FACTORS IN DECISION-MAKING OF WOMEN CONSIDERING TRANSFER OF EMBRYOS WITH MOSAIC RESULTS AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY

In Partial Fulfillment
of the Requirements for the Degree
of Master of Science in Genetic Counseling

By
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CERTIFICATION OF APPROVAL

FACTORS IN DECISION-MAKING OF WOMEN CONSIDERING TRANSFER OF EMBRYOS WITH MOSAIC RESULTS AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY

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Signed Certification of Approval page is on file with the University Library
ACKNOWLEDGEMENTS

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ABSTRACT

Current techniques for preimplantation genetic testing for aneuploidy (PGT-A) following blastocyst biopsy have been shown to significantly improve rates of implantation and ongoing pregnancy and reduce rates of miscarriage following in vitro fertilization (IVF). With the introduction of more sensitive array comparative genomic hybridization (aCGH) and next-generation sequencing (NGS) techniques, detection of embryonic mosaicism has become a possibility. A significant amount of research is currently underway on the outcomes and success of mosaic embryo transfer (MET). Several recent studies have proven that live-birth of a healthy baby is possible after MET. This remains a controversial topic with a small, but expanding, number of IVF providers who will perform the procedure. With outcome data growing, what remains unknown is the experience of this small group of women who undergo MET. The purpose of this study is to determine factors in decision-making of women who have considered transfer of an embryo determined to be mosaic using PGT-A. A total of 59 survey responses were received. Neither demographics, infertility history nor pregnancy history were correlated with MET. Rather, support from health care providers and partners was correlated with a decision to pursue MET.
CHAPTER I
INTRODUCTION

Preimplantation genetic testing was first introduced in the 1990s to significantly reduce the risk of transmission of X-linked disorders, inherited monogenic disorders, unbalanced translocations, and aneuploidy to offspring and reduce morbidity and mortality related to these conditions (Chen et al., 2018). It is well established that rates of aneuploidy in a woman’s eggs is associated with increasing maternal age (Wallach & Simpson, 1980). Aneuploidy rates in preimplantation embryos approach 85% by the age of 43 (Kim et al., 2018). First-trimester pregnancy loss is primarily due to aneuploidy (ASRM, 2018). Screening embryos for aneuploidy allows for the reduction of the most significant reproductive risk in women of advanced maternal age. Meta-analyses have shown a significant decrease in miscarriage rates and increased odds of live birth in cycles of women over 37 when PGT-A had been used prior to transfer (Munne, Grifo, & Wells, 2016; Chang et al., 2016). It has also been demonstrated that the transfer of chromosomally normal blastocysts results in an implantation rate that remains constant, regardless of maternal age at the time of egg retrieval (Harton, Munne, & Surrey, 2015; Platteau et al., 2005). It is justifiable that assisted reproductive success rates would benefit from chromosome screening prior to transfer of embryos. Beyond the ability to assess for embryo selection, PGT-A has the capacity to reduce the incidence of miscarriage and
drastically reduce the risk of children being born with severe congenital anomalies due to a chromosomal imbalance (Scott et al., 2012).

Outcome data on live-birth rates after PGT-A have been highly variable since the development of techniques to determine embryo ploidy prior to transfer (ASRM, 2018). The data generated in the 1990s and early 2000s are markedly different than the data reported in more recent years, in part due to the rapidly advancing technology used to screen for aneuploidy. The first PGT procedure was performed in 1990 using Y specific DNA amplification in hopes of transferring female embryos to reduce the risk of X-linked disease in offspring (Handyside et al., 1990). Not long after, researchers began to attempt to screen for common aneuploidies using fluorescence in situ hybridization (FISH) (Munne et al., 1995). FISH initially screened for three common aneuploidies and later expanded to evaluate 9-12 chromosomes. However, prospective randomized trials failed to show a significant increase in pregnancy rates using this technology (Staessen et al., 2004; Mastenbroek et al., 2007; Mastenbroek et al., 2011). As a result, the American Society for Reproductive Medicine (ASRM) released a formal opinion discouraging its general use (ASRM, 2008).

This lack of utility prompted scientists to reevaluate their methodology. An early assumption of FISH-based PGT-A technologies was that miscarriages due to aneuploidy were much more likely to be due to aneuploidy of certain chromosomes over others. Therefore, experts believed that focusing on these chromosomes would
be most beneficial for reducing miscarriage and increasing ongoing pregnancy rates (Harton, Cinnioglu, & Florentino, 2017). However, recent data have shown that aneuploidy occurs across all 23 chromosome pairs (Mantzouratou & Delhanty, 2011). Therefore, technologies such as FISH that cannot detect aneuploidy in all 23 pairs are at a significant disadvantage. Implementing array comparative genomic hybridization (aCGH) and later, next-generation sequencing (NGS) technologies has demonstrated an increase in pregnancy rates compared to cycles without PGT-A, especially in women of advanced maternal age (Harton et al., 2013; Chang et al., 2016; Rubio et al., 2017; Simon et al., 2018).

Embryonic mosaicism is believed to be a confounder when interpreting PGT-A results (ASRM, 2018). Mosaicism is defined as the presence of two or more cell lines with different genetic compositions in a single sample (Delhanty et al., 1993). This is believed to arise from mitotic errors occurring after fertilization (Sachdev et al., 2017). Mosaic embryos can be classified as fully aneuploid, where two different aneuploid genotypes exist, or diploid-aneuploid mosaic, where one population of the cells is euploid and the other is aneuploid. The percentage of abnormal cells within a diploid-aneuploid mosaic embryo is influenced by the cleavage stage at which the error occurred. Earlier errors occurring during first or second cleavage result in a greater proportion of abnormal cells compared to errors occurring during the third cleavage (Mantzouratou & Delhanty, 2011; Sermon & Viville, 2014; Mantikou et al., 2012).
Traditionally, morphology assessment alone was used to select embryos for transfer; however, this method on its own was an inefficient predictor for reproductive potential of the embryo (Alfarawati et al., 2011). Earlier techniques of embryo biopsy at the cleavage stage did not allow for the detection of mosaicism. Biopsy at the blastocyst stage is increasingly becoming the preferred method for embryo biopsy (Kokkali et al., 2007; De Boer et al., 2004). Cleavage stage biopsy is performed on day 3 embryos composed of at least six cells and involves the removal of typically one cell for subsequent genetic analysis (Hardy & Handyside, 1992). However, limitations of day 3 biopsy include its effect on the reproductive potential of the biopsied embryo and concerns on whether the single cell is representative of the entire embryo (Scott et al., 2013; De Vos & Steirteghsm, 2001). To allow for a more accurate result, the removal of two cells during cleavage stage biopsy has also been proposed. This has even greater concerns for reproductive potential due to the proportion of cell loss from the embryo. (Van de Velde et al., 2001; McArthur et al., 2005; Cohen, Wells, & Munne, 2007). There is an increasing trend toward blastocyst biopsy in recent years (Poli et al., 2019). The blastocyst biopsy technique consists of removing five to ten trophectoderm cells from day 5 or day 6 embryos (Schoolcraft et al., 2010). Since this technique allows for the removal of trophectoderm cells, the inner cell mass, which will go on to form the rest of the fetus, remains undisturbed (De Vos & Steirteghsm, 2001). Also, blastocyst biopsy provides more starting DNA, which would theoretically lead to improved sensitivity and specificity of analysis. In
addition, blastocyst biopsy does not appear to impact reproductive potential of the biopsied embryo (Scott et al., 2013; Kokkali et al., 2007). However, with the increased use of blastocyst trophectoderm biopsy and more sophisticated modalities of subsequent analysis, the frequency of embryos reported as mosaic using PGT-A has become more prominent.

In a retrospective study that compared discrepancies between PGT-A with aCGH and PGT-A with NGS, clinical error rates were found to be comparable between the two technologies (Friedenthal et al., 2017). However, researchers determined that PGT-A with NGS trended toward lower error rates. Array technologies can begin to detect mosaicism when a third of the cells have a chromosomal makeup distinct from others, compared to NGS where discerning low-level mosaicism (20%-50% abnormal cells in the trophectoderm biopsy) is possible (Wells et al., 2014; Rubino et al., 2018).

Although NGS has the advantage of a tighter dynamic range compared with aCGH, more research is required to elucidate the diagnosis of embryonic mosaicism (Fiorentino et al., 2014; Werlin et al., 2017). Several additional limitations of mosaicism detection have been discussed in the literature. The first issue relates to sampling error during biopsy (Scott & Galliano, 2016). The Preimplantation Genetic Diagnosis International Society (PGDIS) recommendations state that, ideally, at least five cells should be biopsied for reliable detection of mosaicism (PGDIS, 2019). However, since knowledge of the distribution of mosaicism in human embryos is
lacking at this time, it is not possible to determine if a random biopsy sample captures
enough cells of different chromosomal complement to allow for the accurate
detection of mosaicism (Scott & Galliano, 2016). Analytical limitations exist as well.
Researchers have questioned whether detection of mosaicism in a biopsy sample is
influenced by noise level in the read distribution resulting from the DNA
amplification or internal company policy cut-offs for low-level mosaicism (Harton et
al., 2017; Rubino et al., 2018; Capalbo et al., 2017). In addition, a 2017 analysis
proposed several mathematical models demonstrating that a single trophectoderm
biopsy at blastocyst stage is unable to determine embryo ploidy accurately enough for
clinical use (Gleicher et al., 2017).

The prevalence of embryos reported as mosaic using PGT-A is estimated to be
5%, although some studies have found rates as high as 20-30% (Kim et al., 2018).
Rates of mosaicism are largely dependent on the chromosomal detection technique
and stage of the embryo at biopsy (Sachdev et al., 2017).

