

## **Assessing the Perception of Fertility Preservation Within the Turner Syndrome Community**

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## ABSTRACT

**Background:** Turner syndrome (TS) is the most common sex chromosome disorder. A hallmark clinical feature of TS is early ovarian failure, which severely decreases a woman's chances of achieving natural pregnancy. Ovarian tissue cryopreservation, an experimental fertility preservation process, may provide women with TS another reproductive option. This study explored the attitudes of the Turner syndrome community regarding possible issues surrounding fertility preservation.

**Methods:** Each individual participated in one semi-structured phone interview. The interview was developed using grounded theory and was based on the current reproductive issues in TS. Participants were asked to reflect on their attitudes and possible experiences with infertility as well as their interest in fertility preservation. Interviews were audio recorded and transcribed; responses were coded and categorized into higher order themes.

**Results:** Eleven participants were interviewed. The issue of infertility was an emotional burden for most, which was not always adequately addressed by doctors. Participants also expressed desire for a woman with TS to have her own biological children. Participants had considered alternative reproductive options, namely adoption. Reactions to experimental fertility preservation by ovarian tissue cryopreservation were mainly positive, but there were some concerns about the surgery. Also, some parents believed the daughter should autonomously make the decision whether to undergo the process once she is of adult age.

**Conclusions:** Past literature found families desire to have personalized, in-depth discussions on fertility (options); genetic counselors can help meet this need. Beyond addressing psychosocial issues of TS, a pediatric genetic counselor can discuss reproductive options with families of girls with TS before it is too late to preserve fertility. By understanding the experiences of parents and women living with TS that create the psychosocial issues surrounding reproductive issues, clinicians can better anticipate and appreciate how the TS community will respond to the prospect of experimental fertility preservation.

## INTRODUCTION

Turner syndrome (TS) is the most common sex chromosome disorder with an incidence of 1/2500 live-born females (Pinsker, 2012) and is caused by the absence or structural abnormality of a sex chromosome, typically an X chromosome. It is a developmental disorder that includes the following clinical features (seen in >50% girls): short stature, low bone mineral density, learning disabilities, and delayed puberty from early ovarian failure. There is a paucity of data on the attitudes among girls and their family members (here called the Turner syndrome community) regarding infertility and emerging reproductive options.

Regardless of karyotype, most girls with TS (95%) develop ovarian failure over time. In girls with TS, ovarian failure may start as early as 18 weeks into fetal life (Reynaud et al., 2004). However, not every girl has complete ovarian dysgenesis by birth. The timeline and rate at which this occurs is less clear, and may be different for each woman with Turner syndrome. Viable oocytes have been found in pubescent girls with classical TS (45, X) without spontaneous pubertal development (Gravholt et al., 2002) and 1-2% of women with TS have spontaneous pregnancies. So, while ovarian failure is a hallmark of Turner syndrome, not every girl will face infertility, and there may be time before ovarian failure occurs to preserve fertility.

Currently, fertility preservation options for women with ovarian failure or disorders of sexual development are not widely clinically available. Research on fertility preservation for individuals with Turner syndrome has made large inroads in identifying the best candidates for fertility preservation and determining how oocytes can be taken before ovarian failure and at what age such preservation is most successful (Visser et al., 2013). However, before offering fertility preservation to a population facing infertility, it is crucial that the attitudes and perceptions of the community toward fertility preservation are assessed (Nieman et al., 2006). This study aims to explore attitudes of girls with Turner syndrome and their parents on infertility, and better understand how important reproductive options would be to the women with Turner syndrome and their parents.

Oncofertility®, or cryopreservation of ovarian follicles for future use before undergoing cancer treatment creates the possibility for women to have biological children after surviving cancer. The process of cryopreservation involves laparoscopic surgery to remove ovarian tissue containing immature oocytes. The tissue is then frozen in strips, to be matured and used later by the patient, either through in-vitro fertilization or transplantation. This process has been largely successful for cancer patients (Woodruff, 2010).

The benefits of follicle retrieval and cryopreservation can reach beyond cancer patients as the process theoretically applies to other women facing infertility. With current research in preserving fertility

in patients with Turner syndrome, expansion of the Oncofertility® model to this population is seemingly inevitable. However, many questions remain, and it is important to better understand the desire of the Turner syndrome community for fertility preservation, as there are special considerations unique to this population, which must be addressed. Current research shows the optimal time to take follicles in girls with TS may be in childhood (Hewitt et al., 2013). This means surgical intervention before the child can give consent; this consideration must be addressed with patients and parents. The integration of a patient karyotype and optimal timing of surgery for cryopreservation is yet to be perfected, but it is a promising approach to providing fertility options to the Turner syndrome population.

## **METHODS**

All aspects of this study were approved by Northwestern University's Institutional Review Board (IRB) and Ann & Robert H. Lurie Children's Hospital of Chicago's IRB.

### ***Participants/Eligibility***

The Turner syndrome patient population at Lurie Children's hospital served as the recruitment population for this project. Per qualitative research recommendations, the recruitment goal for this project was 10-12 individuals from the Turner syndrome community, including women with Turner syndrome and parents of girls with Turner syndrome (Guest et al, 2006). All recruited participants were 18 years old or older.

Recruitment for the project occurred from November 2014 through January 2015. Participants were eligible if they spoke English, were over the age of 18 and had a formal diagnosis of Turner syndrome or a daughter with a formal diagnosis of Turner syndrome. All eligible participants received a recruitment letter in the mail and at least one follow-up phone call.

