Blurring boundaries : interviews with PGT couples about comprehensive chromosome screening

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Abstract

Objective: Comprehensive chromosome examination is a promising approach to Preimplantation Genetic Testing (PGT). Next to testing of specific chromosomes, such as in the case of reduced fertility due to chromosomal translocations, it allows testing of all chromosomes. Hence it potentially reduces the time to pregnancy and the risk of miscarriage. But comprehensive testing also introduces some ethical issues. For example, what is the role of the professional in the decision making regarding embryos with chromosomal abnormalities that are potentially viable? Which chromosomal abnormalities should be communicated to people undergoing fertility treatment? With this paper we wanted to explore the ethical issues related to comprehensive chromosome screening in Preimplantation Genetic Testing
Design: In order to explore these issues, we interviewed seven couples undergoing PGT for chromosomal translocations at the VUB University Hospital, Belgium. We presented them with three fictional cases: the transfer of an embryo with trisomy 21, of an embryo with a sex chromosome aneuploidy and of an embryo with a chromosomal microdeletion.
Results: We found that opinions regarding the role of fertility professionals in deciding which embryos to transfer were mixed. Moreover, where to draw the line between healthy and unhealthy embryos was unclear. We also found that couples, although they thought that comprehensive chromosome testing had certain benefits, also considered the increased waiting time for transfer a heavy burden.
Conclusions: In the light of comprehensive chromosome screening of embryos, persons undergoing fertility treatment may have views on the burdens and benefits of the techniques that are not analogous to the views of professionals.

Keywords

Preimplantation Genetic Testing;
Ethics;
Qualitative research;
Comprehensive Chromosome Screening;

Introduction

Preimplantation Genetic Testing (PGT), formerly named Preimplantation Genetic Diagnosis (PGD) and Preimplantation Genetic Screening (PGS), entails the biopsy and genetic testing of in vitro embryos (1). This is done in two contexts. First, *PGT* is done when a patient is at risk of transmitting a monogenic condition (PGT-M) to their offspring, or when – due to chromosomal translocations – they have little chance of conceiving a child naturally or have a high risk of miscarriages or having a child with an unbalanced translocation (PGT-SR). Second, *PGT for aneuploidy detection* (PGT-A) entails the testing of embryos of patients undergoing IVF as treatment for infertility to enhance the chance of a successful pregnancy and delivery of a healthy baby by selecting the most viable and 'healthiest' embryo. PGT-A, which has traditionally been performed on cleavage stage embryos (day 3) using fluorescence *in situ* hybridization (FISH) is controversial today, as many in vitro embryos are mosaic and it may be impossible to obtain accurate information on the chromosomal status of the entire embryo (2,3). PGT requires embryo biopsy, which can be done at different stages of development. At day three, one or two cells of the cleavage stage embryo can be removed and tested. And at day five the same is true for a number of cells of the trophectoderm of the blastocyst. It has been documented that PGT-A of trophectoderm cells using microarrays improves embryo selection (4). Nevertheless, proper RCT's, taking into account specific categories of patients, transferring fresh or vitrified embryos, using novel technologies are still needed to prove the clinical utility of PGT-A within the frame of IVF (5).

PGT as it is currently practiced has been the subject of some moral debate. First, there have been categorical objections to embryo creation and selection. PGT on in vitro embryos implies that the earliest stages of human life are externalized and subject to observations and manipulations (6). Second, there have been debates about conditions for morally acceptable PGT, for example the question whether requests for testing for lower penetrance mutations or late onset conditions (e.g. HBOC=hereditary breast and ovarian cancer) can be granted (7–10). Currently, microarray technology and other genome wide analysis methods such as haplotyping

are being used. Next Generation Sequencing (NGS) and Massive Parallel Sequencing (MPS) methods are being introduced in the context of PGT. These technologies allow for high resolution screening and for screening of all chromosomes simultaneously, both in the context of PGT-M, PGT-SR and PGT-A. In several centers this comprehensive chromosome examination for couples undergoing PGT for translocations and monogenic disorders is becoming common practice.

