A systematic review exploring the patient decision-making factors and attitudes towards pre-implantation genetic testing for aneuploidy and gender selection

Timothy Bracewell-Milnes¹ | Srdjan Saso² | Benjamin Jones² | Sarah Cato³ | Riya Parikh⁴ | Meen-Yau Thum⁵ | Mark Johnson⁶ | Paula Almeida¹ | Julian Norman-Taylor¹ | Dimitrios Nikolaou¹

Abstract

Introduction: Pre-implantation genetic testing for aneuploidy (PGT-A) is in high demand worldwide, with ongoing debate among medical societies as to which patient groups it should be offered. The psychological aspects for patients regarding its use, lag behind the genomic technological advances, leaving couples with limited decision-making support. The development of this technology also leads to the possibility for its utilization in gender selection. Despite the controversy surrounding these issues, very few studies have investigated the psychological aspects of patients using PGT-A.

Material and methods: This systematic review provides an up-to-date analysis of the psychosocial aspects surrounding PGT for aneuploidy and sex selection, as well as decision-making factors. A systematic search of English peer-reviewed journals of three computerized databases were undertaken following PRISMA guidelines. The qualitative data were extracted using thematic analysis. PROSPERO Registration number: CRD42019126439.

Results: The main outcome measures were patients’ motivations, decision-making factors, attitudes and experiences surrounding the use of PGT for aneuploidy and sex selection. Ten studies were included, four for PGT-A and six for sex selection. Attitudes towards PGT-A were positive, with the main motivating factors being decreasing miscarriage rate, reducing the risk of termination of pregnancy and reducing the time to pregnancy. Consistently raised concerns regarding PGT-A were the financial burden and moral beliefs. The vast majority of patients felt sufficiently knowledgeable to make the decision; however, studies did reveal that a minority misinterpreted certain potential benefits of PGT-A. Studies investigating PGT for sex selection predominantly reported the main motivation was to achieve gender balance.

Abbreviations: ART, assisted reproductive technology; IVF, in vitro fertilization; PGT, pre-implantation genetic testing; PGT-A, pre-implantation testing for aneuploidy.
1 | INTRODUCTION

In vitro fertilization (IVF) is often a last resort for couples who do not achieve pregnancy, usually after 2 years of trying to conceive. Fertility treatment is stressful and is known to have significant psychological impact on couples. Pre-implantation genetic testing (PGT) for aneuploidy (PGT-A) has been available for couples undergoing IVF for nearly 20 years. PGT-A involves retrieving five to ten trophoectoderm cells from a blastocyst and screening for the presence of a normal number of chromosomes, with only euploid embryos selected for transfer.

Requests for PGT-A are now in demand worldwide and have presented both patients and clinicians with the decision of when to use PGT-A as an adjuvant treatment to standard IVF therapy. PGT-A is now the most commonly used alternative to morphological assessment of the embryo, when deciding on which embryo should be selected for transfer.

The rationale for using PGT-A is the well established fact that the rate of aneuploid embryos increases significantly with age. One large study screened over 15,000 embryos and found the aneuploid embryo rate was approximately 25% in young women (30 years of age or younger), 58.2% at age 40, 75.1% at 42 and 88.2% at age 44. The consequences of transferring aneuploid embryos include failed implantation, miscarriage, termination of pregnancy or the birth of a chromosomally abnormal child if prenatal screening did not identify the pregnancy to be high risk.

Patient education surrounding PGT-A varies between different countries and fertility clinics regarding what information patients are given, who is involved in the education process and how patient understanding is gauged. Potential advantages are that PGT-A can improve implantation rates per embryo transfer, reduce miscarriage risk, minimise the risk of a resulting pregnancy with an aneuploid fetus and minimise the time to pregnancy. PGT-A could also reduce multiple pregnancy rates by elective single embryo transfer of euploid embryos without affecting cumulative pregnancy and live birth rates compared with double embryo transfer. However, patients must also be made aware that PGT-A cannot affect the genetic make-up of the embryo, does not increase the live birth rates per egg retrieval, is an invasive procedure with a small risk of damage to the embryos (<1%) and may not reflect the genetic status of the whole embryo due to mosaicism. As PGT-A is still not performed routinely in the majority of fertility clinics worldwide, patients should be informed that PGT-A may not be equally effective in all clinics, and, therefore, they should be made aware of the individual experiences of clinics using PGT-A prior to embarking on treatment.

The rapid advancements of PGT-A have raised numerous concerns regarding the ethical acceptability of some of its potential applications. Nevertheless, PGT-A has evolved without regulation in many of the countries in which it is used, and it is in widespread clinical use and being increasingly utilized worldwide. Indeed, the American Society for Reproductive Medicine (ASRM) advises that the limited number of studies and evidence currently available leaves the value of PGT-A as a universal screening tool for IVF undetermined. The Human Fertilization and Embryology Authority (HFEA) currently states that there is a conflicting body of evidence that PGT-A is beneficial to reproductive outcome and has called for further research. There is ongoing debate as to who benefits most from PGT-A and to which patient groups it should be offered. Currently, the psychology behind why patients become aware of and decide to use PGT-A lags behind the genomic technological advances, leaving couples with limited decision-making support.

1.1 | Pre-genetic testing for gender selection

The development of this genomic technology leads to the possibility for its utilization to satisfy certain parental non-medical desires, namely,
gender selection, with its availability in certain countries likely to become a point of market advantage. Those in favor of PGT for gender selection argue that couples should have reproductive autonomy and privacy with their reproductive choices and that it is preferable to dispose of embryos of the undesired sex, instead of testing for gender when pregnant followed by termination of pregnancy. Those against, argue that using IVF for sex selection encourages the current sexist stereotype that male offspring is preferred, presents unnecessary physical and emotional burden on the woman undergoing potentially unnecessary procedures and goes against the ideal scenario of parents having unconditional love for their children. Organizations such as the American College of Obstetrics and Gynecologists (ACOG) have issued statements suggesting gender selection is an inappropriate use of medical resources and perpetuates gender bias. Despite this opposition the use of PGT for sex selection is legal in a diverse number of countries, including USA, Mexico, Thailand and Italy. Indeed, in these countries the use of embryo testing for sex selection is on the increase, with the Society of Assisted Reproductive Technology (SART) reporting that the use of PGT for gender selection in the USA increased from 9% of PGT cycles in 2005 to 22% in 2008. More recent data from the USA has shown that 57,987 IVF cycles used PGT for aneuploidy and gender selection, which represents 22% of all assisted reproductive technology (ART) cycles. A survey conducted in the USA found that 72.7% of ART clinics in the USA offer gender selection to their patients. Although PGT for gender selection is illegal in the UK and the vast majority of European countries, clinics in the USA have reported a significant surge in fertility patients from countries such as the UK, Europe and Australia.

