ESHRE Task Force on ethics and Law 20: sex selection for non-medical reasons†

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ABSTRACT: This Task Force document revisits the debate about the ethics of sex selection for non-medical reasons in the light of relevant new technological developments. First, as a result of improvement of the Microsoft® flow cytometry method, there is now a proven technique for preconception sex selection that can be combined both with IVF and IUI. Secondly, the scenario where new approaches that are currently being developed for preimplantation genetic screening (PGS) may lead to such screening becoming a routine part of all IVF treatment. In that scenario professionals will more often be confronted with parental requests for transfer of an embryo of a specific sex. Thirdly, the recent development of non-invasive prenatal testing based on cell-free fetal DNA in maternal plasma allows for easy and safe sex determination in the early stages of pregnancy. While stressing the new urgency that these developments give to the debate, the Task Force did not come to a unanimous position with regard to the acceptability of sex selection for non-medical reasons in the context of assisted reproduction. Whereas some think maintaining the current ban is the best approach, others are in favour of allowing sex selection for non-medical reasons under conditions that take account of societal concerns about the possible impact of the practice. By presenting these positions, the document reflects the different views about this issue that also exist in the field. Specific recommendations include the need for a wider delineation of accepted ‘medical reasons’ than in terms of avoiding a serious sex-linked disorder, and for a clarification of the legal position with regard to answering parental requests for ‘additional sex selection’ in the context of medically indicated preimplantation genetic diagnosis, or routine PGS.

Key words: sex selection / ethics / sperm sorting / embryo selection / social sexing

Introduction

Sex selection can be performed at three stages: preconception (selective fertilization with enriched fractions of X- or Y-bearing sperm), pre-implantation (selective transfer of male or female embryos) and prenatal (sex-selective abortion). Sex selection for medical reasons (to avoid the transmission of disease to a next generation) is widely regarded as acceptable. However, sex selection for non-medical reasons (because of a sex preference that the prospective parents would want to see fulfilled) has been the subject of recurrent ethical and public policy debate in many countries. The Task Force has briefly discussed this issue in its earlier document on preimplantation genetic diagnosis (PGD) (Shenfield et al., 2003). This new document revisits the debate about allowing or not allowing sex selection for non-medical reasons in the light of recent technological developments.

Background and Facts

Sex-selective insemination

The only proven technology for preconception sex selection is the Microsoft® flow cytometry method. This method involves staining the sperm with a fluorescent dye and then leading them past a laser beam where the difference in DNA content between X- and
Y-bearing sperm gives a measurable difference in fluorescence. Until recently, one important drawback was the limited yield, as a result of which the technology was only applicable in combination with ICSI. By now, the throughput capacity of the technology has so much improved that flow cytometry can also be combined with IUI (Karabinus, 2009).

A remaining limitation is still less than perfect reliability. In a report from the Microsort® trial, the use of sperm selected as X-bearing led in 92% of the resulting pregnancies to a girl, whereas after the use of Y-sorted sperm, the result was a boy in 83.6% (Karabinus, 2009). Even so, flow cytometry can be a helpful preselection tool for sex selection through PGD or prenatal diagnosis. Such ‘preselection’ will limit the chances that PGD reveals only embryos of the wrong sex, which is not exceptional in women with a low oocyte yield. Similarly, preselection may help to avoid that prenatal diagnosis for sex selection leads to a difficult decision about whether or not to terminate a wanted pregnancy. In the past years, some European centres have used the technology to this end, which involved sending sperm for sorting to licence-holding centres in the USA or Mexico. In the one reported case, this concerned a couple at risk of having a child with Becker’s disease, for whom PGD was no option and who rejected abortion for religious reasons. In this case, flow sorting was done twice as a single-selection method, with the prospective parents and the professionals accepting a less than complete reliability. Happily, a healthy girl was born (De Geyter et al., 2013).

Ever since the technology was developed, there have been concerns about its safety, both in view of the staining with fluorescent dye and the use of a laser. However, extensive use in farm animals has not revealed any harmful effects. In a review based on data of around a million offspring, it was concluded that there is ‘no apparent genotoxic effect from exposure of sperm to Hoechst 33342’ (Garner, 2009). Still, the same review also concluded that embryonic development is slower in sorted than in non-sorted sperm and that fertility rates are also lower. With regard to human use, the latest publication from the Microsoft® trial reports normal pregnancy outcomes and malformation rates in 760 children (Karabinus, 2009).