The introduction of comprehensive chromosome analysis for PGT for translocation carriers and monogenic disorders seems to convey additional benefits. Indeed, by testing for additional chromosomal abnormalities, the chance may increase that a transfer leads to a successful pregnancy (5). Moreover, chromosomal abnormalities that may lead to disabilities unrelated to the indication for PGT can be detected in vitro. However, this introduction may also introduce additional ethical questions. First and foremost, the professionals taking care of individuals in the context of IVF and assisted reproductive technologies have a duty to provide *good clinical care* to these individuals. This implies that the aim of the patient (a child without a specific genetic disorder, or a successful pregnancy and delivery) is always considered first. And although this seems straightforward, there is a chance that these original aims of patients are neglected if embryo testing becomes more comprehensive. For example, this risk is already there at the level of PGT-A (to improve the chance of a successful pregnancy). If comprehensive techniques are used, embryos are checked for aneuploidies of any chromosomes, and embryos with an abnormal number or structure of any chromosome will be routinely discarded, as they probably reduce the chance of a successful pregnancy. So far, this is in accordance with the aim of improving the success rate of IVF and in line with the concept of good clinical care. But if existing policies of not transferring embryos are rigidly applied, professionals may also discard embryos with a fairly good chance of resulting in an euploid child or with viable chromosomal abnormalities that will results in an asymptomatic baby or causing minor health problems that are often considered relatively benign. The latter abnormalities would for example include XXY, Klinefelter syndrome, and XYY, sex chromosome abnormalities. And although patients may welcome extra information that may help them to have a healthy baby, the idea that patients would always want a healthy baby rather than any baby has not sufficiently been checked. For example, in a 2007 study on single embryo transfer, Scotland and colleagues found that some women in IVF treatment would prefer to give birth to a child with a chronic disability than never give birth at all (11). Paradoxically, the patients undergoing comprehensive screening to enhance pregnancy rates, or rather to reduce time to pregnancy or avoid miscarriage may end up with fewer chances of having a baby than if they would have opted for IVF without

comprehensive screening (Vaiarelli et al. 2016). Moreover, conflicts may arise between professionals and patients if the latter request transfer of an embryo with a chromosomal abnormality. Professionals may feel that it is their responsibility not to allow such transfer, but patients may argue that they are ready to accept the risk of a miscarriage of a chromosomal abnormal embryo or the risk of a child with the condition diagnosed in the embryo (12).

Good clinical care in ART also implies making sure that people do not undergo procedures with a high probability of not having the desired outcome, for example if embryos are transferred that have no chance to implant or that have a high risk of ending in a miscarriage. Avoiding such 'futile' medical procedures also fits into the idea that professionals may have some responsibility to make sure that money is spent wisely. But it is far less clear whether this responsibility extends to making sure that no children with serious disabilities are born. One of the authors of this paper (KH) explored some of these questions in focus groups with professionals (13,14).

Material and Methods.

In order to get a more broad perspective on the matter, we decided to interview couples who were offered PGT at the VUB University Hospital.

We used a qualitative research method, as this allowed us to investigate in depth values and opinions of prospective parents. The study was approved by the ethics committee of the VUB University Hospital.

Potential respondents were recruited by the clinical geneticists at VUB, during the period of May 2015- November 2016. Seven couples agreed to participate in the interview. Two of them were offered PGT with FISH analysis of blastomeres after a day 3 biopsy and a fresh embryo transfer. The remaining five were offered PGT with trophectoderm biopsy on day 5 followed by vitrification of the embryos while microarray testing was performed. Qualifying embryos were transferred at the earliest one or two months later. During consultation, the procedure was explained and an informed consent was signed. In the informed consent it was explained that 'abnormal' or undiagnosed embryos were not transferred. They were also told that very rarely and after signing a supplementary informed consent, an embryo with an inconclusive result could , after discussion with the couple, be transferred and followed, in case of pregnancy, by a prenatal diagnosis. All respondents were translocation carriers in the age range of 25-35. Information about the respondents is in table1. The interview schedule contained questions about their current treatment, and their understanding of their current treatment. It also