Despite the controversy and debate surrounding sex selection, surprisingly very few studies have investigated the motivations and attitudes of the patients using or potentially using this option. Insight into patient perspectives of PGT and gender selection could add to this ethical debate and generate new perspectives for couples wanting to rationalise this option.

1.1.1 | Aims

Over 20 years since its first use, the psychological impact of PGT for aneuploidy and gender selection remains poorly defined, with no established clinical guidelines for patient education and counseling. This systematic review aims to synthesise and update the literature regarding patient motivations, decision-making factors, attitudes and experiences of patients using PGT for aneuploidy and sex selection screening. No review has analyzed these psychological factors surrounding PGT together, and it could, therefore, illuminate any gaps in our current knowledge and improve clinical practice.

2 | MATERIAL AND METHODS

2.1 | Search strategy

Three computerized databases (PubMed, Science Direct, SciFinder) were searched systematically using PRISMA guidelines. The search terms and combinations of searches used are listed in Table 1. The

| Databases searched | PubMed, Science Direct, SciFinder |
|--------------------|----------------------------------|
| Search keywords    | [pre-genetic screening OR pre-genetic testing] AND [motivation] [pre-genetic screening OR pre-genetic testing] AND [attitude OR beliefs] [pre-genetic screening OR pre-genetic testing] AND [experience OR satisfaction] [pre-genetic screening OR pre-genetic testing] AND [psychological OR psychosocial] [pre-implantation genetic screening OR pre-implantation genetic testing] AND [motivation] [pre-implantation genetic screening OR pre-implantation genetic testing] AND [attitude OR beliefs] [pre-implantation genetic screening OR pre-implantation genetic testing] AND [experience OR satisfaction] [pre-implantation genetic screening OR pre-implantation genetic testing] AND [psychological OR psychosocial] NOT [pre-genetic diagnosis OR pre-genetic diagnosis for monogenic disorders (PGT-M) OR pre-genetic diagnosis for chromosomal structural re-arrangement (PGT-SR) OR pre-natal diagnosis] |

| Inclusion criteria | 1. Published in English in peer-reviewed journals (no date cut off) 2. Studies focusing on ARTs only 3. Full article available |
|-------------------|-----------------------------------------------------------------|
| Exclusion criteria | 1. Papers not in English 2. Full article not available 3. Studies investigating pre-genetic diagnosis 4. Studies investigating prenatal diagnosis |
search was augmented by the addition of references cited in primary sources.

2.2 | Study selection

Given that PGT is a relatively recent technology, there were no restrictions placed on publication date and inclusion. Only English language peer-reviewed studies that examined the psychosocial aspects of PGT-A, including patient motivations, attitudes, experiences and decision-making process were included. This review aimed to synthesize available data on the topic, so no studies were excluded based on study design. Because this review focused on patients directly involved in PGT-A, the following studies were excluded: those that focused on potential use of PGT-A or couples using PGT for monogenic disorders and chromosomal structural re-arrangement. The full inclusion/exclusion criteria can be found in Table 1.

2.3 | Study screening

Following an initial search, a total of 374 records were screened by the first author (T.B.-M.) based on the inclusion and exclusion criteria, and this process was repeated independently by a second author (S.S.). An overview of the search results and screening process is summarized in the study flow diagram (Figure 1). The screening process was cross-checked by the senior authors (P.A., J.N.-T., D.N.). Any disagreement between the reviewers was resolved by discussion until consensus was reached.

2.4 | Data extraction

A data extraction spreadsheet was developed and agreed between the authors. The selected studies were comprehensively examined and relevant data were extracted for each paper and inputted to the spreadsheet by the first author (T.B.-M.) and cross-checked by the second author (S.S.). Thematic analysis was used to extract key and consistent themes that emerged. Information selected included author details, year of publication and country of the study, study aim, sample size, methodology, sample characteristics, outcome measures and summary of findings. Disagreements regarding extracted data were resolved by discussion and deliberated on by the senior authors (P.A., J.N.-T., D.N.).

3 | RESULTS

3.1 | Search strategy and study selection

After the initial search, 374 records were screened for inclusion. The publications screened dated from 1998 to 2018. A total of 287 studies were excluded based on title alone and 87 abstracts were retained and examined. In addition, 63 abstracts were excluded that were not relevant to the research question. One study was identified after reviewing other relevant studies. Of the 25 full text publications that were examined, 10 met the inclusion criteria. Of the 15 studies that were excluded, one text was not available in English, two were duplicate studies and 12 were review or opinion articles. An overview of the search results and screening process is presented in the study flow diagram (Figure 1).

3.2 | Study characteristics

The study characteristics, sample size, methods, aims, findings and conclusions can be found in Tables 2 and 3. Individual study results are discussed in detail in this section and also summarized in Tables 2 and 3. There were considerable differences in study aim, design, quality, sample size and outcome measures of the 10 studies included for review. Four of the studies investigated patients using PGT-A and six studies examined those who used PGT for gender selection. To collect the data, five of the studies used questionnaires, three studies used an existing database and two used semi-structured interviews. Three of the studies collected data prior to treatment and seven collected their data retrospectively. The sample size range was 21-1500 patients. Of the 10 studies, eight were from the USA, one was from Australia and one was from Lebanon. Thematic analysis was used to extract key and consistent themes that emerged.

3.3 | Motivation and decision-making factors for patients using PGT-A

Quinn et al (2018) performed a cross-sectional survey of 191 subjects after thorough counseling of PGT-A, with 61% of patients opting for PGT-A, and 39% deciding not to pursue this option, with a subsequent analysis of these two groups. Patients planning on using PGT-A rated their main motivating factor as having a healthy baby (57%), reducing the risk of birth defects (18%), reducing the risk of miscarriage (16%) and reducing the time to pregnancy (3%). Another study found that the majority of their participants who elected PGT-A did so because they did not want to terminate a pregnancy, wanting to avoid having a child with a disability, as well as wanting to avoid the disappointment of miscarriage and failed embryo implantation. Katz et al (2002) reported that 96% of their respondents felt that discarding genetically abnormal embryos was significantly "less wrong" than a termination of pregnancy later in pregnancy. Lamb et al (2018) reported that a significant proportion of their participants opting for PGT-A had recurrent failed IVF and wanted more explanation as to why their fertility treatment was not successful. One study found that of their participants who declined PGT-A in a prior IVF cycle, 69% stated they would decline PGT-A in a repeat IVF cycle, and 31% opted for PGT-A in future IVF treatments. Of the patients who accepted PGT-A treatment, 75% would accept...
PGT-A in a repeat IVF cycle. Another study found their participants opted for PGT-A because of their age and the fact they had not been pregnant before, so as to ensure the embryo was chromosomally normal. One study found that 57% of respondents decided to share the decision to use PGT-A with others; of these, 85% felt strongly supported by family and friends. However, 66% of the studies participants did not feel this social support was significant.