Reporting mosaicism with the use of NGS has led to questions regarding the
ongoing reproductive potential of these embryos and the validity of the mosaic
diagnosis (Munne et al., 2016; Munne & Wells, 2017). One of the apprehensions
about transferring mosaic embryos arises from the concern that an aneuploid or
mosaic aneuploid pregnancy may result in a live-born infant with related congenital
anomalies (Lebedev, 2011).
Mosaicism may develop within a diploid embryo for several reasons including anaphase lag, mitotic nondisjunction, inadvertent chromosome demolition, and premature cell division prior to DNA replication. For these reasons, detection of mosaicism has been found to be high in several analyses (Mantzouratou & Delhanty, 2011; Mantikou et al., 2012; Munne & Wells, 2017). At the blastocyst stage, the frequency of embryos reported as mosaic using NGS methods is highly variable between clinics, ranging from 2-40%; however, most clinics report that mosaic embryos represent between 5-10% of embryos tested (Munne at al., 2016; Fragouli, Munne, & Wells, 2019; Munne, 2019; PGDIS, 2019). Several hypotheses of self-correction mechanisms have been proposed. A mouse model shows that abnormal cells may be allocated to the trophectoderm and leave most of the normal cells in the inner cell mass (Bolton et al., 2016). Experimental evidence also shows that euploid cells possess a growth advantage over aneuploid cells and euploid cells may overtake growth and form the majority of the embryo via differential cell proliferation (Wells & Delhanty, 2000). It is also possible that aneuploid cells undergo apoptosis in the developing embryo (Mantikou et al., 2012).

Since a 2015 study by Greco et al. first showed that mosaic aneuploid embryos can develop into healthy euploid newborns, a significant amount of research has been underway on mechanisms of embryo self-correction and the outcomes and success of mosaic embryo transfer (MET; not be confused with "mock embryo transfer," which is also commonly abbreviated to MET). Blastocysts classified as
mosaic by PGT-A have been reported in multiple studies to implant less frequently and miscarry more frequently than embryos classified as euploid (Spinella et al., 2018; Fragouli et al., 2017; Besser et al., 2017; Zhang et al., 2019). However, due to mechanisms still currently under investigation, these embryos can still produce viable pregnancies with seemingly normal chromosomes. (Greco et al., 2015; Victor et al., 2019; Munne et al., 2017). This remains a controversial topic within a small but growing community of IVF providers who will perform MET (Kim et al., 2018).

With reproductive outcome data growing, what remains unknown is the psychosocial experience of this small group of women who undergo mosaic embryo transfer. The most comprehensive paper that addresses part of the patient experience focuses on counseling considerations for chromosomal mosaicism (Besser & Mounts, 2017). In this study, researchers identified several key issues that required further exploration such as individual laboratory and clinic policies, thorough pre- and post-test counseling, as well as prenatal testing considerations.

The most recent guidelines of the Preimplantation Genetic Diagnosis International Society (PGDIS) on chromosomal mosaicism and mosaic embryo transfer acknowledge the challenges of knowing which embryos are safe to transfer (PGDIS, 2019). However, these guidelines are far from exhaustive, and no current literature puts forth clear criteria that governs all possible scenarios. This leads to much confusion and uncertainty for IVF providers on selecting embryos, and many of these decisions are made on a case-by-case basis.
Since a consensus in the community fails to exist, it is difficult to know the communication conducted with women with mosaic embryos regarding risk, benefits, and outcomes and the factors that are affecting their decision-making. Since MET is still relatively rare, women hoping to find support and information have turned to the internet, and many online support communities have formed as a result. This study is based on grounded theory and addresses the psychosocial aspect of MET, which has not been studied thus far. The purpose of this study is to understand the factors that are important in affecting the decision-making process of women faced with the prospect of MET. Identifying key factors in patient decision-making will allow for improved pre-test and post-test counseling with crucial psychosocial support.
CHAPTER II

METHODS

Research Approval: This study received IRB approval from California State University, Stanislaus on February 11, 2019 (Project #1819-058). An electronic consent form was completed by all survey participants (see Appendix 1 for electronic consent).

Eligibility: Eligible participants for this study were women over the age of 18 who had considered proceeding with transfer of embryos with mosaic results after PGT-A. Participants must have considered MET after learning that one or more of their embryos was determined to be mosaic according to their PGT-A results, regardless of whether this transfer had already occurred at the time of survey.

Exclusion Criteria: Participants must have been given the autonomy to make decisions around MET. Participants who expressed that this decision was not available to them were excluded from analysis.

Recruitment: Participants were recruited through a Facebook group called “My Perfect Mosaic Embryo” for women discussing mosaic PGT-A results. The Facebook group had approximately 614 members at the time the survey was posted. The Facebook group was a private group where membership had to be approved by the administrators of the community. After a request to join the community was approved, the administrator was contacted for approval of a survey post. A posting
was made on the Facebook group and included an introductory explanation about the survey and a link to the online consent form and survey. The survey was reposted once, three weeks after the initial posting, and the survey remained open for data collection a total of one month.

**Procedure**: Data was collected using an online survey, which included primarily multiple-choice questions hosted on the Qualtrics survey platform. The survey consisted of approximately 37 questions and took an estimated 10 minutes to complete (see Appendix 1 for the complete survey). The survey was split into five sections. *Section 1: demographic data* consisted of multiple-choice questions eliciting demographic data including race, highest level of education completed, annual household income, religion, and age. If options did not apply, participants could select “other” and write-in a response. For most questions, participants were also given the option to select “prefer not to answer.” The last question in this section was a “yes” or “no” question that asked participants if they had undergone MET. This response affected whether a subsequent section of the survey would be visible to them. *Section 2: infertility and pregnancy history* included multiple-choice questions on the number of times participants had been pregnant, the number of pregnancy losses, and the outcomes of their pregnancies. The next set of questions in this section contained two tables. In the first table, participants selected which infertility treatments they had undergone. The second table aimed to gather information more specifically on the outcomes of their IVF and PGT-A cycles and whether they proceeded with transfer of
a euploid embryo, mosaic embryo, or had no embryos transferred. Section 3: PGT-A process and results included questions aimed to learn more about a patient’s experience with the PGT-A process and their mosaic results. Section 4: participant background, aimed to learn more about the patient’s psychosocial background. Section 5: mosaic embryo transfer was the last section and only displayed to participants that had selected “yes” when asked if they had undergone mosaic embryo transfer at the end of section 1. In this section, participants were asked where they had undergone MET, the outcome MET, what prenatal testing they planned to complete, and their main reason for undergoing MET. The survey was piloted with colleagues including clinic-based genetic counselors, a laboratory-based genetic counselor, and seven students in a genetic counseling training program. As an incentive to participate in the survey, the first 60 participants received a $15 Amazon gift card. Participants were offered the option to click a link to provide their email address to receive the gift card after completing the survey. Participants were also asked to leave their email address if they were receptive to being contacted for a follow-up interview. Statistical analysis was conducted using jamovi 0.9.6.8. Multivariate or chi-square goodness of fit analysis was completed to compare the distribution of participants who selected different variables and to compare between the two groups of participants, those who had undergone MET and those who had not. Mann-Whitney U tests were performed to analyze Likert-type data and ordinal data between the two groups of participants. Fisher’s Exact Test was performed to compare binary data in two-by-two contingency
tables as well as analyze multiple-response questions. A cut-off of \( p < 0.05 \) was used to determine statistical significance. Qualitative analysis of free-text responses was not performed due to insufficient number of responses for statistical significance. If free-text responses echoed sentiment addressed in multiple-choice options, they were recategorized into the corresponding multiple-choice option for statistical analysis and significance.
CHAPTER III

RESULTS

Fifty-nine survey responses were received. Two participants were excluded from statistical analysis because it was determined upon review of their free-text responses that they met exclusion criteria. It was not possible to determine an exact response rate due to the fluctuation of Facebook group members. Membership changed from 614 members when the survey was initially posted to 648 members when data collection concluded. However, despite this fluctuation, the survey response rate was between 9.1-9.6%. The completion rate of the survey was 93% (54/59).

Section 1: Demographic Data

Age: Most participants were between the ages of 36-40 (29/57, 50.1%) and 41-45 (15/57, 26.3%). None of the participants reported being younger than twenty-four or older than forty-five (Table 1; Table 1, Appendix B).

Race: Most participants reported their race as being white/Caucasian (48/57, 84%; Table 1; Table 2, Appendix B).

Highest Completed Level of Education: Half of the participants reported they had achieved at least a graduate degree (28/57, 50%), and most participants held at least an Associate’s degree (46/57, 80.7%; Table 1; Table 3, Appendix B).
**Household Income:** Most participants reported earning more than $100,000 per year (36/53, 67.9%; Table 1; Table 4, Appendix B).

**Religion:** Over half of the participants reported their religion as either Christian or Catholic (37/57, 65%; Table 1; Table 5, Appendix B).

No statistically significant differences occurred in the demographics between participants who had undergone MET and those who had not. Results are summarized in Table 1.
### Table 1

**Summary of Participant Demographic Data**

<table>
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<th>P-value</th>
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<td><strong>Age</strong></td>
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<tr>
<td>25-30 years old</td>
<td>1 (4.5%)</td>
<td>1 (2.9%)</td>
<td>0.957</td>
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<tr>
<td>31-35 years old</td>
<td>4 (18.1%)</td>
<td>7 (20%)</td>
<td></td>
</tr>
<tr>
<td>36-40 years old</td>
<td>11 (50%)</td>
<td>18 (51%)</td>
<td></td>
</tr>
<tr>
<td>41-45 years old</td>
<td>6 (10.5%)</td>
<td>9 (15.8%)</td>
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</tr>
<tr>
<td><strong>Race</strong></td>
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<td></td>
<td>0.513</td>
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<tr>
<td>White/Caucasian</td>
<td>18 (81.8%)</td>
<td>30 (85.7%)</td>
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</tr>
<tr>
<td>African-American</td>
<td>1 (4.5%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>3 (13.6%)</td>
<td>4 (11.4%)</td>
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<tr>
<td>Asian</td>
<td>0</td>
<td>1 (2.9%)</td>
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<tr>
<td><strong>Education</strong></td>
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<tr>
<td>Did not complete high school</td>
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<td>High School Diploma/GED</td>
<td>1 (4.5%)</td>
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<td>Technical training</td>
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<tr>
<td>Some College</td>
<td>3 (13.6%)</td>
<td>3 (8.6%)</td>
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<td>Associate’s degree</td>
<td>1 (4.5%)</td>
<td>1 (2.9%)</td>
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<td>Graduate degree</td>
<td>10 (45%)</td>
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<td><strong>Income</strong></td>
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<tr>
<td>Catholic</td>
<td>8 (36.4%)</td>
<td>11 (31.4%)</td>
<td></td>
</tr>
<tr>
<td>No religious affiliation</td>
<td>1 (4.5%)</td>
<td>10 (28.8%)</td>
<td></td>
</tr>
<tr>
<td>Agnostic</td>
<td>4 (18.2%)</td>
<td>3 (8.6%)</td>
<td></td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>0</td>
<td>1 (2.9%)</td>
<td></td>
</tr>
<tr>
<td>Muslim</td>
<td>1 (4.5%)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Statistical analysis was completed using chi-square goodness of fit test for race and religion and a Mann-Whitney U Test for age, education, and income.

