonly picked pulmonologist or another CF doctor (79%), OBGYN, urologist, or reproductive endocrinologist (76%), and genetic counselor (58%). Parents of pwCF most commonly chose the option that themselves or their partner would be most appropriate (52%), pulmonologist or another CF doctor (38%), or a friend or mentor (33%) (Figure 10).

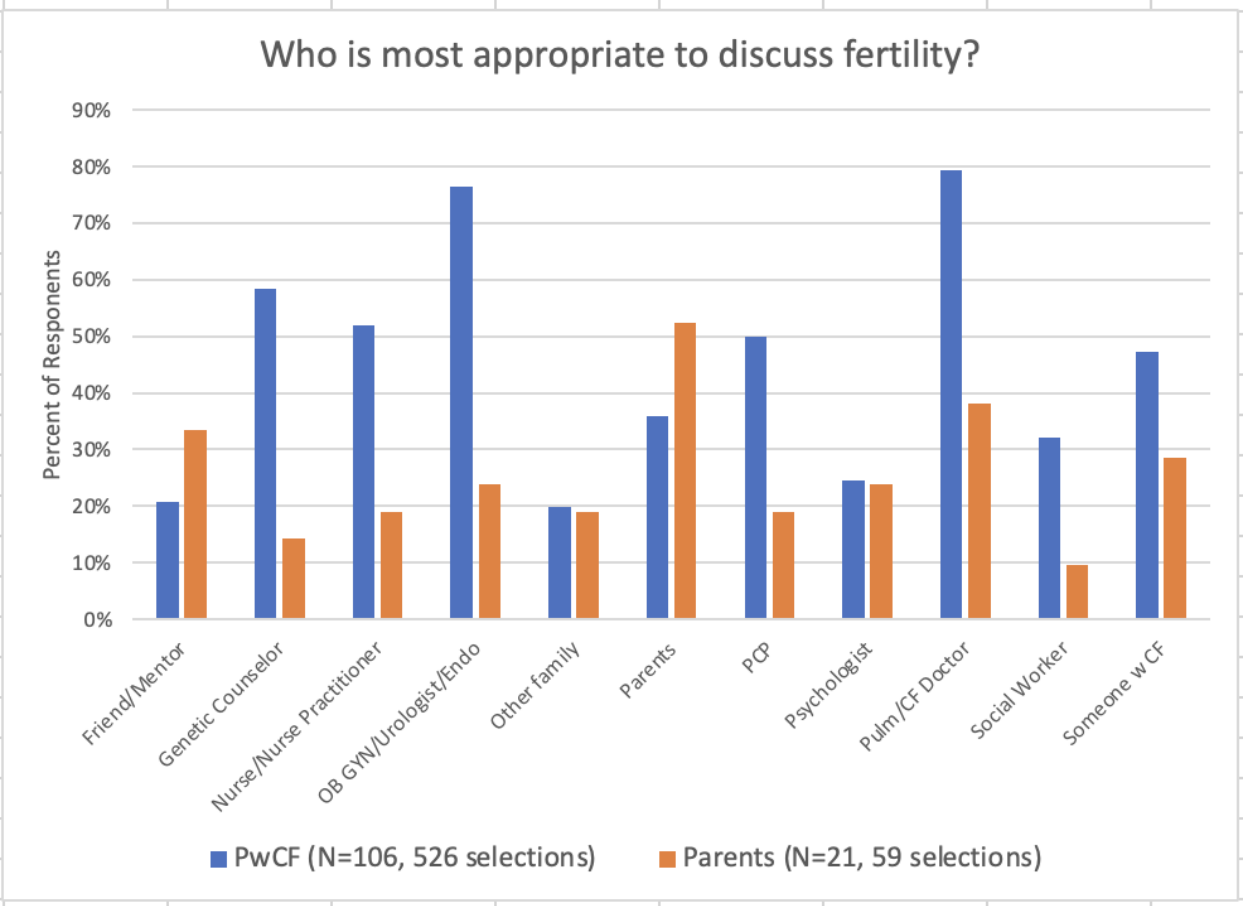

Figure 10. **Support Members Who Would be Most Appropriate for Fertility Conversations in the Future in PwCF and Parents.**

Respondents could select all that applied. [Endo=Endocrinologist; OB GYN= obstetrics gynecologist; PCP= primary care physician; Pulm=Pulmonologist]

When asked when the first fertility conversations should take place, the largest proportion of both the pwCF and parent groups, nearly two thirds of the combined group, selected the teenage years (Table 11). Those who selected the adult years were asked to differentiate between the options ‘as soon as they become an adult’ and ‘when considering family planning’. The groups were split between these options with half of the pwCF and all of the parents indicating

'as soon as they became an adult' and half of the pwCF indicating the conversation should take place when considering family planning (Figure 11). Responses of PwCF and Parents were found to be significantly different (p=0.010).

When should the first fertility conversation take place for individuals with CF			
	PwCF N=108	Parent N=22	Total N=130
Childhood (ages 6-12)	12 (11.1%)	7 (31.8%)	13 (10%)
Teens (ages 13-17)	70 (64.8%)	10 (45.5%)	80 (61.5%)
Adulthood (age 18+)	26 (24.1%)	5 (22.7%)	31 (23.8%)
If adulthood			
As soon as they become an adult	13 (50.0%)	5 (100%)	18 (58.1%)
When considering family planning	13 (50.0%)	0	13 (41.9%)

Table 11. **Assessment of When the First Fertility Conversations Should Take Place.**

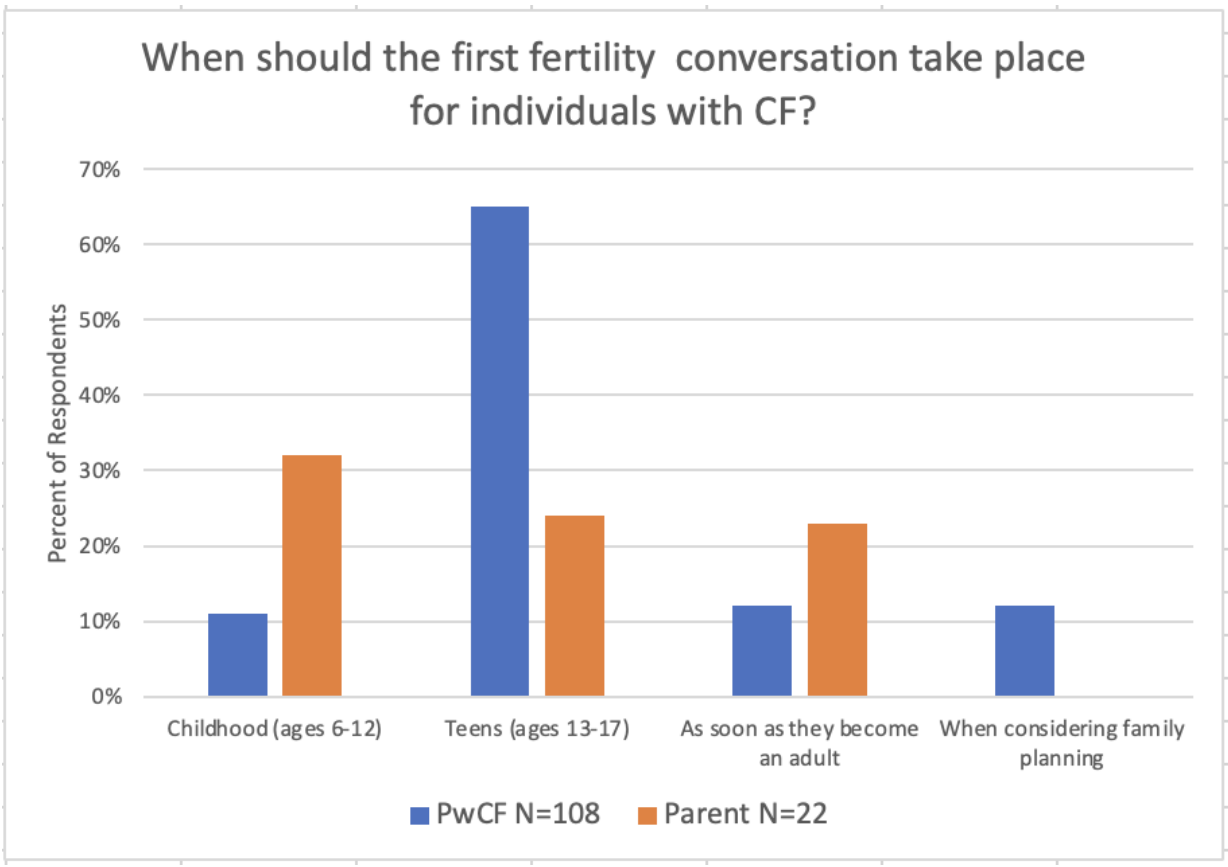

Figure 11. **Distribution of When First Fertility Conversations Should Take Place.**

Responses of pwCF and parents were found to be significantly different; pwCF overwhelmingly preferred the teenage years, but parents were split (p=0.010).

3.7 Short Answer Responses

All groups were asked a variety of different open-ended questions to elicit a better understanding of their personal experiences. The response to these questions was robust and while all are valuable pieces of data and can be found in Appendices I-K, a selection of the responses is also showcased below.

Asked of pwCF and parents:

Were these [fertility] conversations helpful? If so, how?

"No one ever brought it up and I was embarrassed to ask."

(35y Female with CF)

"Knowing the information didn't help make it not a problem"

(31y Female with CF)

"I think that having the social worker who had developed a strong rapport with our our family and child helped the conversation tremendously. The presentation was personalized to my son and not a scripted, factual piece of information. It was a dialogue."

(Mother of a 25y Male with CF).

Did these conversations change your view on fertility/infertility? If so, how?

"Yes. It made me feel less at fault for it. I struggled with infertility (and still do) for 7+ years. Not until a year ago did I know women with CF also struggle too."

(32y Female with CF)

"It made me realize that if I wanted kids id have to adopt because I couldn't afford IVF. "

(31y Male with CF)

Do you feel that you learned something from these [fertility] conversations? If so, what?

"Yes, that there is hope potentially to be a parent one day it just may look different for me"

(27y Female with CF).

"Sometimes your genetics can heavily impact your family planning, but also how to preservers in the presence of hardship."

(32y Male with CF)

"I learned about why it's difficult to get pregnant and why trikafta made it easier to get pregnant for women with CF"

(31y Female with CF)

How do you wish conversations about cystic fibrosis-related infertility had gone for you? How would you hope these conversations would go for people with cystic fibrosis in the future?

"Start earlier. It was alot of my own research"

(31y Female with CF)

"That they would have encouraged me and provided the resources needed instead of just telling me all the worst case scenarios."

(40y Female with CF)

“My only wish is that it was brought up at a younger age.”

(25y Male with CF).

“I would have hoped to have had them earlier before I wanted to have children. I had no idea it could be a struggle for me to get pregnant. And I blamed myself for so much of my infertility for many years. It would have been helpful to have this information. I still feel like I don’t know a lot about it or, especially, how to correct it.”

(32y Female with CF)

"It would be nice to explain it all and plan to be tested without me having to ask about it. Just make it a regular thing so at a certain age you just know it's time to be tested just like other planned CF care."

(31y Male with CF)

“I wish the teams had brought up fertility first, I always had to bring it up and I wish it was talked about sooner. I always believed I could not have children until I was an adult”

(35y Female with CF).

“Although it was awkward sometimes, it was very helpful for my treatment and made the team more confident in my treatment”

(25y Male with CF)

"I wish that our CF clinic had a good plan to introduce this conversation to my child. The plan would ideally be developed with the clinic social worker and be age appropriate. Right now, our clinic seems to avoid having the conversation at all. This conversation should NOT be done by the primary care physician - 99% of them are completely clueless about CF or their knowledge is completely out-of-date."

(Mother of an 11y Male with CF)

Is there anything you would like to share that has not been addressed in this survey?

"I think the conversations need to happen early so parents have time to cope and process. Then they can pass the information on to the child once the child is at the appropriate maturity age (which is different for each child but I believe at least in the teens is when it needs to happen)."

(Mother of a 6y Female with CF).

<u>Asked of providers:</u>

Please explain your thoughts on how adequately fertility is discussed in cystic fibrosis patient care.

"This is not well discussed. This education needs to begin in pediatric clinics and continue through adulthood. In a perfect scenario, this would be a team effort and SW/MH, care coordination/case management would be involved. With the advent of CFTR modulator drugs this is especially important."

(Physician, Pediatric CF Clinic)

"In pediatrics, doctors are often uncomfortable discussing fertility with teens, other than to advise them to use contraception. We could certainly use some guidelines to help us provide better education."

(Social Worker, Pediatric CF Clinic)

"Im sure this differs from center to center, however it is becoming a larger focus as we are seeing a rise in unplanned pregnancies and as patients are leading healthier lives and pursuing parenthood at a higher rate. Guidelines around this topic from the CFF would be helpful."

(Nurse, Adult CF Clinic)

*"Assisted reproductive technologies are extremely expensive and these out-of-pocket costs are often a barrier for patients. I think it is important to recognize that IVF, IUI, sperm extraction, and even adoption fees can make having a family unattainable for many with CF. This does not mean everyone has a "right" to an expensive procedure that is arguably elective, but it is unjust that medical *and administrative* fees prevent people with CF from having families."*

(Physician, Adult CF Clinic)

IV DISCUSSION

CF affects fertility in both males and females. Approximately 95% of men with CF have some degree of vas deferens abnormality, and about 35% of females with CF face infertility due to altered cervical mucus, ovulation issues, or nutritional problems. With highly effective modulator therapy, pregnancy rates in the CF population have risen dramatically. However, there remains a knowledge gap regarding individual fertility capabilities, likely due to inadequate fertility education. Currently, there are no guidelines on when, how, and by whom fertility should be addressed with pwCF.

This study had multiple aims. The first aim was to assess baseline knowledge about the impact of CF on fertility among individuals in the CF community, including pwCF, parents, and providers from CF care centers. The second aim was to assess how fertility impact from CF is addressed in the CF population in the US and identify potential disparities in access to fertility counseling. Lastly, the study aimed to create actionable evidence for the standardization of fertility education for the CF population. The study hypothesized that there would be variation in fertility discussions sampled in the US, including aspects such as the age at which the concept is introduced, the participants involved in the conversation, and the resources explored. Additionally, the study hypothesized that clinics across the country would have different policies and practices regarding how and when fertility is discussed with patients and their families. It was also hypothesized that most pwCF would prefer initiating fertility conversations at a younger age, while parents of children with CF would prefer these conversations to take place after 18 years of age. Finally, it was suspected that both clinics and individuals would agree that there are areas for improvement in fertility discussions within the CF community.

Having collected and analyzed the data, it can be seen that while we were correct in some of these hypotheses, there were others that remain unproven. We can see there is strong variation among those sampled, but overall, the CF community is enthusiastic about the need for improved conversations and working towards care guidelines that include discussions about fertility. Results showed pwCF would prefer fertility conversations in the teens rather than what is actually taking place with most conversations happening in adulthood. While some parents surveyed preferred fertility conversations to happen at older ages, there was a significant number of parents who preferred conversations in the teenage years or even childhood. An ideal time for these conversations might be during the transition between pediatric and adult care, allowing trusted pediatric care teams to initiate discussions that can be continued in the adult clinic.

Descriptive measures collected indicate that things are going well for some individuals, but not for all. While many pwCF scored well on their knowledge exams, indicated that providers initiated meaningful conversations about fertility, and reported overall satisfaction with fertility discussions, a large proportion of pwCF had a different experience. Strikingly, 14% of pwCF reported that no one on their care team had discussed fertility with them.

While ideally multiple CF providers would be comfortable and competent in discussing fertility, without a universal standard to guide these discussions, patients may fall through the cracks and receive this information outside of the clinic setting, at an older age than anticipated, or not at all. We looked at the age of the individuals who said they never had fertility discussed with them to see if this lack of fertility care was something that was isolated to an older population, perhaps prior to modulators and increased fertility knowledge, however alarmingly, the respondents were as young as age 20 and the average age was 41. We also wanted to know if this issue was predominant in one sex over the other, given the different degrees of severity of

fertility implications. The group was relatively evenly split, consisting of 44% females and 56% males. While fertility is an issue for pwCF of both sexes, males are likely to be more significantly impacted given that the issue is structural from birth and has a 95% likelihood of affecting fertility. Over two-thirds of these pwCF indicated that they were diagnosed in childhood because of symptoms. This indicates that many of these individuals had gone through pediatric and adult care teams without ever discussing the fertility impact of CF. Nearly half of the pwCF who indicated no fertility discussions turned to internet sites other than CFF.org for their research, and one-third indicated that they used no resources at all. The internet is a powerful resource and allows many with CF to connect in a way that they are not able to in-person because of the risk of pulmonary infections, however, the internet is also home to rampant misinformation. This data has exposed gaps in care that need to be addressed.