Gebhart et al (2016) reported the additional cost of PGT-A would be approximately $3500 in their clinic, and overall only 21% of patients reported this to be a significant factor in their decision-making process. However, of the 40% of their cohort that declined PGT-A, 67% reported cost as an important determinant, compared to 33% of those who used PGT-A, and this difference was statistically significant. Another study found that 31% of their respondents declined PGT-A primarily to reduce costs of treatment. This was supported by Lamb et al (2018), who reported the financial burden of IVF with PGT-A was a significant decisional factor for all of their 37 respondents, and in general they found those who declined PGT-A did so because they were not willing to pay the additional costs. However, those patients that opted for PGT-A appeared to perform their own cost-effectiveness calculations relating to pay and potential success of IVF and thought that the cost was justified. For example, they quoted they “were not willing to pay for IVF without knowing it was a viable embryo; the cost of PGT-A was instead of transferring all those genetically abnormal embryos”. A significant minority of the same study were unwilling to pay for PGT-A as they felt the cost was not justified. One study found that after thorough counseling, the major reason for declining PGT-A was the fear of having no embryos to transfer (35%), the potential of delaying time to pregnancy (9%) and PGT-A potentially damaging the embryos (7%).

3.4 Attitudes of patients towards PGT-A

Gebhart et al (2016) found that 69% of their 117 respondents felt the decision to use or not use PGT-A was not difficult because they were sufficiently knowledgeable. In all, 69% of their respondents had no prior knowledge of PGT-A before embarking on IVF treatment, and only 9% had moderate or advanced knowledge of PGT-A. However, 93% of participants felt that after counseling on PGT-A they had sufficient knowledge to accept or decline its use at the time of their IVF cycle, with 87% identifying that PGT-A identifies aneuploid embryos and 81% reporting that PGT-A identifies “normal” embryos. Quinn et al (2018) reported 58% of their respondents who decided to undergo PGT-A rated themselves more knowledgeable compared with those who did not (42%, \( P = .02 \)). Studies have consistently reported that the clinic provider was the source of the most information about PGT-A. Another study found 43% of
### TABLE 2
Data extracted from studies investigating the psychological aspects of PGT for medical reasons

| Author, date, country | Sample and method | Study aim | Study findings | Conclusions of study |
|-----------------------|-------------------|-----------|----------------|----------------------|
| Gebhart et al, 2016 USA | 117 patients undergoing PGT. Questionnaire Post-PGT treatment. | Identify the determinants that influence the patient’s decision-making process when deciding to accept or decline PGT | **Attitudes and knowledge:**  
- 60% of respondents accepted PGT.  
- 98% of respondents were Christian and 88% college-educated.  
- 68% had no knowledge of PGS before IVF treatment. After provider education, 93% reported sufficient knowledge to make an informed decision to accept or decline PGT.  
**Motivations/decision-making factors:**  
- The additional cost of screening, the provider information and influence, and social support or acceptance from partner, family and/or friends, were the 3 statistically significant variables affecting the decision. | Several factors contribute to the patient-perceived determinants when choosing to accept or decline PGT, including cost, religious and ethical beliefs and values, social and family support, provider influences, and the past reproductive experience of the patient. |
| Katz et al, 2002 Australia | 48 patients undertaking PGT and 32 control subjects commencing their first IVF cycle. Questionnaire Pre-PGT treatment | Evaluate values a range of social and moral concerns of couples towards PGD and PGT | **Attitudes and knowledge:**  
- PGT was found to be a highly acceptable treatment, with little concern expressed regarding its extension to gender testing.  
**Motivations/decision-making factors:**  
- Patients were strongly in favor of a shared decision-making model in which couples have considerable autonomy over decisions about the embryo(s) to transfer. | The results from this study can be viewed as a source of information to guide PGD programs in improving their services for future patients including counseling sessions, doctor/patient relationships and the development of more sophisticated PGD technology directly related to the specific requirements of the users themselves. |
| Lamb et al, 2018 USA | 37 women undergoing PGT Semi-structured telephone interviews Pre-PGT treatment | Assess decisional factors for why women would accept or decline PGT | **Motivations/decision-making factors:**  
- A number of decisional factors were identified related to values about conception, disability, and TOP, past obstetric history, optimism toward technology, and cost.  
- Other key issues that were identified include the use of expanded carrier screening prior to IVF, maternal age and limited education about PGT due to the complexity about education or IVF alone. | There is a need to develop decision support tools for the increasing choices of genetic testing options for patients seeking IVF. Including patients’ values, past pregnancy experiences and attitudes toward science into the decision-making process may help promote a more informed decision. |
| Quinn et al, 2018 USA | A cross-sectional survey 300 patients initiating IVF cycle were invited to complete a survey on how they decided whether to pursue PGT-A Pre-PGT treatment | Explore how patients make decisions regarding use of PGT-A for IVF | **Motivations/decision-making factors:**  
- 117 (61%) planned PGT-A and 74 (39%) did not. Among those who decided to undergo PGT-A, 56% stated their primary reason was to have a healthy baby, 18% chose PGT-A to reduce the incidence of birth defects, and 16% aimed to decrease the risk of miscarriage.  
- Patients who decided not to pursue PGT-A stated they prioritized avoiding the scenario in which they might have no embryos to transfer (36%) or reducing cost (31%).  
- Both groups rated physicians as the single most important source of information in their decision-making (56% vs 68%, P = NS). | Patients who choose to undergo PGT-A have different priorities from those who do not. Many patients planning PGT-A do so for reasons that are not evidence-based. While patients cite physicians as their primary source of information in the decision-making process, rationales for selecting PGT-A are inconsistent with physician counseling. |

Abbreviations: IVF, in vitro fertilization; PGD, pre-implantation genetic diagnosis; PGT, pre-implantation genetic testing; PGT-A, pre-implantation genetic testing for aneuploidy. TOP, termination of pregnancy.
participants felt their partner had the most influence on their decision, followed by the clinic provider (35%). Close family and friends and the internet were significant other resources of information surrounding PGT-A, with the referring obstetrician and gynecologist most frequently reported as providing the least information (3%).