Section 1 included a “yes” or “no” question on whether participants had undergone MET. Twenty-two participants (38.6%) selected “yes,” and thirty-five (61.4%) selected “no.” Selecting “yes” to this question displayed an additional set of...
questions related to MET prior to the conclusion of the survey. Participants who selected “no” were not shown this set of questions.

**Section 2: Pregnancy & Infertility History**

Participants were asked a series of questions regarding their pregnancy history and infertility. Differences between the two groups of participants were not statistically significant for any variable of pregnancy history and cause of infertility.

Statistical analysis is summarized in Table 2.

**Table 2**

*Statistical Analysis of Participants’ Fertility History*

<table>
<thead>
<tr>
<th>Variable Analyzed</th>
<th>P-value</th>
<th>Test</th>
<th>Sample Size (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy loss</td>
<td>0.772</td>
<td>Fisher’s Exact Test</td>
<td>56</td>
</tr>
<tr>
<td>Number of miscarriages</td>
<td>1.000</td>
<td>Mann-Whitney U Test</td>
<td>58</td>
</tr>
<tr>
<td>Number of full-term deliveries</td>
<td>0.261</td>
<td>Mann-Whitney U Test</td>
<td>48</td>
</tr>
<tr>
<td>Traumatic pregnancy experience</td>
<td>0.201</td>
<td>Fisher’s Exact Test</td>
<td>56</td>
</tr>
<tr>
<td>Cause of infertility</td>
<td>0.085</td>
<td>Mann-Whitney U Test</td>
<td>54</td>
</tr>
</tbody>
</table>

Participants responded to questions with a numerical response by selecting a range of values; responses were translated into numeric values from 1-4 for a Mann-Whitney U Test to compare means between the two groups of participants. Participants selected “yes” or “no” to questions assessing whether they had experienced a pregnancy loss or had experienced a traumatic pregnancy, and Fisher’s Exact Test was performed to analyze responses between the two groups of participants.
Infertility Treatment History: Participants were asked which treatments they had undergone in their last five fertility treatment cycles. Participant responses are summarized in Figure 1.

![Type of IVF Cycle](image)

**Figure 1.** Type of IVF cycle. Summary of participants’ type of IVF cycle in their five most recent IVF cycles (n = 55).

The average number of total IVF cycles was greater in participants who had undergone MET compared to those who had not, but this trend was not statistically significant (M = 3.19, 2.59; p=0.168, Table 3). Statistical analysis of participants’ type of IVF cycle is summarized in Table 3.
Table 3

*Statistical Analysis of Participants’ Five Most Recent IVF Cycles*

<table>
<thead>
<tr>
<th>Variable Analyzed</th>
<th>Mean (MET)</th>
<th>Mean (No MET)</th>
<th>P-value</th>
<th>Sample Size (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number IVF cycles</td>
<td>3.19</td>
<td>2.59</td>
<td>0.168</td>
<td>55</td>
</tr>
<tr>
<td>Number of participants who used a gamete donor (egg or sperm donor)</td>
<td>2.0</td>
<td>2.0</td>
<td>0.632</td>
<td>55</td>
</tr>
<tr>
<td>Number of IVF cycles without PGT-A</td>
<td>1.10</td>
<td>0.79</td>
<td>0.407</td>
<td>55</td>
</tr>
</tbody>
</table>

An Independent Samples T-Test was performed to analyze differences in the means between the two groups of participants for the total number of IVF cycles and the number of IVF cycles without PGT-A. Fisher’s Exact Test was performed to analyze whether the use of a third-party donor was statistically significant between the two groups of participants.

**PGT-A Results:** Participants reported their PGT-A results from IVF cycles that included PGT-A. A breakdown of participants’ PGT-A results from their last five IVF PGT-A cycles is provided in Figure 2.
Figure 2. Results of IVF PGT-A cycles. Summary of participants’ IVF PGT-A results in their five most recent IVF PGT-A cycles.

Statistical analysis was completed to analyze remaining participant cycle result data, and results are summarized in Table 4. The average number of IVF cycles with PGT-A was statistically greater in participants who had undergone MET ($M = 2.52, 1.82; p=0.047$, Table 4). The number of cycles with a mosaic or euploid result was not statistically significant between the two groups of participants (Table 4).
Table 4

<table>
<thead>
<tr>
<th>Variable Analyzed</th>
<th>Mean (MET)</th>
<th>Mean (No MET)</th>
<th>P-value</th>
<th>Sample Size (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number IVF PGT-A cycles</td>
<td>2.52</td>
<td>1.82</td>
<td>0.047*</td>
<td>54</td>
</tr>
<tr>
<td>Number of IVF PGT-A cycles with mosaic results</td>
<td>1.38</td>
<td>1.29</td>
<td>0.632</td>
<td>52</td>
</tr>
<tr>
<td>Number of IVF PGT-A cycles with euploid results</td>
<td>1.29</td>
<td>0.88</td>
<td>0.180</td>
<td>54</td>
</tr>
</tbody>
</table>

An Independent Samples T-Test was performed to analyze differences in the means between the two groups of participants.

Section 3: PGT-A Process and Results

Participants were asked a series of questions presented on a 5-point Likert-type scale to gather information on their understanding of PGT-A results, their trust in the accuracy of PGT-A results, their perceived support from their medical team regarding MET, and their risk perception of MET. The means of the two groups of participants and subsequent statistical analysis are presented in Table 5. A breakdown of participant responses to Likert-type scale questions is provided in Figure 3.
Table 5

*Statistical Analysis of Likert-type Scale Data*

<table>
<thead>
<tr>
<th>Variable Analyzed</th>
<th>Mean</th>
<th>Mean</th>
<th>P-value</th>
<th>Sample Size (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(MET)</td>
<td>(No MET)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Understanding of PGT-A results</td>
<td>3.57</td>
<td>3.76</td>
<td>0.832</td>
<td>54</td>
</tr>
<tr>
<td>Trust in the accuracy of PGT-A results</td>
<td>2.76</td>
<td>2.82</td>
<td>0.874</td>
<td>54</td>
</tr>
<tr>
<td>Support from medical team</td>
<td>4.19</td>
<td>3.42</td>
<td>0.017*</td>
<td>54</td>
</tr>
<tr>
<td>Risk perception of MET</td>
<td>3.05</td>
<td>2.73</td>
<td>0.198</td>
<td>54</td>
</tr>
</tbody>
</table>

Analysis of the variables was completed using a Mann-Whitney U Test to compare means between the two groups of participants. Participants’ original responses were based on a 5 point Likert-type scale and were translated to numeric values ranging from 1-5.

---

**Figure 3.** Composition of Likert-type scale responses. Risk Perception of MET; 1: Not at all risky, 2: Slightly risky, 3: Somewhat risky, 4: Risky, 5: Very risky. Support from Medical Team; 1: Not at all supportive, 2: Slightly supportive, 3: Somewhat supportive, 4: Supportive, 5: Very supportive. Trust in the Accuracy of PGT-A Results; 1: Do not trust them at all, 2: Trust them little, 3: Trust them a moderate amount, 4: Trust them highly, 5: Trust them completely. Understanding of PGT-A Results; 1: Did not understand them at all, 2: Understood them a little bit, 3: Somewhat understood them, 4: Understood them well, 5: Understood them very well (n = 54).
Participants’ perceived support from their medical team was statistically significant between the two groups of participants. Participants who had undergone MET felt their medical team was more supportive of this decision. A breakdown of participant responses and comparison of means regarding support from medical team between those who had undergone MET and those who had not is provided in Figure 4.
Figure 4. Support from medical team regarding MET. a) Summary of participant responses on provider support regarding decision to elect MET. Responses were re-coded for statistical analysis as follows: 1= Not at all supportive, 2= Slightly supportive, 3= Somewhat supportive, 4= Supportive, 5= Very supportive (n = 54). b) Comparison of means between participants who elected MET and those who had not. M = 4.19 (MET), M = 3.42 (No MET) (n = 54).
**Partner Agreement on MET:** Participants were asked how much they felt they and their partner agreed on transferring a mosaic embryo. Participants selected responses presented on a 5-point Likert-type scale. One participant reported that they did not have a partner. Participants who had MET reported higher levels of agreement with their partners compared to those who had not undergone MET ($M = 4.67, 3.97$). The differences in partner agreement were statistically significant between the two groups ($p=0.019$, Mann-Whitney U Test). A breakdown of participant responses and comparison of means regarding partner agreement on MET is provided in Figure 5.
Figure 5. Partner agreement regarding MET. a) Summary of participant responses regarding partner agreement on MET. Responses were re-coded for statistical analysis as follows: 1= Not at all, 2= Little, 3= Moderately, 4= Mostly, 5= Completely. b) Comparison of means between participants who elected MET and those who had not. $M = 4.67$ (MET), $M = 3.97$ (No MET) ($n = 54$).
Initial Discussion of PGT-A: Participants were asked where they had first heard about PGT-A and given the option to choose from several multiple-choice options as well as a free-text option. Over half the participants reported first learning about PGT-A from their fertility clinic (34/54, 63%). A further breakdown is provided in Figure 3. Three participants selected “other.” Of these, two stated they had learned about PGT-A from friends who had done IVF, and one learned from her work as a fertility nurse.

