

EXPERIENCES AND PERSPECTIVES OF PATIENTS WHO
HAVE CONSIDERED OR UNDERGONE TRANSFER
OF EMBRYOS WITH MOSAIC PGT-A RESULTS

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By
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CERTIFICATION OF APPROVAL

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DEDICATION

This thesis is dedicated to my family. My father who gave me perseverance and courage. My mother for her unconditional love and support. My brother who gives me pride and confidence. Sam Jackson who always helps me be my best.

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I want to acknowledge all of the women who were willing to share their experiences with me for this study and their commitment to improve the experiences of women in the future.

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ABSTRACT

To improve implantation rates and pregnancy outcomes, fertility clinics have incorporated advances in embryo genetic testing into their practices. Next-generation sequencing (NGS) technology allows for the reporting of mosaicism through preimplantation genetic testing for aneuploidy (PGT-A). The transfer of embryos with mosaic PGT-A results has resulted in apparently healthy and karyotypically-normal babies, albeit with lower ongoing pregnancy rates than euploid embryo transfer. The ambiguity of mosaic PGT-A results and the lack of consistency and standards in fertility practices surrounding mosaic embryo transfer (MET) leaves patients faced with difficult decisions. The objective of this study was to elucidate the experiences and perspectives of patients who have considered or undergone transfer of embryos with mosaic results with the ultimate goal of improving counseling practices to optimize patient outcomes. Participants were recruited from Facebook mosaic embryo support groups to participate in in-depth interviews. Qualitative analysis found that embryos with mosaic results represented a source of hope and potential for participants. Some participants perceived a discordance between independently gathered information and clinical approaches to MET, which led to distrust and emotional distress. Participants expressed a desire for additional patient-friendly resources and information, provider transparency, and non-directive guidance to aid in decision-making. These findings suggest that the incorporation of genetic counseling in fertility practices could help resolve the issues described by participants

by providing pre-test and post-test counseling, in addition to personalized psychosocial support.

CHAPTER I

INTRODUCTION

Embryonic aneuploidy is known to be one of the primary causes of implantation failure and miscarriage. The development and use of preimplantation genetic testing for aneuploidy (PGT-A, previously known as preimplantation genetic screening or PGS) with in-vitro fertilization (IVF) aims to improve rates of pregnancy and reduce pregnancy loss (Maxwell et al., 2016). By identifying the ploidy status of embryos prior to transfer, euploid embryos can be identified and exclusively considered for transfer, removing one of the principal factors in poor implantation and pregnancy outcomes. Selecting only euploid embryos for transfer also reduces the need to transfer multiple embryos to achieve an acceptable chance of pregnancy, thus reducing pregnancy complications related to fraternal twinning (Forman et al. 2013). Different technical approaches to PGT-A have been adopted in order to improve accuracy and reduce potential damage to the embryo. Next-generation sequencing (NGS) performed on samples of 4-10 trophoctoderm cells biopsied from blastocyst-stage embryos is the current standard method of PGT-A (Victor et al. 2019).

The use of NGS has increased the resolution of PGT-A, allowing for better detection of mosaicism within a biopsied sample (Munné et al. 2020). Embryonic mosaicism is defined by the presence of multiple cell lines with differing numbers of chromosome sets. Mosaicism can be reported through PGT-A if the sample biopsied contains both euploid and aneuploid cells. Embryos are typically reported as mosaic

when the number of aneuploid cells represent between 20% and 80% of the cells within a sample, although some testing laboratories define these thresholds differently. Reports of the rate of mosaicism detected by NGS also vary depending on the testing laboratory (Monahan et al. (2019). Munné et al. (2020) approximate the rate to be 22%, whereas other studies report the rate to be lower; for instance, Stankewicz et al. (2017) found the overall incidence of mosaicism to be 5.4%.

As the reporting of mosaicism becomes more widely accepted, questions about the clinical utility of this category of result are becoming of foremost importance. Greco et al. (2015) published the first study reporting the outcomes after transfer of embryos that received mosaic array comparative genomic hybridization (aCGH) PGT-A results: 6 of 18 transfers resulted in apparently healthy babies with normal karyotypes determined by chorionic villus sampling (CVS). Karyotypes were not possible on the other 12 embryos transferred as they either did not result in pregnancy or resulted in a biochemical pregnancy only. Subsequent studies have continued to report apparently healthy live births from mosaic embryo transfers (METs), albeit at lower rates than euploid transfers. Munné et al.'s (2020) publication involving 253 METs and 2654 euploid transfers showed ongoing pregnancy rates of 37% and 63%, respectively. All of the babies that were karyotyped pre- or postnatally were found to be chromosomally normal. Victor et al.'s (2019) study comparing 100 METs and 478 euploid transfers reported a clinical pregnancy rate of 30.0% and 47.1% ($P < .01$), respectively. Of the MET pregnancies that received post-implantation testing (non-invasive prenatal screening and/or amniocentesis), none of the results

matched the embryo's mosaic PGT-A results. Zhang et al.'s (2018) study of the outcomes of 102 METs matched with 268 control euploid transfers also found that the live birth rate from mosaic embryos was statistically significantly lower (46.6% vs 59.1%). However, the 48 births that resulted from these METs exhibited no statistically significant differences in birth weight or congenital anomalies compared to the euploid transfer group. Of the successful clinical MET pregnancies that were evaluated by karyotyping via amniocentesis, all results were chromosomally normal.

Although these studies have shown that MET results in lower implantation rates, lower ongoing pregnancy rates, and increased miscarriage rates, researchers nonetheless suggest that mosaic embryos be considered for transfer when euploid embryos are not available because of their potential to result in apparently healthy live births (Harton et al., 2017). In light of this finding, several groups have recognized the strong need for additional evidence-based guidance to aid practitioners and patients in MET decision-making. Several recent publications suggest different protocols concerning how best to approach and prioritize the transfer of mosaic embryos. Grati et al. (2018) compared results of cytogenetic analysis from chorionic villus sampling (CVS) and products of conception (POC) in order to determine the likelihood of three adverse outcomes: 1) miscarriage; 2) uniparental disomy (UPD); and 3) mosaicism detected in the cytotrophoblast (which is analogous to NGS results from the trophectoderm) also found in the fetus. Based on their analysis, they developed a scoring system to prioritize which specific mosaic aneuploidies detected by NGS could be considered for transfer; for instance mosaic trisomies 1, 3, 10, 12

and 19 are reported as “the highest priority for transfer because of a very low risk of any of these adverse outcomes.”

In its 2019 position statement on the transfer of mosaic embryos, the Preimplantation Genetic Diagnosis International Society (PGDIS) provides recommendations for providers based on a review of current knowledge and research, including the Grati et al. findings. In contrast to the suggestions of Grati et al., the PGDIS provides more general guidance: care providers should prioritize embryos for transfer with less than 40% mosaicism and give lower priority to “embryos mosaic for chromosomes that are associated with potential for UPD, severe intrauterine growth retardation or liveborn syndromes.” These recommendations are specifically geared towards clinicians and genetic counselors. They also suggest that providers refer to other resources for guidance on how to address psychosocial counseling issues related to MET, in addition to transfer prioritization considerations. Besser et al.’s (2017) commentary provides considerations for pre-test and post-test and prenatal genetic counseling for patients making decisions about their mosaic embryos. Their commentary focuses primarily on issues of informed consent, and also acknowledges the emotional burden that such decision-making can impose on patients and the need for further research in this area. Currently, no published guidance exists which addresses psychosocial issues specifically related to MET, and none of the currently available recommendations have evaluated patient perspectives in order to understand what issues are of foremost importance to patients.

Of the existing literature concerning MET, the majority has focused on quantitative outcomes and parameters. Very little research has been done into understanding the patient experience and decision-making process that is behind these outcomes. To date, only one published paper has focused on the decision-making aspect of MET. Besser et al. (2018) quantitatively assessed factors that influenced how patients made decisions about MET after receiving genetic counseling. From a cohort of 98 participants who received mosaic embryo results and no euploid results from their PGT-A testing, the researchers measured how many of those patients made various decisions, such as transferring their mosaic embryo, pursuing a new cycle, and discarding their embryos. They also measured what factors might have affected these choices, such as number of rounds of IVF completed and maternal age. In discussing the limitations of this study, the authors state: “this study did not assess the reasoning behind patient decisions, nor did it evaluate patient understanding after genetic counseling. Additional research in these areas is essential to establish best practices for genetic counseling about mosaic PGT-A results.” As the authors establish, it is crucial to learn more about the process of patient decision-making concerning MET in order to improve genetic counseling practices and to better guide patients through this difficult experience.