The Microsort® trial was set up with the aim of applying for FDA approval for the technology to be marketed in the USA (Karabinus, 2009). It enrolled patients wanting sex selection both for medical reasons (couples at risk of transmitting a sex-linked disorder), and for ‘family balancing’: couples already having at least one child of one sex and wanting to have a child of the other sex. The halt of the trial in 2011 was explained by the company in terms of high costs and regulatory burdens. As a consequence, the technology is no longer available in the USA, but only in Microsoft®-licensed centres in Mexico and Northern-Cyprus. The university medical centre in Basel (Switzerland) has now also obtained a licence (personal communication Prof. de Geyter, Basel), which will make the method more easily accessible for other European centres in the context of sex selection for medical reasons.

Sex-selective embryo transfer

Although the development of mutation analysis for specific sex-linked disorders has reduced the percentage of sexing procedures, PGD is still being done for this indication. In the USA and other countries where neither sex selection nor access to PGD is regulated, commercial centres also offer the technology for ‘social sexing’. PGD is not available for this purpose in countries with legislation forbidding sex selection for non-medical reasons and/or regulations binding PGD to specific indications. However, professionals in those countries may still be confronted with requests for ‘additional sex selection’ in cases where PGD for a medical indication (other than sex-linked disease) has also revealed embryonic sex. Whether additional selection is possible in such situations will depend on whether the choice of embryos for transfer is not already fully determined by the original indication. Whereas such cases are rare, the scope for additional selection becomes wider with preimplantation genetic screening (PGS) of IVF embryos for aneuploidy, a technology aimed at improving IVF outcomes. Because PGS uses screening panels that also contain probes for the sex chromosomes, a side-effect of this technology is that it provides IVF patients with information about the sex of their embryos prior to transfer. As many prospective parents do have a preference with regard to the sex of their child, it is to be expected that professionals will be confronted with requests for transfer of an embryo of a specific sex. The place of PGS in the future of ART is still very much a matter of debate and research. However, already in view of its present use, the authors of a recent overview of the data collection efforts of ESHRE’s PGD Consortium suggest that our knowledge about social sexing ‘barely scratches the surface’ (Harper et al., 2012).

Sex-selective abortion

In countries where IVF/PGD is not available, prenatal diagnosis followed by the option of abortion is still the only reliable method of sex selection for medical reasons. Until recently, prenatal sex determination depended either on invasive procedures with a 0.3–0.5% miscarriage risk (chorion villus sampling or amniocentesis) or on non-invasive ultrasound (not reliable for sex determination before 13 weeks of gestation). The recent development of non-invasive prenatal testing (NIPT) based on cell-free fetal DNA in maternal plasma allows for easy and safe sex determination already from 7 weeks of gestation (Devaney et al., 2011). The benefit of this test in the context of sex selection for medical reasons is that it will greatly reduce the need for invasive procedures.

On a global level, sex selection is mainly a matter of sex-selective abortions. In the overwhelming majority of cases, it is female fetuses that are aborted. Against this background, it is a concern that NIPT will have the unintended side-effect of making sex determination and sex-selective abortion more easily available for non-medical reasons.

Societal effects of sex selection for non-medical reasons

Sex-selective abortions have led to a serious distortion of the numeric balance between the sexes in several Asian countries. Although there are signs that the trend is levelling off and may even start to reverse in certain regions, the impact on society is long lasting (Gulmoto, 2009). A recent Council of Europe report summarizes the wider societal consequences in terms of a rise of criminality, social unrest and human rights violations, including violence and discrimination against women (Council of Europe, 2011). However, as stressed by the World Health Organization, the availability of sex selection technologies...
should not be regarded as the root cause of these problems (WHO, 2011). The root cause is the culturally embedded preference for male offspring, ‘squeezed’ by fertility decline and population control, with technology as a facilitator (Guilmoto, 2009). The strong preference for sons is based on a complex amalgam of cultural and economic factors, including for example the burden that the dowry system in (regions of) India imposes on the bride’s family (Hvistendahl, 2011).

