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Preimplantation genetic screening: results of a worldwide web-based survey

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KEY MESSAGE

Results of a web-based survey on practices of, and opinions on, preimplantation genetic screening (PGS) are presented. The results clearly emphasize increased utilization and interest in PGS; however, users and non-users of the technique express a need for more robust and evidence-based data on different aspects of PGS.

A B S T R A C T

Our objective was to evaluate and characterize the extent and patterns of worldwide usage of preimplantation genetic screening (PGS) among the assisted reproductive technique community. A prospective, web-based questionnaire with questions relating to practices of, and views on, PGS was directed to users and non-users of PGS. A total of 386 IVF units from 70 countries conducting 342,600 IVF cycles annually responded to the survey. A total of 77% of respondents routinely carry out PGS in their clinics for a variety of indications: advanced maternal age (27%), recurrent implantation failure (32%) and recurrent pregnancy loss (31%). Few (6%) offer PGS to all their patients. In most cycles (72%), trophectoderm biopsy is carried out and either array-comparative genomic hybridization (59%) or next-generation sequencing (16%) are used for genetic analysis. Only 30% of respondents regard PGS as clearly evidenced-based, and most (84%) believe that more randomized controlled trials are needed to support the use of PGS. Despite ongoing debate and lack of robust evidence, most respondents support the use of PGS, and believe that it may aid in transferring only euploid embryos, thereby reducing miscarriage rates and multiple pregnancies, increasing live birth rates and reducing the risk of aneuploid pregnancies and births.

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Introduction

Aneuploidy is widely recognized as a leading embryonic cause for both implantation failure and pregnancy loss in natural and assisted conceptions. The intention of preimplantation genetic screening (PGS) is to prevent aneuploid embryo transfers in infertile patients undergoing IVF. By identifying euploid embryos for transfer, PGS is expected to increase implantation and live birth rates and reduce miscarriage rates per transfer cycle. In the early days of PGS (PGS 1.0), cleavage-stage embryo biopsy using fluorescence in-situ hybridization (FISH) was used for assessing aneuploidy. After initial enthusiasm and widespread use, several randomized controlled trials (Mastenbroek et al., 2007; Staessen et al., 2004) and subsequent meta-analysis (Mastenbroek et al., 2011) failed to show a beneficial effect of PGS on the live birth rate after IVF. The use of PGS 1.0 has declined as it was also discouraged by professional societies (ACOG, 2009; Harper et al., 2010; Practice Committee of Society for Assisted Reproductive Technology, Practice Committee of American Society for Reproductive Medicine, 2008).

Advances in assisted reproduction and molecular genetic technniques have recently allowed the reintroduction of a new form of PGS (PGS 2.0). These improvements consist of the ability to perform comprehensive chromosome screening (CCS) of all 24 chromosomes; the ability to culture embryos to the blastocyst stage and carry out trophectoderm biopsy of several cells; and efficient techniques for embryo vitrification and warming. We are now witnessing a dramatic increase of the use of PGS 2.0 in many patient groups. Nonetheless, debate about the efficiency, pace and mode of introduction of PGS 2.0 into clinical practice is still ongoing (Gleicher et al., 2014; Mastenbroek and Repping, 2014; Sermon et al., 2016).

IVF-Worldwide.com is a comprehensive IVF-focused website linking specialists in IVF centres around the world, providing its members with the ability to communicate and discuss professional issues (www.IVF-Worldwide.com). IVF-Worldwide.com also contains educational materials, and conducts surveys on a variety of issues related to assisted reproduction techniques. The website is non-commercial and has an advisory board of key opinion leaders in the field who also construct and review the surveys posted on the website. The IVF-Worldwide.com platform allows access to a large number of IVF clinics worldwide, and is therefore an excellent tool to conduct large-scale surveys. Surveys are an interesting form of data collection, as they represent the 'wisdom of crowds', but they are only complementary to big data-collection platforms such as the European Society of Human Reproduction and Embryology PGD Consortium data-collection papers that allowed the field to understand trends on the use of genetic technologies in IVF (De Rycke et al., 2015).