Figure 6. Where participants’ first learned about PGT-A. Summary of participant response regarding where they had first heard about PGT-A (n = 54).
**PGT-A Discussions with Providers:** Participants were asked with which providers they had discussed their mosaic PGT-A results. Participants were allowed to select multiple responses. The majority of participants had discussed their results with their reproductive endocrinologist at some point (44/54, 81.5%). Whether or not a participant discussed PGT-A results with a specific provider was not statistically significant between participants who had MET and those who had not. A breakdown of participant responses regarding their discussion of PGT-A results with other providers is provided in Figure 7, and statistical analysis is provided in Table 6.

Table 6

<table>
<thead>
<tr>
<th>Variable Analyzed</th>
<th>Frequency (MET)</th>
<th>Frequency (No MET)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive endocrinologist</td>
<td>17 (81%)</td>
<td>27 (81.8%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Genetic counselor at IVF clinic</td>
<td>4 (19%)</td>
<td>10 (30.3%)</td>
<td>0.526</td>
</tr>
<tr>
<td>Genetic counselor at PGT-A lab</td>
<td>10 (47.6%)</td>
<td>18 (54.6%)</td>
<td>0.781</td>
</tr>
<tr>
<td>Embryologist</td>
<td>5 (23.8%)</td>
<td>9 (27.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>IVF nurse</td>
<td>4 (19%)</td>
<td>8 (24.2%)</td>
<td>0.654</td>
</tr>
</tbody>
</table>

Statistical analysis was completed using Fisher’s Exact Test to analyze responses between the two groups of participants.
Participants’ discussions with providers regarding PGT-A results. Summary of participant responses regarding discussion with providers of PGT-A results. Participants were allowed to select multiple responses. Percentages correspond to what percentage of participants selected having a discussion with the corresponding provider ($n = 54$).

Additionally, the number of providers that participants spoke to about their PGT-A results was not statistically different between the two groups of participants ($p=0.420$, Independent samples T-test). Participants were also asked to select one provider with whom they had mainly discussed their results. Participants reported mainly discussing their results with the genetic counselor at the laboratory that performed the PGT-A (18/46, 39.1%). Less often, participants reported mainly discussing results with the reproductive endocrinologist (15/46, 32.6%) or the genetic counselor at the IVF clinic (13/46, 28.3%).
Resources Given by Providers: Participants were asked if they had been given resources by their providers to help with their decision regarding MET. If participants selected “yes,” they were asked to describe what they had been given. The majority of participants reported that they had not been given any resources to help with their decision-making (41/54, 75.9%). Five participants said they were not sure or couldn’t remember (5/54, 9.3%). Eight participants reported that they had been given resources (8/54, 14.8%). Their responses are described in Table 7.

Table 7

Participant Free-Text Responses When Asked to Describe What Resources They had Been Given by Providers

<table>
<thead>
<tr>
<th>Response</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>“One of our mosaics was recommended for transfer if our euploids don’t work.”</td>
<td></td>
</tr>
<tr>
<td>“Lit on the full expression of our segmental aneuploidy”</td>
<td></td>
</tr>
<tr>
<td>“Consultation”</td>
<td></td>
</tr>
<tr>
<td>“Discussion with a genetic counselor”</td>
<td></td>
</tr>
<tr>
<td>“Second opinion to a genetic counselor and geneticist (doctor who sees children with chromosomal abnormalities)”</td>
<td></td>
</tr>
<tr>
<td>“Strongly discouraged to attempt transfer of our segmental mosaics...one has chromosome 15 implicated, the other chromosome 9...both are associated with uniparental disomy”</td>
<td></td>
</tr>
<tr>
<td>“Referred to a genetic counselor”</td>
<td></td>
</tr>
</tbody>
</table>

Free-text responses revealed that three participants were referred to have a discussion with a genetic counselor, one participant was referred for a consultation but did not specify with whom, and two participants were provided scientific literature.

Possible Outcomes of MET: Participants were asked to select what possible outcomes of MET they had been informed about. Participants were allowed to check all responses that applied. Frequency of participant responses are summarized in Figure 8.
Figure 8. Participants’ knowledge of possible MET outcomes. Summary of participants' knowledge of possible MET outcomes. Participants were allowed to select multiple responses, and frequencies of responses are displayed ($n = 52$).

The mean number of outcomes selected by all the participants was 3.58. For participants who had MET, the average number of outcomes selected was 3.71, and in the group of those who had not had MET, the average was 3.50. This difference was not statistically significant ($p=0.608$, Independent Samples T-Test).

Being informed about a particular possible outcome was not statistically significant between the two groups of participants. Results are summarized in Table 8.
Table 8

**Statistical Analysis of Participants’ Knowledge of Possible MET Outcomes**

<table>
<thead>
<tr>
<th>Variable Analyzed</th>
<th>Frequency (MET)</th>
<th>Frequency (No MET)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>n = 20</em></td>
<td><em>n = 32</em></td>
<td></td>
</tr>
<tr>
<td>Miscarriage</td>
<td>20 (100%)</td>
<td>26 (81.3%)</td>
<td>0.071</td>
</tr>
<tr>
<td>Pregnancy complication</td>
<td>8 (40%)</td>
<td>15 (46.9%)</td>
<td>0.776</td>
</tr>
<tr>
<td>Chromosomal problem at birth</td>
<td>14 (70%)</td>
<td>20 (62.5%)</td>
<td>0.766</td>
</tr>
<tr>
<td>Healthy live-born</td>
<td>17 (85%)</td>
<td>23 (71.8%)</td>
<td>0.330</td>
</tr>
<tr>
<td>Failure to implant</td>
<td>19 (95%)</td>
<td>28 (87.5%)</td>
<td>0.372</td>
</tr>
</tbody>
</table>

Statistical analysis was completed using Fisher’s Exact Test to analyze responses between the two groups of participants.

**Main Concerns Regarding MET:** Participants were asked to select what possible outcomes of MET were their main concerns. Participants were allowed to check all responses that applied. Frequencies of participant responses are summarized in Figure 9.
The mean number of concerns selected by all the participants was 1.91. In the participants that had MET, the average number of concerns selected was 1.76; in the group that had not undergone MET, the average number of concerns was 2.0. This difference was not statistically significant (p=0.465, Independent Samples T-Test).

Further analysis was performed to determine whether participants were more concerned about a particular outcome between the two groups of participants. There were no statistically significant differences. Results are summarized in Table 9.

Figure 9. Participants’ concerns regarding MET. Summary of participants’ concerns regarding MET. Participants were permitted to select multiple responses, and frequencies of responses are displayed (n = 54).
Table 9

**Statistical Analysis of Participants’ Concerns with MET**

<table>
<thead>
<tr>
<th>Variable Analyzed</th>
<th>Frequency (MET)</th>
<th>Frequency (No MET)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage</td>
<td>11 (52.4%)</td>
<td>15 (45.5%)</td>
<td>0.619</td>
</tr>
<tr>
<td>Pregnancy complication</td>
<td>3 (14.3%)</td>
<td>11 (33.3%)</td>
<td>0.119</td>
</tr>
<tr>
<td>Chromosomal problem at birth</td>
<td>17 (90%)</td>
<td>30 (90.1%)</td>
<td>0.485</td>
</tr>
<tr>
<td>Failure to implant</td>
<td>5 (23.8%)</td>
<td>10 (30.3%)</td>
<td>0.604</td>
</tr>
</tbody>
</table>

Statistical analysis was completed using Fisher’s Exact Test to analyze responses between the two groups of participants (n = 54).

**Risk Perception of MET:** Participants were asked how risky they perceived mosaic embryo transfer to be. Participants selected responses presented on a Likert-type scale. Overall, participants who had MET reported perceiving higher levels of risk compared to those who had not undergone MET (M = 3.05, 2.73). The difference in risk perception was not statistically significant between the two groups (p = 0.198, Mann-Whitney U Test).

**Section 4: Participant Background**

Participants were asked several multiple-choice questions to assess certain background and social factors surrounding their mosaic PGT-A results.

**Stress Due to Infertility:** Participants were asked how much stress they felt due to infertility and other pressures. Participants selected responses presented on a 5-point Likert-type scale. The average reported stress levels were overall high in both groups (M = 4.35). The differences in stress levels was not statistically significant between the two groups of women (p = 0.929, Mann-Whitney U Test).
Resources Used to Aid Decision-making After PGT-A: Participants were asked which resources they had used to help make decisions after PGT-A. Participants were allowed to select multiple responses. The majority of participants had used advice from their providers (44/54, 81.5%) as well as medical websites and articles to aid their decision-making (46/54, 85.2%). A breakdown of participant responses regarding their utilization of resources to aid their decision-making is provided in Figure 10. Whether or not a participant employed a particular resource was not statistically significant between participants who had MET and those who had not. A summary of statistical analysis is provided in Table 10.

Figure 10. Resources utilized by participants'. Summary of decision-making resources used by participants. Participants were permitted to select multiple responses, and frequencies of responses are displayed (n = 54).
Table 10

Statistical Analysis of Resources That Participants Utilized to Aid Their Decision-Making After PGT-A Results

<table>
<thead>
<tr>
<th>Resource</th>
<th>P-Value</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advice from providers</td>
<td>0.284</td>
<td>Fisher’s Exact Test</td>
</tr>
<tr>
<td>Advice from family/friends</td>
<td>0.667</td>
<td>Fisher’s Exact Test</td>
</tr>
<tr>
<td>Brochures or pamphlets</td>
<td>1.000</td>
<td>Fisher’s Exact Test</td>
</tr>
<tr>
<td>Medical websites or articles</td>
<td>1.000</td>
<td>Fisher’s Exact Test</td>
</tr>
<tr>
<td>Social networking websites</td>
<td>0.576</td>
<td>Fisher’s Exact Test</td>
</tr>
</tbody>
</table>

Statistical analysis was completed using Fisher’s Exact Test to analyze responses between the two groups of participants (n = 54).

In addition, the average number of resources utilized was 2.6 in both groups of women, and no statistically significant difference was seen between the two groups (p=0.960, Independent Samples T-Test).

**Time Spent Seeking Information:** Participants were asked how many hours they spent a week seeking out information related to this topic. On average, participants spent 3-5 hours a week. No statistically significant difference was found between the two groups of participants (p=0.731, Mann-Whitney U Test).