The objective of this thesis is to conduct a qualitative study of patient perspectives regarding MET in order to inform providers and ultimately to improve the care of patients receiving mosaic PGT-A results. Despite the guidance that has been published so far, there is a considerable lack of consistency in the clinical

approach to mosaic PGT-A results (Kim et al., 2018), as well as significant disagreements over the validity and clinical utility of the use of PGT-A (Takahashi et al., 2018). Although quantitative research will aid in standardizing MET protocols, the lack of qualitative research needs to be addressed in order to optimize how patients are counseled about such a complex subject. Patient-friendly resources in clear layman's terms are not yet readily available; thus, patients must rely on their providers for education, and may resort to less reliable internet searches when additional information is sought. The consideration of whether to transfer an embryo with mosaic results has significant emotional, physical and financial implications for patients. It is crucial that patients considering or undergoing MET be counseled accordingly, to achieve informed consent and promote patient autonomy. Qualitative interviews with patients who have received mosaic PGT-A results and have considered or undergone MET contribute to a deeper understanding into the challenges of the decision-making process as well as the potential emotional impact associated with the entire experience that cannot be represented by quantitative data. Such an understanding is of critical significance, as it informs providers as to best practices to support their patients, and avoids pitfalls that can lead to poor outcomes, extensive emotional burden, lower patient satisfaction and provider distrust.

CHAPTER II

METHODS

This research protocol was reviewed and approved by the California State University, Stanislaus Institutional Review Board, protocol #1920-020, on October 2, 2019.

Recruitment

Participants were recruited through three Facebook groups which provide informational and emotional support to individuals considering or undergoing the transfer of embryos with mosaic results: “My Perfect Mosaic Embryo,” “Mosaic Embryo Discussion and Support,” and “Babies of Mosaic Embryos.” These groups have 1955, 683, and 214 members respectively. All three Facebook groups are private and a request for admission to each group was sent with the intention to recruit for a research study clearly stated in the request. After admission to the groups, an additional request to post a recruitment letter to each group was sent prior to recruitment.

Eligibility

Potential participants were required to have received mosaic PGT-A results and had either made a decision about their mosaic embryos or were in the process of making a decision. Those who reported that they had not been provided with the option to transfer their embryos with mosaic results were not considered eligible since that decision had effectively been made for them. Eligible participants were also

required to meet the following minimum criteria: they had to be at least 18 years old, English-speaking and could not be pregnant at the time of the interview.

Procedure

Upon approval from the group administrator, a recruitment letter was posted to each Facebook group's discussion page. The Facebook recruitment post (appendix A) contained a link to a Qualtrics eligibility survey, preceded by an electronic consent form (appendix B). After consenting to answer the survey questions and providing contact information for follow-up interview scheduling, potential participants responded to 2-4 questions aimed at determining eligibility.

Participants

Forty-one complete survey responses were received, and thirty were found to be eligible for an interview. Four of the eleven remaining responses were found to be ineligible because MET was never made available to them and the remaining seven individuals were pregnant. Using the contact information provided in the Qualtrics survey, eligible participants were sent an email containing a link to schedule their interview, instructions for the day of their interview, as well as a consent form for the interview portion of the study to be signed and returned to the principal investigator by email (Appendix D). Of the eligible participants that were sent a scheduling link, eighteen scheduled interviews; twelve never scheduled interviews despite repeated follow-up email inquiries. Of the eighteen scheduled interviews, three missed their appointments and did not reschedule, one was found to be ineligible during the

interview prompting termination of the interview, and one failed to provide a signed consent form and was thus excluded from analysis. The final number of interviews analyzed was thirteen.

All completed interviews were conducted by the principal investigator using an interview guide composed of nine semi-structured questions, as well as fifteen demographic questions (Appendix C). The nine open-ended questions were organized into three categories with three questions addressing each category: General Experience of/Learning About MET, Knowledge and Decision-Making, and Genetic Counseling Experience. The questions were formulated in a simple open-ended manner aimed at eliciting rich answers from participants, such as: “Tell me about when you first learned of mosaic embryos.” Each question included multiple optional probes to ask if the participant did not answer them during their response to the main question. After the conclusion of the interview, a \$20 Amazon gift card incentive was sent to the participant by email. All thirteen interviews were conducted by phone, audio recorded with verbal permission from the interviewee, and transcribed verbatim using NVivo transcription service. Transcribed interviews were read and edited with the accompanying audio recording for accuracy.

Data Analysis

Upon reading each transcription, the principal investigator highlighted passages of interest and made notes regarding emerging themes. In order to assess the importance and prevalence of different themes, a list of possible descriptive codes was drafted to summarize and quantify the trends commonly expressed within the

interviews (e.g. “experience of the disclosure of mosaic results” and “perception of PGT-A”). Possible codes were narrowed down to a list of nine and scales were developed for each code (e.g. *low/moderate/high*). Each interview was then coded by assigning a rating along the scale for each code. The first three interviews were coded by the principal investigator and then by a second coder. The principal investigator and second coder then discussed the results obtained independently in order to ensure full agreement over the intention of each code and the general understanding about thresholds for assigning ratings according to the coding scales. The remaining interviews were coded independently, and discrepancies were discussed until a consensus was reached as to the best possible rating.

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CHAPTER III

RESULTS

Participant Decisions and Characteristics

Fourteen women were interviewed about their experiences with MET, thirteen of whom submitted signed consent forms allowing for those interviews to be included in this study. Of the thirteen participants whose data is included in this analysis, four had embryos with euploid results in addition to mosaic embryos and were considering MET in the event that their euploid embryos were exhausted. Five participants had only mosaic embryos and were considering MET as the next step in their fertility care. Three participants, all of whom had only mosaic embryos, had made the decision to proceed with MET and had procedures scheduled for the near future at the time of the interview. One participant had undergone MET and has a young child as a result of MET.

The average age of participants was 36.6 at the time of the interview and 34.2 at the time of their first egg retrieval. The majority of participants were white (10/13), had a bachelor's degree or higher (10/13), and had a household income of over 100,000 dollars per year (10/13). The average number of completed IVF cycles was 3, and most participants had at least one child (7/13) and at least one pregnancy loss (8/13).

Table 1

Patient Demographics

| ID # | Age | Race | Religion | Ed. Level | Approx. Income | #of IVF Cycles | Age at 1st Egg retrieval | # of Children | # of Preg. Losses |
|-------------|------------|------------------|-----------------|------------------|-----------------------|-----------------------|---------------------------------|----------------------|--------------------------|
| I1 | 32 | Asian | None | Master's | over 150k | 7 | 27 | 0 | 0 |
| I2 | 28 | African American | Baptist | H.S. | 50-75k | 1 | 28 | 0 | 2 |
| I3 | 38 | White | None | Master's | over 150k | 4 | 31 | 2 | 0 |
| I4 | 39 | White | None | Associate | over 150k | 2 | 38 | 0 | 1 |
| I5 | 40 | White | None | Master's | over 150k | 3 | 38 | 1 | 1 |
| I6 | 32 | White | Catholic | Master's | over 150k | 1 | 32 | 1 | 0 |
| I7 | 28 | White | None | Bachelor's | over 150k | 1 | 28 | 1 | 2 |
| I9 | 41 | White | Catholic | Associate | over 150k | 1 | 40 | 0 | 6 |
| I10 | 42 | White | None | Bachelor's | 100-150k | 5 | 37 | 0 | 2 |
| I11 | 39 | White | None | Bachelor's | 75-100k | 2 | 39 | 0 | 0 |
| I12 | 49 | Asian | None | Master's | 30-50k | 4 | 47 | 1 | 0 |
| I13 | 35 | White | Catholic | Bachelor's | 100-150k | 4 | 32 | 1 | 6 |
| I14 | 33 | White | None | Doctorate | over 150k | 6 | 28 | 1 | 3 |

Experience of the Disclosure of Results

Of the thirteen participants, four outlined a negative experience of their results disclosure, eight described a neutral experience and one expressed a positive experience. Most participants reported that they were not aware of the possibility of receiving mosaic results prior to using PGT-A (9/13), which includes all four participants who had negative results disclosure experiences. This observation suggests that either lack of recall or lack of pre-test counseling that includes anticipatory guidance about the possibility of receiving mosaic results may be a factor contributing to a negative results disclosure experience. Regarding the first time she received mosaic PGT-A results, one participant expressed, “I don't think anyone ever

told me. I don't think anyone really ever told me what to expect when I looked at the results.”