The purpose of the present survey was to evaluate the extent and patterns of PGS usage worldwide, and to gain insights on the views and opinions of the assisted reproductive technique community on the use of PGS 2.0.

Materials and methods

Survey content

Through expert opinion and literature review, the authors developed a questionnaire that was directed to both current users and non-users of PGS. After general questioning on clinic characteristics and demographics, PGS users received a 14-item questionnaire, whereas non-users received a five-item questionnaire. For each question, multiple choice answers were provided, from which a single answer could be chosen in nine questions, whereas in the remaining five questions, multiple answers were allowed.

The web-based questionnaire entitled 'Preimplantation genetic screening (PGS): what is my opinion?' was posted on the IVF-Worldwide.com website on September 20, 2015, and was open for data entry until November 17, 2015. The survey questions can be accessed at the following URL (IVF-Worldwide): http://www.ivf-worldwide.com/survey/preimplantation-genetic-screening-pgs-what-is-my-opinion.html. All registered members of IVF-Worldwide.com were invited by several email messages to participate. The survey contained a demographic section, with questions on the name of the IVF clinic, email address, country, and number of IVF cycles carried out in the most recent year. The medical section of the survey evaluated the practice patterns and opinions of respondents with a series of multiple choice questions.

Quality-assurance methods used

To minimize duplicate reports from a particular unit and possible false data, three parameters were compared with existing data of units registered on the IVF-Worldwide.com website. These parameters included the name of the unit, country, and email address. If all of these parameters from the survey matched the website archive data, this reporting site's data were included in the statistical analyses.

Statistical analysis

The analysis was based on the number of IVF cycles reported by the unit and not on the number of units in the study. Therefore, the relative proportion of answers reflects the total proportion of IVF cycles represented rather than the proportion of individual respondents to the survey questions. Results were calculated by using the following formulas as described in previously reported research from the IVF-Worldwide.com network (Vaisbuch et al., 2012):

Compliance with ethical requirements and conflict of interest statement

The survey does not involve human or animal research and hence a formal Institutional Review Body approval was not obtained. The Survey was available as an open-access questionnaire to the members of the IVF-Worldwide.com who voluntarily answered the study questions. Data collected for this research were anonymous. The authors declare that they have no conflict of interest.

Results

Completed survey forms were received from 386 IVF clinics, originating from 70 countries, from all five continents. These clinics carried out nearly 342,600 IVF cycles annually. The detailed response to all the questions can be accessed through IVF-Worldwide.com at http://www.ivf-worldwide.com/survey/preimplantation-genetic-screening-pgs-what-is-my-opinion/results-preimplantation-genetic-screening-pgs-what-is-my-opinion.html.

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Table 1 – Geographic distribution of IVF units participating in the survey.

Continent	Total				Centers Performing PGS				Centers NOT Performing PGS			
	Annual IVF Cycles	%	Number of units	%	Annual IVF cycles	%	Number of units	%	Annual IVF cycles	%	Number of units	%
USA and Canada	65,800	19.2	97	25.1	63,000	23.9	93	34.3	2800	3.5	4	3.5
South America	18,500	5.4	34	8.8	15,900	6.0	26	9.6	2600	3.3	8	7
Australia and New Zealand	22,300	6.5	21	5.4	20,800	7.9	16	5.9	1500	1.9	5	4.3
Asia	83,900	24.5	78	20.2	62,200	23.6	56	20.7	21,700	27.3	22	19.1
Europe	137,900	40.3	137	35.5	91,600	34.8	70	25.8	46,300	58.2	67	58.3
Africa	14,200	4.1	19	4.9	9600	3.6	10	3.7	4600	5.8	9	7.8
	342,600	100	386	100	263,100	100	271	100	79,500	100	115	100

The geographical and relative size distribution of clinics that responded to the survey are presented in **Table 1**. Analysis of the data according to its source by geographical region failed to reveal any significant difference in response pattern. Results of all survey respondents were compared with the results received from each continent, calculating the absolute difference for each answer, the average difference for all answers was less than 10% (data not shown). The survey revealed that 77% of the clinics that responded routinely carry out PGS.

Which patients are being offered PGS in their treatment cycles?