contained three scenarios to which they had to respond. One scenario included the transfer of an embryo with trisomy 21, one with XXY pattern, and one with a partial chromosomal deletion (46,XY, 9p-) in the analyzed cell(s). This deletion is associated with certain learning difficulties in some cases, but in other cases people with this deletion are symptomless. Interviews were conducted with both partners simultaneously, at their home. Before the start of the actual interviews, it was checked with the couples whether they properly understood the technology used. The interviewer also made sure that both participants had the opportunity to answer the questions, by using prompts when only one of them answered. The shortest interview took 35 minutes, the longest 1h10minutes. The interviews were recorded on tape, subsequently transcribed ad verbatim and coded in NVIVO-10 using an inductive approach. In a first round of open coding all pieces of text were coded into several subthemes. In the next two rounds of coding, the axial coding and the selective coding, the different subthemes were connected into broader concepts (15). The subsequent results were agreed upon by all authors. Selected quotes were translated into English.

Results

Recurring themes in the interviews were burden and benefits of the procedure with microarray, the difficulty of being able to define what is health and what is good life, and the role of the professionals. Themes that were not in the original research question, but that came up consistently in the interviews, were the impact of the longer waiting time of embryo transfer, if vitrification is used and the desire to minimize the impact of miscarriages and/or prenatal diagnoses through PGT. During the interviews, both participants were able to express their opinions and experiences. It was acknowledged in several interviews that the burden of the procedure fell mostly on the woman, but both female and male participants considered this an important consideration when thinking about these new technologies. In fact, participants agreed with one another on most topics, which suggests that these couples had already discussed issues related to the technologies with one another in some depth. One couple disagreed on the question regarding whether they would want the transfer of an embryo with trisomy-21.

Burden & Benefit of procedure with microarray

Weighing burdens and benefits was a recurrent theme in the interviews. Participants agreed that the procedure, with comprehensive chromosome testing using microarrays, would be beneficial, because it would increase the chance of having a successful pregnancy. The fact that with comprehensive chromosome testing using microarrays all chromosomes would be visible,

would, according to some of the participants, eliminate the need for prenatal screening during the pregnancy. This is analogous with the reason that most of the participants gave for choosing the option of PGT in the first place. Although many of them were advised before they started the procedure that they could 'also try naturally', this was not considered a valuable option, as this is clear from the following dialogue:

> G4_M: And because you also had difficulties, mentally, with the insecurity… Because mentally, it is a big question mark, I didn't think she was up to, or it would have been difficult for her to suffer the insecurity of being pregnant or not, and then maybe prenatal…
>
> G4_F: Yes, to have to wait four months until you have had invasive prenatal screening, and then still perhaps you need to choose for pregnancy termination…

So in this quote it becomes apparent that the primary reason why couples decide to take the route of PGT in the case of translocation carriers was reducing insecurities, miscarriages and the burden of having to wait long for the results in case of PND following a spontaneous pregnancy.

One participant described the experience of being counseled to 'try naturally' as follows:

> G2_F: And then they told me, you can always try naturally of course, and then we thought, well it is not about the chance of having one finger more or less, it is about something that is so fundamental that we considered we have to do PGD, and then they immediately agreed. But originally, it was very rational for them like, 'yes you are still young', in their fertility terminology, you do not have to go this route with all these hormones, but then you have to take into account a couple of more miscarriages, and they considered this a fait divers, like, you know how many miscarriages there are, madam, and I thought, yes but that is not actually how this works.

So in this quote, the speaker confronts the more 'rational' counseling of the professionals at the IVF clinic with her own opinion that, although they may have a point, rationally speaking, this is not how things work when you are trying to conceive. The insecurities of having to 'try naturally' were considered more burdensome then the hormonal treatment and IVF. As G2_M continued: "You have been through the miscarriages, and you really do not want that anymore". One couple explicitly mentioned the fact with the new technique, cells from the trophectoderm are taken, not cells from the embryo itself. As G7_F pointed out: "I just think… The idea that they take away a cell of an embryo that has to develop, I can't get my head around it."