Future guidelines addressing fertility discussions should acknowledge the preferences expressed by people with cystic fibrosis (pwCF), parents, and healthcare providers. Many participants in the study emphasized the importance of having conversations about fertility earlier than they personally experienced. According to the participants, the teenage years are seen as the appropriate time to initiate discussions about fertility. Various reasons were provided in open-ended responses as to why earlier conversations are desired, the primary one being that pwCF believe early discussions would allow them more time for family planning. The financial burden associated with pursuing fertility treatments such as IVF, adoption, or other options is significant for individuals with CF. Inadequate insurance coverage and additional costs related to the disease can make these services unaffordable for many. Providing pwCF with more time to plan financially for these services may make them more feasible options. In the US, the average cost of a single IVF cycle is $12,000 before the additional costs of medications, which can range

from $3,000 to $4,000 per cycle. It is important to acknowledge that often couples will need more than one IVF cycle to achieve viable embryos (Patrizio et al, 2022). Insurance coverage in the US for ART services is inconsistent making the costs of IVF the sole responsibility of the pwCF. Seventeen states, however, have passed laws that require insurance to provide at least some coverage for infertility diagnoses and treatments. These states are Arkansas, California, Connecticut, Delaware, Hawaii, Illinois, Louisiana, Maryland, Massachusetts, Montana, New Hampshire, New Jersey, New York, Ohio, Rhode Island, Texas, and West Virginia (Patrizio et al, 2022). Even with insurances providing coverage, it is often limited to few plans. Hopefully, in time more states will implement similar mandates, and coverage for these services will become more substantial.

Understanding how the condition affects their overall health is an integral part of comprehending the condition they live with every day. Participants frequently mentioned the importance of earlier discussions due to their right to understand their bodies and capabilities. Excluding or avoiding fertility discussions denies patients informative and holistic healthcare. Other participants cited their experiences of pain from unexplained infertility as a reason why they would have wanted fertility discussions earlier in their care. Additionally, pwCF reported that understanding their fertility capabilities had an impact on fostering transparency in their relationships.

While many respondents felt they had the opportunity to ask questions about their fertility care, the study revealed that if patients do not know what questions to ask or are unaware that there are questions to be asked, the opportunity for discussion diminishes significantly. Approximately two-thirds of the respondents indicated that their fertility conversations were initiated by the patients themselves, rather than being provided as part of education by their care

team; this is especially notable because our study population was highly educated and may not be reflective of the entire CF community. Without baseline knowledge that fertility is impacted by CF, many patients and parents would not know they need to initiate these conversations. As experts in CF care, it is the responsibility of clinics to provide age-appropriate and timely education to the patients they serve, ideally multiple times throughout the patient's care. Determining who should take the lead in fertility discussions is challenging, considering the varying composition of roles in each CF care center. However, it would be reasonable to consider pulmonologists, nurses, social workers, and genetic counselors, as the latter have already been suggested by many participants and are trained for such sensitive discussions.

It is not uncommon to hear push back in that fertility is not the most pressing issue when faced with a sick child, especially when there are many very important things to discuss with a pwCF and their family. It is imperative that acute medical care comes first in the discussion of what CF is and what needs to happen to make sure that a patient is as healthy as possible, but fertility should still be on the radar. When timing is appropriate and a patient is stable, fertility conversations should be initiated with parents and patients, especially at follow up visits. Based on providers surveyed, over half (55.8%) are bringing up fertility at their first visit with a new diagnosis of CF.

The establishment of fertility discussion guidelines has been relevant in other genetic disorders associated with infertility. The Klinefelter syndrome community has seen the publication of consensus-based guidelines in 2021 by the European Academy of Andrology. (Zitzmann, 2020). These guidelines outline the evaluation and treatment of associated infertility, as well as when and how to initiate discussions in pre-pubertal males. While the fertility issue in Klinefelter syndrome differs from CF, as it involves a time-sensitive fertility preservation aspect

in young men's lives, there is still much to learn about the publication of guidelines for both conditions. The American Academy of Pediatrics published "Counseling in Pediatric Populations at Risk for Infertility and/or Sexual Function Concerns" in 2018 (Nahata, Quinn, & Tishelman, 2018). This set of recommendations applies to CF and many other conditions. Their recommendations address several themes including discussions starting in infancy, providing developmentally appropriate information that evolves with the patient, the importance of shared decision-making, allowing sufficient time for questions, importance of relaying a consistent message across providers, and the need to facilitate a smooth transition to adult care.

Fertility implications for pwCF cannot be considered without also considering the impact of modulators. These therapies have not only extended the life expectancy of people with CF but have also controlled the disease in a way that improves fertility for some women with CF, enabling naturally conceived pregnancies (CF Foundation, 2022). Between 2019 and 2021, the number of pregnancies in women aged 14-45 more than doubled (CF Foundation, 2022). CFTR modulator therapies have improved lung manifestations in women to a degree that allows for safe pregnancy, as well as improved hormone regulation and mucus consistency. Currently, these fertility benefits are limited to women with CF because the use of modulator therapies in males cannot reverse the structural differences (CBAVD) that arise early in development. However, future studies are exploring the administration of CFTR modulator therapies *in utero* to fetuses identified with CF (Fortner et al., 2021; Szentpetery et al., 2022). It is believed that if these therapies are administered early enough, they may prevent the blockage and subsequent degradation of the vas deferens in male fetuses with CF.

This study has certain limitations. Firstly, the survey was only available in English, making it inaccessible to non-English speakers and limiting the generalizability of the data to other populations. This is particularly important considering that non-English speakers in the United States tend to have lower health literacy (Sentell & Braun, 2012), potentially resulting in lower baseline knowledge about fertility and CF. Barriers to initiating fertility conversations with non-English speakers may also exist due to the need for interpreters and translated resources. Additionally, cultural differences surrounding family building, sexual reproduction, and assisted reproductive technologies (ART) may exist among non-English speakers, and not including their voices may have led to missing important cultural nuances in fertility discussions among people with CF and their families.

Examining the demographics of the study participants reveals population skewing that may limit the generalizability of the results to all people with CF, parents, and clinicians. In the sample, 86% of people with CF identified as white, which constitutes a large majority. CF is known to be more common among individuals of white ancestry, and data from the CFF Patient Registry in 2021 showed that 91.4% of people with CF were white, 9.8% were Hispanic, 3.5% were African American, and the remaining 5.1% represented other races combined. While this distribution aligns with the racial distribution of people with CF in the US, there were variations in regional participation, with the Rocky Mountain, Southwest, and Pacific regions being underrepresented compared to other regions. This is significant because ethnic distribution among people with CF can vary dramatically across regions. For example, the sample was less representative of the Pacific region due to both fewer participants from that region and the more diverse racial profile of people with CF in that region compared to the overall distribution across the country.

The majority of the study population had completed at least some college or higher education, with over a quarter of parents and people with CF having partially or fully completed graduate degrees. It is possible that the high education levels of the participants may have skewed the data, as individuals with higher education may have different perspectives on fertility. This being said, these levels of higher education are consistent with what has been published in the 2021 Annual Data Report for the CFF Patient Registry. According to this report, in 2021, 28.9% of adults older than 18 had completed some college, 30.9% were college graduates, and 8.8% held graduate degrees (CF Foundation, 2022).

In comparison to the groups of people with CF (pwCF) and healthcare providers, the parent participant group was small, resulting in limited data collected about their children with CF. Therefore, the responses provided by the few parents cannot be generalized to all parents of pwCF or their children.

Future research should focus on populations that were not adequately represented in this study, specifically non-English speakers, and parents of pwCF. It is hoped that with the development of guidelines, efficacy studies on interventions can determine what works best for pwCF, their families, and healthcare providers, aiming to effectively serve these populations.

Considering the high cost and limited accessibility of assisted reproductive technologies (ART) for many individuals, further research could explore the feasibility of mandating insurance coverage for ART for pwCF. Determining the most cost-effective pathway to ART would be beneficial.

The surveyed parents expressed their interest in having fertility conversations with their children, and pwCF identified their families as key sources of support for discussing fertility. This raises the question of how parents and families can be supported in facilitating fertility

conversations at home. This is another instance where drawing on resources and strategies used for other conditions can provide insights and guidance. The introduction of children's books discussing genetic and chronic conditions has been well-received by parents seeking to normalize and educate their children about these conditions within the family. For instance, Georgina Schlub, a genetic counselor in Australia, collaborated with Sian Greening, Ashley Crook, Jane Fleming, Kristine Barlow-Stewart, and Kathy Tucker to create a book called Emily Goes to the Doctor that was created as a resource for families talking about hereditary cancer syndromes (Schlub et al, 2021). The book is available in two versions, Li Fraumeni and Hereditary Pheochromocytoma and Paraganglioma syndrome, and talks about the reason why the main character, Emily, needs to go to the doctor so often, genetics, and how family history plays a role. The book is a conversation starter for deeper discussions in the family. Creating and piloting an adapted children's book specifically focused on CF and the associated physical differences could be valuable for parents.

V CONCLUSION

This study aimed to assess the knowledge and practices surrounding fertility discussions in the CF community and provide actionable evidence to demonstrate a need for the standardization of fertility education in this community. The findings highlight the need for improved fertility conversations and care guidelines for pwCF, parents, and healthcare providers. The study revealed significant variation in fertility discussions among the sampled population, with conversations mostly taking place in adulthood despite pwCF expressing a preference for initiating discussions in their teenage years. Parents also had diverse views, with some preferring discussions in the teenage years or even childhood. The transition between pediatric and adult care is an ideal time to initiate fertility conversations, allowing trusted pediatric care teams to initiate discussions that can be continued in the adult clinic.

It was concerning to find that a considerable proportion of pwCF had never discussed fertility with their care team. This lack of fertility care was prevalent in both males and females, highlighting the urgent need for standardized guidelines on who should discuss fertility and when. The responsibility lies with clinics to provide age-appropriate and timely education, involving pulmonologists, nurses, social workers, and genetic counselors in these discussions.

If patients or their families are unaware of the impact of CF on fertility or the need for discussions, the opportunity for dialogue diminishes significantly. Therefore, clinics should prioritize providing age-appropriate and timely education multiple times throughout the patient's care. The study emphasized the importance of initiating fertility conversations earlier, as it allows pwCF more time for family planning and financial preparation. Financial burdens associated with fertility treatments, inadequate insurance coverage, and additional costs related

to CF make these services unaffordable for many. Providing pwCF with more time to plan financially for these services may make them more feasible options.

In conclusion, this study underscores the importance of standardized fertility education and discussions for pwCF. By addressing the identified gaps and implementing evidence-based guidelines, healthcare providers can ensure that pwCF and their families receive comprehensive and timely information about the impact of CF on fertility, empowering them to make informed decisions about family planning and reproductive health.

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VII APPENDIX

APPENDIX A: IRB Approval Letter

UCI University of California, Irvine

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD
PAGE 1 OF 3

November 23, 2022

NICOLE CHARLOTTE NEVITT
PEDIATRICS

RE: UCI IRB #1806 Framing Conversations Around Fertility: Experiences of People with Cystic Fibrosis, Their Parents, and Their Clinical Teams

The above-referenced human-subjects research project has been approved by the University of California, Irvine Institutional Review Board (UCI IRB). This approval is limited to the activities described in the approved protocol and extends to the performance of these activities at each respective site identified. In accordance with this approval, the specific conditions for the conduct of this research are listed below, and informed consent from subjects must be obtained unless otherwise indicated below. Additional conditions for the general conduct of human-subjects research are detailed on the attached sheet.

Approval by the Institutional Review Board does not, in and of itself, constitute approval for the implementation of this research. Other institutional clearances and approvals may be required. Research undertaken in conjunction with outside entities, such as drug or device companies, are typically contractual in nature and require an agreement between the University and the entity. Such agreements must be executed by an institutional official in Sponsored Projects, a division in the UCI Office of Research. The University is not obligated to legally defend or indemnify an employee who individually enters into these agreements and investigators are personally liable for contracts they sign. **Accordingly, the project should not begin until all required approvals have been obtained.**

Changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects [21 CFR Part 56.108 (a)(4), and if applicable 45 CFR 4.108 (a)(3)(iii)].

Questions concerning the approval of this research project may be directed to the Office of Research, 160 Aldrich Hall, Irvine, CA 92697-7600; 949-824-6068, 949-824-2125, or 949-824-0665 (biomedical committee) or 949-824-6662 (social-behavioral committee).

Important Reminder: UCI is in Research Phase 4 as of June 22, 2021. UCI's research activities will increase over time in parallel with the stages in California's Pandemic Roadmap and other public health and higher education guidance. Refer to the Office of Research webpage on Research Continuity for more details.

Minimal Risk (Expedited) Review Category: 7

Jessica Sheldon, CIP
Alternate Member, Institutional Review Board
Approval Issued: November 23, 2022
Expiration Date: November 22, 2025
UCI (FWA) 00004071, Approved: January 31, 2003

IRB Determinations as Conditions of Approval:

Study Status:
Informed Consent Determinations:
1. Waiver of Signed Consent Granted
    a. Study Information Sheet Required

APPROVAL CONDITIONS FOR ALL UCI HUMAN RESEARCH PROTOCOLS

POST-APPROVAL INVESTIGATOR RESPONSIBILITIES (PAIR):
In accordance with Federal regulations and HRP policies, there are Investigator responsibilities during the conduct, as well as after completion, of your research. Use the PAIR Worksheet to ensure adherence with your post-approval regulatory responsibilities.

UCI RESEARCH POLICIES:
All individuals engaged in human-subjects research are responsible for compliance with all applicable UCI Research Policies. The Lead Researcher (and Faculty Sponsor, if applicable) of the study is ultimately responsible for assuring all study team members adhere to applicable policies for the conduct of human-subjects research.

LEAD RESEARCHER (LR) RECORDKEEPING RESPONSIBILITIES:
LRs are responsible for the retention of protocol–related records. The following web pages should be reviewed for more information about the LR's recordkeeping responsibilities for the preparation and maintenance of research files: Lead Researcher Recordkeeping Responsibilities and Preparation and Maintenance of a Research Audit File.

APPROVED VERSIONS OF CONSENT DOCUMENTS, INCLUDING STUDY INFORMATION SHEETS:
Unless a waiver of informed consent is granted by the IRB, the consent documents (consent form; study information sheet) with the UCI IRB approval stamp must be used for consenting all human subjects enrolled in this study. Only the current approved version of the consent documents may be used to consent subjects. **Approved consent documents are not to be used beyond the expiration date provided on the IRB approval letter.** IRB approved materials can be found in KR Protocols in the attachments section.

PROTOCOL EXPIRATION:
The UCI IRB approval letter references the protocol expiration date under the IRB Chair's signature authorization. A courtesy email will be sent prior to expiration reminding the Lead Researcher to apply for renewal**. It is the LR's responsibility to apply for renewal to ensure continuous approval throughout the conduct of the study.** Lapses in approval must be avoided to protect the safety and welfare of enrolled subjects.

AMENDMENTS:
The UCI HRP does not require the submission of minor changes to exempt research. For those studies in which a lead researcher (and faculty sponsor (FS), if applicable) has submitted to and received UCI IRB confirmation of exemption, minor changes may be made without notifying the UCI IRB. For more information about this including what constitutes a minor change versus a change that must be prospectively submitted for review and approval by the UCI IRB via a formal amendment, visit Protocol Amendment.

CHANGES IN FINANCIAL INTEREST:
Any changes in the financial relationship between the study sponsor and any of the investigators on the study and/or any new potential conflicts of interest must be reported immediately to the UCI Conflict of Interest Oversight Committee (COIOC). If these changes affect the conduct of the study or result in a change in the text of the approved informed consent document, these changes must also be reported to the UCI IRB via an amendment.

GRANT CONGRUENCE REVIEWS:
If this human subject research is funded or supported by a Federal Agency, it is the LR's responsibility to submit amendments, as necessary, to assure that the IRB protocol continues to be identical in principle and congruent with the scope of work outlined in the proposal application.