### ***Process/Data Collection***

In one semi-structured phone interview, each participant was asked to reflect on her attitudes and possible experiences with infertility. Thirteen questions were crafted to address current reproductive options as well as attitudes toward the experimental fertility preservation process. Mock interviews were practiced with both reproductive endocrinologists and a social science researcher to ensure the interview questions were appropriate, clear and understandable. The lead investigator conducted the phone interviews with each participant. Each interview was audio-recorded and transcribed.

### ***Data Analysis***

Transcripts were coded and analyzed using DeDoose coding software by two investigators. Once all transcripts were coded, investigators reviewed codes and began to combine them into higher order categories and themes. Constant comparative analysis of each interview against the other interviews helped to identify themes. Themes and motifs were categorized and reflected upon for patterns in attitudes toward fertility issues and preservation in the Turner syndrome community, which comprised of both the patient group and the parent group. Data saturation was determined by documenting when no new codes emerged from the data. Frequency counts were obtained for each theme. If the theme occurred in the interview transcript it was counted once. The two coders (RG and NS) did not identify any divergent coding between them and all codes and RG and NS agreed upon their larger themes. The lead investigator discussed the coding themes with a thesis committee member specializing in qualitative research and an outside qualitative researcher to ensure the data was analyzed from many different perspectives for analytic completeness.

## RESULTS

### *Demographics:*

Fifty-one eligible participants were identified from the patient database. Eight individuals did not speak English and thus were unable to participate. Three individuals declined to participate. Of the fourteen eligible individuals recruited, eleven participants were interviewed. See Table 1 for demographics of the eleven participants.

Two trained coders coded each transcript. Inter-rater reliability testing gave a kappa of (.77). Data saturation was achieved before the completion of the 11 interviews.

**Table 1:** Participant Demographic Information

Variable	n (%)	# of Women with TS,	# of Parents
<i>Participants</i>			
Woman with TS	5 (45%)		
Parent of Girl with TS	6 (54%)		
<i>Gender</i>			
Female	11(100%)		
<i>Age (yr)</i>			
18-26	5 (45%)	5	0
27-35	4 (36%)	0	4
36-44	2 (18%)	0	2

<i>Age of Child (yr) of Parent</i>			
0-10y	2 (18%)		
11-20y	4 (36%)		
<i>Racial Background</i>			
Caucasian	7 (63.6%)	2	5
Hispanic/Latino	4 (36.4%)	3	1
<i>Marital Status</i>			
Single	5 (45%)	5	0
Married	6 (54%)	0	6
<i>Highest Level of Education</i>			
High school	2 (18%)	2	0
Some College	3 (27%)	2	1
College/Associates	6 (54.5%)	1	5
<i>Occupational Status</i>			
Student	5 (45%)	5	0
Part-Time	1 (9%)	0	1
Full-Time	4 (36%)	0	4
Not employed	1 (9%)	0	1

### ***Interviews:***

Analysis of the interviews identified eight categories that were organized into three themes based on the topics addressed including: 1) Medical Care for Turner syndrome; 2) Emotional Impact of Reproductive Issues on Turner syndrome Community; and 3) Reactions to the Fertility Preservation Process. Theme (1) encompassed two categories related to life with Turner syndrome including; communication with healthcare professionals about infertility and treatment considerations. Theme (2) contained three categories related to the emotional impact of infertility including; psychosocial effects of infertility, the importance of fertility and perception of possible reproductive options. Theme (3) comprised three categories related to reactions toward the fertility preservation process including attitudes toward the process, opinions on practical issues and how to approach fertility preservation with a girl with TS.

**Table 2.** Themes and Categories from Interviews

<b>Themes</b>	<b>Categories</b>
1) Living with Turner syndrome	#1 Communication with Healthcare Professionals

	#2 Treatment Considerations
2) Emotional Impact of Reproductive Issues on Turner syndrome Community	#3 Psychosocial Effects of Infertility
	#4 Importance of Fertility
	#5 Perceptions of Reproductive Options
3) Reactions to the Idea of the Experimental Fertility Process	#6 Attitudes Toward the Process
	#7 Practical Issues
	#8 How to Approach Fertility Preservation with a Girl with Turner syndrome

### ***Major Themes:***

#### **Theme 1: Medical Care for Turner syndrome**

All participants (N=11) were asked about their healthcare experiences with Turner syndrome. The main categories found in participants' discussion included the communications with healthcare professionals regarding fertility and the treatment considerations made in TS.

#### Category 1: Communication with Healthcare Professionals

Participants recalled having a discussion with their (or their child's) reproductive doctor regarding issues of infertility and pubertal development. When asked if their doctor had spoken about reproductive issues, eight participants said they had had the discussion with their doctor. When participants were asked whether their doctor specifically stated whether women with TS would have children, most participants said that they had had a conversation with the doctor about the slim chances of having children in the future.

Three parents remembered having seen a genetic counselor or a geneticist to discuss their daughter's diagnosis of Turner syndrome. One parent participant who saw a genetics specialist described receiving information from the geneticist that contradicted their doctor, and created confusion for the parent and child:

*"...when we met with the geneticist, they told, we were told in the beginning through Dr. X that the chances of [my daughter] having a baby was slim to none. And when we met with the geneticist...they told her she was able to have children. They said that in front of her, but we had already prior to that told her that she couldn't (Participant 11)."*

## Category 2: Treatment Considerations

Another main category that emerged in discussing life with Turner syndrome was the treatment considerations and health management for girls with TS. Growth hormone is considered standard of care for girls with TS who develop short stature. Most (N=6) participants indicated that they had received or the child was receiving growth hormone therapy. Five parent participants indicated that their daughter with TS used estrogen replacement therapy to help induce her periods and puberty, as well as two women with TS.