Another factor to which participants attributed their negative experiences of results disclosure was a perception that the results were not shared in their entirety. For instance, the participant quoted above recalled another negative results disclosure experience from her second cycle of IVF, which cannot be attributed to her lack of knowledge of the possibility of mosaicism. During this second results disclosure experience, the participant's knowledge of the possibility of receiving mosaic results seemed to influence her experience. She describes that the emotional experience of receiving her results was magnified by her perception that her results were incompletely disclosed to her:

When I got the results from the very last round, the nurse, I don't really know who she was, but she basically just told me on the phone that all of my embryos were abnormal. And I was just shocked, and I actually said, “But are any of them even mosaic?” And she said, “Oh yeah well one is but it's high-level mosaic and then one of them has no results.” So, I just wanted to... I was just so upset at that moment I was speechless. I kind of wish I said to her, “Then why did you tell me they were all abnormal from the start?” It's hard news to hear but then you can kind of soften the blow by actually telling me what's really there.

Another participant reported that the specifics of her mosaic results were never formally reviewed with her and that she had been advised to do another cycle:

So I was going to do another cycle again. And then after that, I got on the phone or I got on the internet and did my own research. And that was when I learned some mosaics are viable. So I called my clinic and asked for more information for the mosaic embryo – “What chromosomes are affected?” They recommended that I email the lab. So I did email the embryologist and she responded just to say the results were a loss of chromosome 17. And it was very... again, I know clinics are really busy and everything, but on further investigation, once I was actually pregnant, the geneticist at my

hospital that works with my ob-gyn wanted more information. So she got in touch with the embryologist and got the full lab report. And it turns out it was only a segmental deletion, which is different than a full loss of chromosome 17. So that information wasn't even presented to me. It was a very small segmental deletion low-level mosaic embryo. That felt like pretty important information that was never even given to me.

These two examples demonstrate different ways in which perceptions of incomplete disclosure can lead to negative experiences of results disclosure: in the first case, the participant perceived that the provider mischaracterized her results during the disclosure, and she maintained that this experience compounded her negative experience. In the second case, the participant reported realizing only retroactively that she was not aware of the specifics of the results of her mosaic embryo, and her negative feelings towards her results disclosure stemmed from her perception that she made a major decision without full knowledge of her circumstances.

Some participants reported that their providers did not distinguish between mosaic embryos and aneuploid embryos:

It was presented to me as I had one mosaic and one abnormal and they would not recommend transferring it. I was devastated. That was a phone call with the clinic nurse, and it was sort of just like a 20-second phone call, "We're sorry it didn't work. You don't have any embryos worth transferring."

For the four participants who were aware of the possibility of mosaicism before doing PGT-A, the results disclosure was not an upsetting experience. Three of these participants described their experience of results disclosure in neutral terms. For instance, one participant who had learned about mosaicism through her own research in Facebook groups explained, "it for sure prepared me and I was not upset when I got the results."

The only participant in the study who expressed having a positive results disclosure experience was one of these four individuals with prior knowledge of mosaicism. She attributed her positive experience to detailed pre-test and post-test counseling that included an introduction to the concept of mosaicism, test parameters and additional resources:

She did a very good job of explaining what some of the limitations are with the science and what to expect. And sort of led us to speak with a genetic counselor who was part of the lab that had done the genetic testing for us. And at that time, our genetic counselor went into a lot of detail as well.

Perception of Mosaic Embryos

Most participants had a positive perception of embryos with mosaic results (8/13). Four participants described neutral feelings about mosaic embryos and one participant felt that having mosaic embryos was negative. Some participants with positive perceptions emphasized their recognition of mosaic embryos as a category distinct from euploid or aneuploid embryos:

We were actually very happy that they were mosaic and not abnormal at that time. We kind of felt... we treated our mosaic embryos like sort of an insurance policy. If the normal embryos did not work out for us, we kind of always had these other mosaic embryos in our back pocket.

This participant expressed a belief that, unlike abnormal embryos, mosaic embryos represent additional attempts at a successful pregnancy. The following participant expressed a similar sentiment:

It was really after everything failed that I was actually happy to have mosaic embryos because I felt like there was a little bit more hope than with the abnormal ones and I wouldn't have to go through another retrieval.

For most participants, mosaic embryos represented additional possibilities of having biological children, as well as providing a sense of security for those that initially had euploid embryos to transfer.

For participants who had a negative experience with results disclosure and who reported that their mosaic embryos were represented as abnormal, learning that mosaic embryos were transferable became a source of hope:

I found myself in a Facebook group and seeing all these pictures of babies that were mosaic embryos and I was really hopeful. I'd kind of gone from that moment after the phone call of feeling like complete despair and that I was never going to have children. And then finding this group of people that are not scientists and don't really know what they're doing but have taken the chance and taken a leap of faith. And it was really encouraging. And that was sort of my only hope at that point. I didn't have any other embryos; I didn't have the money to do another round of IVF.

This participant's testimony shows that the emotional component of hope may be highly dependent on circumstances. However, participants with less emotional attachment still viewed mosaic embryos as a source of hope. Participants who used more neutral language to describe their mosaic embryos seemed motivated by a desire to avoid emotional attachment:

I think it's a delicate balance because I don't see them as children per say. I see them as, you know, hope, or opportunities. But I can't say that I am emotionally attached to them. I don't think they have identities in my mind. I see them as tries, as attempts, as chances. I don't see them as individuals.

All of the above participants held a positive perception of mosaic embryos. Although the degree of emotion with which they described mosaic embryos differs, they all associated them with a tangible source of potential. Participants with neutral perceptions of mosaic embryos employed less favorable language and seemed less

reassured by having this type of result, yet still found the distinction from abnormal embryos notable: “I mean it felt better than just saying abnormal [...] these will be a last resort for us if we do another round and it doesn't work out.”

The sole participant who did not express positive feelings about her mosaic embryo had a single high-level mosaic embryo and had been counseled that transfer would likely result in non-implantation or miscarriage; as such, she effectively considered her mosaic embryo as abnormal and not as a source of opportunity.

Perception of PGT-A

When asked whether they would use PGT-A again, participants were split three ways with four participants responding yes, four participants responding no, and four responding maybe. One participant was not asked. Most participants expressed that they felt PGT-A was somewhat useful (8/13), three participants felt that PGT-A was not useful and two participants found it very useful. Assessing participant perception of the usefulness of PGT-A provides insight into pre-test counseling and informed consent regarding the benefits and limitations of the test. Some of these participants felt that they had been misinformed about or had misunderstood the purpose of using PGT-A. One participant explained that her original motivation for using PGT-A was to prevent her from having to make difficult decisions about terminating pregnancies potentially affected by aneuploidies, but she found that she was having to make challenging decisions when it came to mosaic embryos instead: “I think it was sold to me as, ‘this will prevent you from having to make those hard decisions,’ and that's completely false. So that was super frustrating.”

Another participant explained that she chose to use PGT-A in order to reduce the amount of transfers she would have to undergo, but the test failed to deliver that outcome for her. This participant implied that she was not aware of the limitations of PGT-A, one of which is that it does not ensure a successful single embryo transfer:

Well, for my daughter, we did three retrievals. Ended up transferring a total of eight eggs. We never tested anything. And the only reason why I wanted to do PGS for a second child was because I didn't want to go through all those transfers. I'm like, if we have a normal embryo, we're going to transfer it and everything's going to be good. And after all that, we had a total of three normal embryo transfers, transferred all three in three different transfers and two miscarriages, one that didn't even take. So, in retrospect, I'm like, I went through all that, I was so hopeful that the normal embryos were going to work especially since I had a daughter a couple years ago. So, I've decided that I would never do it again. So, if for any reason we need to do another retrieval, we're not going to test again, we're just going to transfer.