REPORTING A PROBLEM:
In accordance with Federal regulations and HRP policies, only internal (where UCI serves as the IRB of record), Unanticipated Problems must be reported to the UCI IRB. Unanticipated Problems should also be reported to the UCI IRB when UCI is relying on an external IRB, and the incident occurred at UCI or the incident occurred at an offsite location on a study conducted by a UCI LR. Unanticipated Problems must be submitted to the IRB within 5 business days upon the LR's knowledge of the event. For additional information visit the updated HPR webpage on Reporting a Problem.

POSTING OF THE INFORMED CONSENT DOCUMENT:
Clinical trials initially approved by the IRB on or after January 21, 2019, must post one (1) IRB-approved clinical trial consent form at a publicly available federal website. The consent form must be posted after recruitment closes, and no later than 60 days after the last study visit. For additional guidance, refer to the OHRP FAQs on Informed Consent.

CLOSING REPORT:
A closing report should be filed with the UCI IRB when the research concludes. Visit the HRP webpage Closing a Protocol for complete details.

APPENDIX B: Recruitment Flier

CYSTIC FIBROSIS RESEARCH OPPORTUNITY

UC Irvine Health
School of Medicine

HOW DOES CYSTIC FIBROSIS AFFECT FERTILITY?

TELL US WHAT YOU KNOW AND HOW WE CAN BETTER INTEGRATE THESE DISCUSSIONS INTO CYSTIC FIBROSIS CARE!

https://bit.ly/3z9qvKK

SCAN ME

ELIGIBILITY

- Have a diagnosis of cystic fibrosis OR
  Have a child with a diagnosis of cystic fibrosis OR
  Work in a cystic fibrosis care center
- Be 18 years or older
- Be able to read and write in English
- Live in the United States

Participation involves a 10-20 minute anonymous survey. Enter the raffle for a chance to win one of five $20 Amazon gift-cards!

PLEASE CONTACT LEAD RESEARCHER NICOLE NEVITT WITH ANY QUESTIONS AT NNEVITT@HS.UCI.EDU

APPENDIX C: Survey Consent

Start of Block: Survey Consent

University of California, Irvine
Study Information Sheet
Framing Conversations Around Fertility: Experiences of People with Cystic Fibrosis, Their Parents, and Their Clinical Teams
Lead Researcher: Nicole Nevitt, BS Genetic Counseling Graduate Student Department of Pediatrics nnevitt@hs.uci.edu
Faculty Sponsor: Kathryn Singh, MPH, MS, CGC Associate Clinical Professor Department of Pediatrics kesingh@hs.uci.edu
Please read the information below and ask questions about anything that you do not understand. A researcher listed above will be available to answer your questions.

You are being asked to participate in a research study. Participation in this study is voluntary.

You may choose to skip a question. You may refuse to participate or discontinue your involvement at any time without penalty or loss of benefits. You are free to withdraw from this study at any time.

You are being asked to participate in a research study that aims to understand how fertility is discussed as part of cystic fibrosis care throughout the United States. The study will analyze the experiences of patients, parents, and healthcare providers.

You are eligible to participate in this study if you are 18 years or older, are a person with cystic fibrosis OR are a parent of a person with cystic fibrosis, OR work in a cystic fibrosis clinic, can read and write in English, and live in the United States of America.

Participation in this research study involves a one-time, web-based survey. The survey will take about 10-20 minutes to complete.

Possible risks/discomforts associated with the study include psychological distress. This survey discusses the possible fertility complications related to cystic fibrosis. Although this information is freely available to all on the internet, we recognize that it is possible that an individual taking this survey could be learning about fertility implications for the first time by participating in this study. Resources related to cystic fibrosis and fertility will be available throughout the survey and again upon completion of the survey. Please reach out to your health care teams for any questions related to your own medical care.

There are no direct benefits from participation in the study. However, results from this study may be able to be used to help inform fertility discussion guidelines for healthcare providers to follow in the future. This survey is an opportunity to share your experience and relay any feedback to better inform people with cystic fibrosis in the future.

There are no alternative procedures available. The only alternative is not to participate in this study.

There is no cost to you for participation in this study.

All research data collected is anonymous and will be stored securely.

The research team, authorized UCI personnel, and regulatory entities, may have access to your anonymous study records to protect your safety and welfare. While the research team will make every effort to keep your information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

Future Research Use: Researchers will use your information to conduct this study. Once the study is done using your information, we may share it with other researchers so they can use it for other studies in the future. We will not share your name or any other private identifiable information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

We will keep de-identified information until aggregate results of the study are published.

If you have any comments, concerns, or questions regarding the conduct of this research please contact the researchers listed at the top of this form.

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can contact the researcher at the email listed at the top of this form.

Participants may submit their email to be entered in a drawing to win one of 5 available $20 Amazon electronic gift cards. To enter this raffle, you may submit your email address here. Email addresses will be assigned a number and a random number generator will be used to select the 5 winners. Electronic gift cards will be emailed to winners by June 2023. All email addresses collected will be destroyed after prizes are distributed.

Please contact the UCI Institutional Review Board by phone, (949) 824-6662, by e-mail at IRB@research.uci.edu or at 160 Aldrich Hall, Irvine, CA 92697-7600 if you are unable to reach the researchers listed at the top of the form and have general questions; have concerns or complaints about the research; have questions about your rights as a research subject; or have general comments or suggestions.

What is an IRB? An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

APPENDIX D: Survey

Q1.2 Do you agree to participate in this survey?

o I agree (1)

End of Block: Survey Consent

Start of Block: Introduction Question

Q2.1 What is your relationship to the cystic fibrosis community? Note: If you AND your child(ren) have cystic fibrosis, please fill out the entire survey as either a patient OR parent (your choice, but please only pick one and answer all questions from that perspective)

o A person with cystic fibrosis (1)

o A parent of a person(s) with cystic fibrosis (2)

o A healthcare provider at a cystic fibrosis center (3)

End of Block: Introduction Question

Start of Block: Knowledge Assessment

Q3.1 The purpose of the following questions is to capture your background knowledge regarding cystic fibrosis and fertility.

Q3.2 In what way(s) does cystic fibrosis affect fertility in males? Select all that apply.

▢ Fertility is not affected in males with CF (1)

▢ Most males with cystic fibrosis don't make functional sperm (2)

▢ Most males with cystic fibrosis have a problem where sperm are trapped and can't leave the body, either because of a missing tube (congenital bilateral absence of the vas deferens) or a mucus blockage (3)

Q3.3 In what way(s) does cystic fibrosis affect fertility in females? Select all that apply.

▢ Fertility is not affected in females with cystic fibrosis (1)

☐ Females with cystic fibrosis may have differences of mucus in the reproductive tract that can prevent sperm from getting to the egg (2)

☐ Women with cystic fibrosis may have irregularities with hormones that can affect their menstrual cycle (3)

Q3.4 Which of the following ways can males with cystic fibrosis-related infertility have children? Select all that apply.

☐ Adoption (1)

☐ Assisted Reproductive Technologies (IVF, IUI, etc) to achieve a pregnancy (2)

☐ Donor sperm (3)

☐ Hormone regulation therapies (4)

☐ Sexual intercourse (5)

☐ None of the above (6)

☐ Other (7) _____

Q3.5 Which of the following ways can females with cystic fibrosis-related infertility have children? Select all that apply.

☐ Adoption (1)

☐ Assisted Reproductive Technologies (IVF, IUI, etc) to achieve a pregnancy (2)

☐ Donor egg (3)

☐ Hormone regulation therapies (4)

☐ Sexual intercourse (5)

☐ None of the above (6)

☐ Other (7) _____

Q3.6 Does cystic fibrosis-related infertility prevent males from contracting sexually transmitted infections (STIs)?

o Yes (1)

o No (2)

o I don't know (3)

Q3.7 Does cystic fibrosis-related infertility prevent females from contracting sexually transmitted infections (STIs)?

o Yes (1)

o No (2)

o I don't know (3)

End of Block: Knowledge Assessment

Start of Block: Demographics for people with CF

Q4.1 Please answer the following questions to tell us a little bit more about yourself.

Q4.2 How old are you?

_____

Q4.3 In what state do you receive cystic fibrosis care?

o Alabama (1)

o Alaska (2)

o Arizona (3)

o Arkansas (4)

o California (5)

o Colorado (6)

o Connecticut (7)

o Delaware (8)

o Florida (9)

o Georgia (10)

o Hawaii (11)

o Idaho (12)

o Illinois (13)

o Indiana (14)
o Iowa (15)
o Kansas (16)
o Kentucky (17)
o Louisiana (18)
o Maine (19)
o Maryland (20)
o Massachusetts (21)
o Michigan (22)
o Minnesota (23)
o Mississippi (24)
o Missouri (25)
o Montana (26)
o Nebraska (27)
o Nevada (28)
o New Hampshire (29)
o New Jersey (30)
o New Mexico (31)
o New York (32)
o North Carolina (33)
o North Dakota (34)
o Ohio (35)
o Oklahoma (36)
o Oregon (37)
o Pennsylvania (38)
o Rhode Island (39)
o South Carolina (40)
o South Dakota (41)
o Tennessee (42)
o Texas (43)
o Utah (44)
o Vermont (45)
o Virginia (46)

o Washington (47)
o West Virginia (48)
o Wisconsin (49)
o Wyoming (50)

Q4.4 What was your sex assigned at birth?
o Female (1)
o Male (2)
o Other (3) _____

Q4.5 What is your gender identity?
o Female (1)
o Male (2)
o Non-binary (3)
o Other (4) _____

Q4.6 What is your ethnicity?
▢ American Indian or Alaska Native (1)
▢ Asian (2)
▢ Black or African American (3)
▢ Hispanic (4)
▢ Native Hawaiian or Pacific Islander (5)
▢ White (6)
▢ Other (7) _____

Q4.7 What is your highest education level?

o Some high school (1)

o High school graduate (2)

o Some college (3)

o College degree (4)

o Some graduate level (5)

o Graduate degree (MS, MD, JD, PhD, etc) (6)

Q4.8 Do you work in health care?

o Yes (1)

o No (2)

Display This Question:

If Q4.8 = 1

Q4.9 What is your job/role?

_____

Q4.10 What are your CFTR gene variants (mutations)? If you do not know please write 'I don't know.'

_____

_____

_____

_____

_____

Q4.11 How were you diagnosed with cystic fibrosis?

o Newborn screening (1)

o In childhood because of symptoms (2)

o In adulthood because of symptoms (3)

o In adulthood because of infertility (4)

o In adulthood by routine carrier screening (5)

o Other (6) _____

o I don't know (7)

Q4.12 At what age were you diagnosed with cystic fibrosis?

_____

Q4.13 In which state were you diagnosed with cystic fibrosis?

o Not in the US (1) _____

o Alabama (2)

o Alaska (3)

o Arizona (4)

o Arkansas (5)

o California (6)

o Colorado (7)

o Connecticut (8)

o Delaware (9)

o Florida (10)

o Georgia (11)

o Hawaii (12)

o Idaho (13)

o Illinois (14)

o Indiana (15)

o Iowa (16)

o Kansas (17)

o Kentucky (18)

o Louisiana (19)

o Maine (20)
o Maryland (21)
o Massachusetts (22)
o Michigan (23)
o Minnesota (24)
o Mississippi (25)
o Missouri (26)
o Montana (27)
o Nebraska (28)
o Nevada (29)
o New Hampshire (30)
o New Jersey (31)
o New Mexico (32)
o New York (33)
o North Carolina (34)
o North Dakota (35)
o Ohio (36)
o Oklahoma (37)
o Oregon (38)
o Pennsylvania (39)
o Rhode Island (40)
o South Carolina (41)
o South Dakota (42)
o Tennessee (43)
o Texas (44)
o Utah (45)
o Vermont (46)
o Virginia (47)
o Washington (48)
o West Virginia (49)
o Wisconsin (50)
o Wyoming (51)

End of Block: Demographics for people with CF

Start of Block: People with CF Questions

Q5.1 The next set of questions are about your own experience with fertility discussion as part of your cystic fibrosis care.

For more information about cystic fibrosis and fertility, you can visit the Cystic Fibrosis Foundation website: https://www.cff.org/managing-cf/fertility and also talk with your care team.

Q5.2 Who has discussed fertility with you? Select all that apply.

- ☐ Friend/Mentor (1)
- ☐ Genetic Counselor (2)
- ☐ Nurse/Nurse Practitioner (3)
- ☐ Obstetrician Gynecologist/Urologist/Reproductive Endocrinologists (4)
- ☐ Other family member (sibling, extended family) (5)
- ☐ Parents/guardians (6)
- ☐ Primary Care Physician (7)
- ☐ Psychologist (8)
- ☐ Pulmonologist or other cystic fibrosis physician (9)
- ☐ Social Worker (10)
- ☐ Someone else with cystic fibrosis (11)
- ☐ Other (12) _____
- ☐ No one has discussed fertility with me (13)

Skip To: Q5.16 If Q5.2 = 13

Q5.3 At what age(s) were fertility topics discussed with you? Select all that apply.

- ☐ Childhood (ages 6-12) (1)
- ☐ Teens (ages 13-17) (2)

☐ Adulthood (ages 18+) (3)

☐ Other (4) _____

Q5.4 In approximately how many visits with your **pediatric** cystic fibrosis care team has fertility been discussed?

o None (1)

o 1-2 visits (2)

o 3-4 visits (3)

o Many visits (4)

Q5.5 In approximately how many visits with your ***adult*** cystic fibrosis care team was fertility discussed?

o None (1)

o 1-2 visits (2)

o 3-4 visits (3)

o Many visits (4)

Q5.6 What was said in these conversations? Select all that apply.

☐ Assisted Reproductive Technologies (ART) methods such as testicular biopsy and/or in vitro fertilization can help people with cystic fibrosis achieve a pregnancy (1)

☐ Most males with cystic fibrosis are infertile (2)

☐ Infertility in males with cystic fibrosis is due to a problem where sperm are trapped and can't leave the body, either because of a missing tube (congenital bilateral absence of the vas deferens) or a mucus blockage (3)

☐ Infertility in women with cystic fibrosis is due to differences in hormone regulation and/or differences of mucus consistency in the reproductive tract (4)

☐ People with cystic fibrosis can still contract sexually transmitted infections (5)

☐ Women with cystic fibrosis may have trouble getting pregnant (6)

☐ Other (7) _____

Q5.7 Who initiated these conversations? Select all that apply.

☐ I initiated these discussions (1)

☐ My parent/guardian/family member initiated these discussions (2)

☐ My health care provider initiated these discussions (3)

☐ Other (4) _____

Q5.8 Were you comfortable with these discussions?

o Always (1)

o Sometimes (2)

o Never (3)

o I don't remember (4)

Q5.9 Did having these discussions make you feel embarrassed/uncomfortable?

o Always (1)

o Sometimes (2)

o Never (3)

o I don't remember (4)

Q5.10 How much time was spent on fertility discussion?

o Too little (1)

o The right amount (2)

o Too much (3)

o I don't remember (4)

Q5.11 Do you feel that the people leading these conversations on fertility were knowledgeable about the topic?

- o Always (1)
- o Sometimes (2)
- o Never (3)
- o I don't remember (4)

Q5.12 Were these conversations helpful? If so, how?

_____

_____

_____

_____

_____

Q5.13 Do you feel that you learned something from these conversations? If so, what?

_____

_____

_____

_____

_____

Q5.14 Are you satisfied with how conversations on fertility have gone?

- o Yes (1)
- o Somewhat (2)
- o No (3)

Q5.15 Did these conversations change your view on fertility/infertility? If so, how?

_____

_____

_____

_____

_____

Q5.16 Do you feel like you have had appropriate opportunities to ask fertility-related questions to your health care team?

o Yes (1)

o Somewhat (2)

o No (3)

Q5.17 How do you wish conversations about cystic fibrosis-related infertility had gone for you? How would you hope these conversations would go for people with cystic fibrosis in the future?

_____

_____

_____

_____

_____

Q5.18 Which of the following people are most appropriate to discuss fertility with people with cystic fibrosis? Select all that apply.

- ▢ Friend/Mentor (1)
- ▢ Genetic Counselor (2)
- ▢ Nurse/Nurse Practitioner (3)
- ▢ Obstetrician Gynecologist/Urologist/Reproductive Endocrinologist (4)
- ▢ Other family member (sibling, extended family) (5)
- ▢ Parents/guardians (6)
- ▢ Primary Care Physician (7)
- ▢ Psychologist (8)

- ☐ Pulmonologist or other cystic fibrosis physician (9)
- ☐ Social Worker (10)
- ☐ Someone else with cystic fibrosis (11)
- ☐ Other (12) _____

Q5.19 In your opinion, when should the ***first*** fertility conversation take place for individuals with cystic fibrosis?