But although the fact that participants acknowledged that a comprehensive screen of the chromosomes would potentially increase the chance of a successful pregnancy, and that they

considered this an important benefit of the newer procedure, the additional waiting time of approximately three weeks that day-5 microarray screening, followed by vitrification, introduces was seen as burdensome. In fact, this additional waiting time became one of the main topics of the interviews starting from the second interview. For example, G3_M, translocation carrier, had already gone through the FISH procedure with a previous partner at another center, who had undergone six cycles of PGT. He could compare these two procedures very well, and considered the weeks of extra waiting time as psychologically exhausting. He suggested that psychological help should be available during this period. Participants also mentioned that there was a discrepancy between how they had experienced these weeks in which 'nothing' happens and they just had to wait, with how fertility professionals experience the waiting period. For example, one interviewee (G4_F) stated that they were told that they would be contacted with the results 'around a certain date', and she called the waiting for the telephone call 'terrible, really terrible'.

Besides the longer waiting time for the new procedure, participants also named the fact that transfer would not be possible within the same cycle as burdensome (G5_F: "Psychologically is that also difficult. You had all these hormones in your body. You have a pick-up, but then nothing happens with your body"). But one couple (G7) also thought this was an advantage, as in this way the woman's body could first recover from the hormones she had to take for the pickup. Also, although they had been counseled that the vitrification and thawing of the embryos would not add additional risks to the procedure, some of the interviewees still felt that the freezing process, which is practiced in the case of day-5 microarray screening, added an additional factor of insecurity.

Overall, the interviewed couples were in favor of the new technique, as it would probably increase chances of a successful pregnancy and reduce risks of non-implantation and miscarriage. But they often pointed out that longer waiting times where psychologically stressful and that as waiting times are increased, especially those who previously had day 3 biopsy and FISH analysis, also the support from the fertility clinics should be adapted.

The difficulty of defining the good life

The respondents considered the additional information that comprehensive chromosome testing with microarrays could yield, besides the translocation, as an integral part of the aim of the procedure. This means that they did not consider information about chromosomes that were not in their translocation as on a different level than those that were affected by the translocation. For the participants we interviewed, the purpose of the procedure was not primarily to avoid

the transfer of the potentially harmful translocations that they carried, but to increase the chance of a pregnancy, to avoid miscarriage and to increase the chance of having a baby that is healthy at birth. For many interviewees it seemed straightforward that to be able to discard embryos with trisomy 21 was intrinsically part of the main aim of the procedure. As the following interviewee described:

> G5_F: If you are doing PGD, you know that you have so many chances to have faulty embryos, and I think at that point you have to try to do everything to avoid everything. Then it is even better not to have children than a disabled child, because at that point your life stops as well. We have always thought so.

So for this woman, the aim of chromosome testing using PGT already includes testing for any chromosomal abnormalities. She and her partner described themselves as 'very rational' and also attributed their opinions about not transferring an embryo with trisomy 21 to this rationality. Her partner also referred to the potential duty they had, as a couple who had already used health care resources for publicly funded IVF/PGT to avoid more costs to society by avoiding transfer of embryos with a chromosomal abnormality:

> G5_M I find that just. Maybe a heavy word, ethically just, also considering the impact on society. You have already incurred costs in advance, and then again costs… do we have to decide on life and death? Maybe not, but I think we are not at that stage here that we decide on life and death.

Hence, for them, the burden to society was an important factor. This respondent also mentions in this quote the fact that he considers the in vitro embryo not yet as truly a living person. G7_M, however, disagreed with this and thought that, although rationally he understood the viewpoint that embryos are not really living persons, emotionally, he found this difficult. He also was in doubt about whether he would like to have an embryo with trisomy 21 transferred, and thought this was a heartbreaking choice:

> G7_M For me this is really a heartbreaking choice, because I do not know how they feel. Because I think you have children who are perfectly happy, who would be super grateful.