Participants who were unsure about their opinion of the usefulness of PGT-A seemed conflicted about the accuracy and reliability of the test, as well as whether they thought the test was actually appropriate for them individually:

I actually am on the fence about it. I have some concern with the validity of the testing [...] I do believe in the technology. I do think it is incredibly helpful, but I also think you need to filter it through your reproductive endocrinologist, through your doctor to find out if it's something that applies to your specific situation.

Some participants expressed similar “doubts about the legitimacy of the testing,” citing a belief that testing the trophectoderm may not be a “true representation” of the embryo. These participants expressed ambivalence about the testing and seemed conflicted about the reliability of PGT-A. As such, cost seemed to become a deciding factor in their decision to use PGT-A in the future:

It's all a crapshoot of what they're grabbing off and those cells don't even become the baby anyway [...] I think if money was no object, I would

absolutely do another egg retrieval and get them tested because what if they got 10 eggs from me. Every time you do a frozen embryo transfer it's thousands of dollars. So at least weed out the ones they know that are completely not viable. I would get them tested again if money were no object.

One participant who had a child from transferring an embryo that was mosaic for a chromosome 17 segmental deletion explained that the uncertainty of the mosaic PGT-A results of the embryo she had transferred created intense stress throughout her pregnancy:

My pregnancy was definitely a time of serious anxiety and I attribute that all to the mosaicism/PGS testing. It wouldn't have been that way if it had just been an embryo that was just transferred without testing and we didn't know anything about it.

She goes on to describe that the postnatal follow-up continued to create anxiety:

Chromosome 17 is perfectly normal. But there are changes on chromosome 19, which we don't actually know what that means. She's hitting all of her milestones right now and she's perfectly healthy. But again, this is just adding another element of anxiety, right? Because if it hadn't been for the PGS testing, we would never have tested her chromosomes otherwise. And she would just be a healthy baby right now. So it's just been another layer of worry.

Level of Satisfaction with Information and Education

Seven of thirteen participants expressed being somewhat satisfied with the amount of information that their providers supplied them with. Five participants expressed being unsatisfied and one found the amount of information they received satisfactory.

The participant who found the amount of information that was given to her by her provider to be satisfactory explained that her provider did a “great job,” both by providing anticipatory guidance and by clearly defining limitations associated with

PGT-A and mosaic results. This participant described herself as a highly information-seeking individual and expressed understanding that information in this field was limited, a fault she did not attribute to her providers.

Participants who expressed being somewhat satisfied with the level of information that they received were often cognizant that information related to MET was limited. When asked how she felt about the information that she received about concepts such as aneuploidy and mosaicism, one participant responded, “well, I wasn't really given much. But at that time, they may not have known too much.” Some participants explained that although they would have preferred to receive additional information or more thorough explanations of certain concepts, they recognized that this may not have been within the purview of their reproductive endocrinologist.

Although participants expressed varying levels of satisfaction with the amount of information that they were given, they all engaged in independent research and a majority of participants reported that most of the knowledge they had gained about basic concepts related to PGT-A – such as chromosomes, aneuploidy and mosaicism – was “self-taught.” One participant described how she obtained additional information: “I pretty much googled everything, used Facebook groups, and did everything I could to learn more.” In the process of seeking additional information, participants recognized differences between information they received from their PGT providers and information they obtained from other sources, which led to a perception of discordance for some participants.

Participants who described being unsatisfied with the amount of information they were given expressed that this perceived lack of education led to a discrepancy in information and adversely affected them. This is illustrated by the following participant's response:

Once I had a mosaic embryo, I was desperate for information. The clinics, not to criticize in any way because they're busy and they have many patients and they have limited amount of time in your appointments, I just didn't feel like I was educated enough. Even once I knew... sort of knew what mosaicism meant, I didn't feel like I could completely rely on the clinic to give me all the information. So of course, I went to Google and tried to do my own research. And through that process, I ended up connecting with some online groups of women who had mosaic embryos. And much to my surprise, I was seeing not just dozens but like hundreds of people who were transferring embryos and having healthy babies. And that wasn't presented to me at my clinic. Originally, they told me not to transfer the mosaic embryo and to try again and to do another full cycle. And by then I'd done five IVF cycles already and had no money and was 41.

The participant who had a successful MET described that doing research to educate herself was a source of significant anxiety during her pregnancy:

That education piece was like... it was like the glaring omission from my whole experience. Having just, you know... I was pregnant. I was anxious already because of my previous losses. I was anxious because I had no idea what mosaicism meant. I was having to Google and do my own research and it was just – it was... it was awful.

When asked if there was anything additional they wished their provider had explained to them, one participant responded:

Yeah absolutely. Just what mosaicism really means [...] And, you know, to break it down into what most people without that kind of genetic studies background would understand. I think doctors really need to take the time to explain it to us in regular English.

This participant's dissatisfaction stemmed from her perception that they were unable to understand the information that they were given about this complex topic.

Participants specifically acknowledged that communicating this complex information with patients is challenging and requires additional time and attention from providers. However, their testimonies reveal that a perceived lack of communication can undermine a patient's confidence in the patient-provider relationship:

That's my gripe with the whole genetic testing process is that I know some of it really is really nuanced and hard to understand but I think the more information is better, and I think in some ways they might have been shielding some of the patients from information because it's difficult.

Participant Perception of IVF-PGT Providers

Seven of thirteen participants expressed that they had moderate confidence in their reproductive endocrinologist (RE) or clinic as a whole. Four of thirteen expressed that they had low confidence and two expressed that they had a high level of confidence in their RE.

Participants with more moderate views of their providers described turning to alternative sources of education, seeking the most up-to-date information and treatment: "I think that my doctor, while well intended, had a lot of old information so it was helpful for me to see through that Facebook group just kind of, like, more recent trends."

Some participants described feeling a lack of support in their decision making:

So, I mean, I trust [my provider]. She's been doing this for – it's how she had her twins who are 18 years old – so she's been doing this for that long, but she doesn't stay up on the PGS testing, the mosaicism and all that stuff. They're very good about if you want to do it, they'll do it. But the physicians, I think in most of these clinics are pretty hands off.

This sentiment was shared by multiple participants struggling with the uncertainty inherent to making decisions about transferring mosaic embryos. Some participants attributed their moderate confidence to their perception that their clinic was willing to perform MET, yet did not provide the additional support which they felt was warranted considering the decision-making challenges posed by MET. When asked what would have improved her decision-making process, the following participant expressed a desire for more guidance:

If my doctor had had more of the information, I think we probably would have... it would've been easier to make it [the decision] together. And I really love my reproductive endocrinologist and I really trust her, so it was kind of disappointing to have to make this part of the decision on my own. So that would have been super helpful.

When asked whether patients or providers should be in the lead when making transfer decisions, one participant responded:

I guess the provider, because they're really the ones who should be the most knowledgeable. And I'll be honest, I feel like the doctor and the doctors at my clinic and, you know, it's a big clinic with many doctors and I feel like none of them really knew much about mosaicism or weren't comfortable with it. But if they were more comfortable, more knowledgeable it would be nice. If we could really sit down and be like, "okay, the risk with this one, that one..."

The low level of confidence expressed by a minority of participants can be attributed in part to a perceived discordance between information participants had gathered independently and information they were given by their providers. These patients seem to have developed beliefs and expectations about the extent to which providers should engage with patients concerning the topic of mosaic embryo transfer:

One of the reasons why I left my initial clinic was because I think that my doctor was not thinking outside of what was straightforward and easy and standard. I didn't want to accept that answer... It's essentially you are taking what the doctor says at face value and I have firsthand experience in dealing with a doctor who just didn't care to look into this. At this point I suspect that I may know more about mosaicism than he does and that's not fair to the patients that haven't had the chance to do their own research. They could be losing out on chances of having biological children genetically related to them because the doctor just defaults to donor eggs at some point.