- o Childhood (ages 6-12) (1)
- o Teens (ages 13-17) (2)
- o Adulthood (ages 18+) (3)

Display This Question:

If Q5.19 = 3

Q5.20 Should this first conversation happen as soon as someone becomes an adult, or only when considering family planning?

- o As soon as they become an adult (1)
- o When considering family planning (2)
- o Other (3) _____

Q5.21 What resources have you used for your own research on fertility? Select all that apply.

- ☐ Conferences (1)
- ☐ Discussions with my medical team (2)
- ☐ Discussions with my family members (3)
- ☐ Discussions with other people with CF (4)
- ☐ Discussions with friends (5)
- ☐ Cystic Fibrosis Foundation website (cff.org) (6)
- ☐ Other Internet sites (7)

- ☐ Pamphlets from clinic (8)
- ☐ Other (9) _____
- ☐ None (10)

Q5.22 Is there anything you would like to share that has not been addressed in this survey?

_____

_____

_____

_____

_____

End of Block: People with CF Questions

Start of Block: Parent Demographics

Q6.1 Please answer the following questions to give us more information about you and your child(ren) with cystic fibrosis.

Q6.2 What is your parental role?

- o Biological Mother (1)
- o Biological Father (2)
- o Adoptive Mother (3)
- o Adoptive Father (4)
- o Guardian (5)
- o Other (6) _____

Q6.3 What is your ethnicity?

- ☐ American Indian or Alaska Native (1)
- ☐ Asian (2)

- ☐ Black or African American (3)
- ☐ Hispanic (4)
- ☐ Native Hawaiian or Pacific Islander (5)
- ☐ White (6)
- ☐ Other (7) _____

Q6.4 What is your highest education level?

- o Some high school (1)
- o High school graduate (2)
- o Some college (3)
- o College degree (4)
- o Some graduate level (5)
- o Graduate degree (MS, MD, JD, PhD, etc) (6)

Q6.5 Do you work in health care?

- o Yes (1)
- o No (2)

Display This Question:

If Q6.5 = 1

Q6.6 What is your job/role?

_____

Q6.7 How many children with cystic fibrosis do you have? You will be asked a series of questions about each of your children with cystic fibrosis

_____

End of Block: Parent Demographics

Start of Block: Children Block 1

Q7.1 How old is your child with cystic fibrosis?

_____

Q7.2 What state does your child receive cystic fibrosis care in?

- o Alabama (1)
- o Alaska (2)
- o Arizona (3)
- o Arkansas (4)
- o California (5)
- o Colorado (6)
- o Connecticut (7)
- o Delaware (8)
- o Florida (9)
- o Georgia (10)
- o Hawaii (11)
- o Idaho (12)
- o Illinois (13)
- o Indiana (14)
- o Iowa (15)
- o Kansas (16)
- o Kentucky (17)
- o Louisiana (18)
- o Maine (19)
- o Maryland (20)
- o Massachusetts (21)
- o Michigan (22)
- o Minnesota (23)
- o Mississippi (24)
- o Missouri (25)
- o Montana (26)

o Nebraska (27)
o Nevada (28)
o New Hampshire (29)
o New Jersey (30)
o New Mexico (31)
o New York (32)
o North Carolina (33)
o North Dakota (34)
o Ohio (35)
o Oklahoma (36)
o Oregon (37)
o Pennsylvania (38)
o Rhode Island (39)
o South Carolina (40)
o South Dakota (41)
o Tennessee (42)
o Texas (43)
o Utah (44)
o Vermont (45)
o Virginia (46)
o Washington (47)
o West Virginia (48)
o Wisconsin (49)
o Wyoming (50)

Q7.3 What was your child's sex assigned at birth?

o Female (1)
o Male (2)
o Other (3) _____

Q7.4 What is your child's gender identity?

o Female (1)

o Male (2)

o Non-binary (3)

o Other (4) _____

Q7.5 What are your child's CFTR gene variants (mutations)? If you do not know please write 'I don't know.'

_____

_____

_____

_____

_____

Q7.6 How was your child diagnosed with cystic fibrosis?

o Newborn screening (1)

o In childhood because of symptoms (2)

o In adulthood because of symptoms (3)

o In adulthood because of infertility (4)

o In adulthood by routine carrier screening (5)

o I don't know (6)

o Other (7) _____

Q7.7 At what age was your child diagnosed with cystic fibrosis?

_____

Q7.8 In which state was your child diagnosed with cystic fibrosis?

o Not in the US (1) _____

o Alabama (2)

o Alaska (3)

o Arizona (4)

o Arkansas (5)

o California (6)

o Colorado (7)

o Connecticut (8)

o Delaware (9)

o Florida (10)

o Georgia (11)

o Hawaii (12)

o Idaho (13)

o Illinois (14)

o Indiana (15)

o Iowa (16)

o Kansas (17)

o Kentucky (18)

o Louisiana (19)

o Maine (20)

o Maryland (21)

o Massachusetts (22)

o Michigan (23)

o Minnesota (24)

o Mississippi (25)

o Missouri (26)

o Montana (27)

o Nebraska (28)

o Nevada (29)

o New Hampshire (30)

o New Jersey (31)

o New Mexico (32)

o New York (33)

o North Carolina (34)
o North Dakota (35)
o Ohio (36)
o Oklahoma (37)
o Oregon (38)
o Pennsylvania (39)
o Rhode Island (40)
o South Carolina (41)
o South Dakota (42)
o Tennessee (43)
o Texas (44)
o Utah (45)
o Vermont (46)
o Virginia (47)
o Washington (48)
o West Virginia (49)
o Wisconsin (50)
o Wyoming (51)

End of Block: Children Block 1

Start of Block: Parent of people with CF Questions

Q8.1 The next set of questions are about the fertility discussions that you and your child(ren) have had with the cystic fibrosis care team.

If you have more than one child with cystic fibrosis, please answer the following questions based on your combined experience. At the end you will have an opportunity to share what may have been different about each child's experience.

For more information about cystic fibrosis and fertility, please visit the Cystic Fibrosis Foundation website: https://www.cff.org/managing-cf/fertility and talk with your child(ren)'s care team.

Q8.2 Who has discussed fertility with ***your child(ren)***? Select all that apply.

- ☐ Friend/Mentor (1)
- ☐ Genetic Counselor (2)
- ☐ Nurse/Nurse Practitioner (3)
- ☐ Obstetrician Gynecologist/Urologist/Reproductive Endocrinology (4)
- ☐ Other family member (sibling, extended family) (5)
- ☐ Primary Care Physician (6)
- ☐ Psychologist (7)
- ☐ Pulmonologist or other cystic fibrosis doctor (8)
- ☐ Social Worker (9)
- ☐ Someone else with cystic fibrosis (10)
- ☐ You/other parent/guardian (11)
- ☐ Other (12) _____
- ☐ No one has discussed fertility with my child (13)

Q8.3 Who has discussed fertility with ***you***? Select all that apply.

- ☐ Friend/Mentor (1)
- ☐ Genetic Counselor (2)
- ☐ Nurse/Nurse Practitioner (3)
- ☐ Obstetrician Gynecologist/Urologist/Reproductive Endocrinology (4)
- ☐ Other family member (sibling, extended family) (5)
- ☐ Other parent/guardian (6)
- ☐ Primary Care Physician (7)
- ☐ Psychologist (8)
- ☐ Pulmonologist or other cystic fibrosis doctor (9)
- ☐ Social Worker (10)
- ☐ Someone else with cystic fibrosis (11)
- ☐ Other (12) _____
- ☐ No one has discussed fertility with me (13)

Q8.4 At what age(s) were fertility topics discussed with ***your child(ren)***? Select all that apply.

- ☐ Childhood (ages 6-12) (1)
- ☐ Teens (ages 13-17) (2)
- ☐ Adulthood (ages 18+) (3)
- ☐ Other (4) _____
- ☐ It was never discussed (5)

Q8.5 At what age(s) were fertility topics discussed with ***you***? Select all that apply.

- ☐ Infancy/Early Childhood (ages 0-5) (1)
- ☐ Childhood (ages 6-12) (2)
- ☐ Teens (ages 13-17) (3)
- ☐ Adulthood (ages 18+) (4)
- ☐ Other (5) _____
- ☐ It was never discussed (6)

Q8.6 In approximately how many visits with your child(ren)'s pediatric cystic fibrosis care team has fertility been discussed?

- o None (1)
- o 1-2 visits (2)
- o 3-4 visits (3)
- o Many visits (4)

Skip To: Q8.19 If Q8.6 = 1

Q8.7 What was said in these conversations? Select all that apply.

▢ Assisted Reproductive Technologies (ART) methods can help people with cystic fibrosis achieve a pregnancy (1)

▢ Most males with cystic fibrosis are infertile (2)

▢ Infertility in males with cystic fibrosis is due to a problem where sperm are trapped and can't leave the body, either because of a missing tube (congenital bilateral absence of the vas deferens) or a mucus blockage (3)

▢ Infertility in women with cystic fibrosis is due to differences in hormone regulation and differences of mucus consistency in the reproductive tract (4)

▢ People with cystic fibrosis can still contract sexually transmitted infections (5)

▢ Women with cystic fibrosis may have trouble getting pregnant (6)

▢ Other (7) _____

Q8.8 Who initiated these conversations? Select all that apply.

▢ My child initiated discussion (1)

▢ My child's other parent or I initiated discussion (2)

▢ My child's provider initiated discussion (3)

▢ Other (4) _____

Q8.9 Were ***your child(ren)*** comfortable with these discussions?

o Always (1)

o Sometimes (2)

o Never (3)

o I don't remember (4)

Q8.10 Were ***you*** comfortable with these discussions?

o Always (1)

o Sometimes (2)

o Never (3)

o I don't remember (4)

Q8.11 Did having these discussions make ***your child(ren)*** feel embarrassed/uncomfortable?

o Always (1)

o Sometimes (2)

o Never (3)

o I don't remember (4)

Q8.12 Did having these discussions make ***you*** feel embarrassed/uncomfortable?

o Always (1)

o Sometimes (2)

o Never (3)

o I don't remember (4)

Q8.13 How much time was spent on fertility discussion?

o Too little (1)

o The right amount (2)

o Too much (3)

o I don't remember (4)

Q8.14 Do you feel that the people leading these conversations on fertility/infertility were knowledgeable?

o Always (1)

o Sometimes (2)

o Never (3)

o I don't remember (4)

Q8.15 Were these conversations helpful? If so, how?

_____

_____

_____

_____

_____

Q8.16 Do you feel that you/your child(ren) learned something from these conversations? If so, what?

_____

_____

_____

_____

_____

Q8.17 Did these conversations change your view on fertility/infertility? If so, how?

_____

_____

_____

_____

_____

Q8.18 Are you satisfied with how conversations on fertility have gone?

o Yes (1)

o Somewhat (2)

o No (3)

Q8.19 Do you feel like you have had appropriate opportunities to ask fertility-related questions to your child(ren)'s clinicians?

o Yes (1)

o No (2)

Q8.20 How do you wish conversations about cystic fibrosis-related infertility had gone for you/your child(ren)? How would you hope these conversations would go for people with cystic fibrosis and their parents in the future?

_____

_____

_____

_____

_____

Q8.21 Who do you wish had these conversations with your child(ren)? Select all that apply.

- ▢ Friend/Mentor (1)
- ▢ Genetic Counselor (2)
- ▢ Nurse/Nurse Practitioner (3)
- ▢ Obstetrician Gynecologist/Urologist/Reproductive Endocrinologist (4)
- ▢ Other family member (sibling, extended family member) (5)
- ▢ Primary Care Physician (6)
- ▢ Psychologist (7)
- ▢ Pulmonologist or other cystic fibrosis physician (8)
- ▢ Social Worker (9)
- ▢ Someone else with cystic fibrosis (10)
- ▢ You/other parent/guardian (11)
- ▢ Other (12) _____

Q8.22 In your opinion, when should the ***first*** fertility conversations take place for ***individuals*** with cystic fibrosis?

o Childhood (ages 6-12) (1)

o Teens (ages 13-17) (2)

o Adulthood (ages 18+) (3)

Display This Question:

If Q8.22 = 3

Q8.23 Should this first conversation happen as soon as someone becomes an adult, or only when considering family planning?

o As soon as they become an adult (1)

o When considering family planning (2)

o Other (3) _____

Q8.24 In your opinion, when should the ***first*** fertility conversations take place for the ***parents*** of individuals with cystic fibrosis?

o Infancy/Early Childhood (ages 0-5) (1)

o Childhood (ages 6-12) (2)

o Teens (ages 13-17) (3)

o Adulthood (ages 18+) (4)

Q8.25 What resources have you used in your own research on fertility/infertility? Select all that apply.

▢ Conferences (1)

▢ Discussions with my medical team (2)

▢ Discussions with my family members (3)

▢ Discussions with other people with CF (4)

▢ Discussions with friends (5)

▢ Cystic Fibrosis Foundation website (cff.org) (6)

▢ Other Internet sites (7)

▢ Pamphlets from clinic (8)

▢ Other (9) _____

☐ None (10)

Display This Question:

If If How many children with cystic fibrosis do you have? You will be asked a series of questions about each of your children with cystic fibrosis Text Response Is Greater Than 1

Q8.26 Were there notable differences between how fertility was discussed with each of your children with cystic fibrosis?

o Yes (1)

o No (2)

o I don't remember (3)

Display This Question:

If Q8.26 = 1

Q8.27 Please tell us more about any differences you noticed in how fertility was discussed with each of your children with cystic fibrosis.

_____

_____

_____

_____

_____

Q8.28 Is there anything you would like to share that has not been addressed in this survey?

_____

_____

_____

_____

_____

End of Block: Parent of people with CF Questions

Start of Block: CF Center Questions

Display This Question:

If Q2.1 = 3

Q9.1
Which US region is your clinic in?

o Midwest Region (1)

o Northeast Region (2)

o Pacific Region (3)

o Rocky Mountain Region (4)

o Southeast Region (5)

o Southwest Region (6)

Q9.2 What is your job/role in the clinic?

o Dietician (1)

o Genetic Counselor (2)

o Nurse (3)

o Nurse Practitioner (4)

o Physician (5)

o Psychologist (6)

o Social Worker (7)

o Other (8) _____

Q9.3 What is the age range of your patient population?

o Adult (1)

o Pediatric (2)

o Both adult and pediatric (3)

Q9.4 With whom and at what age(s) do you discuss fertility? Select all that apply.

- ▢ Parents in infancy (1)
- ▢ Parents in childhood (2)
- ▢ Parents in teens (3)
- ▢ Patient in childhood (4)
- ▢ Patient in teens (5)
- ▢ Patient during transition to adult care (6)
- ▢ Patient when they turn 18 (7)
- ▢ Patient when they are considering family planning (8)
- ▢ Other (9) _____

Q9.5 When is cystic fibrosis-related infertility discussed in your clinic? Select all that apply.

- ▢ New diagnosis of cystic fibrosis (1)
- ▢ At every follow up visit (2)
- ▢ At least annually during follow up visits (3)
- ▢ Every few years at follow up visits (4)
- ▢ If questions are brought to the team by the patient/family (5)
- ▢ Other (6) _____

Q9.6 Who conducts fertility/infertility discussions in your clinic? Select all that apply.

- ▢ Genetic Counselor (1)
- ▢ Nurse (2)
- ▢ Nurse Practitioner (3)
- ▢ Physician Assistant (4)

- ☐ Pulmonologist (5)
- ☐ Psychologist (6)
- ☐ Social Worker (7)
- ☐ Other (8) _____

Q9.7 What external cystic fibrosis fertility resources do you recommend to patients? Select all that apply.

- ☐ Conferences (1)
- ☐ Discussion with the medical team (2)
- ☐ Discussion with family members (3)
- ☐ Facilitating conversations among other patients with cystic fibrosis (4)
- ☐ Cystic Fibrosis Foundation Website (cff.org) (5)
- ☐ Other Internet sites (6)
- ☐ Pamphlets from clinic (7)
- ☐ Support groups (8)
- ☐ Other (9) _____
- ☐ None (10)

Q9.8 If a male cystic fibrosis patient wants to know how their fertility is being impacted by their diagnosis of cystic fibrosis, how would your clinic respond (both in terms of what you would tell the patient and what evaluations you would order)?

_____

_____

_____

_____

_____

Q9.9 If a female cystic fibrosis patient wants to know how their fertility is being impacted by their diagnosis of cystic fibrosis, how would your clinic respond (both in terms of what you would tell the patient and what evaluations you would order)?