**Self-Perception as a Risk-Taker:** Participants were asked how much they considered themselves to be risk-takers. Participants selected responses presented on a 5-point Likert-type scale. About half of the participants rated themselves to be a moderate risk-taker (29/54, 53.7%). No statistically significant difference was seen between the two groups of participants (p=0.598, Mann-Whitney U Test).

**Additional Information:** Participants were asked if there was any additional information that they would like to share about their experience with MET and provided an open-text response. Common themes included describing their mosaic
embryo results, being upset at the lack of information available, and wishing for better and more productive conversations with infertility medical providers. One woman shared her dissatisfaction with her questions that have gone unanswered. Other women discussed how they wish that some providers were more willing to transfer mosaic embryos. Three women shared details on their ongoing pregnancies following MET. A summary of all participants’ free-text responses is provided in Table 8, Appendix B.

**Section 5: Mosaic Embryo Transfer**

This section of questions was only visible to participants who selected that they had undergone MET. A total of 20 participants completed this series of questions.

**Location of MET clinic:** Participants were asked where the clinic in which they had undergone MET was located. Most participants were located in the United States (16/20, 80%). A more detailed breakdown of geographical location is provided in Figure 11.
Figure 11. Location of MET. Geographical location where participants had undergone their mosaic embryo transfer. United States (Southwest) = AZ, TX, NM, OK. United States (Southeast) = WV, VA, KY, TN, NC, SC, GA, AL, MS, AK, LA, FL. United States (Northeast) = ME, MA, RI, CT, NH, VT, NY, PA, NJ, DE, MD. United States (Midwest) = OH, IN, MI, IL, MO, WI, MN, IA, KS, NE, ND, SD. United States (West) = CO, WY, MT, ID, WA, OR, UT, NV, CA, AK, HI (n = 20).

**Outcome of MET:** Participants were asked to select the outcome of their mosaic embryo transfer. Most patients reported an ongoing pregnancy (13/20, 65%) or live-birth of a healthy baby (4/20, 20%). More detail about MET outcomes is provided in Figure 12.
Figure 12. Outcomes of MET. Summary of participants’ reported outcomes of MET (n = 20).

It is important to note that the pregnancy rates displayed in Figure 12 are not representative of what is reported in the literature. The average clinical pregnancy rate following MET is 30-40% (Munne et al., 2017; Victor et al., 2019).

**Prenatal Testing after MET:** Participants were asked which prenatal testing they completed or planned to complete following MET. Participants were allowed to select more than one response. Most participants had completed or planned to complete some sort of testing (14/20, 70%). A breakdown of participant responses is provided in Figure 13.
Figure 13. Prenatal testing considered after MET. Summary of prenatal testing options considered by participants. Participants were permitted to select multiple responses, and frequencies of responses are displayed ($n = 20$).

**Main Reason for Proceeding with MET:** Participants were asked to select their main reason for proceeding with MET. Most participants reported that they proceeded with MET because they felt it was their last chance to have a baby (12/20, 60%). Participant responses are summarized in Figure 14.
Figure 14. Main reason for proceeding with MET. Participants’ main reasons for proceeding with MET (n = 20).

Additional Information: Participants were asked an open-text question asking if they would like to share any additional information about their experience with MET. The themes in the participants’ responses were similar to previous open-text responses. One participant described her thoughts as follows, “There are so many complexities including that only some types of mosaics are ‘fit’ to be transferred. Clearer communication on the different types of embryos etc. is needed to support patients and their decision-making.” One participant also mentioned the potential use of a gestational carrier in the future and therefore saving her euploid embryos for possible surrogacy. Another participant’s responses included further IVF cycles as being cost-prohibitive: “IVF is so expensive and I am 38 years old and our retrieval
resulted in 2 low-level and 2 high-level mosaics and 1 abnormal. We can’t afford another cycle.” Participant free-text responses are summarized in Table 9, Appendix B.
CHAPTER IV

DISCUSSION

The need for more understanding of women’s experiences when faced with mosaic PGT-A results is apparent in the responses of the participants of this current study. This study had several findings that may help guide further research. Results show that women use input from their providers as a powerful decision-making tool. In this cohort of women, 67% of women reported that a genetic counselor, either at their IVF clinic or PGT-A lab, was the primary provider with whom they discussed their PGT-A results, and 75% of women reported speaking to either a lab-based or clinic-based genetic counselor about their PGT-A results (Figure 7). This highlights the importance of genetic counselors in supporting patient decision-making when presented with this type of result. In addition, many women reported speaking to both counselors, which alludes to the overlapping yet distinct role of both types of genetic counselors in the decision-making process.

The data collected in this study did not show a statistical difference between participants in the two groups who had spoken to a genetic counselor or who had not. Women who had MET and women who had not had spoken to a genetic counselor at similar rates (Figure 7). Conversely, the level of support that women felt from their medical team was statistically significant between women who had MET and women who had not (Table 5; Figure 4). Women who elected MET rated their medical...
providers as being significantly more supportive of their decision than those women who not elected MET. It is unknown if providers encouraged MET; however, one participant cited that her main reason for MET was that her doctor recommended to do so (Figure 14). It is also possible that participants who rated their providers as less supportive were not given the decision to elect MET, and therefore did not undergo MET.

When it came to resources utilized to aid their decision-making, the majority of participants had utilized advice from their providers (44/54, 81.5%) as well as medical websites and articles (46/54, 85.2%; Figure 10). While this is further evidence for the importance of discussions with providers, the only resource that may be influencing decision-making more is medical and scientific articles. It is not known whether these articles were peer-reviewed or literature from professional organizations. It is important for providers to be aware of the influence of outside resources on the decision-making of women considering MET. In contrast, it was clear that most women were not utilizing information in brochures or pamphlets, whether or not they had been provided the literature by their clinic. Few women were utilizing advice from their family or friends when making decisions after PGT-A. It is possible this could be due to many couples electing not to share their IVF or other infertility treatments with those in their social circle rather than the lack of influence of friends and family. Fifty-seven percent (32/56) of participants reported utilizing social networking websites (Figure 10). This number is likely higher than in the general population due to the method of recruitment. Additionally, given that this
survey was posted on a Facebook group, this result implies that although 100% of participants are part of an online support community, not all of them are using social media to make decisions regarding MET.

Although this particular study was only open to women who had considered MET, the results of this study showed partner agreement to be a significant factor in decision-making. Women who had elected MET rated stronger partner agreement regarding MET than women who did not (Figure 5). This highlights the importance of partners in decision-making, as well as the benefit of educating and involving them in the conversation.

Of note in this study, none of the demographic variables surveyed proved statistically significant in MET decision-making (Table 1). While one participant did note in her free-text response that another IVF cycle was cost-prohibitive, no statistically significant difference in income levels was seen between the two groups.

An assumption of this study was that women with longer and more complicated infertility histories would be more likely to transfer an embryo with mosaic results (Besser et al., 2019). Overall, no difference was seen between the two groups in the number of reported prior miscarriages, pregnancy losses, or traumatic pregnancy experiences (Table 2). Additionally, this finding challenges assumptions that women with more traumatic pregnancy histories may be more likely elect MET; instead, pregnancy history may not be an important factor in decision-making.

Based on free-text comments, there appears to be a strong desire by women who are considering MET to receive comprehensive counseling and have their
questions regarding long-term outcomes answered. Presently, this is a struggle for medical providers due to the limited outcome data currently available (Besser et al., 2019).

It is also important to note that for some women undergoing PGT-A, their pursuit of IVF may not be due to an underlying fertility issue but rather one of heritable risks. In this cohort of women, two participants reported pursuing PGT-A with concurrent preimplantation genetic testing for monogenic (single gene) disorders (PGT-M), and both women had MET. Due to the small sample size of this study, it is unknown how this may have factored into their decision-making.

Since data is still emerging around MET and the full scope of risks is still unknown, it is not surprising that most participants rated MET to be “somewhat risky” (31/56, 55.4%). However, risk perception of MET was not statistically different between the two groups of participants, and neither was participants’ perception of how much they consider themselves to be a risk-taker. More exploration is needed on participants’ understandings of MET risks to clarify how risk perception may be related to a willingness to assume risk by electing MET.

Besser et al. (2019) found that increased age and previous number of egg retrievals were found to be significant positive contributors to the decision to pursue MET. In this cohort of women, age was not found to be a statistically significant difference between women who had MET and those who had not, but the total number of IVF PGT-A cycles was significantly higher in women who elected MET (p=0.047, Table 4). Pursuing additional fertility treatment may lead to increased
physical, psychological, and financial burden, and therefore MET may be a more preferable option for some patients (Besser et al., 2019).

A committee opinion put forth by ASRM states that at minimum IVF clinics should provide information to patients concerning procedures that are not performed by the treating clinic (ASRM, 2014). Participant free-text responses revealed that at least one participant was not aware of her IVF providers’ policy on MET until she received mosaic results following PGT-A (Table 8, Appendix B). This reveals a possible gap in the pre-test counseling women are receiving.

Current counseling recommendations and guidelines state that women receive prenatal genetic counseling and discuss prenatal testing options and limitations following MET (Besser & Mounts, 2017). Besser et al. (2019) found that 6/11 (54.5%) of women underwent an amniocentesis after MET. In this current study, 14/20 (70%) of women considered prenatal testing, and 45% pursued or planned to pursue an amniocentesis (9/20; Figure 13). One participant reported considering chorionic villus sampling (CVS). This was noteworthy since amniocentesis is often recommended over CVS after MET due to the chorionic villus having been derived from the trophoderm cells upon which the PGT-A was previously performed. CVS analyzes placental cells which are of trophodermal origin. Therefore, it is possible that abnormal results of a CVS may underlie confined placental mosaicism rather than true fetal aneuploidy (Besser & Mounts, 2017). There is a need for more insight into patient decision-making around prenatal testing after MET.
In one study, 17% of women with mosaic embryos elected to maintain these embryos in cryogenic storage rather than discarding or transferring them (Besser et al., 2019). Although participants in this current study were not surveyed on what they had ultimately done with their mosaic embryos if they did not elect MET, it is possible that some of these women have kept these embryos in storage and may transfer at a later date.