Although multiple answers were allowed for this question, answers were almost equally distributed (90%) for three major indications: advanced maternal age (AMA) (>35 years [27%]); patients who had experienced repeated implantation failure (RIF) (32%); patients who had experienced recurrent pregnancy loss (RPL) and normal parental karyotype (31%). PGS was offered to all patients in only 6% of the clinics, and mainly to good-prognosis patients in 4%.

Is ovarian reserve a major factor in the inclusion criteria for PGS in your clinic?

Most clinics (62%) do not include ovarian reserve in the inclusion criteria for PGS, whereas 38% do include it.

Are patients with low ovarian reserve excluded from PGS?

Most clinics (83%) do not exclude patients with low ovarian reserve (LOR) from PGS, whereas the remaining (17%) do so. All patients are included irrespective of ovarian reserve in most responding clinics (67%).

Is a minimum number of blastocysts necessary for inclusion irrespective of ovarian reserve?

In 56% of the clinics, a stipulation of a minimum number of blastocysts is not necessary for inclusion, irrespective of ovarian reserve, whereas, in 44%, a minimum number of blastocysts is necessary for inclusion.

To what extent is PGS being used in your clinic?

In 47% of the clinics, PGS is used in less than 10% of the cycles, and,in only 7%, it is used in more than 50% of cycles (**Figure 1**).

Who is responsible for funding the PGS part of the cycle?

In most clinics (97%), PGS is being funded by patients out-of-pocket. It is covered by insurance companies in 1%, and the the public health system in 1%. Another 1% of respondents answered 'other/unspecified option'.

At what stage of development are the majority of embryo biopsies being carried out in your clinic?

In 72% of the clinics, embryo biopsies are carried out at the blastocyst stage. In 25% of clinics, biopsies are carried out at the cleavage stage, and in 3% polar body (I and II) biopsies are predominantly carried out (**Figure 2**).

Do you carry out PGS on frozen–thawed embryos if the patient failed a non-PGS cycle?

In most clinics (68%), PGS is carried out on frozen-thawed embryos if a fresh non-PGS cycle has failed.

Which method of genetic testing is predominantly used in your clinic for determination of embryo ploidy status?

The most frequently used technique is array comparative genomic hybridization (aCGH) (59%) followed by next-generation sequencing (16%), FISH (9%), single nucleotide polymorphism microarray (SNP) (7%) and real-time quantitative polymerase chain reaction (5%) (**Figure 3**).

Where is genetic testing being carried out?

Most clinics (69%) use a centralized referral laboratory, 23% use an in-house genetic laboratory and 8% report on using both.

Which method of embryo transfer is preferred in your clinic after PGS?

In 49% of clinics, frozen–thawed embryo transfer is predominantly used, 22% prefer fresh transfers, and in 29% of clinics both methods are used.

How many euploid embryos do you normally transfer?

In 34% of clinics, single embryo transfer (SET) is carried out for all cases after PGS, and, in 21%, SET is carried out only in good-prognosis

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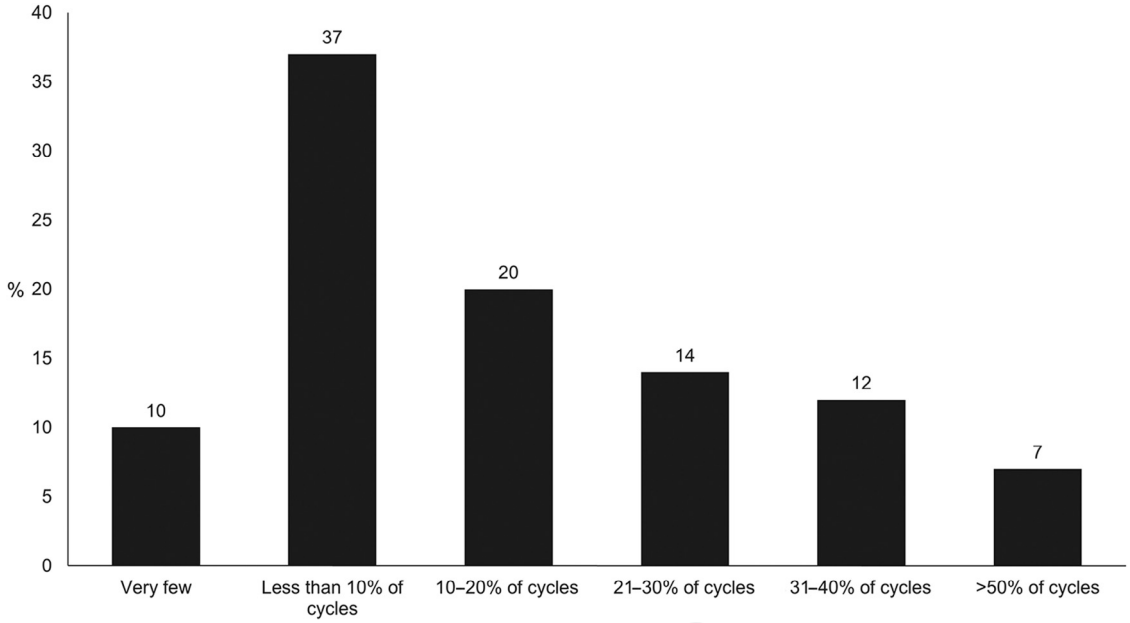