_____

_____

_____

_____

_____

Q9.10 What is your protocol for connecting patients with Assisted Reproductive Technologies (ART)?

o Refer patient back to primary care (1)

o Provide direct referral to ART provider (2)

o Clinic is not involved in referring patient to ART services (3)

o Other (4) _____

Q9.11 Assess this statement: Fertility is adequately discussed in cystic fibrosis patient care in the United States.

o Strongly disagree (1)

o Somewhat disagree (2)

o Neither agree nor disagree (3)

o Somewhat agree (4)

o Strongly agree (5)

Q9.12 Please explain your thoughts on how adequately fertility is discussed in cystic fibrosis patient care**.**

_____

_____

_____

_____

_____

Q9.13 Is there anything you would like to share that has not been addressed in this survey?

_____

_____

_____

_____

_____

End of Block: CF Center Questions

APPENDIX E: Knowledge Assessment Scoring Guide

Highest possible: 20

Lowest possible: 0

Q3.1 The purpose of the following questions is to capture your background knowledge regarding cystic fibrosis and fertility.

Q3.2 In what way(s) does cystic fibrosis affect fertility in males? Select all that apply. Q total: 3

- ☐ Fertility is not affected in males with CF (1) **+1** if **NOT selected**
- ☐ Most males with cystic fibrosis don't make functional sperm (2) **+1** if **NOT selected**
- ☐ Most males with cystic fibrosis have a problem where sperm are trapped and can't leave the body, either because of a missing tube (congenital bilateral absence of the vas deferens) or a mucus blockage (3) **+1** if **selected**

Q3.3 In what way(s) does cystic fibrosis affect fertility in females? Select all that apply. Q total: 3

- ☐ Fertility is not affected in females with cystic fibrosis (1) **+1** if **NOT selected**
- ☐ Females with cystic fibrosis may have differences of mucus in the reproductive tract that can prevent sperm from getting to the egg (2) **+1** if **selected**
- ☐ Women with cystic fibrosis may have irregularities with hormones that can affect their menstrual cycle (3) **+1** if **selected**

Q3.4 Which of the following ways can males with cystic fibrosis-related infertility have children? Select all that apply. Q total: 6

- ☐ Adoption (1) **+1 if selected**
- ☐ Assisted Reproductive Technologies (IVF, IUI, etc) to achieve a pregnancy (2) **+1 if selected**
- ☐ Donor sperm (3) **+1 if selected**
- ☐ Hormone regulation therapies (4) **+1 if NOT selected**
- ☐ Sexual intercourse (5) **+1 if NOT selected**
- ☐ None of the above (6) **+1 if NOT selected**
- ☐ Other (7) _____

X→

Q3.5 Which of the following ways can females with cystic fibrosis-related infertility have children? Select all that apply. Q total: 6

- ☐ Adoption (1) **+1 if selected**
- ☐ Assisted Reproductive Technologies (IVF, IUI, etc) to achieve a pregnancy (2) **+1 if selected**
- ☐ Donor egg (3) **+1 if NOT selected**
- ☐ Hormone regulation therapies (4) **+1 if selected**
- ☐ Sexual intercourse (5) **+1 if selected**
- ☐ None of the above (6) **+1 if NOT selected**
- ☐ Other (7) _____

X→

Q3.6 Does cystic fibrosis-related infertility prevent males from contracting sexually transmitted infections (STIs)? Q total: 1

- Yes (1)
- No (2) **+1** if **selected**
- I don't know (3)

Q3.7 Does cystic fibrosis-related infertility prevent females from contracting sexually transmitted infections (STIs)? Q total: 1

- Yes (1)
- No (2) **+1** if **selected**
- I don't know (3)

APPENDIX F: "Other" open-text Responses From Table 6: Initiation of Fertility Conversations in PwCF and Parents.

Who initiated fertility conversations?
When I got pregnant
I don't honestly remember. However it was not the main point of concern so it was only briefly mentioned
Don't remember
After finding out I was already pregnant

APPENDIX G: "Other" Open-Text Responses From Table 8: Fertility Conversation Timing by Providers.

With whom and at what age(s) do you discuss fertility?
When they ask
When patient is getting married even if not planning children right away
We discuss it with all of our adults regularly
unknown
Review Annually and as needed
Periodically during adult care visits
Patients who transition from another center
only if they ask
Never
Initiation of modulators, at patient request, during routine visits if relevant
i don't
I do not. That is left up to the medical professional.
I am not sure when the MD discusses fertility
has not come up for me yet, newer to this role
first visit when transitioning to new center
As needed; as requested by patient or other team member.
Anyone who is following in my clinic
Any of my patients who are of reproductive age

APPENDIX H: "Other" Open-Text Responses From Table 9: Fertility Conversation Initiation by Providers.

When is cystic fibrosis-related infertility discussed in your clinic?
working on developing new process for education
When the patient expresses the desire to have a family;
we ask them annually if they have questions about family planning
Unsure
unsure
unknown
transition
Start of modulators
patient Age 16
It depends on the patient.
If I have never discussed infertility in the past, I will discuss it, then depending on what the patient expresses, this will affect how often I revisit the topic. This could be every visit, annually or every few years.
I don't know.
don't know
Depends on the patient
Annually after the age of 12
AGE 10

APPENDIX I: Free response answers- PwCF:

Were these conversations helpful? If so, how?
Yes. They explained to me why I had no ejaculate
Yes. Informative and honest about the possible fertility struggles
Yes; otherwise I was left wondering
Yes, very helpful. I was a member of the first vertex modulator clinical trial and they were very concerned about unwanted pregnancy while on the trial. They wanted my highschool girlfriend to be on birth control and have a diaphragm but she didn't have insurance and couldn't get on the pill. Instead we opted to do a semen analysis and my pediatric pulmonologist informed me I was "shooting blanks" and was able to participate in the trial.
Yes, they helped me understand my disease and it's affects on my body.
Yes, they allowed me to be informed in fertility amongst people with cystic fibrosis, and what I can do to have a better chance at being fertile
Yes, my wife and i have wanted to have a child togther.
Yes, My wife and I ended up pursuing IVF
Yes, my wife and I are expecting after 5 years
Yes, I wanted to have a family and my care team explained in detail the issues we could face when trying to get pregnant
Yes, I actually attended a CF presentation with my now wife newly into our relationship so we knew what to expect upfront.
Yes, gave me a realistic expectation on life.
Yes we were able to conceive a healthy baby girl through IVF due to these discussions. We used IVF due to my husband being a carrier
Yes because it opened up the discussion for me to be able to ask questions.
Yes because it lead us finding out that I was 100% not going to have a child naturally
Yes because it helped me get my son!

yes
yes
When i was you ger, i didn't think children would be an option. As i got older and more was learned about CF, i felt like maybe. Eventually with medical assistance, i was able to have a child. So yes.
We had infertility due to reasons unrelated to my CF. My CF was discovered as an adult through genetic testing done due to our recurrent miscarriage issues. So the conversations were surprising and gave us even more insight into why it possibly was difficult for us to conceive. It was another layer added on top of many others though, so it wasn't necessarily helpful or unhelpful. It was just more information and another diagnosis.
We did IVF to get pregnant with our first and felt there was a lack of communication and knowledge between reproductive medicine and my care team. Granted, they were in very different cities that were about 3 hours apart.
Understand the occurrence of disease
They brought the subject up, which I appreciated, because I wanted to know things but was often afraid to ask about having babies because I was afraid they'd just tell me no instead of helping me make an informed decision.
These discussions provided me ample knowledge of what I can expect and the options available to me.
The most useful conversations were those that initiated when I wanted to become pregnant.
The conversations were helpful in some ways they helped me understand I might have trouble having a baby when the time was right and understanding my options
Somewhat. Not enough is discussed about fertility and CF
Somewhat, atleast I had a knowledge that the possibility of having children naturally was very low
Sometimes? Often I felt i had more information than my CF team about IVF
Some help ， Be psychologically comfortable
People who have a better understanding of cystic fibrosis can still have sexually transmitted diseases
Not really. I wish this was talked about more

Not really. I learned more from other CF patients and then told my doctors my plans.
Not really, I was diagnosed while pregnant, as an adult.
Not really-- it was all basic stuff that I knew. I am sure they helped some people, but I needed guidance on vaginal health that my team could not provide. I also have no interest in pregnancy or childbirth so fertility-related conversations are not helpful to me
Not really
Not necessarily, my situation ended up being completely different in the end. So generalities used didn’t fit my case
Not exactly
No one ever brought it up and I was embarrassed to ask.
No just said most likely I can't have kids and reffed me to a doctor to be tested.
No help, can't solve the problem
no
My CF team at KU has been extremely supportive of me in regards to the possible approaches of my wife and I having children and assisted us wherever possible through our 3 failed IVF attempts
Led me to have a sperm count done
Knowing the information didn’t help make it not a problem
It offered education on something I had a lot of unknowns with
It let me know there was a good chance I would need other methods to have children.
It helps. It guides my treatment
It confirmed the research i had done on CF infertility
I’m not interested in having children, but they were helpful in understanding my options.
I only remember the conversations I've had as an adult, and those were initiated mostly by me. They were helpful because I asked the questions I needed to know.
I don't know

Honest conversation
Helped to inform me on this subject
General awareness.
Gave me information I didn’t know about
By the time I was diagnosed with CF I already had two adult sons (adopted).
As I was post menopausal, it was conversational and did not pertain to me as I already had 2 children and 3 grandchildren when I was diagnosed.
Additional context was good to know
A little

Do you feel that you learned something from these conversations? If so, what?
You know the basics of the disease
Yes. Why I can't have kids
Yes. It was made clear that as a woman with CF I could still get pregnant but that there might be issues due to mucus.
Yes. I learned that thicker mucus/CF could have been another contributor to our issues.
Yes. How to have a healthy pregnancy.
Yes, to make me more aware of my illness, to understand the harm of this disease caused by the inconvenience of life
Yes, the basics of reproduction with cf.
Yes, that there is hope potentially to be a parent one day it just may look different for me
Yes, that having kids is something I don't want to do.

Yes, that a sperm count is needed to confirm infertility in men.
Yes, previously I was unaware of fertility implications of CF.
Yes, my wife and I are expecting after 5 years
Yes, just because I couldn't have kids there would be a way if I wanted.
Yes, I knew some basic possibilities prior to ever trying, but also felt knowledge was very limited.
Yes, I had a successful roegnancy and did jot realize cf could impact my fertility until I had trouble conceiving and started discussing
Yes we discovered the course we would have to take.
Yes that through Ivf they could genetically test the embryos to make sure we wouldn't have a baby with cf
Yes I learned safe sex and a safe way to get pregnant
Yes I did. I learned about reasons I may be struggling with infertility
Yes
yes
Yeah, that I could still have kids via IVF
Women with cystic fibrosis can have trouble conceiving
Was already educated.
Trikafta and the other modulator medications have made a huge difference for CF women's fertility
The reason why this occurs
The fact that I can't have kids and insurance in my state doesn't pay for ivf
that the possibility of having children naturally was very low
That doctors don't want CF adults to have children.
Somewhat. The conersation was very short because i was not interested in becoming pregnant

Sometimes your genetics can heavily impact your family planning, but also how to preservers in the presence of hardship.
Not really
Not really
No
No
no
Like everything
Learned it is possible to use my own sperm to have kids of my own.
Know some life precautions
Keep a positive attitude
Just that people with cf have reproductive issues
It’s been so long that I don’t remember what I learned or where i learned it.
It's possible to carry a baby with my lung function
I originally didn't know that my infertility was due to an absence of vas deferens.
I learned that males have a harder time with fertility than females. And about possible options should fertility be a problem for me.
I learned it was possible for me to have kids; but did not learn much about the possible challenges to fertility, or what the process should be.
I learned about why it’s difficult to get pregnant and why trikafta made it easier to get pregnant for women with CF
I had unexplained infertility, so there was no real answer to the problem.
I don't know
I did learn how my cystic fibrosis could affect my body when it came time to have a family
Humor is the best medicine!!

How important it is to work out and take medications consistently
Absolutely, that there can be challenges in our future and we were provided options and steps to tackle when we were ready.

Did these conversations change your view on fertility/infertility? If so, how?
Yes. It made me feel less at fault for it. I struggled with infertility (and still do) for 7+ years. Not until a year ago did I know women with CF also struggle too.
Yes. I wanted kids, but am ok with not due to possible spreading cf to them
Yes. After talking with my care team. I found out it could actually be a possibility with ivf.
Yes, understanding that it was yet another negative side effect of having CF.
Yes, the original disease brought infertility can be adjuvant treatment
Yes, more information was helpful
Yes, I know that I'm not infertile just there is a hurdle to cross.
Yes, but i'm not sure how.
Yes I was able to get pregnant twice and have healthy pregnancies both times with help from care team.
yes， promising， pleasing
They gave me much more hope
Some
Nothing to say
Not really. My urologist described the procedures taken for CF men to have children and it made me realize it would be incredibly expensive, unless you're lucky with the insurance plans your employer offers.
Not really. Just made me value my medications a lot

Not really. I haven't been interested in getting pregnant for most of my adult life so they weren't conversations that I sought out.
Not really, I always knew I was gonna be infertile. I found out in an encyclopedia in 7th grade, nothing has changed my mind about it since then.
Not necessarily.
No. Didn't change
No.
No.
No.
No.
No
No
No
No
No
No
No
No
No
No
No
no
no
N/A

Made me determined to have a child anyway
Know the cause of infertility and release the psychological pressure
It made me realize that if I wanted kids id have to adopt because I couldn't afford IVF
It eased the pain slightly and let us know the possibilities prior to all procedures.
It did and didn’t at the same time it made me more aware of how many people do have a problem with infertility
I wish i had more info. My cycle has always been very Irregular and now that im older and thinking of starting a family, i wish i had more info
I was not aware of fertility issues before I was diagnoed. I had no problem getting pregnant or carrying to full term.
I have a very mild case of CF so it was hard to know if It played a role. After many tests by fertility specialists it was unknown infertility. We tried naturally for 6 years. I was able to conceive twins through 1 round of IVF.
I had no views.
I grew up knowing that I would have a hard time getting pregnant. But the age of Trikafta changed all of that.
I don't know
After Trikafta came out yes! I thought I would never have a child tell Trikafta came along and I got pregnant!
A little. I was fertile so was my husband we just wanted to prevent cf

How do you wish conversations about cystic fibrosis-related infertility had gone for you? How would you hope these conversations would go for people with cystic fibrosis in the future?
Younger people should have the oppotunrity to ask questions. Our clinic offers forums and counseling.
Would of talk to me about it more and was brought up to me starting when I was 18 and older not when I was 35

What I know about male infertility came from joining a CF webinar about infertility, not from my doctors. I'm female, so it doesn't directly apply to me, but now I am wondering if I have incorrect information.
To acknowledge this issue before they become adults trying for a child.
They were great for me. I was diagnosed at 24 so I had already looked deep into the condition before my first appointment and was already aware my fertility was most likely impacted. Overall my health team discussed exactly what I wanted to know and a plan of action for family planning.
They went well for me
They went just fine. My wife's blood was tested for a large panel of CF mutations to see if she was a carrier and then to understand chances of having children with CF.
They are doing a better job these days educating cf patients. 30 yrs ago they didn’t talk about it.
That they would have encouraged me and provided the resources needed instead of just telling me all the worst case scenarios.
Start earlier. It was alot of my own research
Start at an appropriate age and talk scientifically about it. Tell them what to expect but give them all of the knowledge.
Psychological and physical comfort
Patients need to be more aware of the options that are available to them
no
N/A; CF diagnosed at age 56; wife had hysterectomy.
N/A
N/A
My only wish is that it was brought up at a younger age.
My drs never discussed that with me. I hope every Dr explains anyone who has CF to tell them at a younger age what CF entails
More proactive conversations starting upon transition to the adult clinic, for educational purposes

More commonplace
Mime with my doctor went well I just asked how to go sbout having children and it was smooth
Letting them know that when they are ready for the conversation the staff would be more than willing to talk. When your not ready you don’t listen and it would just frighten you.
Let the patient understand his condition more clearly
It would be nice to explain it all and plan to be tested without me having to ask about it. Just make it a regular thing so at a certain age you just know it's time to be tested just like other planned CF care.
Informative and educated conversations
I would hope to have better options presented to me for the financial struggle that fertility can lead too
I would have like for it to be a more open conversation that includes all options (including adoption)
I would have hoped to have had them earlier before I wanted to have children. I had no idea it could be a struggle for me to get pregnant. And I blamed myself for so much of my infertility for many years. It would have been helpful to have this information. I still feel like I don’t know a lot about it or, especially, how to correct it.
I would have been horribly embarrassed by it as a teenager but more discussion of STDs and safe sexual practices would have been welcome for a late-teenaged me.
I wished the clinic would’ve brought it up, or asked if I had questions. I was too embarrassed to ask. It would’ve been great if they brought it up when I was a teen. I assumed I couldn’t have kids until much later.
I wish this was discussed when I was a preteen so I understood everything better
I wish they would have brought it up. I ended up going to a Reproductive Medicine team and had to start all the conversations on my own. No one ever mentioned the lack of ability to conceive with having CF. I have a more mild case of CF, so it seemed like no one thought fertility would be an issue.
I wish they recommended possible places to confirm if I was infertile or not. They told me to go any local sperm donor place.