One study revealed a lack of patient understanding regarding PGT-A and previous parental genetic carrier screening. Parental carrier screening is standard clinical practice for IVF patients in the USA. However, Lamb et al (2018) reported that, of those declining PGT-A, some participants felt they had already done parental carrier screening and, therefore, PGT-A of embryos was not necessary. Lamb et al (2018) also asked questions about the type of information received, and the vast majority of respondents reported they were given information on PGT-A verbally. Lamb et al (2018) reported that a significant proportion of respondents declined PGT-A for religious reasons, with others also stating the genetic status of the embryo was not relevant, as they would not terminate a pregnancy under any circumstances. Another study found that 49% of those surveyed stated religious beliefs did not impact their decision to accept or decline PGT-A, but 36% found religious beliefs to be moderately important, and 16% felt religious beliefs were extremely important. Studies consistently showed that patients strongly preferred to discard genetically abnormal embryos to requiring a termination of pregnancy because of a genetic problem.

Lamb et al (2018) reported one of the significant differences they identified among patients accepting or declining PGT-A was their opinion of science, with those choosing PGT-A holding a much more optimistic view that technological advancements in science can enhance reproductive outcomes. A minority of respondents expressed a will to keep the IVF process as "natural" as possible, as well as some questioning the reliability of the technology, with one patient concerned that the embryos would be harmed by the PGT-A process. Indeed, Gebhart et al (2016) reported 51% expressed some concern that PGT-A could harm their embryos. Another study reported that potential harm from the biopsy to the embryo was their most influential decision in not going ahead with PGT-A.

3.5 Motivations, decision-making factors and knowledge of PGT for gender selection

Six studies investigated patients who used PGT for sex selection: four studies found there was no statistically significant difference between couples wanting a male or a female child, whereas two studies found that their participants had a preference for male offspring. Studies report that the majority of their participants had 2 (28%-44%) or 3 (28%-30%) existing children of the same gender. Studies also consistently reported that couples with existing children were using gender selection technologies to have a child of the opposite sex, thus achieving gender balance in the family. Sharp et al (2010) performed structured interviews with 18 participants and reported their motivations to pursue gender selection included: age-related concerns for one of the parents (78%); a desire to limit family size (72%); the gender makeup of their own families (67%); desire for a child of a particular sex (61%); desire to pass on the family name (61%); and the desire to enhance the experience of current children (50%). Couples also consistently cited a desire for same gendered-parenting experiences, meaning a father wanting the experience of raising a son and vice versa for the mother.

The only study from a non-western population looked at the medical and non-medical indications for the use of PGT overall in 192 couples in its first 3 years of use in Lebanon and found that motivations for PGT use were non-medical gender selection (96.3%), known parental chromosomal aneuploidy (3.1%) and known balanced translocation (0.5%). Therefore, only 3.7% of their patients were using PGT for medical reasons. Of those using PGT for gender selection, 94.1% were for the selection of male offspring and 5.9% for the selection of a daughter. In this Lebanese cohort, if the couple using PGT for gender selection were also infertile, then 100% of couples wanted to use PGT for selection of a son. Gleicher et al (2007) also reported statistically significant gender choices dependent on a couple’s ethnicity, with an obvious gender bias in favor of male offspring among Chinese, Arab and Indian couples. In contrast, caucasian and Hispanic couples appeared to prefer female offspring. One study found there was almost always strong agreement between the couple regarding their choice to pursue IVF and gender selection.

The only study to investigate any moral issues their participants had with using gender selection technologies found the major concerns to be: the potential psychological impact on their current children (67%); the creation and destruction of potentially healthy embryos (67%); negative feeling from family members (61%); financial costs (56%); and religious concerns (50%). Indeed, the highly private way in which these patients conceptualized the decision to pursue gender selection was reflected by the fact that almost all couples stated they had not discussed this option with any close family or friends.

These findings were supported by studies whose patients were using PGT for medical reasons. Lamb et al (2018) reported that a significant minority of their participants found that knowing the sex of the baby was a positive addition to the decision-making process, although they all denied using PGT for sex selection. Gebhart et al (2015) reported that 89% of respondents did not find gender selection significant and that this did not influence their decision-making process.

4 DISCUSSION

This systematic review provides an up-to-date analysis of the psychological aspects of PGT for aneuploidy and gender selection. It also explores the motivations, attitudes and experiences around
### TABLE 3 Data extracted from studies investigating the psychological aspects of PGT users for gender selection

| Author, date, country | Sample and method | Study aim | Study findings | Conclusions of study |
|-----------------------|-------------------|-----------|----------------|----------------------|
| Jain et al, 2005 USA | Cross-sectional survey of 1500 consecutive fertility patients at a fertility center. | To determine the demand and preferences of infertility patients for sex selection and the method and sex they would choose, and to investigate the relation between these choices and their demographic and socioeconomic characteristics. | Motivations/decision-making factors:  
- 40.8% wanted to select the sex of their next child for no added cost. Of these patients, 45.9% had no living children and 48.4% had children of the same sex.  
- After adjustment for observed predictors of gender preference, we found a significant preference for a female child among women who were older, not religious, willing to pay for sex selection, had more living children, had only sons, or had a diagnosis of male infertility. Nulliparous women did not significantly prefer one sex over the other.  
- Among parous women, those with only daughters significantly desired to select a male child, whereas those with sons significantly desired to select a female child. | There is significant demand among infertility patients for PGT for sex selection, with a significant portion of this demand coming from patients who do not have any children or who have children all of one sex. |
| Gleicher et al, 2007 USA | 92 IVF patients between 2004 and 2006 undergoing gender selection for family-balancing purposes. Their choices were then also investigated stratified for the ethnicity of the couple. | To investigate the notion that if offered gender selection patients would opt for male gender | Motivations/decision-making factors:  
- Among 92 cycles, 36 cycles were selected for female and 56 for male ($P = .037$). There were considerable differences in gender selection patterns among different ethnicities, with certain nationalities selecting males (Chinese 21/22, Arabic 5/6, Indian 5/5). Gender choices thus varied in a statistically significant way between ethnicities ($P < .001$).  
- Of the remaining ethnicities, however, the majority selected female gender (34/59) rather than male (25/59). | In an ethnically mixed patient population, elective gender selection for family balancing purposes in most ethnic groups does not represent a discriminatory procedure against female equality. However, cultural preference for male offspring is maintained in certain ethnic groups. |
| Missmer et al, 2007 USA | Cross-sectional survey of 1350 consecutive fertility patients at a fertility center. | To assess patients demands and preferences for non-medical sex selection. | Motivations/decision-making factors:  
- 49% of participants wanted to select the sex of their next child for no added cost. Of these patients, 56% had no living children and 37% had children all of one sex.  
- There was a significant preference for a female child among women who had only sons, had more living children or were single.  
- Nulliparous women did not significantly prefer one sex over the other.  
- Among parous women, those with only sons significantly desired to select a male child, whereas those with sons significantly desired to select a female child. | There is significant demand among infertility patients for PGT for sex selection, with a significant portion of this demand coming from patients who do not have any children or who have children all of one sex. |
| Coils et al, 2009 USA | Couples were selected from PGD cycles performed in the referring facilities in 2007-2008. Centers performing these PGD cycles were asked to provide information on the indications for PGD and whether gender selection was mentioned. | To identify whether there was any gender selection preference for patients selecting PGT for non-medical reassess. Its secondary aims were to assess whether families with same-gender children chose to use PGT to select offspring of the opposite sex. | Motivations/decision-making factors:  
- 3339 PGD cycles were reviewed and, of these, 11.4% were used for gender selection.  
- In general, there is no deviation in preference towards any specific gender except for a preference of males in some ethnic populations of Chinese, Indian and Middle Eastern origin that represent a small percentage of the US population.  
- In cases where only normal embryos of the non-desired gender are available, 45.5% of the couples elect to cancel the transfer and 54.5% of them continue with the transfer; this was strongly linked to cultural and ethnic background of the parents. | Based on these facts, it seems that objections to gender selection formulated by ethics committees and scientific societies are not well founded. |