This participant describes leaving her provider because her expectations, developed through independent research, were not consistent with the approach taken by her provider. For some this perception of discordance seemed to lead to feelings of distrust regarding their providers. For instance, one participant suspected that clinics and PGT lab genetic counselors might be motivated by a potential conflict of interest:

Maybe it's a conspiracy theory, but [...] I suspect there may be providers and genetic counselors that do know the true value and the potential of mosaic embryos – they're just not willing to share it with patients because there's no advantage to it for them. I don't know how to overcome that, but it is, you know, a factor in causing frustration for myself and other patients who are doing round after round after round.

Participant Perception of Genetic Counseling

Most participants had access to a genetic counselor to discuss their results after completing PGT-A testing (11/13), and most of those were genetic counselors affiliated with the lab that did their PGT-A testing (10/11); of the participants who had contact with a lab genetic counselor, three also spoke with an independent genetic counselor, and one participant spoke only with an independent genetic counselor. When asked about the utility of genetic counseling, seven participants described it as very helpful, four described it as somewhat helpful and one described it as not

helpful. One participant was not familiar with genetic counseling and thus did not have an opinion.

Despite recognizing the potential utility of genetic counseling, some participants, in particular those who spoke with lab genetic counselors, perceived conservative counseling practices regarding the transfer of mosaic embryos as possibly stemming from a financial conflict of interest. Five participants expressed concerns that these genetic counselors were possibly biased, three felt that they definitely biased, and two described them as unbiased. One of these participants described what she perceived as potential motivations for these genetic counselors to discourage patients from using MET:

I understand that they're in the business of providing genetic results [...] 1) Financially it's more advantageous to them if I do more rounds and do more testing and come up with more euploid, so financially it wouldn't be in their best interest to advocate transfer of mosaics and then 2) for liability purposes, if a mosaic embryo were to become some kind of, I don't know, a child with some kind of abnormality then maybe liability-wise they don't want to be on the hook for a patient suing them saying that "well they said that they have no knowledge of this specific genetic abnormality causing this type of disease but here it is, it has manifested and we have a child who needs disability support for the rest of their life." So they don't want that kind of risk exposure.

For this participant, along with several others, over-emphasis on the risks of MET influenced their perception of genetic counseling, and lab genetic counselors in particular, leading them to misattribute standard practices to ulterior motives.

As previously noted, participants experienced a sense of discordance between information they received from genetic counselors and other resources. One participant explained:

I wish that the genetic counselor would have acknowledged the reality that mosaic embryos do become healthy children. Because the way it was presented to me it was almost like it rarely happens. And based on personal experiences of actual women in the Facebook group and seeing the reality that I'm experiencing on social media is that it happens a lot more often than what the genetic counselors have let on [...] I just don't think it was accurate the way it was presented to me by a genetic counselor.

Some participants expressed a desire for greater access to genetic counseling.

One participant explained that despite wanting to speak to an independent genetic counselor, she was not aware of a formalized process for doing so:

I'm going to have to go on that group and ask where they're getting these genetic counselors they're talking to. I don't even know how to go about doing that. I don't. I mean I guess I could google genetic counselors. I don't want just anyone; I want one that is versed in this process. I mean it's too bad that it's not more of a known thing. Even... it would be nice if my clinic even said, "here's a list of three or four genetic counselors we recommend."

One participant described the aspects of genetic counseling that were particularly helpful to her and her partner:

It was definitely helpful because as much as I can read online it's not like I really understand... I guess just most helpful was the fact that she was able to explain things in layman's terms and especially for my husband because I feel like I just am constantly researching and reading up on different comments that people make and posts and whatever and he kind of doesn't. He's not in that realm at all. So, I feel like for him to kind of get what I've been trying to explain because I feel like I read things and I can't really put it understandably. I feel like I get it in my head but when I try to explain he's like, 'huh?' So that was very helpful because she was able to. Then I feel like he understood as opposed to before I feel like he didn't get what I was talking about probably because I wasn't really doing a good job.

Another participant described the genetic counseling process as a means of translating complex information:

So the genetic counselors that we spoke with were very knowledgeable. I do think that they were very well versed in the information that they translated for us. I think that it was explained to us in a very easy way to understand for

someone who has a good background and also for someone who just may be just starting the process and not really understanding what the tests actually are or what they signify.

Multiple participants expressed that one of the beneficial aspects of genetic counseling was the facilitation of decision-making:

My husband and I both met with a genetic counselor to talk about our specific mosaic embryos and what any associated syndromes would be or anything like that. And that was really helpful in making the decision.

Some participants felt that speaking to a genetic counselor should be “mandatory,” due to the potential risk that could come with transferring a mosaic embryo without sufficient knowledge:

I can't see how anyone would ever transfer a mosaic without talking to a genetic counselor because there are syndromes that these children can be born with. It doesn't mean that every single mosaic will self-correct and it will be good; there are still issues that your child could have. You know, people need to understand that.

Participant Perception of the Risk Associated with MET

Although most participants viewed mosaic embryos as having reproductive potential, the majority of participants described MET as being associated with some risk (11/13). One participant described MET as high risk (1/13) and one participant associated it with no risk. The majority of participants (9/13) reported that they would use prenatal genetic testing for a pregnancy achieved using a mosaic embryo; the remaining four participants were unsure whether they would. Many participants were very knowledgeable about the availability of prenatal testing options. For instance,

one participant who had never been pregnant responded, “absolutely CVS at the earliest available time,” when asked what type of testing she planned on using.

The intention to use prenatal testing seemed to be motivated by an awareness of the potential risks of mosaic embryo transfer, such as aneuploidy and pregnancy loss. One participant expressed, “my biggest fear is having a late-term miscarriage.”

However, many participants found data showing favorable outcomes to be reassuring:

It's going to be very tricky because I could see it causing a lot of problems in our marriage because if, God forbid, something is wrong with that child. But I don't think there's any documented. I've been reading trying to find mosaic embryos – if a child was ever born not healthy, and I'm not seeing any results to that fact. Either you get pregnant and it's fine or you get pregnant, you miscarry, which would, I mean, that would be an awful, awful thing to go through. But I mean I've been through it and it's awful. But it's – I don't know. It's something that happens.

The birth defect one is probably the one that is most on my worry list. However, I see that there is now a study that says that, of course, you don't know how many of them were terminated, but none of the live births have had the same defect that was listed in the PGS testing... So the miscarriage, you know, I think for women who have had lots of miscarriages it's one of these things, it's like, is this another emotional toll? But they did tell me the miscarriage would be probably within the first eight weeks. So it's not a later month of miscarriage. So that part I kind of would be glad for, that it would be an earlier miscarriage.

The willingness of participants to accept an uncomfortable level of risk alludes to the hope for a biological child from MET, and to the importance of receiving skilled counseling from providers. The participant that had undergone a successful MET expressed that she associated it with a high level of risk. When asked whether she considered herself to be a risk-taker in her every-day life, she responded:

No, I'm definitely not. I normally play it safe. So that was another factor, right? I don't know. I'm not a risk-taker on a normal day. So this was sort of like, way out of my comfort zone.

When asked whether patients should be allowed to make the decision about which embryos to transfer, one participant expressed the view that the provider's opinion is indispensable:

I personally don't think that a patient should have that option if they are not educated on their options. I think they can be told about it from their RE, fertility doctor and then they can go home, do their study, speak to some common folk about it and make a decision from there and come back. But if they don't have any means of knowing what's going on, I really personally don't think that we should have that choice to choose, especially when it comes to an abnormal and/or mosaic, depending the kind. So just a little more education behind it, I'm all for being able to pick. But if I didn't know anything, I don't want that option.

One of the participants with a scheduled MET was reassured by her understanding that her embryo's mosaic result was a non-viable aneuploidy that would not result in a pregnancy if present in the whole embryo:

You need to understand the issue with your embryo and what it means. Like Turner syndrome, there's a couple of syndromes that if your embryo has issues with those chromosomes that you need to understand if your child is born with that, what would that mean. My issue is either my child is going to be completely healthy or it's not going to be a child, but that's where I'm at and I'm fine with that. If they told me that if this embryo does implant your child could possibly have some kind of syndrome, I wouldn't have implanted it.