Figure 1 – To what extent is preimplantation genetic screening being used in your clinic? Results are expressed in percentage, which represents the proportion of replies from the clinics relative to the number of cycles carried out in each clinic. Figure adapted from the IVF-Worldwide (2017).

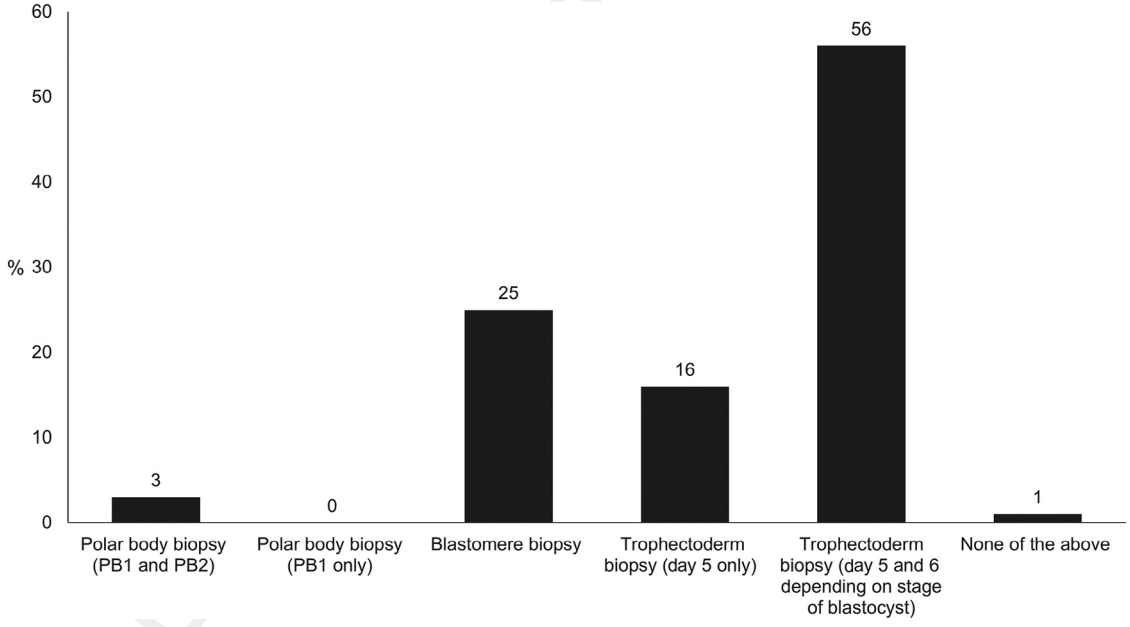

Figure 2 – At what stage of development are the majority of embryo biopsies being performed in your clinic? Results are expressed in percentage, which represents the proportion of replies from the clinics relative to the number of cycles performed in each clinic. Figure adapted the IVF-Worldwide (2017).

patients. In 33% of clinics, the decision on the number of embryos to be transferred is based on patients' request, and, in 12% of clinics, double embryo transfers are predominantly carried out.