(Continues)
TABLE 3 (Continued)

| Author, date, country | Sample and method | Study aim | Study findings | Conclusions of study |
|-----------------------|-------------------|-----------|----------------|----------------------|
| Sharp et al, 2010 USA | 18 couples participated in ethnographic interviews from November 2005 to April 2006. These interviews explored couples’ motivations for pursuing sex selection, moral beliefs and attitudes regarding sex selection and sources of moral ambivalence about the use of IVF/PGD for sex selection. | To characterize the moral attitudes and beliefs of couples actively pursuing IVF/PGD solely for purposes related to sex selection. | Motivations/decision-making factors:  
- Couples reported a combination of motivations for pursuing sex selection, including a desire to limit family size, concerns about parental age and financial concerns about multiple pregnancies.  
- Couples compared their decision to choices about TOP, maintaining that individuals have a right to make such decisions privately.  
Attitudes:  
- Couples frequently expressed anxiety about telling their other children and family members about their plans to use IVF/PGD for sex selection. Few couples cited concerns about the physical/emotional burden of IVF/PGD or emotional burdens of IVF/PGD. | The study’s findings suggest that couples pursuing IVF/PGD for sex selection view this as an ethically complex decision and express considerable uncertainty about the ethical acceptability of this practice. |
| Farra et al, 2014 Lebanon | Retrospective cohort study of 192 couples undergoing PGT between 2004 and 2007. Post-PGT treatment | To describe the motivations for the utilization of PGS during the first 3 years of its availability in Lebanon. | Motivations/decision-making factors:  
- When gender selection was sought, the selection of a son was desired in 94.1% of cases.  
- Of couples undergoing PGT for sex selection, 16.2% were childless, 8.6% had one child of the opposite gender, 28.1% had two same-gender children, 29.7% had three same-gender children, and 11.9% had four or more. | Our findings demonstrate the morally questionable consequences of self-regulated systems in which physicians are the sole gatekeepers of norms and ethics. |

Abbreviations: IVF, in vitro fertilization; PGD, pre-implantation genetic diagnosis; PGT, pre-implantation genetic testing; TOP, termination of pregnancy.

PGT-A use and reports on the patient decision-making process. To the best of our knowledge this is the first systematic review to investigate this topic.

4.1 | Patients selecting PGT-A

Understanding factors that influence couples in the decision-making process for PGT-A treatment can help providers to integrate this information and improve patient education, counseling and the shared decision-making process. It is established that patients only recall a small volume of the information that is given by medical practitioners across different specialties,\(^{40}\) despite attempts to improve retention with numerous interventions.\(^{41,42}\) In addition to information recall of patients being low, the information that is retained is often inaccurate or misunderstood;\(^{43}\) the reasons for this include both healthcare professional factors (inadequate communication skills, overuse of medical terminology) and patient factors (lack of basic understanding, preconceived notions).\(^ {44}\) Nonetheless, it is a basic principle of medical care to provide patients with an adequate amount of information at a level they can understand, especially in a field such as reproductive medicine, where a significant proportion of services are privately funded.

Unfortunately, studies consistently showed couples did not accurately understand PGT-A and its limitations and there is, therefore, a need to improve the patient education process. For example, studies showed women opted to undergo PGT-A to have genetically normal offspring,\(^ {34,45}\) with Quinn et al (2018) reporting 75% of patients selected PGT-A to have a “healthy baby” or to reduce the risk of birth defects. PGT-A certainly has the potential to reduce aneuploid live births; however, the majority of aneuploid pregnancies will fail to implant, miscarry or are detected by prenatal screening and/or testing. Indeed, the incidence of babies born with aneuploidy in developed countries is a relatively rare phenomenon and this has not been studied with regard to the use of PGT-A.\(^ {46}\) Of more concern, Lamb et al (2018) reported a common response was that previous parental carrier screening eliminated their risk of certain genetic conditions and, therefore, PGT-A would not provide any additional genetic information and was not required.\(^ {14}\) An increased aneuploidy risk is not usually “carried” by a parent and each pregnancy carries a risk for aneuploidy mainly determined by maternal age. However, it is not questioned that PGT-A does not screen for birth defects and by no means guarantees a healthy live birth. Additionally, Gebhart et al (2016) reported 81% of their participants had PGT-A to have a “normal” embryo. Therefore, it appears that improved counseling is needed to educate patients on the differences between assessing chromosomal number and single gene disorders and chromosomal rearrangement, as well as the other multiple etiologies that lead to birth defects.

In one study, 16% of respondents selected PGT-A to reduce their miscarriage risk, and the theory behind this is justifiable, since it is
well established that a significant proportion of miscarriages are due to transferring aneuploid embryos. However, one study examined patients with recurrent spontaneous miscarriage and found similar pregnancy and live birth rates among those patients who decided to undergo PGT-A and those who opted for expectant management. This study reported 26% of patients did not have an euploid embryo to transfer after IVF and, therefore, suggested fertility clinics should counsel patients not only on success rates with PGT-A per euploid embryo transferred but also on live birth rate per initiated IVF-PGT-A cycle. Another study found PGT-A eliminates the negative impact of maternal age on the implantation and miscarriage rate per embryo transfer, assuming there were sufficient embryos to perform PGT-A on.