Participant Desire for Additional Non-Directive Guidance

In light of the risks and uncertainties participants associated with MET, eleven of thirteen participants expressed a strong level of desire for additional non-directive guidance. One participant had a moderate level of desire for additional guidance and one had a low level of desire.

Although most participants expressed a desire for additional information, they also expressed desire for an expert-led approach to determining what information was most useful to them. For instance, one participant who described herself as having an information-seeking personality expressed that she would have benefitted from additional guidance to manage the information she was given:

I would have liked a lot more guidance in the beginning. A lot of what I was coming up with was research that I did on my own and I presented to my clinic and said, “Hey, can we talk about this more?” I understand that their time is very limited. They have a lot of patients and their patients do require a lot of hands on application. I do understand their time and resources are limited. But I also think to the clinic, sometimes they come at patients with all of this information on the first day: it's option paralysis. And it causes a lot of anxiety, stress, because then you fully understand everything that could go wrong. So I think it's a very, very difficult balance to give a patient enough information so they understand what's happening, but not give them too much information about what's happening or what could happen.

This participant expressed the need for additional guidance in the early stages of her care. The desire for additional guidance was also pronounced after receiving mosaic PGT-A results. One participant expressed simply: “we just need to be guided better sometimes.”

Decision-making seemed to be one of the most difficult aspects of receiving mosaic PGT-A results. One participant who described struggling with decision-making explained that Facebook support groups became an important source of support:

I found that's part of why I needed a break, and part of what is so taxing about this process is that you got to make the decisions and there's no guidance. There's just no guidance and these are, like, decisions I feel like I need a lot more education to make a lot of the time so I just – that group actually has been really, really helpful. I don't know what people did before things like

this, it's crazy but I post questions when I have questions and reach out to other people who post and just try to make decisions based on that.

The participant above expressed that she utilized the Facebook support group as a resource that could provide guidance based on her particular questions. Similarly, the following participant described the beneficial role of receiving individualized care:

So it would be really helpful if they gave – if they chimed in more, but unfortunately, they don't. It's just volume, this clinic goes on volume. Like it's just mass mass mass people. That's why I'm really lucky to have found the nurse practitioner I go to every time because at least I have her individual attention where other people don't even have that. They see a different nurse every single time they go.

Another participant recognized that a possible solution to receiving personalized facilitation of decision-making might be for a genetic counselor to take on this role because of their specific skill set and knowledge base:

I don't expect [my doctor] to have the specific knowledge of what each one of my mosaics could potentially present if it became a pregnancy, I just don't think that he has the time and resources to look up every single scenario, whereas for me I would. I guess that's where the genetic counselor fills the gap a little bit.

CHAPTER IV

DISCUSSION

The objectives of this study were to gather and elucidate the opinions and experiences of women who have received mosaic PGT-A results and have considered or undergone MET. The results of this qualitative analysis contribute to the ongoing discussion about clinical practices and policies regarding MET. Qualitative research assessing how patients are making decisions about their mosaic embryos has yet to be published.

Previous studies have proposed that, because MET has the potential to give patients additional opportunities for healthy biological children, it should be considered (Viotti et al., 2019). These previous studies have also shown through outcomes data that patients are making the decision to use MET and have thus implied that it is a procedure that patients will continue to elect (Besser et al., 2018). The findings of this study are consistent with other studies regarding the desirability of MET for patients. It further elucidates this desire in patients' own words. Besser et al. (2018) quantitatively established that patients who did not have euploid embryos are making the decision to use MET. Some of the participants (4/13) in this study had euploid embryos in addition to mosaic embryos and were considering MET as an alternative to additional cycles of IVF, in the event that their euploid embryo transfers were unsuccessful. Thus, this study showed that some patients who do have euploid embryos to transfer may also consider their mosaic embryos for future transfer.

Although most participants perceived mosaic embryos favorably as having reproductive potential and a source of hope, the complexity and uncertainty associated with MET poses decision-making challenges for providers and their patients. Qualitative analysis of patient perspectives further demonstrates the patient desire for result-specific transfer guidance proposed by Grati et al. (2018) and the PGDIS (2019). These resources provide suggestions for a clinical approach to MET, but a consensus on standardized practices of MET have yet to be established and patient-oriented resources have yet to be created. The findings of this study showed that a desire for additional information and guidance throughout the experience of making decisions about mosaic PGT-A results was an important aspect of the patient experience. For some, this need for supplemental support contributed to the emotional challenges posed by infertility. Participants expressed a desire for additional individualized attention and guidance with balanced information from their providers.

Seeking to address their desire for additional information and support, participants utilized Facebook support groups. Despite the potentially unreliable nature of online resources, which patients are often cautioned against, the widespread use of the internet as a resource is practically inevitable. As one participant expressed: “A doctor will sit there and say, ‘Don't go on the internet, don't go on the Internet’ and guess what? Every woman in the fertility clinic is doing it. She's going on the Internet.” This study allows for the examination of the role that these online support groups can play in the experiences of patients who have received mosaic results. Most participants described that this resource created a platform where patients could

support each other on an individual basis with emotional, practical and decisional guidance. Despite the assistance that patients reported receiving from these support groups, they did not eliminate the desire for additional guidance and individualized attention from providers.

Some participants expressed a low-level of confidence in their providers. This low-level of confidence might be attributable to a discordance between what participants experienced in Facebook groups and what they experienced in clinic. From a clinical perspective, MET is not widely practiced and remains controversial (Kim et al., 2018). In line with their ethical responsibilities, providers may choose to take a conservative approach to the topic of mosaic embryos until additional clinical outcomes data emerge and as long-term risks remain unknown. Some participants described the experience of discovering the anecdotes of successful METs as seen in groups such as “Babies of Mosaic Embryos,” and they reported feeling a discrepancy between their impressions of MET and the manner in which MET was conveyed to them by their provider. Some participants expressed awareness that providers and clinics are limited in their availability and resources. For other participants, this feeling of discordance seemed to create doubt about the potential motives of providers, including REs as well as genetic counselors.

The findings of this study support the efforts made by Besser et al. (2017) to suggest detailed pre-test and post-test counseling practice suggestions. One aspect of the experience of receiving mosaic PGT-A results that led to distress for some participants was a results disclosure experience that they perceived as negative. These

negative experiences of the disclosure of results could be attributable in part to limited anticipatory guidance and pre-test counseling. These findings suggest that a more standardized incorporation of pre-test genetic counseling might contribute to resolving this issue.

The findings of this study, when considered comprehensively, suggest that fully incorporating genetic counselors into the process of administering PGT-A would likely improve patient experiences. These interviews demonstrate that MET was an emotionally charged issue for many patients, and they show that participants valued and desired additional non-directive guidance, personalized decision-making support and patient-friendly education. Genetic counselors are trained in skills which address the needs that participants in this study expressed (ACGC, 2019). Providing pre-test counseling that includes a simple introduction to mosaicism, a warning about the potential for ambiguous results and an upfront discussion about the limitations of PGT-A could prevent or lessen the surprise and confusion experienced by some patients receiving unexpected mosaic results. Post-test counseling with complete results disclosure and a result-specific conversation, including appropriate resources, has the potential to increase patient autonomy to make informed decisions with the support and expertise of their provider. These genetic counseling practices could also strengthen trust between patients and providers by reducing an impression of discordance between anecdotal information and clinic-based practices.

Lessons Learned from Patient Experiences with MET

The following is a summary of points to consider for fertility clinics utilizing PGT-A reports that include mosaic results:

- Access to pre- and post-PGT genetic counseling services could address many of the concerns and desires of patients expressed in these interviews.
- Pre-test genetic counseling should inform patients of the possibility of mosaic results, the potential for uncertain implications, and the need for decision-making. A simple and concise description of mosaicism should include potential outcomes of transfer (seemingly healthy children, unknown long-term effects, reduced pregnancy rates and increased miscarriage rates).
- Acknowledging and responding to questions about anecdotal references to successful METs could help to maintain rapport with patients. Providers should be clear about their clinic's experience with and policies concerning MET and advise patients that genetic counselors are available to provide additional counseling. Similarly, addressing laboratory policies about MET could help in preventing the potential misconception of a conflict of interest.
- In the event that a patient receives mosaic results, information regarding what is known and/or what is not known about a particular PGT-A result is desired. Advising patients about various resources can help patients manage additional independent research.