To what extent do you think that PGS is evidence-based?

Only 30% of respondents regard PGS as clearly evidenced-based, and 37% regard it as 'most likely' evidence-based. On the other hand, 9% regard PGS as 'not evidence-based' or 'probably not evidence-based' (7%), and for 18% it is undecided.

Do you think more randomized trials are needed to support the use of PGS?

Most respondents (84%) believe that more randomized trials are needed to support the use of PGS.

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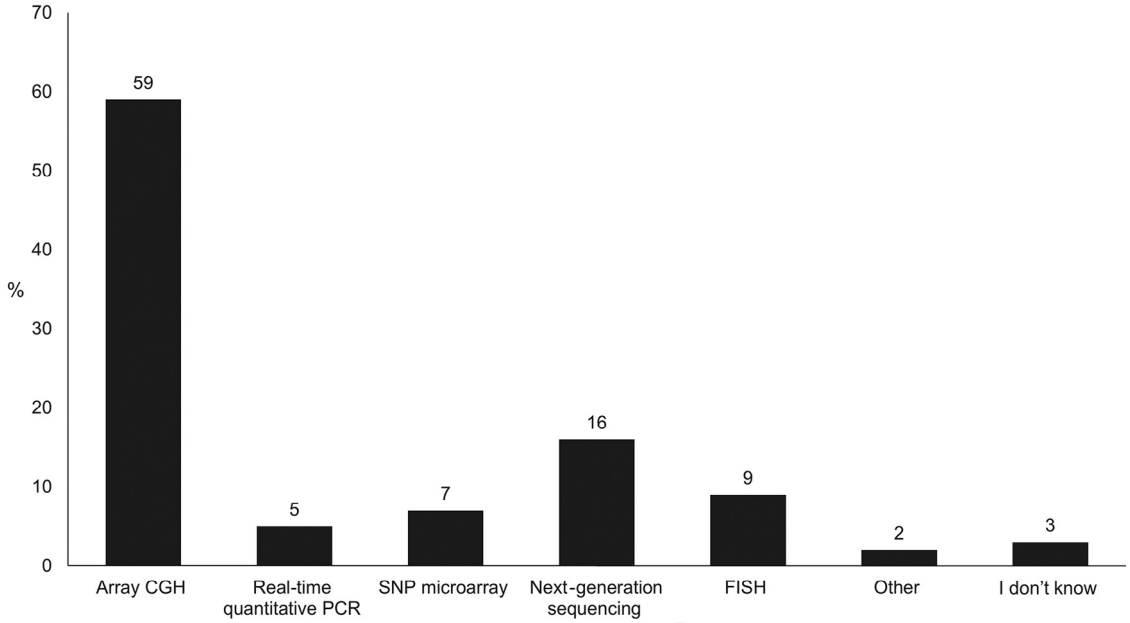

Figure 3 – Which method of genetic testing is predominantly used in your clinic for determination of embryo ploidy status? Results are expressed in percentage, which represents the proportion of replies from the clinics relative to the number of cycles performed in each clinic. CGH, comparative genomic hybridization; FISH, fluorescence in-situ hybridization; PCR, polymerase chain reaction; SNP, single nucleotide polymorphism. Figure adapted the IVF-Worldwide (2017).

Do you believe PGS can (do the following)?

A total of 78% of the respondents believe that PGS can only prevent the transfer of aneuploid embryos, 72% believe it can reduce miscarriage rates, and 60% believe PGS can increase live birth rates.

Is PGS regulated in your country?

In 30% of the clinics, PGS is regulated, including the number of embryos transferred; in 57%, it is not; and in 13% the answer was 'none of the above'.

Questions for units where PGS is not being used

Most respondents in such units (63%) replied that PGS is carried out in other centres in their country, whereas 37% responded that it is not carried out. The reasons why PGS is not carried out include lack of technical skill and staff (23%); lack of patient demand (20%); initial investment and cost issues (15%); or PGS is banned by law (23%). Most respondents (66%) believe that, at present, it is clinically justified to offer PGS. If PGS would became available, it should be offered to the following patient groups: patients who have experienced RIF (63%), patients who have experienced RPL (44%), patients of AMA (36%), good-prognosis patients (1%), all patients (11%) and none (9%). With ovarian reserve, most respondents (59%) believe that a minimum number of embryos/blastocysts is necessary for inclusion in a PGS programme.