G2_F, explicitly mentioned the difference between prenatal screening for trisomy 21 and preimplantation screening. She was not sure if she would really want to terminate the pregnancy at that point. However, not transferring the embryo was seen as avoiding such difficult choices during pregnancy.

From the discussion based on the Down syndrome case it was also clear that often these couples did not base their decision on potential *wellbeing* of the child alone. For example, one respondent, G3_F stated that "I know that they can be happy, but you are never sure. They can grow old, what if you are no longer there". Other considerations included the increased risk that a disabled child would be bullied and the burden to the family and to the society at large of having to care for a disabled person. This was corroborated by G6_M, who had experience living with his disabled brother, and who thought that it is extremely burdensome for all family members involved, but also for the society at large. Respondents often considered Down syndrome a life-long disability with great impact on the family.

When discussing the next scenario, the transfer of a male embryo with an extra X chromosome ('Klinefelter syndrome'), the difficulties of delineating what is a valuable life or what is important information to know about one's child became apparent. Most participants would consider transferring an embryo that has an extra X chromosome, although some suggested that it would be better to try another cycle and freeze this one. One person (G7_F) explicitly referred to infertility as a reason not to transfer such embryo: she thought it unfair that she would inflict the same problem she had on her child. The difference with the trisomy-21 scenario was described by one person as follows: "... that he is not always in the hospital or with the doctor, that he can have a decent life without medication or operations." (G1_M) In the following quote the importance of autonomous functioning is even more clear:

> G4_M: I find someone with for example learning problems, there are other things that you can do in your life than becoming a professor. I mean there are hundreds of alternatives. Someone with a learning disability can be perfectly autonomous, and do something he loves doing in another area, I would not have a problem with that at all. But it is the [lack of] autonomy that would scare me and the fact that they are by definition younger than you. There is a certain moment that they have to be autonomous, or function without you, and then there is a big question mark what happens next.

Hence, this and other respondents made a clear distinction between on the one hand, congenital medical problems, that would affect the child's potential to autonomous functioning and that would imply medical interventions, and on the other hand other issues such as learning problems or problems related to physical appearances, which they did not consider a sufficient reason not to transfer. For example, G1_M remarked that "at a later age, other medications can be invented", suggesting that PGT was also primarily for congenital disorders. Also respondents insisted that the aim of PGT was, besides increasing the chance of a successful pregnancy, to avoid 'problems', not 'selecting super humans'.

Especially when we discussed the third scenario, that of a structural chromosomal abnormality being a partial deletion which may or may not lead to medical problems, it became clear that this was an important distinction that these couples insisted on. They saw the potential of this technology to screen for even more genetic differences, and introducing even more uncertainty, and wondered where the line should be drawn. Often they actually mentioned the idea that it is possible to 'know too much': for example respondent G3_F drew the analogy with breast cancer screening, where she had read that it is not always good to screen for everything. In this respect, G4_M stated that "the situation can escalate quickly to the entire genetic constitution or genetic modification of a child. Because in the end that is what happens. It is a technique that intervenes so that you can have a baby and then you have the choice between two healthy ones, but what if they are both boys and you want a girl?". Hence, this respondent clearly saw dangers in a technology that was primarily aimed at offering couples with genetic or chromosomal abnormalities the chance to reproduce, but that could easily escalate into screening for the perfect baby. In this respect, G4_F stated that she would not mind that an embryo with a small chance of potential problems would be transferred, as she considered this insecurity "part of the package of having children". She and other respondents also thought that knowing too much about one's child could lead to anxiety, and to the child having to grow up under constant scrutiny, which would affect the way the child would be raised.