In Western countries, son preference is only weak or even absent. Surveys consistently show that only a small minority of couples say they would want to make use of sex selection, and that of those who would consider this, most would do so in order to have a family with children of both sexes (Dahl et al., 2006). Given the lack of a strong sex preference, there is no reason to think that in Western countries, the wider availability of sex selection technologies will lead to a distortion of the sex ratio (Van Balen, 2006).

Legislation
An overview of all 36 countries with laws or policies regarding sex selection, including 25 European countries (Darnovsky, 2009), shows that (with Israel as a qualified exception) none of these allow sex selection for non-medical reasons. Article 14 of the Convention on Human Rights and Biomedicine (Council of Europe) states that ‘the use of techniques of medically assisted procreation shall not be allowed for the purpose of choosing a future child’s sex, except where serious hereditary sex-related disease is to be avoided’. In most jurisdictions, this prohibition applies only to the use of assisted reproductive technologies. Whereas some Asian countries, including India and China, have enacted specific legislation also forbidding the use of prenatal diagnosis for sex determination without a medical reason, in most other countries this is a matter of professional regulations and guidelines. Legislation forbidding sex selection typically contains a clause in which an exception is made for cases where there is a medical reason. The reasoning behind this is that the specific moral concerns related to the idea of allowing people to choose a child of a specific sex do not apply to cases where this preference is instrumental to the wish for a healthy child. As in the European Convention, this exception is usually formulated in terms of avoiding the birth of a child with a serious ‘sex-linked disorder’. On a strict understanding, this refers to a specific type of monogenetic disorder, where 50% of the male offspring of a female carrier will have the disease. The German Embryos Protection Act explicitly follows this understanding, stating that sex selection is forbidden except when done to avoid the transmission of Duchenne Muscular Dystrophy or an equally serious sex-linked disease. A wider account is given in the amended British Human Fertilisation and Embryology (HFE) Act of 2008, where the exception is defined as allowing sex selection ‘in cases where there is a particular risk that a woman will give birth to a child who will have or develop a serious gender-related disability, illness or other medical condition that (…) affects only one sex, or affects one sex more than the other’.

General Ethical Principles
In this section, the Task Force discusses the ethical arguments for and against allowing sex selection for non-medical reasons in Western countries.

Respect for persons
Those rejecting all forms of sex selection for non-medical reasons suspect that sexist motives will be at work in most if not all cases and argue that this renders the practice deeply problematic from a moral point of view. ‘Sexism’ refers to the discriminative belief that one sex is better than the other or to stereotyping views about gender role behaviour. This would also apply to sex selection aimed at having a ‘balanced family’. Although not necessarily based on a view about the supremacy of one sex, this application would still be sexist in the sense of expressing and reinforcing preconceived gender role expectations.

Opponents of this view argue that although individual requests for sex selection may flow from a sexist parental motivation, it cannot be maintained that this is necessarily the case. For instance, prospective parents may find it beneficial for their children to have the experience of growing up in a family of both boys and girls. These commentators do not agree that seeing a difference between what boys and girls might contribute to family life would necessarily stand in the way of valuing one’s children for their own sake and allowing them to grow into autonomous individuals. According to these authors, it is not sex selection for non-medical reasons, but the categorical ban of this practice that stands in opposition to the principle of respect for persons: it infringes the right to self-determination in what many people regard as a fundamental dimension of their lives.

Do no harm
It has been suggested that sex selection by parents with stereotyped gender role expectations may negatively affect the welfare of their children. Being raised to fulfill such expectations would restrict a child’s development, or lead to emotional harm as a result of the understanding of being only conditionally wanted. On the other hand, sex selection might in certain cases make a positive contribution to the quality of parent–child relationships, as children would not have to bear the burden of being wanted less because of their sex. More fundamentally, those critical of the present ban argue that speculative fears do not suffice when it comes to justifying restrictive legislation.

On a societal level, distortion of the sex ratio as a result of sex-selective abortions in countries with a strong parental preference for a boy is a most serious concern. But as stated, it seems that there is no reason to fear such effects in Western countries.