Discussion

The results of this survey clearly emphasize increased interest among the assisted reproduction technique community in PGS. With respondents from 386 IVF clinics, originating from 70 countries and representing about 342,600 annual IVF cycles, it is a survey with one of the highest response rates ever published by IVF-Worldwide.com (IVF-Worldwide, 2017). As no regional differences were noted in the response patterns of the study respondents, it seems that physicians and researchers worldwide share similar guidelines on, and practices of, PGS. The diversities in the responses obtained for many of the questions raised in the study represent the fact that PGS 2.0 is still in a constant process of development, with many issues yet to be resolved.

Although no updated worldwide registry is available that can provide data on the precise utilization rate of PGS, it seems that the survey respondents are heavily biased towards PGS, as 77% of the clinics represented in the survey routinely carry out PGS. In the USA, the most recent national summary report on assisted reproduction techniques by the Centers for Disease Control and Prevention for 2014 stated that, only 4% of 208,604 cycles carried out were PGD, PGS, or both (CDC, 2017). The Society for Assisted Reproductive Technology reported that 165 out of 458 (36%) participating clinics used PGD, PGS, or both (SART, 2017). As PGS is recently gaining popularity in the USA, it is likely that the above figures are an underestimation. Although no updated hard data are available, most estimate the current rate today to be over 20% of IVF cycles in the USA. Obviously, clinicians who carry out PGS were likely to be attracted by the survey, which explains the high utilization rates of PGS among respondents, which is the major weakness of the study. Another weakness of the survey is that it did not address the problem of embryo mosaicism. Embryonic mosaicism within PGS has been the topic of a recent survey and a study, the results of which are now available (IVF-Worldwide, 2017; Weissman et al., 2017).

The most common indications for PGS in this survey are for poor-prognosis patients (AMA, RIF and RPL). High-quality data, namely randomized controlled trials, that support the use of PGS for these indications, are however, lacking. Advanced maternal age is a common indication for PGS (27%) among respondents. Rubio et al. (2013)

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conducted a randomized controlled trial in patients of AMA, in which single-cell day-3 biopsy and FISH for nine chromosomes (PGS 1.0) with subsequent fresh blastocyst transfer were used in patients aged 41–44 years (Rubio et al., 2013). A significant two-fold increase in live-birth rate per patient was found in the PGS group compared with the non-PGS blastocyst group ([32.3% versus 15.5%], respectively (OR 2.585; CI 1.262 to 5.295). In a recent multicentre RCT in slightly younger patients of AMA (38–41 years), the same group (Rubio et al., 2017) further showed that PGS (day 3 biopsy and aCGH for 24 chromosomes) significantly improved the delivery rate after the first transfer attempt (52.9% versus 24.2% for control) and per patient (36.0% versus 21.9%, respectively). In addition, PGS dramatically reduced miscarriage rates (2.7% with PGS versus 39.0% for control). No significant differences were observed in the cumulative delivery rates per patient 6 months after closing the study.

Retrospective studies using PGS 2.0 in patients of AMA have also yielded promising results. In a retrospective multicentre study, Harton et al. (2013) demonstrated that, with transfer of euploid embryos, implantation and pregnancy rates were not significantly different between younger and older patients, up to 42 years of age. Implantation and pregnancy rates declined in patients over 42 years of age, as did the fraction of patients who had euploid embryos available for transfer, a condition that worsened with advancing maternal age. Similar results were reported in another retrospective study for patients of AMA aged 40–43 years (Lee et al., 2015). Ubaldi et al. (2015) reported a significant increase in live birth rate per transferred embryo in patients of AMA after PGS, while maintaining a low multiple pregnancy rate with the elective transfer of a single euploid blastocyst.