## **Theme 2: Emotional Impact of Reproductive Issues on Turner syndrome Community**

The emotional impact of reproductive issues surrounding Turner syndrome was evident in discussions with participants. Three main categories emerged, including the psychosocial effects of infertility, the importance of fertility to participants and the emotional support given by parents to girls with TS.

## Category 3: Psychosocial Effects of Infertility

Infertility was discussed as a main issue in TS and something that most participants said their doctors had spoken about. Parents described having a personally difficult time accepting their daughter's infertility:

*"... I just have to accept that myself, it's something I just haven't done yet..., I just think it's something I kinda don't like to face. Do you know what I mean? Like kinda try not to act like she has it, but I know she does. If that makes any sense (Participant 3)."*

## Category 4: Importance of Fertility

As understanding their child's likely infertility was an emotional burden for parents of girls with TS, parents and women with TS were also asked to comment what fertility meant to them. One parent commented on the common desire parents have for their daughters and how difficult it is to see her daughter want children:

*"I think that's something that every parent wants, like how do you explain that to your child once she get older that she can't have children on her own and she's not the same as her sister or her cousin, in terms of like her, she has like even baby dolls, she carries them around... (Participant 5)."*

One parent remarked on how fertility is the most important concern after physical health:

*"These fertility issues, once you know they're healthy, that's what hits you the most. You think Ugh! She's never going to be able to have her own child. Those are the thoughts. That's the question: Will she be able to? That I would say is the second*



*thing, once you know that the hearts okay, the kidney, you know, they're gonna be okay, the next thing is that (Participant 9)."*

Four of five women with TS interviewed also expressed a desire to one day have children of their own. One woman with Turner syndrome said she did not think having children was important to her.

#### Category 5: Decision-Making in Reproductive Options

Participants were asked whether they had thought about the reproductive options that are available to women with TS and whether they considered any of them for their daughters. A parent participant explained how she would show her daughter that adoption was okay, and how she would break the news earlier than later:

*"Oh, we've been putting it in her head now. I think what we're saying is okay for her right now. That way she can get the hang of it. Our plans, between my husband and I, we want to have two more of our own, we want to adopt two. So, her to see that that's gonna be okay if she can't have kids. But still, I did explain to her that she might not be able to, so we're trying to introduce the idea of adoption, so that way it that won't be such a like, a heartache for her because she can't have kids of her own (Participant 7)."*

Three of the four women with TS interviewed said they considered adoption as a possible reproductive option. One participant added that she thinks about all the reproductive options available:

*"Well I just thought like, I would think that if I want to be able to I would obviously want kids, so I'd try things you know, other than not having them myself. So yeah, I've thought about you know, a donor, surrogate mother and all of that (Participant 8)."*

Although adoption was the most considered option, some parents thought about egg donation, either from the mother of the child with TS or from a relative. One parent discussed how donations expanded options for women:

*"I know people that had babies, did it naturally, I know people that did surrogates. I went back and forth, I'm not going to lie, doing the egg donor, like holding my eggs, getting them frozen for her. I know there are some parents who have done that, but I think there are a million ways to take it (Participant 3)."*

Another parent remarked on egg donation, citing the cost as a reason to have a relative donate.

Finally, some participants discussed the option of gestational surrogacy. Gestational surrogacy allows for a biologically related child to be carried to term by another woman. One parent participant said she would advise her daughter to use a surrogate:

*"I think, if it was me talking to my daughter, I would tell her to do the surrogate because she would go through that risk and taking the chance because it's her heart. I*

*would definitely definitely try to convince her to have the surrogate so that way she could become a mother (Participant 7)."*

On the topic of surrogacy, one woman with TS remarked:

*"Honestly, I think why not? If that person can help bring my child into the world, I don't see a big deal with it. I mean, as long as they are okay with it. I wouldn't care about having a surrogate at the end of the day; what's important is having a child of my own (Participant 1)."*

### **Theme 3: Reactions to the Idea of the Experimental Fertility Process**

Finally, the interviewer reserved a part of the interview to give the participants information about the fertility preservation process of ovarian tissue cryopreservation. Responses organized into three different categories: attitudes toward the process; practical Issues; and how to approach fertility preservation with a girl with Turner syndrome.

#### Category 6: Attitudes Toward the Process

The overall attitude from the participants regarding the general idea of fertility preservation was positive. Most parents of girls with TS had a positive response to the idea of fertility preservation. Women with Turner syndrome thought it was something they would appreciate later in life. One woman with TS expressed caution but support for the process:

*"I mean, I think that it would be a good thing to help women with Turner syndrome be able to be pregnant later on, more options. But I can't say anything because it's really experimental, but I think the idea is a good one (Participant 1)."*

When asked to consider how she may have felt if her parents had consented to fertility surgery for her when she was a young girl, one participant replied: *"I would have been happy (Participant 2)."*

Participants were asked if the fact that having children in the future cannot be guaranteed changes their opinion on pursuing fertility preservation. A few participants brought up the idea of taking risks in life as a rationale to pursue fertility preservation regardless of the fact that a future successful pregnancy cannot be guaranteed by this process. One participant stated:

*"...Nothing's guaranteed at 100%. It's always an option, it's always there, you can give it a try if it works, it works, if it doesn't, it doesn't you know. You're never gonna have that doubt- what if I had done it? You know? (Participant 5)."*

A woman with TS also expressed a similar feeling when considering pursuing the process even if a pregnancy is not guaranteed: *"Not much in life is a guarantee (Participant 2)."*

Nine participants said they would have definitely or likely pursued fertility preservation if the option were available. Two participants (both were parents) said they were uncomfortable with the

process and would not have pursued fertility preservation. Most participants said they would hypothetically consent to the fertility preservation process of ovarian tissue cryopreservation. One participant saw the benefit of the surgery, even if the woman were to decide later on not to use the tissue: *“Um, yeah I think for some people it would be really useful and I guess by doing, you don’t necessarily have to use them. But it allows you the option to use them in the future (Participant 10).”* One parent expressed a desire to support her child and avoid regret she might feel from not pursuing an option for her daughter:

*“I think you know, if she does want to do it, why not, I’ll do it, I’ll probably just try to do it as much as a can to help her have children in the long run. I would want her to have her own children. If it’s out there, if it’s an option that I have, if they offer it, or there’s the possibility, I would consider it (Participant 5). I think yeah, if they gave me that option, yes. If it would help her in the future, I don’t want her to like know “you could’ve done that” and can’t go back. “Why didn’t you do this?” I think that if it’s worth doing, if there’s results, why not? (Participant 5).”*

Some participants expressed uncertainty about whether they would hypothetically pursue fertility preservation. Only one parent voiced concern about the practical issue of cost of the process as a reason she might not pursue the process:

*“Yeah, if insurance covers it, I don’t know. It’s a lot of finance, too. How much of a responsibility does that fall on an individual, and as far as expense? Because the expense could be astronomical, too. I don’t want to commit to that myself (Participant 6).”*

A woman with TS said she would need to have more information and a discussion with her doctor in order to make that decision:

*“Maybe, like I said, I would really have to talk to my doctor about the risks, but I am not discarding the option... but right now its like I’m one of those people, its whatever God has planned for you (Participant 1).”*

Two parents of girls with TS stated that they would not choose ovarian tissue banking for their daughter. One participant, although she believed the process’s end result would be positive, found the process would interfere with her faith:

*“I want her to have that joy, but at the same time, if it was me, I wouldn’t go through that. I kinda feel like, I don’t know... It’s messing with God’s work, you know what I mean? [My daughter] was given to us with Turners for a reason, so, yeah... I wouldn’t do it (Participant 11).”*

### Category 7: Practical Issues

Participants were asked about concerns they might have had with the practical issues of the fertility preservation process. This included concerns about (early) surgery, amount of ovarian tissue

taken, and whether pregnancy risks would create a barrier to pursuing the process. Overall, early surgery received mixed, sometimes uncertain opinions from participants.

A woman with TS stated that the idea of surgery is scary, but not unreasonable:

*"I guess just the word "surgery" in general is kind of... a red flag or something that would make me a little anxious... Um... I'd say if all the parties involved are willing and understand all the risks associated with it, then I think it would be okay (Participant 10)."*

One woman with TS reacted to the idea of surgery by saying:

*"My concerns would be the surgery; whether it would actually work or not, or just put my life in jeopardy? When told the surgery was a small risk, she responded: "Honestly, if I would be a young girl, I wouldn't know exactly what's going on; I don't think it would be that big of a deal; a lot of parents wouldn't feel comfortable having their child have that surgery, but others might be thinking toward the future, their children might be able to have children one day, if the doctor says they might not be able to have children, then obviously they might want to do this (Participant 1)."*

A parent expressed immediate concern about the surgery: *"Um, that's cutting my daughter, I don't like it. [Laughs]...But just to do that procedure at that young age, that would scare me because what if trying did work? (Participant 7)."*

Another parent was concerned with the possible consequences and risks of undergoing the fertility preservation process: *"It sounds extensive... What would her commitment level be, after removing that, how would that affect her health and her long terms side effects from that (Participant 6)."*

Participants were also asked if early surgery would be something they would be okay with. One woman with TS responded that she would have some ambivalence over an early surgery:

*"I probably would. I mean like I would understand if they were really... probably. I would want to do it but I wouldn't want to do it at the same time. I wouldn't really understand, you know? (Participant 8)."*

A parent responded similarly:

*"I mean, I would be very concerned because of obviously the age being a huge factor...if I felt like it was going to help her and not hurt her, then I would be on board with it. Plus, the idea of getting pregnant, and possibilities for the future. Absolutely. (Participant 3)."*

Participants were asked whether the amount of ovarian tissue taken in surgery mattered to them. The amount of ovarian tissue taken was not an important issue for most participants, but some did find taking a whole ovary dangerous. One participant preferred the least amount to be taken: *"Um, yeah I think that would kind of make a difference. I think the less invasive a surgery is, the less intense it is, for*

*lack of a better adjective, I think um, that that makes it more attractive and possibly less dangerous as well (Participant 10). ”*

Most other participants (N=6) did not seem to care about the amount of ovarian tissue taken. One participant invoked the idea that the surgery would be a benefit for her in the future: *“I can’t answer that question. That is not that big of a deal to me; if it’s entirely taken out so I can have children in the future, I can function without it, it would be for a greater cause (Participant 1). ”*

Participants were asked if the cardiac risks of pregnancy for some women with TS were a barrier to pursuing the fertility preservation option. Some participants were unsure, but most said it would be up to the individual, knowing the risks. One woman with TS expressed uncertainty about this decision:

*“Well I think that’s a case by case basis. Every individual person going through it might feel differently about that...I don’t know. I just think it would...be the experience I would want to go through myself. I would miss out on certain parts of it if someone else is carrying it for me (Participant 10). ”*

One parent commented on the difficulties of making that decision:

*“I think that well if they have a heart condition that they wouldn’t be able to carry it, that it’d have to be with someone else. I think that would be a little bit... that makes it harder to do. But no, basically if you can have a biological child whether someone else has to carry it for you. It’s a little harder. If you don’t have a heart condition, you’ll always have that experience and do it yourself. I think it would be a little bit easier to make this decision (Participant 5). ”*

Another parent responded with uncertainty over her child’s understanding of this process:

*“I don’t know how she would feel about that. I don’t think she would understand that. I don’t know how much she understands about someone else carrying your baby. I don’t know. I mean, she may be okay with it (Participant 6). ”*

#### Category 8: How to Approach Fertility Preservation with a Girl with Turner syndrome

Fertility preservation via ovarian tissue cryopreservation may be more effective in preserving fertility when done at an early age in girls with TS. Participants were asked to think about what they believed would be the earliest acceptable age to discuss this process; have the surgery; and to have the girl with TS to see the doctor alone. Overall, participants believed the average acceptable age to discuss the process with a girl with TS was when she was 16 years old; the ages ranged from 8 years old to 18 years old. Participants believed the average acceptable age to have the surgery is 18 years old; the ages ranged from 6 years old to “adulthood”. Participants believed the average acceptable age to see the reproductive doctor alone was 16 years old; the ages ranged from 16-18 years old.

One parent described her rationale for girls underdoing the surgery at a young age (i.e. no consent):

*“Um, I think it’s fine to have, at whatever age. I mean the parent makes most of the decision until they can actually talk. If they do it when they are 3, well then the parents are making all the decisions. But you know, having open communication with my daughter, she would do it probably. If I talked to her about it. She would be okay. She’s had her tonsils and adenoids taken out. She doesn’t mind the idea of extra things, I don’t think...(Participant 6).”*

Some parents spoke to the idea of waiting for their daughters to be of adult age to make a decision about reproductive options like fertility preservation on their own. When asked whether she would consider the preservation option for her daughter or other girls with TS, three parents discussed their hesitation. One parent responded:

*“...I think it would be selfish on our part, because of the fact that “oh we want her to have kids, we want her to have kids” but I think that would be a decision that the child needs to make when they’re older...I would wait until she’s older. I believe in trying first on her own if you can, and then if it’s whatever, if it’s been a couple years and she can’t get pregnant then I would consider it Option B... (Participant 7)”*

## DISCUSSION

### *Theme 1: Living with Turner syndrome*

Most participants recalled talking to the reproductive doctor or pediatrician about the reproductive issues involved in Turner syndrome. Many of the participants stated that they were told they or their daughters would almost definitively not be able to have their own biological children, and that the discussion on infertility generally stopped there. As fertility preservation options become clinically available to girls with TS, the reproductive doctors may be the healthcare professionals that first educate patients and families on these options. Studies involving cancer patients receiving information about fertility preservation cited a need for more individual counseling on the options (Goossens et al., 2014). One study looking at fertility counseling stated that oncologists should refer all their patients to fertility counseling, which should include an in-depth discussion on the process (Lambertini et al., 2013). Another fertility counseling study found that “specialized counseling about reproductive loss and pursuing fertility preservation is associated with a reported lower quality of life for [cancer] survivors” (Letourneau et al., 2012). Counseling skills and adequate time are indicated by past studies as necessary to have a helpful discussion about fertility preservation with patients. So, a genetic counselor may play an important role in this process.

When Turner syndrome is suspected, a genetic counselor can speak to the patient and parents to help them better understand risks, medical management and genetic information. Most diagnoses of Turner syndrome are made when the girl is around 5 years of age, in a specialized pediatric clinic (Pinsker, 2012). The opportunity to meet with a genetic counselor and discuss the diagnosis can also occur at this time. The genetic counselor, in helping parents to understand the syndrome, can discuss the infertility issues that are a hallmark of the chromosomal disorder. It may be appropriate in that session to discuss potential fertility preservation options available. Research has shown that time is a crucial factor in obtaining viable oocytes before gonadal dysgenesis occurs (Hewitt et al., 2013). Although there are no clear guidelines as to what the best age is, the time at which the parents are most likely to meet with the genetic counselor (early in the girl’s life) could be key in preserving the fertility of the child. Specifically, because it can be overwhelming when first hearing a medical diagnosis, perhaps a post-diagnosis follow up visit with a genetic counselor would be appropriate. Although most participants in this study did not recall seeing a genetic counselor after the diagnosis of Turner syndrome, and those who did reported they not find the session particularly useful, the skills of a genetic counselor make she or he an appropriate healthcare professional to discuss the sensitive issue of infertility and possible fertility preservation options available with child and/or her parents.

When asked about the treatment and medical management girls with TS had received, most participants mentioned that they or their daughters had used growth hormone therapy (GHT) in an effort to increase final adult height. This therapy is considered a standard practice by the Clinical Practice Guidelines for TS (Bondy et al., 2007). It is a time-sensitive treatment, in that it does not help achieve a taller adult height once the child has finished growing. Ovarian tissue cryopreservation for girls with TS may be similarly time-sensitive. Pointing out the similarities in receiving treatment within a certain time frame for both GHT and fertility preservation may help parents better understand why girls with TS would need to have the surgical intervention to save their fertility at an earlier age than waiting until adulthood.