Patients who selected PGT-A also rated reducing the time to pregnancy as a significant factor. There is evidence that PGT-A testing significantly improves the chances of a live birth per embryo transfer but patients need to understand the difference between this and time to live birth after starting an IVF cycle. However, a recent study did report that using PGT-A reduced the time in fertility treatment by approximately 4 months. Unfortunately, while time to a live birth when utilizing PGT-A is an ideal outcome measure, this has not been assessed in a randomized controlled trial.

4.2 | Reasons for patients not selecting PGT-A

PGT-A is an expensive procedure and, understandably, the associated costs were a consistently raised reason to decide not to go ahead with PGT-A. However, although PGT-A is associated with cost, it is unclear whether its use offsets these additional costs by increasing pregnancy rates per embryo transfer, thus reducing the number of transfers required. A recent study investigated the cost effectiveness of PGT-A of achieving a live birth in women over 37 years of age, and concluded the use of PGT-A to be a cost-effective strategy, reducing costs of fertility treatment overall. Another study by Neal et al (2018) showed that for patients with more than one embryo for transfer, IVF with PGT-A reduced healthcare costs by on average US$931-2411, shortened treatment time by 4 months, reduced the number of embryo transfers required and reduced miscarriage rates when compared with IVF alone. A minority of participants from studies consistently reported they declined PGT-A due to concern about harming the embryo. This concern should be acknowledged; however, patients should be reassured that data do not support that PGT-A damages blastocyst-stage embryos in experienced fertility centers. Indeed, a study in which one embryo was biopsied with subsequent transfer without influence from the PGT-A result found that blastocyst biopsy did not appear to impact on implantation rates.

For those considering its use, thorough patient education and counseling must be given, addressing the current limitations of the clinical effectiveness of PGT-A. This is particularly relevant, since most studies have reported patients who participate in PGT-A have significant misconceptions and gaps in knowledge surrounding its use.

4.3 | PGT for gender selection

The use of PGT for non-medical interventions has been deeply criticized internationally by medical societies, and its utilization is the center of much ethical debate. Indeed, the American Society for Reproductive Medicine "actively discourages purely elective use of PGT for social sex selection" and this view is supported by other organizations including the Human Fertilization and Embryology Authority and the American College of Obstetrics and Gynecologists. However, more relevant are the moral attitudes and beliefs of couples who are using PGT for that purpose. Sharp et al (2010) reported that couples pursuing IVF for gender selection had a wide range of motivations to do so. They broadly split their rationale for choosing gender selection into self-interests, such as a desire for specific parenting experiences, and family-centered interests, such as a hope to enhance family dynamics.

One of the major concerns regarding gender selection in the biomedical ethical literature is that it is inherently sexist and perpetuates gender discrimination. Sharp et al (2010) reported that a couples’ desire for gender balance in the family is more complex and not inherently sexist, with them generally expressing a desire to use gender selection to achieve a gender balanced family, in contrast to a simple desire to have a son. Indeed, the majority of studies found there was no difference between couples wanting a male child and those wanting to have a female child. However, a study from Lebanon found an extreme desire for a male offspring, with 94.1% of those who used PGT wanting a son.

Couples felt the use of gender selection was a personal one and not a larger societal one. Much of patients’ moral decision-making process involved weighing moral issues for themselves, future children and their immediate families. Larger societal implications to allow PGT for gender selection were not apparent in their personal decision-making process. However, it should be noted that couples did consistently report moral concerns about this approach to have a child, and although the majority felt the benefits outweighed the risks, and, therefore, continued with PGT for gender selection, the majority continued to raise concerns about the process. For example, a significant number of couples in various studies had experienced having a child of the opposite sex they had hoped for, but did not feel that child was less loved because of this initial disappointment. Patients were also ambivalent regarding their choice to disclose they had used PGT for gender selection to close friends and family. Disposing of unused embryos created via ART was another consistent source of concern for couples. Couples also identified numerous moral concerns regarding gender selection, including the negative impact the use of gender selection could have on their other children and on their personal relationships with close family members. Couples also reported their strong beliefs surrounding reproductive liberty and privacy.

These issues raised, confirm the importance of fertility clinics in countries offering PGT for sex selection offering extensive pre-decisional and post-treatment counseling to patients using this
technology, with the existing counseling models for PGT for monogenic disorders or PGT for chromosomal structural re-arrangement being appropriate counseling models to base this on. Patients need to be made aware during counseling that the effect of PGT-A is also highly dependent on the IVF center performing the procedure. In the wrong hands, PGT-A could be detrimental, with euploid embryos incorrectly classified as aneuploid and discarded, or increased risk of damage to the embryo during biopsy. Patients, therefore, should be made aware of the individual experiences of clinics using PGT-A prior to embarking on treatment.

There were some methodological limitations identified in the studies included in the systematic review. First, the majority of studies used a relatively small sample size and were single-centered studies. Second, the majority of the studies used existing databases or closed-ended surveys to gather their data. Although subjects in the studies using questionnaires were invited to write in additional factors that influenced their decision-making process, it is possible that respondents would not have volunteered this information in a questionnaire tool. This could mean that additional factors might have played a role and are unreported. It is also likely that some of the survey content in the studies was misunderstood by patients; for example, using PGT-A to “have a healthy baby” was commonly selected but this cannot be guaranteed by PGT-A, and studies consistently reported they had counseled patients about this. Interview-based studies would be able to clarify this with patients and ensure the questionnaire did not cause misunderstanding. Third, there is a significant risk of sampling bias, with the views of those who declined to participate in the studies interviews/questionnaires not reported. Patients with more positive attitudes and experiences are more likely to participate, thus leading to potentially significant publication bias. Fourth, studies consistently only invited female patients to participate in the questionnaires, meaning the male partners’ motivations, attitudes and experiences are under-reported. Fifth, only English language studies were included, again allowing for potential bias. Sixth, some of the studies investigating PGT for sex selection were retrospective and used databases, meaning information bias could occur from inaccurate record-keeping. In these studies there was some desired demographic and medical data not collected, restricting analysis. Seventh, there are no studies following up couples long term, thus there are no data investigating longer term consequences of using this technology. Finally, the majority of study participants had a high socioeconomic and educational status, with the majority having a university degree. This population is likely to have better access to ARTs, meaning the views of other populations have not been captured. The demographics of those who chose not to participate in PGT for aneuploidy or gender selection remains unknown.