Overall, the results of this study show that most women were aware of at least some of the possible complications and outcomes of MET (Figure 8). Of the five possible outcomes, women on average were aware of about three to four outcomes. Women were aware of the risks for miscarriage, failed implantation, and chromosomal problems at birth and equally aware about the possibility of an apparently healthy live-birth. Women were least aware about the possibility of a pregnancy complication with only 24/54 (44%) participants reporting this was a risk that was discussed with them. While research is limited in this area, pregnancies resulting from conception with mosaic embryos may have a higher risk of prenatal and perinatal complications, due to the possibility of persisting placental mosaicism (Besser & Mounts, 2017). This reveals another possible gap in the counseling that these women are receiving.

When asked which of the concerns of MET was paramount to them, 46/54 (85%) of women reported the risk for a chromosomal abnormality at birth is their main concern following MET (Figure 9). Recent data shows that it is possible that risk for chromosomal abnormality in live-borns may not be as significant once
successful implantation has been established. In a recent analysis of live-birth rates after MET compared to euploid embryo transfer, while the live-birth rate was significantly lower after MET, there were no reported congenital anomalies, and all infants were seemingly healthy (Zhang et al., 2019).

Since this study did not sample women from a specific center, it is less likely that overall trends of patient decision-making were influenced by center-specific policies and procedures. It is important to note that the majority of participants who reported undergoing MET were from the United States; therefore, it is unknown how decision-making may vary internationally for women considering MET. For example, one participant explained in her free-text response that she was from Spain and had been advised to undergo MET without a discussion with a genetic counselor (Table 8, Appendix B). More research is necessary regarding the counseling women are receiving and the services they have available internationally.

It was also noted that in several cases, after obtaining mosaic results, women did not utilize PGT-A in subsequent IVF cycles. Perhaps, women may realize after receiving mosaic results that this is information they would rather not have. Rates of IVF without PGT-A went from 34% in the first cycle to 46% in women pursuing a fifth (or greater) IVF cycle (Figure 1). More exploration is necessary when determining possible causes of this decline of PGT-A utilization in subsequent IVF cycles. Besser & Mounts (2019) highlight the importance of discussing PGT-A risks, benefits, limitations, and the four possible results of testing embryo chromosome testing (euploid, aneuploid, mosaic, test failure/insufficient DNA) with women
pursuing PGT-A. It is possible that women were not fully counseled on PGT-A when they received their results or that they were not anticipating how complicated their decision-making may be. This could also be due to the additional cost of PGT-A to an already costly procedure. A study by Gebhart et al. (2016) that analyzed decision-making and PGS (PGT-A) reported that 16% of patients considering PGT-A considered the decision of whether to accept or decline PGT-A to be a difficult or extremely difficult decision.

A survey looking at MET practices across the United States was completed by 252 assisted reproductive technology (ART) clinics and found clinics in the Northeastern United States were more likely to have undergone MET compared to other regions (Kim et al., 2018). The data from our current study showed similar rates between most areas compared to the 2018 analysis. The exception was the Southwestern United States where in this study only one participant reported undergoing MET. This is likely because, since this study was surveying actual recipients of MET, there was a much smaller sample size compared to the 2018 analysis surveying ART clinics.

**Limitations of This Study**

This study has several limitations. First, women were surveyed from an online Facebook group titled “My Perfect Mosaic Embryo.” The name of the Facebook group itself implies potential ascertainment bias. By using the adjective “perfect” to refer to one’s mosaic embryo, women in this group may hold more hopeful and positive opinions on MET compared to the general population of women considering
MET. Second, women who have either already undergone MET or seriously considered MET are more likely to have searched for support communities; therefore, the proportion of women who underwent MET after considering mosaic PGT-A in this study may be overestimated. Third, many women who selected “No” when asked if they had ever undergone MET may still go on to transfer at a later time. Fourth, women were not surveyed regarding the extent or type of embryonic mosaicism, and, therefore, it is not possible to know if the findings of this study would apply for different classifications of mosaicism. More research is emerging on differing rates of embryo implantation and live-birth depending on type of aneuploidy (segmental vs. whole chromosome), and it is possible this may factor into decision-making (Zhang et al., 2019). In addition, since this survey was not IVF center- or PGT-A-lab-specific, it is likely that a lab’s methodology, threshold, reporting, and classification of mosaicism differs between participants. Fifth, the information was provided via self-report, with no access to patient charts to confirm or complete certain medical history and patient information. The low response rate of the survey could have several possible causes. First, although the group members varied from 614 to 648, it is likely that not all of these were active members of the community. It is a common occurrence in discussion forums and support groups for individuals to cease active participation in that community once the subject matter is no longer relevant to them (Ussher et al., 2005). This is also a possible reason for why 65% of participants that had undergone MET reported an ongoing pregnancy (Figure 12), which is significantly higher than the average clinical pregnancy rate of 30-40% following
MET (Munne et al., 2017; Victor et al., 2019). It is important to note that the results of this study should not be used to suggest implantation or reproductive potential since the study did not attempt to control for all METs. This study could also have been hindered by the small sample size. The subset of women who elected MET was only comprised of 22 participants. Therefore, this study should be treated as an exploratory study, with more research necessary to make conclusions regarding the correlations assessed. Finally, the exclusion criteria was not explicitly mentioned in the informed consent, nor were participants asked in the survey whether they were given the option to make decisions around MET. Therefore, it is possible that more participants met exclusion criteria but failed to mention their lack of autonomy surrounding decision-making in the free-text responses.

**Future Research**

This study was formulated using a grounded theory approach. To our knowledge, this particular patient population has not been surveyed previously regarding their psychosocial experience. This study provided some initial insight into the infertility history of patients considering MET, which health care providers patients are speaking to, and patients’ overall understanding and feelings toward PGT-A. The findings of this study can assist in the development of future surveys and interviews for women considering MET. Because most participants reported using advice from providers after PGT-A, determining which information is the most helpful to patients would aid in providing them with the best care possible. Performing a similar study on a larger scale and within multiple clinics would help to
confirm if the findings of this study can apply to the majority of the population.

Finally, since this study was a survey and the questions were primarily multiple choice, interviewing women from the same population would provide further insight. Open-ended interviews would provide the opportunity to learn more about women’s stories and emotional journeys. It would also allow researchers to ask more questions about women’s perceptions regarding the counseling they received from providers. At the end of this survey, participants were asked if they would be interested in being contacted for a follow-up interview. Four participants left their email address, and two women left messages on the survey posting that they had not left their email address, but would still be interested in being contacted.
CHAPTER V

CONCLUSION

Women considering MET are typically being provided some level of counseling, including possible risks and outcomes, but this study reveals that this discussion may not be adequate. Decision-making is complicated by the differing opinions of providers and practices of clinics regarding MET (Kim et al., 2018). According to the findings of this study, support from health care providers and partners was correlated with a decision to pursue MET. Comparatively, reasons that participants did pursue MET included a greater number of previous IVF PGT-A cycles and feeling like this embryo was their last chance to have a baby. In conclusion, this study found that women considering MET would prefer more comprehensive counseling and more information regarding outcomes and success rates of MET.
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APPENDICES
APPENDIX A

STUDY SURVEY & INFORMED CONSENT

California State University, Stanislaus
Online Consent to Participate in Research

California State University, Stanislaus
Reena Dhaliwal
Rdhalwal909@gmail.com

Factors in Decision-making of Women who have Considered Mosaic Embryo Transfer After Mosaic PGT-A results.

Dear participant,
The Principal Investigator, Reena Dhaliwal, is a student at California State University, Stanislaus conducting research for a Master’s degree in Genetic counseling. This study seeks to learn about patient perspectives and factors in decision-making of women who have considered mosaic embryo transfer after receiving a mosaic result following PGT-A (pre-implantation genetic testing for aneuploidy, formerly called PGS or CCS). Your participation will require approximately 10 minutes and is completed online at your computer. Completing this survey has very little risk to you, however some of the questions may make you feel upset or worried. If this should happen, or if you have any other concerns, a genetic counselor is available to talk with you by phone. Please contact Lauri Black at lauriblack@pacreprogc.com if you experience distress related to this survey.

The survey will not collect your name, medical record number or any other identifying information. You can stop taking the survey at any time. It is possible that you will not benefit directly by participating in this study. However, future patients, genetic counselors and other medical providers may benefit from your participation. The results of this study may help medical providers on how to better guide and help women in a similar situation. The researcher will not keep your research data to use in the future.

There is no cost to you beyond the time and effort required to complete the survey above. Compensation for participating in this research will be a $15 Amazon gift card to the first 60 participants. To receive the gift card, you will need to provide an email address to which the gift card will be delivered electronically. At the end of the survey you will also be asked if you would like to leave your email address to be potentially contacted for a follow-up phone interview regarding your experience with
mosaic embryo transfer. By providing your email you may be contacted in the future but you can decline to participate in any further research. There is no anticipated commercial profit related to this research. Your participation is voluntary. You may refuse to participate or stop participation at any time without penalty or loss of benefits. If you have any questions about this research, you may contact me, Reena Dhaliwal, at rdhaliwal909@gmail.com or my faculty sponsor, Dr. 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.

If you agree and wish to participate in this research study, please select “agree” below. Selecting agree indicates that you have read the information above and agree to participate voluntarily, and are at least 18 years. Please feel free to print a copy of this consent page to keep for your records.

If you agree and wish to participate in this research study, please select “agree” below. Selecting agree indicates that you have read the information above and agree to participate voluntarily, and are at least 18 years of age.