Rubio et al. (2013) also conducted a randomized controlled trial in patients who had experienced RIF, and found no significant differences in live birth rates among patients who underwent PGS compared with patients who did not (47.9% versus 27.9%, respectively). In a retrospective study, Rodrigo et al. (2014) reported on 188 PGS cycles in patients who had eperienced RIF using aCGH on cleavage-stage biopsies with subsequent blastocyst transfer. Both fresh and cryopreserved oocytes and embryos were included. Although 71.5% of all embryos analysed were aneuploid, in 78.8% patients at least one euploid embryo was available for transfer, resulting in a favourable delivery rate of 43.1%. Similarly, Greco et al. (2014) carried out trophectoderm biopsy and aCGH in 43 patients who had experienced RIF (RIF-PGS group) and compared results with 33 patients who had not experienced RIF and did not undergo PGS (RIF non-PGS) and 45 good-prognosis patients also underwent PGS (non-RIF PGS). A single euploid blastocyst was transferred in both RIF-PGS and non-RIF-PGS groups. Similar clinical pregnancy and implantation rates were obtained in the RIF-PGS and non-RIF-PGS groups (68.3% and 70.5%, respectively). In contrast, a significantly lower clinical pregnancy rate (21.2%) was observed in patients who had experienced RIF who did not undergo PGS. Although the favourable results reported in retrospective studies (Fragouli et al., 2010; Greco et al., 2014; Rodrigo et al., 2014) support the application of PGS in patients who had experienced RIF, no RCT using CCS in this challenging patient population has been conducted.

Patients with low ovarian reserve (LOR) and diminished ovarian response (DOR) are frequently encountered in assisted reproduction technique programs, and could theoretically benefit the most from PGS. Data on PGS outcomes in patiens with LOR and DOR, are, however, scant. The available randomized controlled trials on PGS either included only young and good-prognosis patients (Yang et al., 2012), or patients who had a minimum of two blastocysts at the time of randomization (Forman et al., 2013; Scott et al., 2013a). The minimum number of blastocysts needed to obtain at least one euploid embryo for transfer according to age and ovarian reserve test is currently unknown. Although a matter of debate, it has previously been suggested that infertile patients with hormonal evidence of DOR have a significantly higher percentage of aneuploid blastocysts (Katz-Jaffe et al., 2013). It has also been proposed that, for patients with DOR, blastocyst culture and transfer is either ineffective or, indeed, may actually be detrimental (Gleicher et al., 2015). Women with DOR are more likely not to reach embryo transfer at all simply because their embryos may not reach the blastocyst stage. Strategies directed at improving the outcome of patients with LOR and DOR by PGS include the accumulation of vitrified oocytes or blastocysts in multiple cycles (Chamayou et al., 2017), by dual-stimulation (Ubaldi et al., 2016) or by polar body biopsy (Montag et al., 2013). In addition, the use of polar body biopsy rather than trophectoderm biopsy for CCS is the only available method for PGS in some countries mainly due to legal reasons, as embryo biopsy is not permitted.

In the early days of PGS (PGS 1.0), FISH had the advantage of a rapid turnaround time of several hours. In addition, FISH does not require DNA amplification, so errors that originate in the amplification process, such as allele drop-out, are avoided. In the context of PGS however, FISH has serious limitations, such as the limited number of chromosomes amenable to simultaneous diagnosis, hybridization errors that may lead to over- or under-scoring of specific probes, and the subjective nature of interpretation, which may lead to erroneous results (Brezina et al., 2016; Handyside, 2013; Harper and Sengupta, 2012). According to the survey results, the extent of FISH usage has declined to only 9% of all PGS cycles reported.

Microarray techniques, such as aCGH and SNP require whole-genome amplification, and both have the ability to evaluate the ploidy status of all 23 chromosome pairs. Many of the clinics performing PGS (59% in our Survey) have shifted towards the use of a-CGH because results can usually be obtained within 12 h enabling transfer of fresh embryos, when warranted. The limitations of aCGH include its relatively high cost, possible errors introduced during DNA amplification, and the inability to detect triploidy or uniparental disomy (UPD) (Brezina et al., 2016; Wilton et al., 2009). Conversely, SNP microarrays can also detect relatively small deletions and duplications as well as UPD. SNP microarrays, however, usually require several days for a result, and their use necessitates freezing the whole cohort of embryos (Handyside, 2013). According to our survey, only 7% of clinics are predominantly using SNP microarrays for PGS.