I wish there was just more open discussion in this topic now that we are reaching these situations more. I have had 0 trouble with getting pregnant, but anticipated issues so I wish I had known better. My sister on the other hand has been unable, and I wish we had known more tools than just the rumors. Preparing the teenagers of today that the world is open, and having full fertility discussions prior to intercourse maybe by bringing a OB onto the team or something in teenage or early adult years to be able to discuss this area of CF with. OBs still are very limited on their knowledge of how pregnancy and CF goes.
I wish the teams had brought up fertility first, I always had to bring it up and I wish it was talked about sooner. I always believed I could not have children until I was an adult
I wish the conversation started earlier and there was more research on barriers for a woman to get pregnant.
I wish that doctors were able to pin down which problem a person has more quickly so that pregnancy could have been achieved sooner.
I wish more urologists who aren't familiar with CF would become more knowledgeable. I had a urologist who told me to not pursue IVF and got a second opinion and then 2 successful round of IVF.
I wish it was brought up by then and that they had shared more about it with me especially initially
I wish I was explained everything a little bit better then just one time I don’t feel like we covered all the facts about how it could be hard for me or how it could not be a problem at all
I wish I could just conceive easy like everyone else
I think this subject should be brought up early so that people with CF understand the impacts on their reproductive system.
I think they went as good as they could!
I think the social worker asking is most appropriate. Especially if the social worker is the same sex/gender as patient
I had wished there was a way to fix my problem without major surgery, or using a lab.
I had none - I read about it in an encyclopedia. I was diagnosed in the 60s
I had my son prior to being diagnosed with CF. As far as I know, CF did not affect my ability to conceive since I became pregnant within a few months of our decision to have a baby. I would hope that anyone with CF would be able to have fertility discussions when they were of an age to be thinking of their plans for a family.

I had infertility problems before I knew I had CF. I had carrier screen for IVF
I felt uncomfortable asking about having children because I worried my healthcare team would strongarm me into deciding not to instead of give me accurate information; I wish people had shared more with me about the hormonal imbalances - that was never brought up, and I spent 7 years trying to conceive with wonky hormones, never knowing it was tied to CF.
I feel like the conversation I had with my doctor was at the correct age however it could have taken place earlier.
I don’t recall how I learned but i remember learning on my own. I think it should be included in sexual education however that Is handled either through school or through a conversation with parents
I don't want people talking about me，I hope patients can communicate more with each other
I don't know
I don't have any complaints about how the conversations went.
I do not know what could have been discussed that was not that would have given a better understanding of the situation.
I am overall satisfied
I always brought up the topic but I think it would be a beneficial conversation to talk about family planning and options especially now that CFers are living longer
follow and understand the science
CF was a small (if any) part of our issues so I don't have any wishes regarding how the conversations related to CF went. If we didn't have the other issues I would have loved to have been warned (if I would be known about my CF prior to trying to conceive) about how thicker cervical mucus can make it difficult to conceive and to have been offered solutions to that problem. From what I understand that is the main problem is causes in fertility in women.
Although it was awkward sometimes, it was very helpful for my treatment and made the team more confident in my treatment
Actively influence and avoid marital conflicts

Is there anything you would like to share that has not been addressed in this survey?

This is so important, especially for women with CF. I know it's a new world now with Trikafta, but I experienced years of hurt and suffering trying to conceive with CF and never really had a medical professional discussion my fertility as relates to CF with me; either the CF docs were not very knowledgeable about fertility and didn't offer much information, or fertility doctors didn't know much about CF, so I had to try to put together information on my own.
There is no
There are lots of CF patients with successful pregnancies. Pregnancy itself is not a disease. CF is simply a barrier for some. We shouldn't be treated as outcasts for choosing to have families. We should also be supported in our decisions. I had a perfect natural and planned conception, pregnancy and childbirth (even at 45% FEV1!) in spite of my CF providers trying to unnecessarily intervene constantly in my pregnancy and birth. (I finally fired them and went back to an old provider at 20 weeks pregnant.) They need to be telling these good stories as well. We need to have a database for pregnancy that is accessible. My OB poured herself into trying to research CF pregnancy and came up with almost nothing. fyi - this survey platform sucks! It's super glitchy and its taken me 20 min to type this paragraph. Buttons dont click, the captcha took 6 tries, and its constantly causing errors in my typing
Thank you for looking into this topic. It's one I never thought we'd see the CF community talking about because I never imagined our life expectancy would grow so much. Means a lot to know someone is willing to consider our lives past childhood.
Some of the symptoms of the disease, cystic fibrosis, affect the cells that produce mucus, sweat and digestive juices. These secreted liquids are usually thin and slippery. But people with CF have a faulty gene that causes secretions to become sticky. Instead of acting as a lubricant, these secretions clog pipes, catheters and passages, especially in the lungs and pancreas.
Since I was diagnosed so late in life, I already had the family that I chose to have. I only learned that people with CF have fertility issues some years after my diagnosis. I feel fortunate that I was not impacted when I was ready to have a child.
nothing else
Nope
None
No.
No.
No

No
No
No
No
No
no
no
no
N/A
N/A
N/A
My mutations are df508 & w1282x- couldn’t remember the last one and it wouldn’t let me go back
I've gotten pregnant three times, each of which was on the first try. Unfortunately, I have miscarried twice and am still very early in the third, but at least getting pregnant is not our problem.
I would like to share my experiences with fertility, I was told i had a 50/50 chance of having a baby and if I did get pregnant that there was a bunch of complications that would happen and how I would have to have pills or ivf or some other sort of fertility treatment to even have a baby. Well when I turned 19 a week after my birthday I found out I was 5-6 weeks along all of my doctors was shocked that I didn’t take no pills or treatments or anything to get pregnant as easy as I did well through the whole nine months I didn’t have any complications I had a very healthy pregnancy no cystic fibrosis doctors was not concerned in the least, the whole nine months and even before I quit taking my medicine I’ve been doing really good my health is great no problems at all I had a healthy baby boy who is thriving and is now 6 months old and is doing fantastic he doesn’t have cystic fibrosis or anything. I just wanted to share my fertility story
I think it would be great to provide pamphlets that show the varying degrees of fertility and infertility of CFers to those later adolescents and young adults. I believe our stories are generalized but are vastly different. It would have been encouraging to know that even post treatments for NTM I would one day have additional children would have been encouraging, but

also knowing that like the regular population there are CFers that have infertility will help younger CFers know they aren’t alone.
I had two healthy babies because of Trikafta
I found out I was infertile in my mid 20s but didn't know why at the time. It wasn't until my late 40s, when my two sons (adopted) were grown that a misdiagnosis of Immotila Cilia was given as the cause. This was corrected when I was 62 and diagnosed with CF at National Jewish through genetic testing.
I feel like since Trikafta came out it has been a game changer for fertility in women!!! Ik if it wasn't for Trikafta I would not have my son today!!!
How fertility changes with CFTR modulatrs
Find a way for CF patients to explore IVF with no out of pocket cost expected. Make it a set testing for all patients at a certain age who have CF
Fertility was only ever discussed with me by my care team at one visit and hasn’t been mentioned again. While I don’t feel like it needs discussed at every visit, information should be easily accessible. And patient decisions on fertility should be respected, even in cases like mine where I do not ever plan to have biological children.
Feel confidante with the person(s) you speak with about fertility. Do what's best for you, not someone else.
Embryo adoption is a great alternative for infertility. This is an option not widely known and great for CF patients that potentially have a spouse that is a carrier as well.
Be quite satisfied
After my egg retrieval it was determined that my eggs had a hard shell coating that didn’t allow the sperm to enter. The ICSI technique was used to create the embryo. Implanted 2 snd conceived twin boys who are now 8. I was 39 when I had them. I wished I would have started the process sooner so I could have had more.

APPENDIX J: Free response answers- Parents

Were these conversations helpful? If so, how?
yes, even though my son is still a child and not sexually active, it does help to know the challenges he could potentially face later on in life.
These conversations have been very helpful to me. Pay attention to diet, pay attention to rest and keep a happy mood
Not yet
no
It was a quick conversation where I asked if my daughter would be able to get pregnant. It was helpful as I was new to the CF community and worried about everything.
It helps. Exercise regularly
It does. It'll give me a better idea of what's going on
I think that having the social worker who had developed a strong rapport with our our family and child helped the conversation tremendously. The presentation was personalized to my son and not a scripted, factual piece of information. It was a dialogue.
I learned about the fertility plan that can be realized through technology
I already knew this information from researching, but it was helpful to have the pediatrician point out the missing vas deferens. My child was only about 1, so he had/has no opinion on the matter.
Good
A little help, at least to make the child feel less inferior
...

Do you feel that you/your child(ren) learned something from these conversations? If so, what?
Yes...there are many ways to still have children and not all male children with CF are sterile, so protection is necessary.

We havent talked to him in detail about this due to his age
These talks are of great help to children, pay attention to life diet, rest time and have a good mentality
No. He's too young.
no
Let me know how to talk to kids
I learned to face the positive, positive treatment
I learned something. My daughter was too little to understand.
How can you better protect yourself
Do breathing exercises and cough on purpose
....

Did these conversations change your view on fertility/infertility? If so, how?
Yes, I will cooperate with the doctor's treatment plan
These conversations helped me gain a new understanding of fertility and listen to the advice of professional doctors in this field
No. I hope my son chooses not to pass on his CF mutations, to be honest. But it's his choice, not mine.
No.
no
no
Lament the progress of technology and address the concerns of parents about this disease
It does make me not discriminate
I was more thankful for all the advances that are available in case my daughter has issues.

Eat a high-calorie diet and take vitamin supplements if necessary
...

How do you wish conversations about cystic fibrosis-related infertility had gone for you/your child(ren)? How would you hope these conversations would go for people with cystic fibrosis and their parents in the future?
Will let a person optimistic face, must actively cooperate with the doctor
To be honest, I'd hope that people are given ample time to consider the ramifications of passing on CF mutations, and that other options for having children are discussed.
There was hope. That was huge in the conversation. Hope that my daughter would be a mother and live a full and happy life.
The conversations have always been productive with our care team.
Technology changes Lives
Teach your children self-care as they get older
Starting at 12 is appropriate with an introduction and then progressively more in depth through the years. My son is 31 and married and only my husband and I discussed with him his fertility issues even when the drs knew he was getting married
no
N/A due to age
My daughter with CF is so young, fertility is not a remotely immediate concern or something that needs a long or involved discussion at this point. However, the thought her likely having a hard time with having babies does make me grieve that much more over the CF diagnosis.
I wish that our CF clinic had a good plan to introduce this conversation to my child. The plan would ideally be developed with the clinic social worker and be age appropriate. Right now, our clinic seems to avoid having the conversation at all. This conversation should NOT be done by the primary care physician - 99% of them are completely clueless about CF or their knowledge is completely out-of-date.
I think it went well.

I prefer the discussion to be between the physicians and the parents until my child is 18.
I hope the child will not feel inferior and return to a normal mentality
Hopefully, this conversation will happen around us, and cystic fibrosis patients will be greatly helped in the future. Safe and effective fertility treatments will be available in the future
....

Is there anything you would like to share that has not been addressed in this survey?
There's a lot of sensitivity on using IVF & PGT, but I think those options should be part of the conversation, especially for individuals with CF who may have a partner who's a carrier. Hopefully insurance will cover PGT more in the future and increase access.
there is no
No.
No
no
I think this is a pretty thorough survey
I think the conversations need to happen early so parents have time to cope and process. Then they can pass the information on to the child once the child is at the appropriate maturity age (which is different for each child but I believe at least in the teens is when it needs to happen).
I hope parents can understand the children's mood and mentality, and take the initiative to guide the children slowly
I guess I'd like the initial conversation about my child's likely fertility challenges due to CF to take place in her first couple years of life and just go over the physical reasons why, and the resources and accessibility of those resources that can be used to overcome my child's future CF-related fertility issues.
I am very excited about this discussion and want to share with you that infertility patients with cystic fibrosis can get effective and safe treatment to solve the problem of infertility

I am completely clueless about how to determine if my son's vas deferens did not form correctly because apparently a small percentage of males with CF can have children through regular intercourse. I'm also worried that my son may need to monitor his sperm production at some point, as I've heard that some in males with CF their body stops making sperm, but I'm not sure if that's incorrect information. And is there a possibility that a surgery could repair the vas deferens? I've heard about vasectomies being reversed before, could the same surgery apply here? There needs to be more information for males on how they can preserve their fertility. Should they be banking their sperm (can they bank their sperm over the long term?). If they find a long-term partner, should they immediate start trying to make embryos? I feel like most clinics lack a formal plan to address these questions, everyone is just silent on the issue for both parents and preteen/teen patients. And there is no way of knowing how proactive we can be as parents to preserve fertility. Unfortunately there is a lack of urology representation in CF clinics (same with GI representation, but I won't get into that here).
Don't
...

APPENDIX K: Free response answers- Providers

If a male cystic fibrosis patient wants to know how their fertility is being impacted by their diagnosis of cystic fibrosis, how would your clinic respond (both in terms of what you would tell the patient and what evaluations you would order)?
Yes, we can refer you to a fertility specialist
Would typically discuss the common impact of CF on fertility. Males will often time have viable sperm but the sperm have no way to exit the body. I would usually refer to the provider to discuss and provide referrals to the patient for sperm count testing and options for insemination. Will also discuss sexual health and prevention of STIs.
Would tell them that if they have 2 disease causing mutations they have a high likelihood (over 90%) of having absence of the vas defferens and thus infertility. The initial test would be a semen analysis. Depending on the findings and their wishes to have a child we would then recommend referral of patient and partner to an infertility urologist and infertility specialist in the Gyn group.
would start with a conversation about how fertility can be impacted. would work with the team to order semen analysis and/or urology consultation if the patient and family desired it.
would describe what congenital absence of the Vas Deferens means sperm count studies
We would provide the patient with education on the fertility issues associated with CF in males and the almost universal CBAVD. Education would be provided on how a patient could still father a child. We would often use this opportunity to talk about STDs or if the pt is actively looking to have children the need to have the partner checked for CF carrier status. We may order a sperm count or refer to a urologist we work with if the patient wants to pursue it further.
We would provide him the current information on fertility in males with CF and then recommended him to adolescent clinic if there are additional questions or family planning needs.
We would have a verbal discussion and an ultrasound may be ordered
We would explain that approximately 98-99% of males with CF do have infertility but a urologist can confirm this with certainty and a urology referral is placed. Most men with CBAVD/obstructive azoospermia can have biological children with the use of in vitro fertilizations with ICSI, and explain the process.

We would explain how CF affects male fertility with the appropriate explanation, including that this does not reduce STI acquisition and that while most men are infertile it isn't 100%. Discuss contraceptive and STI prevention etc. Would consider semen analysis if warranted by urologist with specialty training in fertility/andrology/male health, who could perform workup and offer options including TESE etc. Adoption would be covered etc.
We would discuss this open and factually. Options to become a parent are briefly discussed. Then, offer referrals to urology for ultrasound of vas deferens. Also refer to adolescent med to discuss STI prevention.
we would discuss their specific mutations, what practitioners know about the mutations and how they effect fertility. we refer to the urology department as needed or requested. We always recommend the use of a barrier method to prevent STDs
We would discuss CBAVD and refer to Urology for sperm count and further workup.
We usually provide education about how most males with CF do not have a vas deferens and therefore, sperm cannot leave the body. We let them know that when they are ready to be tested, we can give them orders to get semen tested to see if sperm are able to get through or not. If the patient is ready to proceed and talk more, we discuss next steps such as referral to urology and starting IVF.
We recommend consult with Urology to discuss testing that could be provided to confirm infertility
We provide order for sperm analysis and discuss options for infertility specialists if patient indicates wish to pursue further.
We provide education about how CF causes infertility in males. We would also order a sperm count to confirm azoospermia and discuss referral to a urology/reproductive medicine specialist if they are actively wanting to conceive a child. We also discuss partner screening for CF carrier status and have a protocol in place for our providers to order this for partners of CF patients.
We educate our CF patient on the chances of infertility and their options. If males want to know more about their fertility, we have a few options. If it is a couple trying to have a child we send them to are female fertility clinic, many times insurance will cover the testing better if they use this approach. If they are not looking at having a child at this time we can do one of 2 things, send them to our male infertility clinic or we just order a serum analyses.
We discuss how CF may affect the reproductive anatomy, and if the patient is interested, we place a referral for testing with expert physicians in the urology clinic. In addition, we discuss genetic counseling and the IVF procedure. Depending on the patient's preference, we place referrals to the appropriate specialists.
We are looking into developing a better process to address this question.