- [ ] I agree to participate
- [ ] I do not agree to participate

Skip To: End of Survey If... = I do not agree to participate

End of Block: Informed Consent

Start of Block: Demographics
Q2 What is your race/ethnicity?
☐ White/Caucasian
☐ African/American
☐ Hispanic or Latino
☐ Asian
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Prefer not to answer
☐ Other (please specify)
________________________________________________

Q3 What is your highest completed level of education?
☐ Did not complete high school
☐ High school diploma/GED
☐ Some college
☐ Associate's degree
☐ Bachelor's degree
☐ Graduate degree
☐ Technical training
☐ Prefer not to answer

Q4 What is your household income?
☐ Under $30,000
☐ $30,000-$50,000
☐ $50,000-$75,000
☐ $100,000-$150,000
☐ Above $150,000
☐ Prefer not to answer
Q5 What religion do you identify with?
   ○ Christian
   ○ Catholic
   ○ Jewish
   ○ Muslim
   ○ Hindu
   ○ Agnostic
   ○ Other (please specify _______________________________________________________________________
   ○ No religious affiliation
   ○ Prefer not to answer

Q6 What is your age?
   ○ 18-25 years old
   ○ 25-30 years old
   ○ 31-35 years old
   ○ 36-40 years old
   ○ 41-45 years old
   ○ 45 years or older

Q7 Have you undergone mosaic embryo transfer?
   ○ Yes
   ○ No

End of Block: Demographics

Start of Block: Pregnancy History
Q8 How long had you been trying to get pregnant prior to beginning fertility treatment (i.e. having intercourse without birth control)?

- less than 1 year
- 1-2 years
- greater than 2 years

Q9 What is the total number of all of your pregnancies (including losses)?

- 0
- 1-3
- 3-5
- greater than 5

*Skip To: Q13 If What is the total number of all of your pregnancies (including losses)? = 0*

Q10 Have you experienced a pregnancy loss?

- Yes
- No

*Skip To: Q12 If Have you experienced a pregnancy loss? = No*

Q11 Number of miscarriages (less than 20 weeks gestation)?

- 1-3
- 3-5
- greater than 5
Q12 Number of full term deliveries?
   ○ 0
   ○ 1-3
   ○ 3-5
   ○ greater than 5

Q13 Have you had a traumatic pregnancy experience? If so, please explain.
   ○ Yes
   ○ No

Q14 What is the cause of your infertility (if known)?
   ○ Female factor
   ○ Male factor
   ○ Both female factor and male factor
   ○ Other (please specify)

End of Block: Pregnancy History

Start of Block: Infertility History
Q15 In your last five fertility treatment cycles, which treatment processes have you undergone?

(PGT-A: Preimplantation genetic testing for aneuploidy)

<table>
<thead>
<tr>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>Cycle 3</th>
<th>Cycle 4</th>
<th>Cycle 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF without PGT-A</td>
<td>IVF with PGT-A (using own sperm &amp; eggs)</td>
<td>IVF with PGT-A and 3rd party (sperm donor, egg donor, gestational carrier)</td>
<td></td>
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</tr>
</tbody>
</table>
Q16 For cycles that included PGT-A, what types of results did you receive and what type of transfer was done?

Euploid: Normal chromosomes  
Mosaic: Both normal and abnormal chromosomes

<table>
<thead>
<tr>
<th></th>
<th>Some euploid &amp; no mosaic</th>
<th>Some euploid &amp; some mosaic</th>
<th>No euploid &amp; no mosaic</th>
<th>No euploid and some mosaic</th>
<th>No embryo transfer</th>
<th>Euploid embryo transfer</th>
<th>Mosaic embryo Transfer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st PGT-A cycle</td>
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<td>2nd PGT-A cycle</td>
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<td>3rd PGT-A cycle</td>
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<tr>
<td>4th PGT-A cycle</td>
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</tr>
<tr>
<td>5th PGT-A cycle</td>
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<td></td>
</tr>
</tbody>
</table>

End of Block: Infertility History

Start of Block: PGT-A Process
Q17 Where did you first hear about PGT-A?

- Researching online
- From a discussion forum or online community
- Fertility Clinic
- Genetic Counselor
- Other (please specify)

- Not sure/Don't remember
- Other doctor

Q18 Which provider(s) have you spoken with about your PGT-A results? (check all that apply)

- Reproductive endocrinologist
- Genetic Counselor associated with or at IVF center
- Genetic Counselor at laboratory that performed PGT-A
- Other (please specify)

- Not sure/Don't remember
- Embryologist
- IVF Nurse
Q19 Which provider did you **mainly** discuss your PGT-A results with?

- [ ] Reproductive endocrinologist
- [ ] Genetic Counselor associated with or at IVF center
- [ ] Genetic Counselor at laboratory that performed PGT-A
- [ ] Other (please specify)

- [ ] Not sure/Don't remember
- [ ] Embryologist
- [ ] IVF Nurse

Q20 How well did you feel you understood your test results?

- [ ] Understood them very well (28)
- [ ] Understood them well (29)
- [ ] Somewhat understood them (30)
- [ ] Understood them a little bit (31)
- [ ] Did not understand them at all (32)

Q21 How much do you trust the accuracy of your PGT-A results?

- [ ] A great deal
- [ ] A lot
- [ ] A moderate amount
- [ ] A little
- [ ] None at all
Q22 Were you given any resources by your providers to help with your decision regarding transfer?

○ Yes (please describe what you were given)

____________________________

○ Not sure/Don't remember

○ No

Q23 How much support did you feel you received from your medical team regarding your decision to transfer or not to transfer?

☐ A great deal

☐ A lot

☐ A moderate amount

☐ A little

☐ None at all

Q24 I was told that possible outcome(s) of mosaic embryo transfer are ________.

(check all that apply)

☐ Failure to implant

☐ Miscarriage

☐ Pregnancy complication

☐ Chromosomal problem at birth

☐ Healthy live born baby

☐ Other (please specify)

____________________________
Q25 What were your main concern(s) regarding transferring a mosaic embryo? (check all that apply)

- □ Failure to implant
- □ Miscarriage (2)
- □ Pregnancy complication
- □ Chromosomal problem at birth
- □ Other (please specify)

Q26 How risky do you perceive mosaic embryo transfer to be?

- □ Very risky
- □ Risky
- □ Somewhat risky
- □ Slightly risky
- □ Not at all risky

End of Block: PGT-A Process

Start of Block: Background

Q27 Estimate the level of stress you feel due to infertility and other pressures.

- □ A great deal
- □ A lot
- □ A moderate amount
- □ A little
- □ None at all
Q28 How much did you and your partner agree on implanting mosaic embryos?

- A great deal
- A lot
- A moderate amount
- A little
- None at all
- I don't have a partner

Q29 Which resources did you use to help you make decisions after PGT-A? (check all that apply)

- Advice from provider(s)
- Advice from family members or friends
- Brochures or pamphlets
- Medical websites or scientific articles
- Parenting/Pregnancy websites
- Social networking websites (ex. Facebook)
- Other (please specify)

__________________________________________________________________________

Q30 How many hours a week do you spend seeking information related to this topic?

- less than 1 hour
- 1-3 hours
- 3-5 hours
- 5-7 hours
- greater than 7 hours
Q31 How much do you consider yourself to be risk-taker?
   - A great deal
   - A lot
   - A moderate amount
   - A little
   - None at all

Q32 Is there anything more about your experience with mosaic embryo transfer that you would like to share?
   - Yes ________________________________________________
   - No

End of Block: Background

Start of Block: Only women who have undergone MET

Display This Question:
   If Have you undergone mosaic embryo transfer? = Yes

Q33 What part of the world is the clinic where you had mosaic embryo transfer
   - United States (West)
   - United States (Midwest)
   - United States (Northeast)
   - United States (Southeast)
   - United States (Southwest)
   - Canada
   - Europe
   - Asia
   - Other (please specify)
Q34 What was the outcome of your mosaic embryo transfer?
- Failure to implant
- First trimester miscarriage
- Second or third trimester miscarriage
- Ongoing pregnancy
- Live birth of a healthy baby

Q35 Which prenatal testing, if any, did you complete or plan to complete after your mosaic embryo transfer?

- Amniocentesis
- NIPT (Non-invasive prenatal testing)
- Maternal Serum Screening
- Chorionic Villus Sampling (CVS)
- I chose not to do any prenatal screening

Q36 What was your main reason in proceeding with mosaic embryo transfer?
- I felt this embryo was my last chance to have a baby
- I was not concerned about the risks or felt they were manageable
- I felt that this embryo should have a chance
- My doctor recommended that I transfer this embryo
Q37 Is there anything more about your decision to transfer that you would like to share?

- Yes ________________________________________________
- No

End of Block: Only women who have undergone MET

End of Survey: Message & Links

Thank you for taking the time to complete this survey. To receive your $15 Amazon gift card, please click the link below to leave your email address. The gift card will be delivered to your email within 2 days of submission. Your responses to the survey will not be linked to your email.

https://csustan.co1.qualtrics.com/jfe/preview/SV_eefUK9dhwoAcUzbf?
Q_SurveyVersionID=current&Q_CHL=preview

If you would be interested in potentially being contacted for a follow-up interview regarding your experiences with PGT-A and mosaic embryo transfer, please click the link below to leave an email address where you can be contacted. Your responses to the survey will not be linked to your email. You can always choose to decline further participation if you are contacted.

https://csustan.co1.qualtrics.com/jfe/preview/SV_bqtJTjX1hXTFFn7?
Q_SurveyVersionID=current&Q_CHL=preview
APPENDIX B

PARTICIPANT DEMOGRAPHIC INFORMATION & FREE TEXT RESPONSES

Table 1

Summary of Participant Age Data

<table>
<thead>
<tr>
<th>Age</th>
<th>Number (n = 57)</th>
<th>Percent</th>
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<tbody>
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<td>18-24 years old</td>
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<td>3.5%</td>
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<td>31-35 years old</td>
<td>11</td>
<td>19.3%</td>
</tr>
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<td>36-40 years old</td>
<td>29</td>
<td>50.1%</td>
</tr>
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<td>41-45 years old</td>
<td>15</td>
<td>26.3%</td>
</tr>
<tr>
<td>Older than 45</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 2

Summary of Participant Race Data

<table>
<thead>
<tr>
<th>Race</th>
<th>Number (n = 57)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>White/Caucasian</td>
<td>48</td>
<td>84.2%</td>
</tr>
<tr>
<td>African-American</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>7</td>
<td>12.3%</td>
</tr>
<tr>
<td>Asian</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 3