Role of the professional (clinical and laboratory geneticists, fertility specialists, psychologists)

The couples had certain ideas about what they considered acceptable for the health of their future child or not, and which decisions they would make in this respect. Opinions varied, however, on the role of the professional with regard to transfer decisions. One couple thought that the choice whether to transfer an embryo with a certain abnormality should be entirely up to the parents, and that all the information about the embryo should be conveyed to the prospective parents: G1_M: "I think that they always have to tell you, worrisome or not, everybody has the right to know if something is wrong, even if it is only 1% or 5%." This was explained by the fact that they had chosen for the treatment, and that this granted them the right to decide for themselves which level of insecurity was acceptable to allow transfer. For others, the answer was less straightforward. Especially in the light of uncertainty, doctors could take the decision not to tell people about risk factors, if the risks were statistically low. The reason why they thought professionals could be allowed to make decisions for them (e.g. not to tell

them if a mutation with a relatively small chance to have bad effects) was that uncertainties would cause anxiety for people undergoing fertility treatment:

> G2_M: Because, if you have to decide all for yourself, I think it becomes really burdensome, because if something goes wrong anyway, and it has been your decision…

With regard to transfer decisions, for example in trisomy 21, one couple drew the analogy with prenatal screening. They considered it reasonable that couples could decide this for themselves, because you have the same choice for prenatal diagnosis. Couple G5, who stated that they were strong believers in medical science, thought that professionals could take such decisions without further explanation, and that the fertility professionals could take up a decision making role.

> G5_M "I would just say is was a bad embryo, and not give any more comments. In this way², you didn't create hope and you didn't create disappointment."

This respondent also referred to the circumstances surrounding transfer decisions (i.e. during already burdensome fertility treatment) as too emotional for the couple to make the 'right' choices. Indeed, several couples considered that the fertility specialist was, next to someone with the technically relevant skills, also someone who was responsible to make sure that right decisions were made regarding the treatment as a whole. For example, she or he should make sure that the couples would not undergo more cycles then they could handle, and should provide necessary guidance throughout the process. Also, the specialist should make sure that couples receive all necessary information throughout the process, and that this information should be not conflicting between professionals. If possible, the supporting role could also be taken up by a psychologist or case manager. For example, G6_F, who considered the waiting time very burdensome, stated that: "There should be someone, who, for example, calls and asks how are you doing. Because psychologically as a couple it is really heavy. And you don't hear anything from them."

This idea that professionals also bore some kind of responsibility towards the wellbeing of the couple during the treatment, when they were not physically at the fertility center, was mentioned by several couples.

With regard to the capacity of fertility specialists and geneticists to make, as individuals, the right transfer decisions, the following respondent was not very sure:

> G4_M: I honestly think there should be a framework[1]. I do not think that it is up to the individual doctor to decide on that. I think it should be a panel of experts who design beforehand a framework with a number of guidelines for the doctor. I think it is dangerous if you leave it to the individual decisional capacity of one person whether or not to transfer a certain kind of embryo.

This respondent also referred to such transfer decisions as a choice between 'life and death', suggesting that even at this stage the decisions to be made were too complex to be left to individuals, even if they were doctors.

Discussion

A central theme that emerged from the discussions with these couples was that of *blurring boundaries*. Although they all saw the benefit of PGT over prenatal screening or 'trying the natural way' or of PGT using arrays over PGT using FISH, this endorsement of the technique was not absolute. And although respondents acknowledged that there was a difference between the transfer of an embryo with trisomy 21 and one with XXY (in the analyzed cells), probably resulting in Down syndrome, respectively Klinefelter syndrome, the boundary of what is a 'healthy' enough embryo and what is not was difficult to draw.

We had expected that the main themes that would arise from this study would be the additional information generated by the use of arrays. However, it became clear quickly that often these couples considered the (extra) burden of the additional weeks of waiting time and the extra procedure of freezing the embryo before transfer as important too. Although they admitted that the enhanced chance of a successful pregnancy was one of the primary benefits of the comprehensive procedure, and they would therefore prefer the use of comprehensive chromosome screening using microarrays over FISH, the additional burden of the procedure was not to be neglected. This is consistent with the findings of Cipoletti et al, who describe the period during fertility treatment as one of lack of control and associated with anxiety and worry (Cipolletta and Faccio, 2013) . Our respondents often described similar feelings too.