Justice
Even if sex selection is not inherently sexist, its application in countries with a strong culturally mediated gender preference may reinforce societal patterns of inequality between the sexes (FIGO, 2006). Some commentators think it is naive to say that such effects need not be feared in Western countries. They are concerned that the marketing of sex selection technologies will reify sex differences and reinforce latent gender stereotypes also in seemingly non-sexist western societies. Others are less convinced about this or regard this type of argument as again too speculative to serve as a basis for public policy.

A specific concern is that if sex selection leads to more first-born males, men will profit more from the supposed advantage of this position. This would be a further way in which sex selection might contribute to social inequalities. However, this presupposes that sex selection will be used for selecting the sex of the first-born child. Even in most
countries with a strong preference for boys, this seems not to be the case (Hvistendahl, 2011).

**Slippery slope**

A final category of general concerns is that sex selection for non-medical reasons would be a step on a slippery slope towards the ‘designer child’. If one allows parents to choose the sex of their children, the door is opened to allow them to choose all other kinds of non-health-related characteristics. It is feared that sex selection is the thin end of the wedge that will inevitably lead to a morally reprehensible ‘commodification’ of children. Others have argued that slippery slope arguments are by definition speculative, that choosing offspring characteristics is not as such morally wrong, and that it will always be possible in principle to distinguish between selecting for characteristics that would limit a child’s chances of having a fulfilled life, and selection for other characteristics.

**Specific Ethical Considerations**

**The distinction between medical and non-medical reasons**

Sex selection for medical reasons is widely regarded as acceptable because it is aimed at avoiding health risks rather than at providing the prospective parents with a child of a specific sex. However, the way in which this distinction is usually drawn seems too strict.

As acknowledged in the British HFE Act, sex selection is not ‘medical’ only when aimed at avoiding sex-linked diseases such as Duchenne muscular dystrophy or haemophilia, but also when chosen in the light of a risk of transmitting a non-Mendelian disorder with an unequal sex incidence. Although in such cases sex selection cannot exclude the birth of a child with the relevant disorder, it can reduce the risk of an affected child. It can of course be asked whether that is enough to justify a sex-selective procedure. This will depend on the seriousness of the disorder and the amount of risk reduction that can be achieved, but also on the burdens and costs related to the type of procedure (Pennings, 2002). If the potential health benefits are small, IVF/PGD may be disproportional, whereas this need not be the case when sperm sorting with IUI can be chosen. But the point here is that whatever the proportionality of the procedure, the motive would still be health related, rather than based on a preference for a child of a specific sex for its own sake.

A further category not accounted for in the legal distinction between medical and non-medical reasons is sex selection for reasons of transgenerational health. For instance, a couple of which the male partner is a haemophilia patient will not have affected children themselves, but because any daughters will be (healthy) carriers, their grandchildren are potentially at risk. In such cases, sex selection aimed at the birth of a boy would serve the double aim of protecting their grandchildren are potentially at risk. In such cases, sex selection for other characteristics.

**Ethical aspects of specific methods for sex selection**

A safe, cheap and fully reliable method for sex-selective insemination would be the morally preferred method for sex selection both for medical and non-medical reasons. Although the proven effectiveness of Microsort® means that preconception sex selection is no longer a hypothetical concept, this technology still has limitations that are relevant from a moral point of view. First, the still existing safety concerns raise the question whether the technology can responsibly be offered to prospective parents. Given the debate about the need for the field to proceed with greater care when introducing new reproductive technologies into clinical practice, one might argue that as long as safety concerns cannot be fully answered, flow-cytometry may only be used for medical reasons, more specifically in cases where preselection can significantly add to the effectiveness of PGD aimed at avoiding the birth of a child with a serious sex-linked disease (HFEA, 2003). However, this seems too strict, given reassuring data not only from 760 children in the Microsort® trial, but also from the large scale use of flow cytometry in farm animals over more than 20 years. Centres offering the technology should commit themselves to careful monitoring and follow-up in order to provide data for assessing the longer term safety of the technology. As part of informed consent, patients (and non-patient users) should be clearly informed that safety data are still limited and that flow cytometry is not yet an established technology.