Real-time polymerase chain reacton (PCR) or quantitative PCR, used by 5% of respondents, can detect whole chromosome copy number as well as smaller copy number variations along a given chromosome. Real-time PCR can rapidly evaluate all 23 chromosome pairs within 4–12 h. It only tests a relatively small number of loci along each chromosome; however, and is labour-intensive, making it difficult to evaluate multiple samples simultaneously. Although it can identify triploidy, this technique cannot detect structural chromosomal aberrations or UPD (Brezina et al., 2016; Handyside, 2013).

Next-generation sequencing (NGS) is increasingly used for CCS of all 23 chromosome pairs (Brezina et al., 2016; Handyside, 2013). This technique amplifies embryonic DNA and compares millions of fragmented DNA sequences with a reference genome. It can analyse specific DNA sequences along each chromosome and can also determine point mutations. Next-generation sequencing can therefore be used concurrently for both PGS and PGD, when indicated. The broad diagnostic applications of NGS are likely to increase its use in the

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future. This is reflected by the fact that NGS was the second most commonly used technique (16%). Although the survey data are relatively recent (second half of 2015), the technical landscape of PGS is currently undergoing a dramatic change. It is highly likely that most PGS cases are now being carried out by NGS rather than aCGH.

In centres in which PGS is routinely carried out, 72% carry out trophectoderm biopsies, whereas only 25% carry out blastomere biopsy from day 3 cleavage-stage embryos. Only 3% of respondents carry out PGS on polar bodies. Trophectoderm biopsy has been shown to be safer and more accurate than cleavage-stage blastomere biopsy. Embryos that underwent trophectoderm biopsy have been shown to have a higher implantation rate (47.6%) compared with those undergoing blastomere biopsy (26.7%) (Kokkali et al., 2007). Moreover, blastomere biopsy has been shown to have a detrimental effect on the embryo's reproductive potential, resulting in 39% relative decrement in the chance of delivery when compared with trophectoderm biopsy (Scott et al., 2013b). In a recently published questionnaire on PGS practices, most respondents preferred blastocyst biopsy (Sermon et al., 2016).

Most clinics (69%) use a centralized referral laboratory for PGS. Although many inconsistencies have been reported between different techniques and laboratories (Esfandiari et al., 2013), arising, at least in part, from embryonic mosaicism, it has also been shown that trophectoderm biopsy provides highly consistent and reproducible laboratory and clinical outcomes across multiple practitioners from different IVF centres when all of the embryologists received identical training and use similar equipment (Capalbo et al., 2016). Interestingly, it has recently been shown that while using aCGH in a single reference laboratory, euploidy rates in donor egg cycles were found to differ significantly between fertility centres (Munne et al., 2017). These data indicate that validation and standardization of the techniques and commercial platforms used for PGS are necessary in order to ensure high accuracy, consistency and reproducibility of PGS.

With the use of PGS, it should also be possible to reduce multiple pregnancy rate if favourable live birth rates can be achieved after the transfer of a single euploid embryo. This has already been demonstrated by Forman et al. (2013) in a randomized controlled trial conducted in good-prognosis patients, including a favourable perinatal outcome (Forman et al., 2014). In the present survey, 88% of respondents would consider SET under certain circumstances. Only 34% uniformly carry out SET in all cases, whereas 12% prefer double embryo transfer to all patients.

Despite the ongoing debate and lack of robust ranodmized controlled trials, most respondents believe that PGS may aid in transferring only euploid embryos, thereby reducing miscarriage rates and increasing live birth rates. Both users and non-users of PGS regard patients who had experienced RIF, RPL and were of AMA as the best candidates for PGS, and only a minority believe it should be offered to all patients. Most respondents generally agreed that more RCTs are needed before the role of PGS 2.0 can be determined. This is also the view that is frequently expressed in the many verbal and written debates on the future of PGS that we are currently witnessing. The results of ongoing ranodmized controlled trials on different aspects of PGS are awaited with interest.

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