### ***Theme 2: Emotional Impact of Reproductive Issues on Turner syndrome Community***

The emotional impact of reproductive issues discussed by both parents and women with TS were categorized into two major topics, including the importance of the idea of fertility and the consideration of alternative reproductive options. While interpreting these emotional issues, it is important to consider that the parents interviewed in this study were all mothers of girls with TS and that there may be a gender bias regarding the importance of having one's own children.

The impact of infertility on a woman can be devastating and can also be perceived as a loss of femininity by those who suffer from it (Schover, 1999). Participants in this study reported comparable emotions. Most participants, especially parents, revealed strong emotional reactions to infertility and shared that the idea of fertility was important to them. Many stated that after they received the diagnosis, infertility was the second most important issue to them, after physical health issues. These reactions were similar to those seen in cancer patients and parents wishing to preserve fertility before cancer treatment. A study by Neiman et al. (2007) addressed how patients with cancer and their parents felt about a loss of fertility due to cancer treatments and fertility preservation. The participants in the study largely noted that infertility was not necessarily the primary concern at the time of diagnosis, but that it became more important with time. Similarly, the women with TS in this study predicted that in the future, fertility and having their own children might be much more important to them.

Participants in this study commented on the reproductive options they had considered for themselves or their daughters. The most commonly considered option was adoption, but some had mentioned egg donation through a relative or surrogacy. Parents who had considered future reproductive options believed it was important ensure that their daughters had opportunities available to them when they wanted to start a family of their own. Participants of the cancer study previously discussed echoed a similar sentiment and noted that having reproductive choices was meaningful to them (Nieman et al.,



2007). This strong emotional desire for mothers to want their daughters to one day experience pregnancy and have their own children spoke to their consideration of every available reproductive option.

### ***Theme 3: Reactions to the Idea of the Experimental Fertility Process***

To our knowledge, the attitudes and reactions to the idea of fertility preservation via ovarian tissue cryopreservation have not been previously studied in the Turner syndrome population. To better understand how fertility preservation may be received in the TS community, participants were asked to discuss their general reaction to the idea of the process, the practical issues involved, and their opinions on how to approach the process with a girl with TS. Overall, both parents and women with TS related a positive attitude toward the possibility of fertility preservation. This response is comparable to that seen in another qualitative study on reactions to fertility preservation, where parents and women with cancer both stated they would have wanted fertility preservation as an option when they were being treated for cancer (Nieman et al., 2007). The supportive reaction by participants in the TS study is perhaps not surprising; in discussing considerations of reproductive options for their daughters, parents expressed a desire to have as many opportunities as possible.

Just as the overall reactions in the TS population to fertility preservation have not previously been evaluated in the TS population, opinions surrounding the practical issues of preservation have not previously been published. Most participants responded that they did not care about the amount of ovarian tissue taken, and that the risks that pregnancy poses for some women with TS do not negate the benefit of fertility preservation. Many were open to the idea of a gestational surrogate in the case that a pregnancy would be deemed too risky. Most participants also stated that even though the process did not guarantee pregnancy, the surgery was still worth pursuing. While the opinions of individuals on the practical issues of a surgical process do not necessarily impact how the process might be technically performed, it is important to be cognizant of how the practical issues surrounding fertility preservation might affect those in the TS community.

This study also aimed to identify how and when participants thought it best to approach the preservation process with girls with TS. There are not yet guidelines detailing the best age for the preservation process. However, it is known that ovarian failure can even begin prenatally in girls with TS, and that over time, most of them experience complete ovarian failure. It is similar to the ovarian failure in girls with galactosemia, where the ovaries are damaged at an early age. And, similar to what is suggested in Turner syndrome, Bosch et al. (2013) estimated that the success rate of fertility preservation for girls with galactosemia is likely lower than for women diagnosed with cancer. So, while the clinical data on fertility preservation for TS and other disorders that cause ovarian failure is still uncertain, the

investigators considered it important to query participants on the appropriate age to discuss the process with a girl with TS and the earliest age appropriate to have her undergo the process. Most participants stated without prompting that the process would be best discussed in the teenage years, and that the surgery be performed in the late teenage years, or when the woman is legally an adult. When asked if they would be okay with the surgery when the girl is younger, around 5 years of age, the reactions were mixed; some said it would be permissible, some did not approve of the idea of surgery at a young age when the girl could not knowledgeably make her own decision. The wariness that some participants expressed could predict future decisional conflict regarding fertility preservation, especially because it is likely that the preservation process would need to be performed at an early age to have the best chance of preserving viable ovarian tissue.

### ***Conclusion***

Current fertility preservation techniques include embryo freezing, oocyte cryopreservation and ovarian tissue cryopreservation (Salama et al., 2013). These methods have been successful in preserving the fertility of cancer patients, and theoretically can be applied to other women who face impending infertility for genetic or other iatrogenic reasons. Ovarian tissue cryopreservation is still considered experimental, but is currently used to preserve fertility and restore puberty for prepubescent girls with cancer. In vitro maturation of oocytes from the ovarian tissue can create an opportunity for girls with Turner syndrome to preserve viable tissue before complete ovarian failure occurs and thus to have their own biological children in the future. A genetic counselor has the appropriate skills needed to assume the role of counseling on this potential preservation option. Discussing reproductive options with families of girls with TS and other genetic disorders that cause ovarian failure could educate the families about their options before it is too late to preserve fertility. This study began to address some of the emotional and practical issues of infertility and possible fertility preservation within the TS community. By understanding the experiences of parents and women living with TS that create the psychosocial issues surrounding reproductive issues, clinicians and counselors will perhaps better anticipate how the TS community may respond to the prospect of experimental fertility preservation.