Very high rate of infertility (98%) but sperm production is OK, just trapped. There is still potential for having a family in many ways including adoption, sperm donor, and sperm harvesting-ICSI-IVF process. Offer to refer to Urology if desired to test for sperm count in ejaculate, the only way to know for sure. And still use protection to prevent STDs.
usually refer the female to a fertility specialist(physician) and refer the male to a urologist.
unknown
unknown
Ultrasound of the vas deferens or semen analysis (depending on age)
treatment
Tell them that most males have infertility due to CAVD. Referral to urology to assess for CAVD. We would briefly discuss different reproductive options, and refer patient to IVF center if they had CAVD and were interested.
Suspect CBAVD, check ultrasound, refer to fertility specialist
Schedule a meeting with Pulmonologist or Genetic counselor about fertility, and the next steps patients can take.
Review genotype Discuss timing of family planning/conception for realistic goals for w/u and interventions if needed. Urology referral to Urologist familiar with CF males. Listen to their concerns and questions and develop a plan for addressing.
Referral to urology. We have a local group with whom we have a relationship and provide referrals.
referral to genetic counselor, referral to fertility/urology
refer to Urology, sperm count
Refer to urologist for exam and talk about going to a fertility specialist if that is necessary. Talk about sperm production and the vas deferens being the focus of assessment. Adoption, extraction of sperm and IVF. Refer to CF Foundation web site and Peer Connect
Question is too open ended for a survey -- depends on the patient
Pulmonologist or APN would discuss medical information/details as well as a referral to a fertility specialist for evaluation. Social Worker would discuss infertility resources and behavioral health impact of infertility.
Pulmonologist either talks to them/family or refers to fertility clinic

Provider usually discusses common themes with male patients that have CF. As the nurse, I would provide them CFF Resources and educational materials (including Peer-Connect). Provider usually will educate on tests/referral to specialist for further work-up and/or inquire to pursue.
Physician would discuss statistics surrounding males with CF and fertility. Would conduct an evaluation to determine whether patient has a vas deferens, may order a sperm sample, provide follow up support as needed.
Our pulmonologist would address the question and provide education. The social worker could also join the conversation to provide support and resources for reproduction health for the future.
NP/MD have discussion with patient and/or significant other. Discuss defects and anatomy issues. Discuss testing for fertility and places to go. Discuss other options for having children, resources and any further testing. Discuss carrier status of baby and significant other testing. Costs of various processes.
Not sure on the evaluations but we would explain to him the possibility of being infertile, what this mean and looks like, and his options.
MD/NP discussion, refer to Urology for testing
MD orders sperm count test. MD explains which genetic codes usually do not have a vas deferens. MD discusses STD's every visit when checking for high risk behaviours.
Many/most men with CF have an absence of the vas deferens such that men can make normal sperm and have normal sexual function however the sperm cannot be delivered to a female partner through intercourse. A referral to a GU or infertility specialist will be ordered to perform a semen analysis.
In our clinic if a patient brings this up the MD will answer questions and refer them to a urologist.
In order to determine how CF impacts fertility, we would order a semen analysis.
I would tell them they are likely infertile. I emphasize that infertile does not equal sterile. We talking about the pathophysiology. If patients are interested in investigating, I typically will order a semen analysis for confirmation.
I would tell the patient that an assessment by a urologist would be helpful to see the sperm count and to have a full urological examination.

I would talk to the patient about statistics for CBAVD and what that means in lay terms. I would talk about sperm analysis being the usual first step to assess this and then discuss options such as sperm extraction that exist to assist in reproduction if CBAVD is present. We also discuss carrier status of partner and how to assess if the patient's partner is a carrier. We would refer to a fertility specialist to have sperm analysis. We do sometimes order partner carrier screening via Genzyme 97 mutation analysis.
I would educate that patient regarding the estimated rates of bilateral absence of Vas Deferens. I recommend referral to our men's health clinic and check a seaman analysis. We have many men who have chosen to pursue parenthood via IVF
I would discuss with them the reasons why (potential/probable CBAVD, lower sperm count), discuss that there are options at having biological children as well as other options (adoptions, surrogacy, foster, etc.). Would order sperm test to assess presence/absence of sperm. Discuss genetic testing for partner. and discuss next steps thereafter.
I offer the patient an explanation of why they are infertile, what they would need to do to have a biological child, and referral to reproductive medicine if needed.
I explain that most men with cf have CAVD and if interested we can check for that. I refer them to my colleague in urology who is the male infertility expert. The urologist first gets a semen sample to look for sperm presence.
I explain that > 95% of men with CF have CBAVD and that their fertility is affected by this factor. I refer my male patients to the Fertility Clinic for semen analysis and consultation. I also always offer a referral to Genetic Counseling.
I can't answer that question. I would recommend patient speak with our clinic nurse and or doctor for starters. They would be able to speak on the impact of their diagnosis on fertility.
I can address their questions head on in clinic, usually with a pretty frank discussion about how CF impacts male fertility. If the patient is interested in more information and/or pursuing a family, we have a few urologists in the area who are well-versed in our patient population that we refer to.
I am in pediatrics, so we would rarely recommend sperm analysis - however when I worked with both adults and peds, we recommended sperm analysis often. I answer all questions related to fertility (and everything else) with (I hope) sensitivity and an awareness of age-appropriate ability to process information.
Have a discussion with pt and then have refer them to male reproductive specialist who will run tests to evaluate fertility.
genetic counselor vas deferens check sperm count

explain what the common issue is and refer for sperm analysis and fertility clinic
Evaluate as required
education, referral to urologist
Doctor would review the normal CF reproduction system with patient and family if asked and would recommend they follow up with a specific urologist whom works with CF patients in this area.
Discussing with and referring to urology
Discuss that most males with CF has congenital absence of the vas deferens but it doesn't always mean sperm doesn't work. It may be that sperm doesn't have a way of getting out. We can do a semen analysis (send them with instruction sheet we have for this). Discuss having them speak to genetic counselor. (I've only had to do this once since I don't have an outpatient panel of patients).
Discuss CAVD, order u/s testes and refer to Urology.
Depends on their CFTR variants, but in most cases I would explain that he is likely infertile, that we can refer him for semen evaluation, and that even if he does have CBAVD, he has options including ART, adoption, fostering...I would explain the potential expense of those options and the challenges of being a parent with CF. I'd refer him both to CFF.org as well as peer-to-peer info (CFRESCH website for parenthood information) or direct peer-to-peer with one of our adult males with CF who has become a parent.
Depending on age, further discussion with patient and parent to developed shared-decision on next best steps which may include psychosocial support, referral to fertility clinic/assessment.
Decreased fertility, good response to assisted fertility technologies, referral to fertility specialist
CT, refer to reproductive specialist if needed
Counseling. Sperm count. Referral to infertility clinic.
Check for absence of vas deferens, discuss possible fertility implications as well as STI protection, provide resources (CFF.org e.g.), discuss family planning preferences.
Assess if this topic had been introduced while in peds care. As a social worker, my conversation will focus more on values of family planning. If this is the first time a patient hears of infertility, I will defer to MD for disclosure and evaluations. Afterwards, I go back in to discuss different options and provide resources.

All males get counseling about the ability to get a female pregnant if they have not had confirmation of a CAVD. If they haven't, we refer for semen analysis, ultrasound of testis and referral to our male fertility clinic (if in SF); urology if unable to come into San Francisco.
Age appropriately and with referral.
>95% of male CF is infertile. He can produce normal sperms but they are trapped because of absence of Soren canal to penis. Order US of scrotum, sperm count and refer to Urology
-CF is a multi system condition and one of the systems often/usually affected in males is the reproductive tract. -Sexual function is normal but this means a man with CF usually can't get a woman pregnant without extra medical assistance from a fertility specialist. -Explain the vas deferent as a "piece of the male piping" that carries sperm out of the body -Sperm are made, but there's a roadblock issue where the vas is absent (usually) or blocked -Men with CF can become biological fathers using a minimally invasive procedure to retrieve sperm in a fertility doctor's office. The female partner must also have egg retrieval so the egg and sperm can be combined in IVF (ask have you heard of that?…explain…). -Many men with CF have successfully had biological kids this way, but it can be taxing, physically, psychologically and financially (discuss in context of patient). -There are also many other ways to build a family including adoption, sperm donor, partner with someone with kids, not have kids, etc. The right choice is the one that fits you and your family and goals. (Discuss more if desired). -If pursuing biological paternity the partner should have CF carrier testing. Usually the fertility center will do this as part of a couple's work up, but we are happy to help. Would order: Traditional semen analysis from fertility clinic, but have started mentioning availability of home male fertility kits

If a female cystic fibrosis patient wants to know how their fertility is being impacted by their diagnosis of cystic fibrosis, how would your clinic respond (both in terms of what you would tell the patient and what evaluations you would order)?
Would tell them that they are normally fertile but cervical/vaginal mucus may impair conception. Would then refer them to a GYN fertility specialist whether or not they had normal or abnormal menstrual cycles. Referral would be offered whether or not there was a plan to have a child.
would start with a conversation about how fertility can be impacted. would work with the team to refer to gyn/endo for consultation if patient and family desired it

Would discuss the common impact of CF on bodily fluids which may be thicker and prohibit sperm from reaching the egg for fertilization. Will also discuss the impact of Trikafta on a woman's body and the increase of Trikafta babies. Will mention the importance of birth control and use of condoms to prevent STI.
Women with CF may take longer to conceive with sexual Intercourse than age matched peers without CF. Referral to ART specialist will depend on age of first attempting to have a child.
Women with CF can get usually get pregnant, especially with modulators, so important to prevent when not desired and plan/optimize health and meds when desired (explore and discuss). Without Trikafta, many women can still get pregnant but some have trouble due to thicker cervical mucus, amenorrhea related to body weight or endocrine issues, etc, so see fertility specialist early if natural conception is desired and does not occur. Also discuss genetic risk and offer to do carrier testing for the male partner in clinic. Order nothing if just starting conception journey but review med list, PFTs, nutritional status, annual labs.
We would recommend the patient follow with OBGYN to have a better understanding of fertility tracking and status. We would discuss how pH and mucus viscosity could be an impact. We would discuss nutritional status and impact on normal menses. We would talk about physical impact/risks with carrying out a pregnancy. We would talk about following with a high risk OB. We would review medications and discuss safety in pregnancy. For women on modulators (particularly Trikafta) we would discuss impact of modulator on fertility.
We would provide her the current information on fertility in females with CF and then recommended him to adolescent clinic if there are additional questions or family planning needs.
We would discuss the impact of CF on cervical mucus and other endocrine impacts on fertility and refer to Gynecology or REI for further evaluation.
We usually let them know the information out there indicates a similar fertility rate compared with the general population. If on Trikafta, we might discuss how Trikafta has improved fertility rates in women with CF. We also refer to their OBGYN if they are having fertility issues so they can get tested if needed.
We send her to her GYN or our female fertility clinic
We recommend consult with MFM or adolescent medicine to discuss testing and treatment that could be provided for the infertility
We provide referral to Maternal Fetal Medicine.

We provide education on how fertility is impacted in females with CF, and explain that females are generally considered "sub fertile" rather than infertile. This would include a discussion about the need to use birth control to prevent pregnancy, impact of modulators on fertility, impact of poorly controlled diabetes or malnutrition on fertility, etc. We also discuss the importance of stable lung health prior to trying to become pregnant and need for high risk OB if patient becomes pregnant. We would encourage the patient to establish with OB early on, however dont necessarily recommend any specific fertility workup on females unless they have been trying to get pregnant for 6 months without success. We also discuss partner screening prior to pregnancy and have a protocol in place for our providers to order this for partners of CF patients.
We inform the patient that they are likely fertile but their fertility may be reduced. We also educate them regarding the clinical experience with ETI and the increased number of pregnancies
We have open discussion about baseline health, comorbid conditions, the type of family planning they are considering, their timeline and will refer to our wonderful high-risk OB/GYN team. We do not order any additional or fertility-specific tests, but continue with their usual CF care. If a patient becomes pregnant, we follow more closely, in conjunction with their OB/GYN provider.
We have many pregnant patients in Clinic. They all socialize on line with chat rooms. Dr. discusses family planning, STD's and how to plan for pregnancy and if an option depending on their health and lung function.
We have an open and honest discussion about female fertility in CF, and how it's a misconception that women with CF cannot get pregnant (especially in the age of modulators). Patients who are not interested in getting pregnant at this time are always encouraged to use some form of birth control method. Those who are interested in becoming pregnant are sometimes referred to our high-risk pregnancy specialists, genetic counselors, or endocrinologists. Sometimes they just want to try to become pregnant 'naturally,' without additional intervention. We do discuss the importance of prenatal care including vitamin levels and bone health, etc. Those who are pregnant, we encourage to receive care at our center where we have OB specialists who are familiar with our population.
We discuss their nutritional status and overall growth, how that may effect fertility. the role that mucus in the genitals can play. also how regular their periods have been. we refer to our adolescent medicine colleagues, or to the patients ob gyn for hormonal evaluation if needed, and/or prescription birth control. we always recommend a barrier method of birth control as well to prevent STD
We discuss the implications of CF in fertility and discuss referral and evaluation by the OB group at our institution. If the patient prefers, we place referrals for further evaluation with Obstetrics. In addition, we discuss genetic counseling and the IVF procedure. Depending on the patient's preference, we place referrals to the appropriate specialists.