5 | CONCLUSION

Fertility patients are especially vulnerable to treatments and technologies that have the potential to improve their IVF outcome. Screening embryos for chromosomal aneuploidy offers many theoretical benefits. However, until randomized controlled trials show a definite positive outcome for certain populations using this technology, fertility clinics should ensure adequate counseling to allow better patient interpretation. Regarding the use of PGT for sex selection, the full range of issues raised for the use of PGT for sex selection has not yet been examined adequately for the numerous regulating authorities internationally to make sweeping ethical statements concerning its use. Studies consistently report that it is naïve to suggest couples use this simply to have a child of a particular sex, but instead make decisions based on a diversity of moral values and cultural perspectives. These perspectives allow a more practically orientated discussion surrounding ethical considerations and the use of ART for gender selection. An increasing number of women are choosing to have pre-genetic testing of embryos globally, and patient preferences are likely to remain significant where a potential clinical balance of interests exists. There is a need to develop decision support tools for couples for the increasing genetic testing options available.

CONFLICT OF INTEREST

None.

ORCID

Timothy Bracewell-Milnes https://orcid.org/0000-0001-9827-4816

Benjamin Jones https://orcid.org/0000-0002-0391-0443

REFERENCES

1. Cousineau TM, Domar AD. Psychological impact of infertility. Best Pract Res Clin Obstet Gynaecol. 2007;21:293-308.
2. Rubio C, Rodrigo L, Mir P, et al. Use of array comparative genomic hybridization (array-CGH) for embryo assessment: clinical results. Fertil Steril. 2013;99:1044-1048.
3. Geraedts JP, De Wert GM. Preimplantation genetic diagnosis. Clin Genet. 2009;76:315-325.
4. Martin J, Cervera A, Mir P, Martinez-Connejero JL, Pellicer A, Simon C. The impact of next-generation sequencing technology on preimplantation genetic diagnosis and screening. Fertil Steril. 2013;99(4):1054-1061.e3.
5. Wong KM, Repping S, Vandenbroek S. Limitations of embryo selection methods. Semin Reprod Med. 2014;32:127-133.
6. Minasi MG, Fiorentino F, Ruberti A, et al. Genetic diseases and aneuploidies can be detected with a single blastocyst biopsy: a successful clinical approach. Hum Reprod. 2017;32:1770-1777.
7. Scott RT Jr, Ferry K, Su J, Tao X, Scott K, Treff NR. Comprehensive chromosome screening is highly predictive of the reproductive potential of human embryos: a prospective, blinded, nonelection study. Fertil Steril. 2012;97:870-875.
8. Franasiak JM, Forman EJ, Hong KH, et al. The nature of aneuploidy with increasing age of the female partner: a review of 15,169 consecutive trophectoderm biopsies evaluated with comprehensive chromosomal screening. Fertil Steril. 2014;101(3):656-663.e1.
9. McGowan ML, Burant CJ, Moran R, Farrell R. Patient education and informed consent for preimplantation genetic diagnosis: health literacy for genetics and assisted reproductive technology. Genet Med. 2009;11:640-645.
10. Zheng Z, Zhao X, Xu B, Yao N. What should we focus on before preimplantation genetic diagnosis/screening? Arch Med Sci. 2018;14:1119-1124.
11. Meldrum DR. Introduction: preimplantation genetic screening is alive and very well. Fertil Steril. 2013;100:593-594.
12. López-Regalado ML, Clavero A, Gonzalvo MC, et al. Randomised clinical trial comparing elective single-embryo transfer followed by single-embryo cryotransfer versus double embryo transfer. *Eur J Obstet Gynecol Reprod Biol*. 2014;178:192-198.

13. Dahdouh EM, Balayla J, García-Velasco JA. Preimplantation genetic screening using comprehensive chromosome screening: evidence and remaining challenges. *Hum Reprod*. 2015;30:1515-1516.

14. Lamb B, Johnson E, Francis L, et al. Pre-implantation genetic testing: decisional factors to accept or decline among in vitro fertilization patients. *J Assist Reprod Genet*. 2018;35:1605-1612.

15. Brezina PR, Kutteh WH, Bailey AP, Ke RW. Preimplantation genetic screening (PGS) is an excellent tool, but not perfect: a guide to counseling patients considering PGS. *Fertil Steril*. 2016;105:49-50.

16. Harper JC, Geraedts J, Borry P, et al. Current issues in medically assisted reproduction and genetics in Europe: research, clinical practice, ethics, legal issues and policy. *European Society of Human Genetics and European Society of Human Reproduction and Embryology*. *Eur J Hum Genet*. 2013;21(Suppl 2):S1-S21.

17. The use of preimplantation genetic testing for aneuploidy (PGT-A): a committee opinion. *Fertil Steril*. 2018;109:429-436.

18. Human Fertilisation & Embryology Authority. Treatment add-ons. [https://www.hfea.gov.uk/treatments/explore-all-treatments/treatment-add-ons/ Accessed on August, 2020.](https://www.hfea.gov.uk/treatments/explore-all-treatments/treatment-add-ons/

19. Hershberger PE, Gallo AM, Kavanaugh K, Olshansky E, Schwartz A, Tur-Kaspa I. The decision-making process of genetically at-risk couples considering preimplantation genetic diagnosis: initial findings from a grounded theory study. *Soc Sci Med*. 2012;74:1536-1543.

20. Whittaker AM. Reproduction opportunists in the new global sex trade: PGD and non-medical sex selection. *Reprod Biomed Online*. 2011;23:609-617.

21. Merhi ZO, Pal L. Gender, “tailored” conceptions: should the option of embryo gender selection be available to infertile couples undergoing assisted reproductive technology? *J Med Ethics*. 2008;34:590-593.

22. Savulescu J, Dahl E. Sex selection and preimplantation diagnosis: a response to the Ethics Committee of the American Society of Reproductive Medicine. *Hum Reprod*. 2000;15:1879-1880.

23. Levy N. Against sex selection. *South Med J*. 2007;100(1):107-109; discussion 10-1.

24. Blyth E, Frith L, Crawshaw M. Ethical objections to sex selection, indeed, sexist? *Clin Genet*. 2014;86:177-180.

25. Naini P, Lewis J, Rajanna K, Weir AB 3rd. Evaluation of a method to improve the consent process: improved data retention with stag-nant comprehension. *J Cancer Educ*. 2013;28:38-42.