- Counseling that includes balanced information can aid patients in making informed decisions in the context of their specific results and personal circumstances after receiving mosaic results.

Limitations of the Study

The primary limitation of this study is that all participants were recruited from Facebook support groups. Although these groups include members from a variety of different locations and fertility clinics, the decision to seek out and join an online support group could indicate the existence of unmet needs. As such, there is the possibility that ascertainment and self-selection bias affected the findings of this study: members of Facebook support groups may have had a negative experience which led them to join a support group, and those who volunteered to participate in the study may have been those who felt the most compelled to voice those experiences. The perspectives of these participants may not be generalizable to the greater patient population represented by all patients who have considered MET following PGT-A. Nonetheless, examining the experiences of these participants illuminates the factors which may have led to their negative circumstances, and the results of this study offer insights that could optimize experiences for future patients.

The findings of this study also relied entirely on participant reports, and none of the information provided was corroborated by additional investigation. It is possible that some discrepancies could be identified between the perceived experiences of patients and the actual information given or care administered by

providers. However, the focus of this study was how participants experienced their care, rather than a thorough review of care protocols.

The sample size of thirteen interviews obtained for this study also represents a small fraction of the total membership of these Facebook support groups. One of the consequences of this small sample size was that not all possible scenarios of those considering or undergoing MET were represented. For instance, there were no participants who had undergone MET and subsequently miscarried or received positive prenatal testing results. Participants with these different experiences could have different opinions and perspectives than those interviewed. Lastly, there was a lack of diversity in the participant sample; most participants were white, non-religious, had higher education and had an approximate household income over 100,000 dollars per year.

CHAPTER V

CONCLUSION

This study elucidated the experiences and opinions of women who received mosaic PGT-A results and considered or underwent the transfer of those embryos. This is the first study to take a qualitative approach to exploring the topic of MET from a patient perspective. Overall, the findings illustrate a broadly shared desire for an increased level of balanced information and guidance from providers concerning mosaic PGT-A results, even among patients who have euploid embryos in addition to mosaic embryos.

Participants expressed that they viewed mosaic embryos as having reproductive potential and being a source of hope. The challenges and uncertainties associated with MET led participants to seek education outside of their clinical setting. For some participants, information and expectations derived from independent research differed from what they experienced in a clinical setting, which led to a perception of discordance. Participants described a need for additional result-specific transfer resources to aid in decision-making about their embryos with mosaic results and used Facebook support groups as a way of satisfying this need.

This qualitative study provides the first insight into the patient experience of MET in order to inform providers and policy-makers working towards improving practices and guidelines. The findings of this study suggest that a broader incorporation of genetic counseling into the care of patients using PGT-A could

improve patient education, provide psychosocial support, and facilitate decision making.

Future Studies

Future research could expand on this study by recruiting patients from sources other than Facebook support groups in order to assess whether the findings shown here are generalizable to the broader patient population. A mixed methods approach could quantify which patients use Facebook support groups and whether that use is associated with any particular outcome or has an effect on a patient's decision-making.

Other future studies could assess the guidance practices of genetic counselors affiliated and unaffiliated with PGT-A labs and evaluate patients' experiences of those services. Such research could assess how patient' perceptions of genetic counseling differ when provided by laboratory-affiliated or non-laboratory affiliated genetic counselors.

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APPENDICES

APPENDIX A

FACEBOOK RECRUITMENT POST

Hello everyone, my name is Eva Gabor-Fourcade and I am a graduate student in the Genetic Counseling Program at California State University, Stanislaus. For my Master's thesis research project, I am conducting phone interviews with women who have considered or undergone mosaic embryo transfer after mosaic preimplantation genetic testing for aneuploidy (PGT-A) results to learn more about patient perspectives and factors in decision-making.

I am hoping that providing these perspectives to medical providers will help improve their practices for the benefit of future patients.

The interviews will consist of questions seeking to learn more about your experience and opinions and will take between 30-45 minutes. A \$20 amazon gift card will be provided upon completion of the interview.

If you are interested in participating, the link below will have you review a consent form for a brief eligibility survey (<5 mins). If you agree to provide consent, you will be asked to answer a few questions to ensure your eligibility for the study and to provide your email address so that we can contact you to schedule an interview.

Please note that to participate you must be 18 years old or older, English-speaking, and cannot be pregnant at the time of the interview.

If you have any questions about the research, please contact me at egaborfourcade@csustan.edu.
Thank you.

*This post has been approved by the admin of this group.

https://csustan.co1.qualtrics.com/jfe/preview/SV_9pNJ2blO74xNnI9?Q_SurveyVersionID=current&Q_CHL=preview

APPENDIX B
ELIGIBILITY SURVEY

Start of Block: Survey Informed Consent

Informed Consent to Participate in Research
Patient experiences with Mosaic Embryo Transfer:
A Qualitative Study.

Eva Gabor-Fourcade
evagaborfourcade@csustan.edu

Purpose of the Research

The Principal Investigator, Eva Gabor-Fourcade, is a student at California State University, Stanislaus conducting research for a master's degree in genetic counseling.

The purpose of this research is to learn more about the experiences and opinions of patients that have considered mosaic embryo transfer (MET) with the goal of improving the practices of medical providers for the benefit of future patients.

Procedures

If you wish to participate in this study, the following will occur upon providing consent to this statement:

- You will be prompted to answer a few questions (<5 mins) to confirm your eligibility for the interview portion of the study.
- You will be asked to provide your email address to that the researcher may correspond with you about a follow-up interview.
- You will be contacted via email to let you know of your eligibility status.
- If you are eligible, you will schedule an interview with the researcher at your convenience. The interview will take about 45-60 minutes of your time and will be audiotaped with your consent for accuracy and analysis.

Potential Risks or Discomforts

There are no anticipated risks associated with this taking this brief survey.

Potential Benefits of the Research

There are no direct benefits to you by completing this study. However, it is possible that practices involving MET could be improved for future patients as a result of the information derived from this study.

Confidentiality

The information collected by the researcher will be protected from all inappropriate disclosure under the law. All information, including questionnaire responses, and audio recordings of the interview, will be kept in a secure location on a password protected device. Only the researcher, and her research team, will have access to the data.

The researcher will not keep your research data to use for future research.

Costs

There is no cost to you beyond the time and effort required to complete the procedure(s) listed above.

Compensation

There is no anticipated commercial profit related to this research.

Participation and Withdrawal

Your participation is voluntary. You may refuse to participate or stop participation at any time without penalty or loss of benefits.

Questions

If you have any questions about this research, you may contact me, Eva Gabor-Fourcade at egaborfourcade@csustan.edu or my faculty sponsor, Janey Youngblom at jyoungblom1@csustan.edu.

If you have any questions regarding your rights and participation as a research subject, please contact the IRB Administrator by phone (209) 667-3493 or email IRBadmin@csustan.edu.

Consent

Clicking the “I consent to participate” button below indicates that you are 18 years of age or older and that you consent to participate in this study. Please feel free to print a copy of this consent page to keep for your records.

I consent to participate, begin eligibility study (1)

- I do not consent to participate (2)

Skip To: End of Survey If Informed Consent to Participate in Research Patient experiences with Mosaic Embryo Transfer: A Q... = I do not consent to participate

Page Break

End of Block: Informed Consent

Start of Block: Eligibility Survey

Q1 When you initially received mosaic PGT-A results for your embryo(s), were you given the option of transferring them?

- Yes (1)
- No (2)
- Other (3) _____
-

Q2 Have you ever transferred an embryo that received mosaic PGT-A (PGS) results?

- Yes (1)
- No (2)
- Other (3) _____

Skip To: Q3 If Have you ever transferred an embryo that received mosaic PGT-A (PGS) results? = Yes

Q3 Are you currently pregnant?

- Yes (1)
- No (2)
- Other (3) _____

Skip To: Q4 If Are you currently pregnant? = No

Q4 Do you have a child that was conceived from an embryo that received mosaic PGT-A results?