### ***Limitations***

As this study is an exploratory, single-center pilot study, the data and results are not necessarily generalizable to the entire Turner syndrome population. The participants in this study may represent a biased sample since the population from which participants were recruited all received care at Lurie Children's Hospital in Chicago, IL. Additionally, we did not obtain perspectives from fathers of girls with TS as mothers were the only participants who were willing to respond or who were reached by phone.

Because most participants (63%) identified as White/Caucasian, a lack of ethnic diversity also limits the generalizations from this study. Finally, this study did not encompass all of the questions that need to be addressed by the TS community. Rather, this study aimed to simply begin exploring the reproductive issues involved in TS and how fertility preservation may be perceived in the community.

### ***Future Directions***

Future directions are guided by this study's limitations. Further research is needed to better understand the implications of fertility preservation in this population. Since a study of this nature has not previously been published, replication studies, with a larger, more diverse group of participants from the Turner syndrome community are essential.

Clinical investigation into the viability of this option for women with TS must also be continued, as ovarian tissue cryopreservation is still considered experimental. Issues, both physical and psychosocial, unique to Turner syndrome that may impact the manner in which ovarian tissue cryopreservation might be implemented must be explored to determine who might benefit from this process and investigate the practical issues including amount of tissue needed and timing of surgery.

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## APPENDIX F: SATURATION GRID

Codes	1	2	3	4	5	6	7	8	9	10	11	Totals
Amt of ovary matters								X		X		2
Anything to help			X		X		X		X		X	5
Appreciation of surgery				X						X		2
Biological child important	X			X	X			X				4
Biological child not important						X			X			2
Can have children	X			X		X		X		X	X	6
Cannot have children										X		1
Changes everything					X				X			2
Child's happiness			X		X	X	X				X	5
Child/woman is infertile			X				X				X	3
Considers adoption	X	X	X		X	X	X	X	X		X	9
Considers donor			X		X			X	X			4
Considers options			X		X	X	X	X	X	X	X	8
Considers surrogacy	X	X					X	X	X			5
Daughter's decision					X	X	X				X	4
Decide as adult					X	X	X					3
Demographics	X	X	X	X	X	X	X	X	X	X	X	11
Discuss infertility		X				X	X				X	4
Doesn't matter	X	X		X	X			X				5
Early surgery ok		X	X	X	X			X				5
Early surgery okay	X	X		X				X		X		5
Fertility irrelevant	X			X						X		3
Fertility a main concern					X							1
Fertility important		X		X	X				X		X	5
Infertility is upsetting			X								X	2
Infertility is complex									X		X	2
Future Fertility Discussion			X						X			2
GC experience					X	X					X	3
Great idea	X	X		X	X			X	X			6
Hadn't heard of process	X	X	X	X	X	X	X	X			X	9
Happy		X							X			2
Haven't considered options	X			X			X		X			4
Heard of process									X	X		2
IVF Concern	X											1
Infertility denial			X									1
Infertility hard			X		X		X				X	4
Infertility history											X	1
History of TS diagnosis		X	X		X	X	X	X	X	X	X	9
Info on TS infertility	X	X		X	X	X	X	X	X		X	9
Issues in TS	X	X	X	X	X	X	X	X	X	X	X	11
Keep faith					X							1
Long journey			X				X				X	3
Maternal donation			X						X			2
Maybe to process	X		X	X	X	X	X			X	X	8
Medicated periods	X	X	X	X				X	X	X		7
No periods							X					1
Mess with fate	X										X	2
Mild symptoms									X			1
Misc	X	X	X	X	X	X	X	X	X	X	X	11
Missing pregnancy								X		X		2
No GC	X	X	X	X			X	X	X	X		8
No banking when young							X				X	2
No concerns		X		X	X	X	X	X				5
No estrogen						X	X				X	3
No fertility conversation	X			X	X	X		X	X	X		7
No regrets					X							1
No to early surgery							X				X	2
Probably no to process											X	1
Process interesting	X		X	X	X			X	X			6
Reproductive issues with doctor	X	X	X	X	X			X		X	X	8
Risks create barrier				X							X	2
Risks not a barrier	X	X	X	X	X	X			X			7
Scared of surgery							X			X		2
Short stature		X	X		X		X		X			5
Social outreach			X								X	2
Support child							X				X	2
Surgery concern	X		X	X		X	X		X	X	X	8
Surgery when adult	X						X					2
Surgery when older			X				X			X		3
Surrogacy concerns					X		X			X	X	4
Surrogacy difficult					X					X		2
Surrogate okay	X			X	X			X				4
TS normalized			X			X			X			3
Take risks		X	X		X							3
Traumatizing experience			X		X		X				X	4
Unaware of infertility			X			X						2
Unaware of risks				X				X	X	X		4
Universal desire					X	X			X			3
Unsure if fertile	X			X	X			X	X	X		6
Unsure if risks create barrier	X	X		X		X		X		X		6
Unsure if wants children	X									X		2
Unsure of hormone issues			X						X			2
Unsure of options	X					X						2
Unsure of worth		X				X		X		X		4
Uses GHT			X		X	X	X		X		X	6
Wants children	X	X	X	X	X	X		X	X		X	9
Wants options			X		X		X		X			4
Wants tissue banking	X		X	X	X	X		X	X			6
When Dx'd	X	X		X	X		X	X		X	X	8
When to discuss the process	X	X	X	X	X	X	X	X	X	X	X	11
When to have surgery	X	X	X	X	X	X	X	X	X	X	X	11
When to see doctor alone	X	X	X			X	X	X		X	X	8
Will consider options in future									X	X		2
Wonderful			X		X		X		X	X		5
Yes to process		X	X	X	X			X	X	X		7
Young dx	X				X	X					X	4