We are looking into developing a better process to address this question.
unknown
unknown
Trikafta has made a big difference for fertility in females. Would discuss egg donation, genetics, surrogacy, adoption, sexual intercourse. Talk about CF Foundation website resources and Peer Connect program
treatment
That females with CF are thought to have reduced fertility, but some do have children and they may or may not need any assistive reproductive technologies. Would defer to the CF pulmonary provider about any work up.
tell them what we know, likely is OK and suggest they see our family planning specialist
Some women with CF have a harder time getting pregnant, likely related to cervical mucus. CFTR modulators may increase natural fertility. Patient's health needs to be optimized prior to conception and throughout pregnancy. Also need to review medications for possible teratogenicity prior to conception. Reproductive technologies are also an option.
Since we are pediatric pulmonary, we would refer them to an adult urologist and onto an adult CF provider to help manage their concern.
She might have more difficulty to be pregnant. Refer to adolescent medicine or gynecology
Schedule a meeting with Pulmonologist or Genetic counselor about fertility, and the next steps patients can take.
Referral to OBGYN (our CF/high risk OBGYN) with whom we have a relationship with in clinic.
referral to genetic counselor, referral to fertility
refer to reproductive or endocrine specialist if needed
refer to Ob GYN
Refer to gyn/ob colleagues here at our facility or local specialist in their area
Question is too open ended for a survey -- depends on the patient
Pulmonologist or APN would discuss medical information/details as well as a referral t a fertility specialist for evaluation. Social Worker would discuss infertility resources and behavioral health

impact of infertility.
Pulmonologist either talks to them/family or refers to fertility clinic
Provider usually discusses common themes with female patients that have CF. As the nurse, I would provide them CFF Resources and educational materials (including Peer-Connect). Provider usually will educate on tests/referral to specialist for further work-up and/or inquire to pursue.
Physician would discuss fertility changes if patient is on a modulator, discuss potential risks of pregnancy in CF patients, encourage use of birth control/order birth control, and then encourage to discuss fertility needs with adult CF team once ready to have child
Our pulmonologist would address the question and provide education. The social worker could also join the conversation to provide support and resources for reproduction health for the future.
Our MD would answer any questions and then refer them to a gynecologist that is familiar with CF.
open and honest conversations would be facilitated, with referrals to adolescent med to prevent unwanted pregnancy and STI
NP/MD has discussion about fertility now with modulators and without. Discuss carrier status of baby and then discuss need for testing on significant other. Discuss pregnancy timeline, visits, etc... Provide pamphlets with information, if wanted. Discuss some medication/therapy changes with pregnancy. Discuss high risk OB. Discuss other options for having children. Costs of various processes.
Not sure on the evaluations but we would explain to her the possibility of being infertile, what this mean and looks like, and her options.
Modulator eligible or not is helpful to know. Discuss gyn history, referral to OB/GYN familiar with CF Discussions involving center Genetic Counselor with visit and f/u as needed. Mild, Moderate, Advanced CF important to know Partner with CF team to determine their specific concerns and providers concerns. Work to optimize health and support goals as feasible. Let them know our experiences with patients like them. Discuss gyn issues: menses, exacerbations as they relate to cycle and hemoptysis, Contraception preferences, family plan/goals, Assure have regular GYN eval, mammography, Pap tests, contraception plan until ready to have a family at all encounters or at least annually. Be aware of their family structure, partner(s), pronouns, vulnerabilities, etc.
MD/NP discussion, Ob referral

If the patient is on a modulator, we would tell them that new research is encouraging and suggest that they can conceive naturally. If they aren't on a modulator, we'd refer them to an OBGYN.
I would order a GYN consult and tell the patient about relative infertility and how assessment by a GYN would be helpful.
I would ask either the NP or physician to discuss with the couple what options they have.
I personally haven't had to discuss this with a female. It has been other members of the team.
I gene rally tell them that as far as we know their fertility is not impacted, and if on trikafta likely has improved fertility. If they don't want to be pregnant I counsel on birth control. I do refer my patients to ob gyn for further eval if trying to get pregnant and can't. Also refer partner for genetic testing.
I explain that CF affects female fertility by causing thickened mucus in the reproductive tract and that depending on the overall health of the patient, there are other factors that can affect female fertility in CF such as malnutrition and frequency of exacerbations. I also explain the effect that Trikafta has had on improving female fertility in CF. I offer a referral to Maternal Fetal Medicine for pre-conception counseling and to Genetic Counseling.
I can't answer that. I would recommend patient speak with our clinic nurse and or doctor for starters. They would be able to speak on the impact of their diagnosis on fertility.
I am in pediatrics, so we don't often send a young woman for testing, however when I worked with both adults and peds (prior to Trikafta) we would recommend that a young woman who did not want to get pregnant us birth control, even if pregnancy was " less likely" - and for women who wanted to become pregnant, we encouraged them to find and work closely with an OB-GYN - and to ask , early on, about the potential need for IVF
Have them see gynecology if concerns after failed attempts at pregnancy or miscarriages.
genetic counselor GYN consult.
fertility specialist PRN Many patients are getting pregnant with Trikfata. Please start your prenatal vitamin now and call us when you are pregnant (if patient is stable and weight is okay.
Fertility is sometimes a little reduced due to thickened cervical mucus which could make it a bit more difficult for sperm to get through. But in most cases, getting pregnant naturally is possible. Should use contraception if you do not wish to get pregnant, and as always you should practice safe sex to avoid STDs.

Explain that sticky/thick mucus can interfere with fertility, but especially with Trikafta we are seeing rise in (planned & unplanned) pregnancy; discuss possible fertility implications as well as STI protection, provide resources (CFF.org e.g.), discuss family planning preferences.
Evaluate as required
education, referral to GYN with knowledge of CF
Education provided about the issues associated with fertility in women with CF. Birth control options might be discussed. For patients on highly effective modulators we would share anecdotal information that women are getting pregnant much easier (ie, the patient may need to start using birth control). We would discuss the need to test the partner for CF carrier status. We would defer any testing to the pts OB/GYN. We have a few OBs that we have worked with closely that we might refer the pt to if they desire it.
Discussion. Referral to Maternal Fetal specialist as needed
Discuss thickened cervical mucus, (and how CFTR HEMT modulators greatly correct that) and chances of pregnancy. Would discuss genetic testing for partner, and also discuss all options of parenthood (biological children, adoption, surrogacy, foster, etc.), and the ART options if needed.
Discuss thick mucous in reproductive organs and refer to high risk pregnancy clinic (IVF)
discuss the impact that thicker cervical mucus has on sperm motility and successful penetration of the cervix
discuss cervical mucus issue but that it is not a guarantee against pregnancy, stil might need birth control. refer to perinatology to discuss issues and mention that IUI can soemtimes be helpful.
Depends on their CFTR variants/modulator eligibility, but in general I would explain that most females with CF are fertile (particularly in setting of HEMT). I would also tell her that some females with CF have a more difficult time getting pregnant (associated with older age and PI per the literature) and that we would refer her to an ob/gyn if she was having difficulty getting pregnant as there are options to assist. I'd also talk about the potential impacts of pregnancy and parenthood on her health.
Depending on age, further discussion with patient and parent to developed shared-decision on next best steps which may include psychosocial support, referral to fertility clinic/assessment.
Decreased fertility, good response to assisted fertility technologies, referral to fertility specialist
Counseling. Referral to infertility clinic.

Assess for what the patient and their partner have discussed/considering, provide resources and referrals. MD will refer to high risk OB and ask partner to get genetic testing via their PCP
As above, explanation of how CF affects fertility, but emphasize that most women with CF are fertile. increased fertility with modulators is emphasized as well, so options for contraception covered including discussion of STI prevention. Not sure specific evaluations are needed unless unable to conceive and otherwise indicated.
Age appropriately and with referral.
A verbal discussion would be had.

Please explain your thoughts on how adequately fertility is discussed in cystic fibrosis patient care
Working in pediatrics we rarely address this. It's always a question of when it's appropriate to first bring up. You don't want to overwhelm parents who just found out their newborn has CF and are learning how to care for them that they also will most likely struggle to conceive their own children naturally. For patients you want them to find out from us before they find out somewhere else but parents all have different comfort levels of what age that is appropriate.
we rarely discuss fertility in CF clinic/care, usually p the couple has inquired about their fertility options.
We probably think about it less as care providers than patients do as individuals.
We have protocols for when we will bring it up and are open to discussion at any time.
We have genetic counselors that are happy to discuss all of this in detail, explain the process, coordinate partner carrier screening etc. Unfortunately the adult pulmonologists tend to forget about us and don't refer.
we discuss sexual activity around age 13-14, if the patient is sexually active we discuss fertility then. if they deny sexual activity we start discussing safe sex and fertility issues at age 17-18.
We discuss fertility as part of our annual visits.
We are not a pediatric center (only adult), but I feel that CF care has historically been complex and things like fertility took a backstage position to pressing infection risks and/or comorbid conditions. Many young male adults get to our center and have never heard that they could be infertile or have never been asked about their thoughts on family planning. We screen both male

and females at each clinic visit.
Usually just discussed when brought up by the patient, not a routine point of discussion.
Unfortunately, being pediatric pulmonary we really do not deal often with the details but do discuss with family when they are first diagnosis. Once a year it is reviewed with teenagers and primarily, they are referred to urology for validation concerns.
This is not well discussed. This education needs to begin in pediatric clinics and continue through adulthood. In a perfect scenario, this would be a team effort and SW/MH, care coordination/case management would be involved. With the advent of CFTR modulator drugs this is especially important.
This is not discussed as the main providers for CF care are pulmonologists. Pulm is not trained in this and should not be. All subspecialist should know their limitations and thus refer out when appropriate. The patients however do not want "to see yet another doctor" and thus never fill the referral and then we can't adequately discuss this topic.
Respect their choice they are free
Previous survey and qualitative data has repeatedly demonstrated that it's inadequately discussed.
Patients are aware of infertility at various levels of understanding. We mention when discussing CF in general as part of general education. We answer in depth when patients ask about infertility or about having children.
Our team has been working towards being more proactive with this discussion. It has been a talking point for patients transitioning from a pediatric program or new to our clinic. I think there is room for improvement of discussion and resources but we have improved broaching this subject with patients over the last 18months.
Our doctors discuss annually to see if patient is interested or considering family planning.
Our clinic as a whole has increased our discussion of fertility in CF since the approval of Trikafta. I cannot comment on other clinics.
Not enough. A gap between dx and transition/adult clinic unless family or patient asks.
not adequately discussed..
most people now know issues

It would be helpful to have more of a script for discussion at various ages and in teenagers and adults...
It often falls through the cracks. Fertility after transplant is a deficit too and I would love clinician education on this.
It is well discussed
it is probably most often discussed when a patient asks, but not as part of routine discussions
It is often a neglected topic of discussion, still for many an awkward topic of conversation. Even if discussed, probably not early/often enough. The parents (especially of a male CF child) are typically told at diagnosis so the patient themselves doesn't hear it for a long time. Even the parents may not remember it because there is so much information and shock at the time of diagnosis.
It is not brought up regularly enough in pediatric clinic.
It is improving, particularly given the surge in fertility after starting ETI/Trikafta. but there is still ongoing misinformation prevalent with persistent belief that females are infertile etc being noted in patients. Again, this is improving, but also should include spreading some information among primary care, as able, since while almost all people with CF are connected with a care center, there are some who are missed and this is an emerging need.
In pediatrics, doctors are often uncomfortable discussing fertility with teens, other than to advise them to use contraception. We could certainly use some guidelines to help us provide better education.
Im sure this differs from center to center, however it is becoming a larger focus as we are seeing a rise in unplanned pregnancies and as patients are leading healthier lives and pursuing parenthood at a higher rate. Guidelines around this topic from the CFF would be helpful.
I'm not directly involved so am neutral on this subject
I think we should talk about it earlier, but also we need better resources/information to give to patients on all the different options.
I think this is very dependent on the care team, pediatric versus adult clinic, and specific center.
I think our clinic is very good about discussing, as we discuss birth control as well. I have had several patients though move from other clinics and were disappointed in not talking about reproduction as much as they would have liked. So I think we are missing out on discussions.
I think it is probably not adequately addressed.

I think it is discussed from a medical standpoint-ie what is or isn't physically functional and what are ways around that, but resources for families or pwCF are fairly limited or at least not housed within the clinic
I think it is an issue that takes backstage to other more pressing issues. I think it should be brought up to the parents at diagnosis and discussed with the patient by pedi CF providers in the teen years at the latest. It should be brought up again during the transition process and then on a PRN basis during the adult years.
I think fertility in adequately discussed in pediatrics. However, provided PwCF are living longer the discussion needs to change in adults.
I suspect it is in most instances but have no idea what triggers are used or how and when discussed outside our own program
I see a pattern that fertility is not usually discussed with patients with ALD or transplanted. For these patient, it is important that they are told while in peds care of their fertility concerns. Once they get to adult care, we hear repeatedly that they wish they were told sooner. Adult clinics tend to pick of the pieces.
I rarely brought up during CF Care in childhood
I personally have made this a huge focus of my annual review with patients because I do not feel it is adequately discussed. I think people hesitate to ask about it or don't know if we will know the answers. I like to bring it up and open the discussion so that all patients know they can ask now or in the future if they ever had any questions.
I know from my experience in my care center, we do not address fertility enough. It is only addressed if the patient specifically asks about it.
I have a lot of male patients who have not been given the full story of how their fertility is affected by CF. Since we are an adult center, we are not talking about this until they are 18. Every year when the annual psychosocial assessment is performed, we ask our patients what questions they have about family planning and this has opened the door for them to be able to ask questions. I think it is hard to bring up, especially when you are a teenager, if the door isn't being opened by the provider to discuss fertility.
I feel we could do a better job as we only address when patient asks.
I feel like we try to touch on it annually, but we could probably do a better job.
I feel like the discussion needs to begin when patients are still in the pediatric clinic (starting around age 12) and should be done annually until patients transition to adult clinic.

I feel like it is discussed fairly regularly, but since we work in pediatrics it is not a primary component of our regular interactions with patients unless they raise concerns. It is mentioned at diagnosis, during transition preparation, and intermittently throughout their time with us. However, I am unsure how systematically it is being addressed with both parents and patients following initial disclosure.
I encountered resistance from the medical team in terms of "we aren't urologisits, we are pulmonologists. Discussions around sex and reproduction with patients is historically avoided, or assumed will take place in adult care clinic.
I believe the that we do not start early enough and depend on parents to bring it up in CF children's teenage years
i believe it is adequately discussed in our clinic but based on conversations with others i am concerned it is not elsewhere
I am really deficient in the area of fertility. I will have to make an effort to get more educated in that area.
I am not sure whether our providers in our peds or adult clinics have a standard protocol for addressing fertility and where providers refer to when patients ask for referrals.
I am aware of what we do but not globally. Would be interested in attending a session that reviews trends and data.
I always discuss as an adult provider, but it’s not regularly discussed in pediatric clinic setting it seems
Fertility is not adequately discussed. There is not enough time to discuss everything we need to discuss with CF patients.
Fertility is a sensitive topic and should be addressed on an individual basis, determined by the needs and goals of the patient. I do not think there is a "standard approach" to discussing fertility in the clinic setting.
Excellent at our center
don't really know.
Discussed and addressed well in our clinic, but there is always room to improve on this.
Could be discussed more.
busy clinic - SW often asks teens about sexual activity and that opens discussion. Physician answers questions and will discuss at times- sometimes comes up when asking about menarche/menstrual issues - don't always do good job of giving teens time away from parents during visit either.

Based on discussions with parents, patients from other centers, and presentations at conference, fertility discussion varies by clinic and provider.
As life expectancy increases, we see a need to discuss this sooner. Patients can expect to live to see grandkids:) As the SW I would like to have a way to talk about this with parents early. This would allow them to be prepared to talk to their kids about their unique fertility differences as they get older
A discussion is had between the patient and their significant other if they express desire to have a child. It is discussed at initial visit with Adult CF team once the patient transitions to adulthood. STIs are discussed and the use of HEMs in CF patients.

Is there anything you would like to share that has not been addressed in this survey?
Weight issues could affect menarche/hormones in females but less common with use of CFTR modulators - as probably is cervical mucus issues. Risks of pregnancy with severe lung disease should prompt counseling as well.
We use the CFF handout.
We have a preclinic questionnaire where patients can indicate concerns. One of the boxes they can check is “sexual/reproductive health.” I try to get to everyone at around annual intervals without overdoing this topic, and this helps to make sure I’m not missing people at times they want this info. For our teen boys in our transition program, they get it usually at age 14 even if they don’t check the box.
We are currently having discussions with our cystic fibrosis team of who should be responsible from the team to have these discussions with patient/family members and how often. As well as the best way to approach the subject
There needs to be more availability of peer programs for CF patients to discuss fertility - including spouses/partners of CF patients. As Trikafta is emerging, there needs to be updated information about fertility as patients have access at an early age.
Thanks for the survey.
Surrogate pregnancy is an option for females with CF and severe lung disease. It’s also necessary to discuss what will happen to children if the patient is severely ill. Pregnancy post transplant of lung or liver is possible but is usually difficult. We’ve helped various patients in that last situation.

Please re-iterate the role that genetic counselors can have in these conversations and care.
Part of my pharmacist review with the patient is asking (when appropriate) are you currently pregnant or trying to become pregnant? If no, what are you doing to prevent pregnancy? If yes, discuss medications and safety in pregnancy and answer answer questions about pregnancy in CF. If no methods to prevent and not interested in pregnancy, discuss options for birth control and offer to help connect the patient with resources to obtain. For any patients of child baring potential and men, I ask if their partners know their carrier status or would like to find out. I track if people have gone through menopause, had hysterectomy, tubal ligation, vasectomy, etc. I've found that even if patient find this awkward at first, when I explain that I'm trying to proactively help people understand options and that they can talk to us in clinic, maybe people will reach out in the future for help.
Not that I can think of at this time.
Not sure if the effects of Trikafta change this effect on the reproductive system.
No.
No.
No additional thoughts at this time.
No
No
No
No
No
No
no
no
no
no
no

no
no
Need more resources about fertility in CF for patients, caregivers and providers
n/a
Just that I am now aware that I can get a little more exposure to fertility issues in our clinic.
It is fantastic to see this effort gaining more traction. It is heartbreaking to learn that a male learned about infertility on the internet and not from us.
How often is pulmonary disease discussed in reproductive medicine clinics?
Better education materials needed for teenage years. You have to start early and continue to build on the knowledge we have and continue to develop.
Assisted reproductive technologies are extremely expensive and these out-of-pocket costs are often a barrier for patients. I think it is important to recognize that IVF, IUI, sperm extraction, and even adoption fees can make having a family unattainable for many with CF. This does not mean everyone has a "right" to an expensive procedure that is arguably elective, but it is unjust that medical *and administrative* fees prevent people with CF from having families.
Although we discus fertility/infertility with all our patients they almost always set the timing of proceeding with a full infertility evaluation by our ART colleagues