- Yes (1)
- No (2)
- Other (3) _____
-

Q5 Please provide the email address where you would like to be contacted for interview scheduling.

End of Block: Eligibility Survey

APPENDIX C

INTERVIEW GUIDE

Introduction:

Informed consent will have been received via email prior to interview.

Hello, is this ____? My name is Eva. Thank you for agreeing to be interviewed for my research. Let me tell you a little more about what we're doing today. I'm a graduate student in the Genetic Counseling Program at California State University, Stanislaus and I'm conducting a series of interviews with the goal of getting a better understanding of people's experiences who have considered mosaic embryo transfer. Learning more about your experience is important to help improve the practices of genetic counselors and fertility care providers in an effort to create a better experience for people making decisions about mosaic embryo transfer.

The interview itself should take about 45-60 minutes and will include questions related to your experience with IVF and mosaic embryo transfer. All of your answers will be completely de-identified, and your information will be kept confidential. This study is voluntary, and you do not have to answer any questions that you do not feel comfortable with.

Do you have any questions before we begin?

Demographic Information:

1. Age:
2. Race/Ethnicity:
3. Religion:
4. Education Level:
5. Household income: Under \$30k/year, 30-50k, 50-75k, 75-100k, 100-150k, over 150k
6. # of rounds of IVF before MET:
7. Age at egg retrieval (s):
8. # of children before considering/undergoing MET:
9. # of SABs before considering/undergoing MET:

Try to obtain these from conversation:

10. Access to a GC during fertility process? Yes or No
11. Prenatal testing after MET transfer:

12. Outcome of MET if done:

Questions in italics are probes/follow-up question options that will only be asked depending on the interviewee's answer to the primary question.

General experience/learning about MET

1. Tell me about when you first learned of mosaic embryos.

-Did you know ahead of time that there was a possibility that your PGS/PGT-A (preimplantation genetic testing) results could show that you had mosaic embryos?

-If so, how were you feeling about that before you got the results

-If not, do you wish you had known that there was a chance of mosaic results before going ahead with PGT-A?

-Would you use PGT-A again in the future? Why or why not?

- What were your complete PGT-A results (mix of euploid and mosaic embryos, mix of aneuploid and mosaic, mix of euploid/aneuploid/mosaic, only mosaic embryos, what kinds of mosaic embryos)?

2. How did you feel about your PGT-A results?

-Did you feel emotionally connected to your embryos?

-Did learning that some of your embryos were mosaic change the way you felt about your embryos?

- Who provided you with the PGT-A results?

3. How did you initially learn about the possibility of transferring your mosaic embryos?

-Where or from whom did you obtain this information?

-What was your initial reaction when you first learned about the possibility of mosaic embryo transfer? Did it strike you as particularly positive or negative?

-Are there particular aspects you liked or wished could have been different regarding the general process of learning about MET?

I'd like to shift gears a little now and talk more about how you made decisions during this experience.

Knowledge & Decision-Making

4. Tell me about your decision-making process and the decision you made, if any yet.

-What factors did you take into consideration during your decision-making process? (e.g. finances, emotional burden, negative outcome, your particular PGT-A results (e.g. chromosome(s) involved), etc)

-What is your reproductive history and do you feel like it had an effect on your decision about MET?

-Did your provider/clinic's policy on MET influence your decision?

-Who did you consult during this process? Your doctor, nurse, embryologist, genetic counselor in the clinic or at the lab, family, friends, social media, therapist, spiritual support person, etc?

-What resources/information did you use? Internet search, written material provided by your clinic or lab, laboratory website, etc

-What other options were you considering? (egg donor, adoption, etc)

5. How do you feel about the amount of information you were given about aneuploidy, mosaicism and the specific results of your embryos? Did you feel like you understood the information well enough to make informed decisions about what to do with your embryos?

-Is there anything you wish you had known?

-Did your provider refer you to any resources to consult on your own?

-Did you get most of your knowledge from your providers or from a different source?

What or who was the most helpful resource to you in your decision making and why?

-What level of understanding of concepts like aneuploidy and mosaicism do you think is necessary in order to feel confident in your decision-making?

-Do you think that patients should make their own decisions about which embryos to transfer or do you feel that the decision should be in the hands of the providers?

6. How did you feel about your decision(s) (confident, unsure, etc.)?
- *How did you feel you were supported when you were making these decisions?*
 - By providers: were they encouraging or discouraging?*
 - What about your friends and family?*
 - Did you think that the option of using prenatal testing for aneuploidy (amniocentesis, CVS, NIPT) gave you some peace of mind?*
 - Do you have any suggestions regarding what would have been helpful for you during this decision-making process?*
 - (e.g. additional resources, connecting with other women who have gone through the process, access to additional professionals, etc.)*
-

Now I'd like to hear more about you experience with Genetic Counseling.

Genetic Counseling experience

7. Did you have access to a genetic counselor during your experience?
- What was most helpful about meeting with the Genetic Counselor?*
 - Was there anything that you did not like about meeting with the genetic counselor?*
 - If you did not have access to a genetic counselor, do you wish that you had and why?*
 - (If participant answers "yes", skip to final question)*
8. What do you wish genetic counselors incorporated more into their practices when helping with a decision about mosaic embryo transfer?
9. Is there anything else that I haven't asked you about that you would like to discuss or a question that you think would be useful to ask other interviewees?

Conclusion:

Thank you so much for participating in this interview. You will receive a \$20 Amazon gift card via email within the next 3 days. Please feel free to use my contact information at any time if you have any questions or would like to discuss anything further.

APPENDIX D

INTERVIEW INFORMED CONSENT

California State University, Stanislaus
Informed Consent to Participate in Research
Patient Experiences and Decision-Making
with Mosaic Embryo Transfer: A Qualitative Study.

Purpose of the Research

The Principal Investigator, Eva Gabor-Fourcade, is a student at California State University, Stanislaus conducting research for a master's degree in genetic counseling.

The purpose of this research is to learn more about the experiences and opinions of patients that have considered or undergone mosaic embryo transfer (MET) with the goal of improving the practices of medical providers for the benefit of future patients.

Procedures

To be eligible to participate in this study you must be 18 years old or older, English speaking and you must not be pregnant at the time of the interview.

If you wish to participate in this study, the following will occur upon providing consent to this statement:

- The researcher will communicate with you via email to schedule a telephone interview at your convenience.
- The interview will take about 45-60 minutes of your time and will be audiotaped for accuracy and analysis.

Potential Risks or Discomforts

There are no anticipated risks associated with this study. It's possible that some interview questions could be emotionally triggering or make you feel uncomfortable, however you are not required to answer any questions that you do not wish to and contact for a genetic counselor will be available upon request.

Potential Benefits of the Research

There are no direct benefits to you by completing this study. However, it is possible that practices involving MET could be improved for future patients as a result of information derived from this study.

Confidentiality

The information collected by the researcher will be protected from all inappropriate disclosure under the law. Audio recordings of the interview will be stored in a secure location on a password protected device. Audiotaped interviews will be de-identified and transcribed, upon which the original recordings will be destroyed. Only the researcher, and her research team, will have access to this information.

The researcher will not keep your research data to use for future research or other purpose.

Costs

There is no cost to you beyond the time and effort required to complete the procedure(s) listed above.

Compensation

Compensation for participating in this research will be a \$20 Amazon gift card that will be emailed to you upon completion of the interview.

There is no anticipated commercial profit related to this research.

Participation and Withdrawal

Your participation is voluntary. You may refuse to participate or stop participation at any time without penalty or loss of benefits.

Questions

If you have any questions about this research, you may contact me, Eva Gabor-Fourcade, at egaborfourcade@csustan.edu or my faculty sponsor, Janey Youngblom at jyoungblom1@csustan.edu.

If you have any questions regarding your rights and participation as a research subject, please contact the IRB Administrator by phone (209) 667-3493 or email IRBadmin@csustan.edu.

Consent

I have read and understand the information provided above. All of my questions, if any, have been answered to my satisfaction. I consent to take part in this study. I have been given a copy of this form.

In addition to agreeing to participate, I also consent to having the interview *audio* recorded.

Signature _____ Date _____
Name (printed) _____