APPEN  
DIX G:  
CODEB  
OOK

## AND FREQUENCY OF CODES

<b>Codes</b>	<b>Frequency</b>	<b>N=11</b>
<b>Amt of ovary matters</b>	2	18%
<b>Anything to help</b>	5	73%
<b>Appreciation of surgery</b>	2	18%
<b>Biological child important</b>	4	36.40%
<b>Biological child not important</b>	2	18%
<b>Can have children</b>	6	54.50%
<b>Cannot have children</b>	1	9%
<b>Changes everything</b>	2	18%
<b>Child's happiness</b>	5	45.50%
<b>Child/woman is infertile</b>	3	27.30%
<b>Considers adoption</b>	9	81.80%
<b>Considers donor</b>	4	36.40%
<b>Considers options</b>	8	72.70%
<b>Considers surrogacy</b>	5	45.50%
<b>Daughter's decision</b>	4	36.40%
<b>Decide as adult</b>	3	27.30%
<b>Demographics</b>	11	100%
<b>Discuss infertility</b>	4	36.40%
<b>Doesn't matter</b>	5	45.50%
<b>Early surgery ok</b>	5	45.50%
<b>Early surgery okay</b>	5	45.50%
<b>Fertility irrelevant</b>	3	27.30%
<b>Fertility a main concern</b>	1	9%
<b>Fertility important</b>	5	45.50%
<b>Infertility is upsetting</b>	2	18%
<b>Fertility is complex</b>	2	18%
<b>Future Fertility Discussion</b>	2	18%
<b>GC experience</b>	3	27.30%
<b>Great idea</b>	6	54.50%
<b>Hadn't heard of process</b>	9	81.80%
<b>Happy</b>	2	18%
<b>Haven't considered options</b>	4	36.40%
<b>Heard of process</b>	2	18%
<b>IVF Concern</b>	1	9%
<b>Infertility denial</b>	1	9%
<b>Infertility hard</b>	4	36.40%
<b>Infertility history</b>	1	9%
<b>History of TS diagnosis</b>	9	81.80%
<b>Info on TS infertility</b>	9	81.80%



<b>Issues in TS</b>	11	100%
<b>Keep faith</b>	1	9%
<b>Long journey</b>	3	27.30%
<b>Maternal donation</b>	2	18%
<b>Maybe to process</b>	8	72.70%
<b>Medicated periods</b>	7	63.60%
<b>No periods</b>	1	9%
<b>Mess with fate</b>	2	18%
<b>Mild symptoms</b>	1	9%
<b>Misc</b>	11	100%
<b>Missing pregnancy</b>	2	18%
<b>No GC</b>	8	72.70%
<b>No banking when young</b>	2	18%
<b>No concerns</b>	5	45.50%
<b>No estrogen</b>	3	27.30%
<b>No fertility conversation</b>	7	63.60%
<b>No regrets</b>	1	9%
<b>No to early surgery</b>	2	18%
<b>Probably no to process</b>	1	9%
<b>Process interesting</b>	6	54.50%
<b>Reproductive issues with doctor</b>	8	72.70%
<b>Risks create barrier</b>	2	18%
<b>Risks not a barrier</b>	7	63.60%
<b>Scared of surgery</b>	2	18%
<b>Short stature</b>	5	45.50%
<b>Social outreach</b>	2	18%
<b>Support child</b>	2	18%
<b>Surgery concern</b>	8	72.70%
<b>Surgery when adult</b>	2	18%
<b>Surgery when older</b>	3	27.30%
<b>Surrogacy concerns</b>	4	36.40%
<b>Surrogacy difficult</b>	2	18%
<b>Surrogate okay</b>	4	36.40%
<b>TS normalized</b>	3	27.30%
<b>Take risks</b>	3	27.30%
<b>Traumatizing experience</b>	4	36.40%
<b>Unaware of infertility</b>	2	18%
<b>Unaware of risks</b>	4	36.40%
<b>Universal desire</b>	3	27.30%
<b>Unsure if fertile</b>	6	54.50%
<b>Unsure if risks create barrier</b>	6	54.50%

<b>Unsure if wants children</b>	2	18%
<b>Unsure of hormone issues</b>	2	18%
<b>Unsure of options</b>	2	18%
<b>Unsure of worth</b>	4	36.40%
<b>Uses GHT</b>	6	54.50%
<b>Wants children</b>	9	81.80%
<b>Wants options</b>	4	36.40%
<b>Wants tissue banking</b>	6	54.50%
<b>When Dx'd</b>	8	72.70%
<b>When to discuss the process</b>	11	100%
<b>When to have surgery</b>	11	100%
<b>When to see doctor alone</b>	8	72.70%
<b>Will consider options in future</b>	2	18%
<b>Wonderful</b>	5	45.50%
<b>Yes to process</b>	7	63.60%
<b>Young dx</b>	4	36.40%