Summary of Participant Education Data

<table>
<thead>
<tr>
<th>Education</th>
<th>Number (n = 57)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not complete high school</td>
<td>2</td>
<td>3.5%</td>
</tr>
<tr>
<td>High School Diploma/GED</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>Some College</td>
<td>6</td>
<td>10.5%</td>
</tr>
<tr>
<td>Technical training</td>
<td>2</td>
<td>3.5%</td>
</tr>
<tr>
<td>Associate’s degree</td>
<td>2</td>
<td>3.5%</td>
</tr>
<tr>
<td>Associate’s degree</td>
<td>2</td>
<td>3.5%</td>
</tr>
<tr>
<td>Bachelor’s degree</td>
<td>16</td>
<td>28.1%</td>
</tr>
<tr>
<td>Graduate Degree</td>
<td>28</td>
<td>49.1%</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>
Table 4

Summary of Participant Income Data

<table>
<thead>
<tr>
<th>Income</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under $30,000</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>$30,000-$50,000</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>$50,000-$75,000</td>
<td>12</td>
<td>21.1%</td>
</tr>
<tr>
<td>$100,000-$150,000</td>
<td>14</td>
<td>24.6%</td>
</tr>
<tr>
<td>Above $150,000</td>
<td>22</td>
<td>38.6%</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 5

Summary of Participant Religion Data

<table>
<thead>
<tr>
<th>Religion</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christian</td>
<td>18</td>
<td>31.2%</td>
</tr>
<tr>
<td>Catholic</td>
<td>19</td>
<td>33.3%</td>
</tr>
<tr>
<td>Jewish</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Muslim</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>Hindu</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Agnostic</td>
<td>7</td>
<td>12.3%</td>
</tr>
<tr>
<td>No religious affiliation</td>
<td>11</td>
<td>19.3%</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>
Table 6

*Participant Free-Text Responses Regarding Traumatic Pregnancy Experience*

<table>
<thead>
<tr>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Multiple losses, 2 at home, hemorrhage”</td>
</tr>
<tr>
<td>“Had to do a selective reduction for T18 during first pregnancy”</td>
</tr>
<tr>
<td>“A 14 week miscarriage in 2016 and a termination for medical reasons at 22 weeks in 2017”</td>
</tr>
<tr>
<td>“I had a traumatic twin birth with broken ribs, a vaginal and c section, an abruption and severe post partum preeclampsia that left me in ICU for days.”</td>
</tr>
<tr>
<td>“Placenta would not detach and I hemorrhaged with my second child.”</td>
</tr>
<tr>
<td>“I ectopic that required an emergency laparatomy.”</td>
</tr>
<tr>
<td>“Emergency c section”</td>
</tr>
<tr>
<td>“Currently 20w pregnant with my mosaic embryo. I also transferred another embryo with this one and initially both embryos stuck. We heard heartbeats in both, and lost the non-mosaic baby at 8w. I’ve also had a subchorionic hemorrhage and several large bleeding episodes throughout the pregnancy. Additionally, because of the fetal demise of the twin, NIPT testing was inconclusive and we weren’t sure if my mosaic embryo or my normal embryo stuck. My mosaic baby is a girl and my normal embryo was a boy. It wasn’t until 19w that we were able to find out via ultrasound that our girl was the surviving twin. It has been quite the rollercoaster of events. We are now considering amniocentesis for peace of mind that our daughter is normal.”</td>
</tr>
<tr>
<td>“My son has cystic fibrosis so the pregnancy was difficult and felt like every appointment brought bad news.”</td>
</tr>
<tr>
<td>“Miscarriage at 8 weeks”</td>
</tr>
<tr>
<td>“PPROM at 19w, delivery at 32w.”</td>
</tr>
<tr>
<td>“Yes, termination for Trisomy 18 at 14 weeks.”</td>
</tr>
<tr>
<td>“Fertility treatment in and of itself is traumatic. Miscarriage after fertility treatment feels particularly cruel. Social and career disruption due to infertility diagnosis.”</td>
</tr>
<tr>
<td>“Breech with emergency c section”</td>
</tr>
</tbody>
</table>

Table 7

*Participant Free-Text Responses Regarding Cause of Their Infertility*

<table>
<thead>
<tr>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Unknown secondary infertility”</td>
</tr>
<tr>
<td>“Unexplained infertility”</td>
</tr>
<tr>
<td>“Doing PGD”</td>
</tr>
<tr>
<td>“Removed tubes”</td>
</tr>
<tr>
<td>“Blocked and then removed fallopian tubes”</td>
</tr>
<tr>
<td>“Emergency c section”</td>
</tr>
<tr>
<td>“Unexplained”</td>
</tr>
<tr>
<td>“Not infertile. Krabbe disease killed our first born son”</td>
</tr>
<tr>
<td>“Secondary infertility, age related” “Fertility treatment in and of itself is traumatic. Miscarriage after fertility treatment feels particularly cruel. Social and career disruption due to infertility diagnosis.”</td>
</tr>
</tbody>
</table>
Table 8

Participant Free-Text Responses Providing Additional Information Regarding MET

“My first retrieval resulted in a mosaic and a monosomy 2, then did 3 more cycles in hopes of getting a normal and was suggested I transfer mosaic as last resort. Then I switched drs to one who was willing to transfer 3day embryos. I will still transfer mosaic if needed.”

“It is a complex mosaic with 5 affected chromosomes but we were advised to transfer without a discussion with a genetic counsellor (we are in Spain)”

“I am deeply conflicted about transferring our mosaics for the reasons listed above. I hope to never have to make the decision. We have 2 euploid embryos cryopreserved.”

“We transferred 2 mosaic embryos. 1 low level monosomy 6 male and 1 high level monosomy 22 female. Currently 22 weeks pregnant with the male embryo. The stress from transfer to week 14 was extreme.”

“Emergency c section”

“Just that we have 2 mosaic embryos that we plan on transferring at some point. I wish we could’ve transferred them in chronological order but our doctor wants to save them for last”

Fertility specialists need to better explain the risks and opportunities associated with mosaic embryos, including summarising to extent possible the latest research available and its implications

Wish my provider was not so hesitant about the transfer, I waited weeks in limbo to determine if he was going to transfer and still don’t know. I am determined to do the transfer and found another clinic that will transfer our mosaic embryo. I wish I would have asked I. The beginning if he would transfer a mosaic before beginning care.”

“For women who do not have other embryos and do not wish to use donor embryos, throwing out mosaics throws out every chance of having a baby”

“I wish more providers were educated on mosaicism. My obgyn and the high-risk perinatology group I see weren’t familiar with mosaic transfer. I have been personally judged by many providers for choosing to transfer a mosaic embryo, even though my daughter appears to be perfectly normal. Infertility is hard enough.. I shouldn't be asked "why" and chastised about my decision”

“Currently 16 weeks with my mosaic embryo. It is a 56 mb gain on chromosome 5. MaterniT genome test came back normal and cvys normal”

“My transfer of a monosomy 1 mosaic was successful. I have an almost-10 month old baby girl that is happy and more importantly healthy. She was our last chance of having another child and I felt I appreciated the risk. I trust that the results of the testing are accurate, in that it gives accurate data on the cells tested, but that the deductions then made from that bit of information to reach a conclusion on the embryo in its entirety may be flawed. My fertility doctor supported us in transferring our Baby Mo, but when his practice was purchased by another practice that did not want me to talk about the success because transferring mosaic embryos was against their policy. This saddens me, and I hope your research encourages a change of thinking amongst practitioners and provides patients hope they may not otherwise have and an opportunity to make an informed decision.”

“It's difficult to answer the question since there are so many levels of risk with mosaics. We kept a monosomy 19 (a "safe," lethal defect while we discarded a very wanted girl with monosomy 21 - not a good choice for us. We have a special needs child and thus accepted less risk than if we had no kids.”

“Currently 6 weeks pregnant with mosaic embryo that could result in live birth with the genetic condition that it was mosaic for. I have a lot of anxiety in regard to this, wondering if the baby will be safe and healthy.”
“I have a -19 and dup 14 (q21.1-31.1) I transferred them both on 2/14 and am currently pregnant. Unsure of how many implanted, will know 3/15. I wish there was more info out there about my partial trisomy mosaic 14, since I know live births can happen with this chromosome disorder but since mine is such a small duplication, of this issue is actually in the embryo and doesn’t fix itself, will the outcomes be the same as a full duplication on a chromosome? It’s hard to find info about partials anywhere, only full chromosome issues. I wish I knew more about my dup 14, I know my -19 will either not implant, miscarry or result in a healthy baby. Thank you and I hope you can help to better educate woman in the future!”

“At the time of transfer, I felt confident about my decision based on my conversation with my RE. Since transfer, I have done much more research on my own and feel very little confidence in the transfer. I'm currently 22 weeks pregnant and ultrasound is showing some soft markers which could be a genetic abnormality. In retrospect, I should have had much more information than I did, but it was hard to find and my IVF clinic did not seem to have many answers either. Thanks for doing this research - it is so desperately needed”

Table 9

Participant Free-Text Responses Providing Additional Information Regarding Their Decision to have MET

“There are so many complexities including that only some types of mosaics are ‘fit’ to be transferred. Clearer communication on the different types of embryos etc. is needed to support patients and their decision making.“It is a complex mosaic with 5 affected chromosomes but we were advised to transfer without a discussion with a genetic counsellor (we are in Spain)”

“Was very difficult not to have the amnio but didn't want additional risk when no one can tell me if the baby will have the duplication or if she does how the gene will express itself”

“I had 6 euploid embryos leftover that I could have transferred. I chose to transfer a mosaic because I had transferred 4 normal embryos with no implantation. I wanted to try another transfer and was encouraged to do 2 embryos, however, I didn't want to use 2 more euploid embryos because in the event that I needed a surrogate, I would need the euploids. I used a normal boy and a mosaic girl. Only the mosaic girl resulted in ongoing pregnancy. Out of 6 embryos over 3 transfer, 5 of the embryos being normal, only my mosaic embryo has stuck beyond 8 weeks.”

“It was my last embryo, but I also didn't want to wonder what if. My "normal" embryos didn't take, so I tried this one and it worked. I had an amnio and microarray analysis”

“We are doing genetic testing at birth, on advice of MFM against amnio with perfect anatomy scans and other screening thus far (21 weeks on 03/10)”

“IVF is so expensive and I am 38 years old and our retrieval resulting in 2 low level and 2 high level mosaics and 1 abnormal. We can’t afford another cycle”

“I don't know yet what prenatal genetic testing I want to do”