26. Langdon JJ, Hardin R, Learmonth I. Informed consent for total hip arthroplasty: does a written information sheet improve recall by patients? *Ann R Coll Surg Engl*. 2002;84:404-408.

27. Anderson JL, Dodman S, Kopelman M, Fleming A. Patient information recall in a rheumatology clinic. *Rheumatol Rehabil*. 1979;18:18-22.

28. Ley P. Memory for medical information. *Br J Soc Clin Psychol*. 1979;18:245-255.

29. Quinn G, Vadaparampil S, Wilson C, et al. Attitudes of high-risk women toward preimplantation genetic diagnosis. *Fertil Steril*. 2009;91:2361-2368.

30. Hassold T, Hunt P. To err (meiotically) is human: the genesis of human aneuploidy. *Nat Rev Genet*. 2001;2:280-291.

31. Blue NR, Page JM, Silver RM. Genetic abnormalities and pregnancy loss. *Semin Perinatol*. 2019;43:66-73.

32. Murugappan G, Shahine LK, Perfetto C, Hickok LR, Latii RB. Intent to treat analysis of in vitro fertilization and preimplantation genetic screening versus expectant management in patients with recurrent pregnancy loss. *Hum Reprod*. 2016;31:1668-1674.

33. Neal SA, Morin SJ, Fransasi JM, et al. Preimplantation genetic testing for aneuploidy is cost-effective, shortens treatment time, and reduces the risk of failed embryo transfer and clinical miscarriage. *Fertil Steril*. 2018;110:896-904.

34. Dahdouh EM, Balayla J, García-Velasco JA. Impact of blastocyst biopsy and comprehensive chromosome screening technology on preimplantation genetic screening: a systematic review of randomized controlled trials. *Reprod Biomed Online*. 2015;30:281-289.

35. Cedars MI. Fresh versus frozen: initial transfer or cumulative cycle results: how do we interpret results and design studies? *Fertil Steril*. 2016;105:188-193.

36. Katz MG, Fitzgerald L, Bankier A, Savulescu J, Cran D. Issues and concerns of couples presenting for preimplantation genetic diagnosis (PGD). *Prenat Diagn*. 2002;22:1117-1122.

37. Quin MM, Juarez-Hernandez F, Dunn M, Okamura RJ, Cedars MI, Rosen MP. Decision-making surrounding the use of preimplantation genetic testing for aneuploidy reveals misunderstanding regarding its benefit. *J Assist Reprod Genet*. 2018;35:2155-2159.

38. Jain T, Missmer SA, Gupta RS, Hornstein MD. Preimplantation sex selection demand and preferences in an infertility population. *Fertil Steril*. 2005;83:649-658.

39. Gleiher N, Barad DH. The choice of gender: is elective gender selection, indeed, sexist? *Hum Reprod*. 2007;22:3038-3041.

40. Turner P, Williams C. Informed consent: patients listen and read, but what information do they retain? *N Z Med J*. 2002;115:U218.

41. Naini P, Lewis J, Rajanna K, Weir AB 3rd. Evaluation of a method to improve the consent process: improved data retention with stagnant comprehension. *Hum Reprod*. 2000;15(Suppl 2):S1-S21.

42. Langdon JJ, Hardin R, Learmonth I. Informed consent for total hip arthroplasty: does a written information sheet improve recall by patients? *Ann R Coll Surg Engl*. 2002;84:404-408.

43. Anderson JL, Dodman S, Kopelman M, Fleming A. Patient information recall in a rheumatology clinic. *Rheumatol Rehabil*. 1979;18:18-22.

44. Ley P. Memory for medical information. *Br J Soc Clin Psychol*. 1979;18:245-255.

45. Quinn G, Vadaparampil S, Wilson C, et al. Attitudes of high-risk women toward preimplantation genetic diagnosis. *Fertil Steril*. 2009;91:2361-2368.

46. Hassold T, Hunt P. To err (meiotically) is human: the genesis of human aneuploidy. *Nat Rev Genet*. 2001;2:280-291.

47. Blue NR, Page JM, Silver RM. Genetic abnormalities and pregnancy loss. *Semin Perinatol*. 2019;43:66-73.

48. Murugappan G, Shahine LK, Perfetto C, Hickok LR, Latii RB. Intent to treat analysis of in vitro fertilization and preimplantation genetic screening versus expectant management in patients with recurrent pregnancy loss. *Hum Reprod*. 2016;31:1668-1674.

49. Neal SA, Morin SJ, Fransasi JM, et al. Preimplantation genetic testing for aneuploidy is cost-effective, shortens treatment time, and reduces the risk of failed embryo transfer and clinical miscarriage. *Fertil Steril*. 2018;110:896-904.

50. Dahdouh EM, Balayla J, García-Velasco JA. Impact of blastocyst biopsy and comprehensive chromosome screening technology on preimplantation genetic screening: a systematic review of randomized controlled trials. *Reprod Biomed Online*. 2015;30:281-289.

51. Cedars MI. Fresh versus frozen: initial transfer or cumulative cycle results: how do we interpret results and design studies? *Fertil Steril*. 2016;105:188-193.

52. Collins SC, Xu X, Mak W. Cost-effectiveness of preimplantation genetic screening for women older than 37 undergoing in vitro fertilization. *J Assist Reprod Genet*. 2017;34:1515-1522.

53. Scott RT Jr, Upham KM, Forman EJ, Zhao T, Treff NR. Cleavage-stage biopsy significantly impairs human embryonic implantation potential while blastocyst biopsy does not: a randomized and paired clinical trial. *Fertil Steril*. 2013;100:624-630.
54. Preconception gender selection for nonmedical reasons. *Fertil Steril.* 2001;75:861-864.
55. Cohen J. Gender selection: is there a European view? *J Assist Reprod Genet.* 2002;19:417-419.
56. Pastore LM, Cordeiro Mitchell CN, Rubin LR, Nicoloro-SantaBarbara J, Genoff Garzon MC, Lobel M. Patients’ preimplantation genetic testing decision-making experience: an opinion on related psychological frameworks. *Hum Reprod Open.* 2019;2019:hoz019.
57. Thornton A, Lee P. Publication bias in meta-analysis: its causes and consequences. *J Clin Epidemiol.* 2000;53(2):207-216.

**How to cite this article:** Bracewell-Milnes T, Saso S, Jones B, et al. A systematic review exploring the patient decision-making factors and attitudes towards pre-implantation genetic testing for aneuploidy and gender selection. *Acta Obstet Gynecol Scand.* 2021;100:17-29. [https://doi.org/10.1111/aogs.13973](https://doi.org/10.1111/aogs.13973)