One of the often quoted principles with regard to reproductive ethics is that of reproductive liberty (or procreative freedom). The idea of *procreative liberty* was first discussed in depth by John Robertson in his seminal work *Children of Choice: Freedom and the New Reproductive Technologies* (6). Here, it is defined as the right individuals have to decide for themselves whether they want to reproduce or not. It also includes the right to decide, in principle, on the

[1] It is important to mention that at the VUB fertility center a framework categorizing embryos in three groups was used: 'normal' results and always transferred; 'abnormal' result and never transferred, inconclusive results with the possibility to transfer and prenatal testing in case of pregnancy

genetic characteristics of the children. However, most of our respondents did not express such a desire to exercise their procreative freedom. Indeed, many felt that in the case of congenital disabilities such as the ones associated with trisomy 21 there was some duty not to transfer such embryo. Remarkably, the reasons for this were often related to the burden that such a child would pose on the family and society, rather than the wellbeing of the child herself. Some couples even linked this to the fact that their fertility treatment already costed a lot of money, which then could be spared by avoiding the birth of children that would cost society. As an alternative to procreative liberty, Bonnie Steinbock has framed the idea of *procreative responsibility*. She defines this as the duty of prospective parents to consider the impact of their reproductive decisions on any offspring they have (16). She gives the example of PGT for cystic fibrosis, and argues that if a patient is using IVF/ICSI to have a child, the decision to test the embryos for CF seems a "no-brainer" in terms of responsible parenthood. But she agrees that it would impose too much a burden on people who can conceive naturally to have to undergo PGT and test the resulting embryos for a genetic disease.

For the couples we interviewed, it was hard to draw the line between which were acceptable health risks and which not. They all agreed that the aim of such procedure was not making perfect babies, and as such this corresponds to the findings in the seminal study by Roberts and Franklin with prospective parents in a PGT trajectory. They describe how couples expressed a feeling of a parental duty to avoid grave suffering and premature death and how they clearly resented any association with 'designer babies' (17). One of the key words in defining where to draw the line between which embryo to select for transfer and which one to discard was the potential for autonomous functioning. Indeed, one of the major worries was the fact that children with disabilities would live longer than their parents and would require continuous support. Remarkably, none of the couples blamed society for the lack of support for disabled persons, and none suggested that more money should be spent to provide such support.

Another topic that we discussed was that of professional responsibility. From the discussion on the burden and the time waiting for results and transfer of the procedure itself, it became clear that the couples expected good information and support from the fertility professionals during the procedure. With regard to transfer decisions, opinions varied: one couple believed that professionals have a mere informational role to play, and that the decision to transfer also an embryo with a potential disability was up to the couple. Others thought the role would be more advisory, and still others gave professionals decisional capacity with regard to whether to transfer a certain embryo or not. Scholars have agreed that the professionals involved in helping patients to conceive have some responsibility towards the outcome of the procedure, the future

child. Specifically, this relates to the welfare of the future child. In documents of for instance, ESHRE, the HFEA, and the Dutch Health Council this has been translated to mean that professionals should refrain from offering assisted reproduction if they think that a child is at risk of serious harm. The precise implications are a matter of debate, but this may entail that patients are refused fertility treatment because there is a history of child abuse, or because the prospective parents suffer from a genetic disease that would lead to the child becoming an orphan prematurely (18). But with regard to embryo selection, the upper and lower boundaries of reasonable wellbeing are hard to draw (19). Would transferring an embryo potentially prone to depression or schizophrenia violate the high risk of serious harm standard? What should be done with embryos with genetic abnormalities that are risk factors rather than mendelian disorders? If standards are set too high, infertile patients whose primary wish is to have a baby to take home would end up with no chance at a child at all. Indeed, the use of genomic data for embryo selection raises important questions about the conditions for ART. On the one hand, there is the patient already burdened with genetic disease in the family or with infertility who may initially be drawn to the idea that comprehensive screening may eliminate some suffering in their future child, but who are ultimately faced with even fewer reproductive options. On the other hand, there is the wish of many professionals to optimize outcome and not to willingly bring into existence a child with potentially severe health problems. It also remains unclear how the idea of non-directiveness, which states that professionals should give enough information to patients to enable them to make an informed choice, translates to the context of the in vitro embryo, where they are more actively involved in transfer decisions. In any case, informed consent procedures should be clear about what will happen with an embryo if a genetic and chromosomal abnormality is detected, and which abnormalities will be communicated to the prospective parents. For example, it should be made clear when and if they have the choice to transfer an embryo with a certain abnormality. With the introduction of techniques such as whole genome sequencing in the fertility clinic, deciding which information should be generated, whether embryos with certain genetic or chromosomal abnormalities will always be discarded, and when patients should be given the choice, will become of utmost importance (5).

Our study has several limitations. Given the limited scope of the study (interview of couples with translocations who were offered PGT with FISH or comprehensive chromosome testing), we have only conducted 7 interviews, with 14 interviewees. We have used a qualitative rather than a quantitative approach, which makes our findings not generalizable to the entire population of couples undergoing IVF/PGT, as this is not the primary aim of qualitative research.

We believe to have demonstrated that qualitative studies like this are indispensable companions to the introduction of new techniques, as they reveal specific issues that may not be analogous to the issues raised by the professionals themselves. We hope to have shown that in the light of comprehensive chromosome screening of embryos, persons undergoing fertility treatment may have views on the burdens and benefits of the techniques that are not analogous to the views of professionals. Ideally this study is followed by both qualitative and quantitative studies in other centers, taking into account the evolving novel techniques, which can lead to ranking embryos as transferrable as first priority followed by transferrable as second priority and non-transferrable for instance (5).

Author statement

Kristien Hens, Inge Liebaers and Christine de Die – Smulders were involved in the original design of the study and the interview guide. Kristien Hens, Inge Liebaers and Maryse Bonduelle were involved in recruitment of the participants. Kristien Hens did the actual interviews, transcribed them and did the first-pass analysis. All four authors agreed on the results. Kristien Hens did the initial write-up of the article, all four authors contributed to the writing of the final version. We declare no conflict of interest.

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Tables

Table 1: participants

Code participant (number & gender)	**Translocation Carrier**	**Technique used**	**Stage of treatment at time of interview**
G1_M	X	Microarray	First cycle PGT test done, two good embryos cryopreserved , will be transferred the next cycle
G1_F			
G2_M		Microarray	After three miscarriages, PGT, now pregnant. idem
G2_F	X		

G3_M	X	Microarray	G3_M had already finished 6 PGT attempts with a previous partner (FISH). With the current partner, first try, four embryos had made it to day five, but they were all unbalanced.
G3_F			
G4_M			Had already had one transfer, but this ended in an ectopic pregnancy. Next attempt will be with frozen embryos.
G4_F	X	Microarray	
G5_M	X	FISH	Pregnant after four attempts. First two attempts were at a different fertility center without PGT.
G5_F			
G6_M	X	FISH	Already had one child, almost two years old. First PGT attempt ended in miscarriage.
G6_F			
G7_M		Microarray	First attempt, waiting for microarray results
G7_F	X		

Table 2: summary of themes originating from the interviews

Burden and benefit	PGT benefit over prenatal diagnosis PGT benefit over trying naturally Burden of miscarriages PGT-with-microarray has benefits over FISH Increased chance of pregnancy Possibility to check for other chromosomal abnormalities Less intrusive PGT with microarray and vitrification introduces longer waiting time compared to classic FISH More anxiety ...More time to recover
Avoiding health related problems in offspring	Avoiding congenital handicaps Value of "autonomous life" But also: burden to family/society Not: selecting perfect babies Not: knowing everything

Role of the professional	From mere information providing To decision capacity Also: psychological assistance

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