A second limitation is the imperfect reliability of the technique. In 8% of the cases where selection is for a girl, a boy will be born, and 16% of those who use the technology to have a boy, will have a girl. This need not be a problem when the technique is used as a pre-selection tool in the context of a medical procedure, but otherwise there is a chance of failure. If the aim is to avoid or reduce health risks, a less than complete reliability may well be acceptable, provided this does not entail a high risk of serious harm (Pennings et al., 2007). If sperm sorting were to be used for non-medical reasons, a specific concern is that a failure may have adverse consequences for the welfare of children born to parents who have gone to great lengths to have a child of the other sex. Clearly, this is an important aspect that centres offering this technology would have to address as part of pretreatment implications counselling. For prospective parents unable to cope in a responsible way with technology failure, IVF/PGD would be the better choice of method in this respect.

Although a reliable sex selection technology, PGD is burdensome, costly and may raise ethical concerns related to the use of embryos. Because of these material and immaterial costs, IVF/PGD is, in
many countries, only available for parents at risk of transmitting a serious genetic disease, which excludes its use for securing a parental sex preference. Even so, professionals may still be confronted with requests for ‘additional sex selection’ from prospective parents with a medical indication for IVF/PGD. As indicated, developments in the context of PGS may provide wider occasion for such parental requests. Ethically, this is a different situation than where ‘social sexing’ would be the reason for doing IVF/PGD \( (\text{ASRM, 1999}) \). As no extra medical procedures are needed, there can at least be debate about why it would be wrong to fulfill such requests. However, in countries with legislation banning sex selection, the question arises whether doctors performing PGD or PGS for medical reasons are legally allowed to do so. This will depend on the precise formulation of the relevant law in each country. Even if additional sex selection (not involving any extra procedures or use of techniques) is not against the letter of the law, it may still violate its spirit. A practical solution would be to leave the selection of the embryos for transfer to a professional who is not aware of the couple’s preference.

Sex selection for non-medical reasons through prenatal diagnosis followed by abortion in case of a fetus of the ‘wrong’ sex is widely regarded as morally problematic, precisely because it entails a termination of pregnancy. This is indeed the method most often used in countries where sex selection has led to a distorted sex ratio. Attempts to forbid the use of prenatal diagnosis and abortion for sex selection (other than for medical reasons) have had the adverse effect of making safe medical abortion less easily available for women who need such procedures for whatever reason \( (\text{WHO, 2011}) \). In Western countries, abortion does not seem to be widely used as a means of sex selection, reflecting the lack of a strong sex preference. But as with the new technology of NIPT, information about fetal sex can be obtained in a risk-free manner in the early stages of pregnancy; this would also allow sex-selective abortion to be performed much earlier. And since many persons regard early abortions less problematic than later ones, the advent of NIPT may make sex-selective abortion a more acceptable method for those who would currently not contemplate an abortion just for sex selection.

**Beyond symbolic legislation**

The categorical prohibition of sex selection for non-medical reasons as adopted in many Western countries has been described ‘as a surrogate campaign to eliminate sexist discrimination’ \( (\text{Dickens et al., 2005}) \). Until now, this legislation has indeed largely been of symbolic value, as there was no preconception method of proven effectiveness, and as the prohibition of social sexing through PGD does not add anything to regulations that in many countries already bind the use of this technology to strictly medical indications. As a result of the developments described in this document, this may be subject to change.

First, flow cytometry is now available with IUI such that those who want to use a preconception method for choosing the sex of their (next) child are effectively deprived of what for them may be a worthwhile option. As for those who would want to use it for this purpose, this method is currently only available in Mexico and North Cyprus, the prohibition of sex selection may add to the growing stream of those seeking reproductive treatment abroad.

Secondly, in the scenario where new approaches currently developed for PGS would lead to such screening becoming a routine part of all IVF treatment, this will provide many IVF patients with the option of asking the doctor to preferentially transfer a female or male embryo in cases where the choice is not fully determined by medical criteria. Assuming that the legislators have meant to also forbid additional sex selection, this is a further area where the ban may lose its symbolic nature and come to deprive people of a reproductive option that they would want to pursue.

At the same time, the advent of NIPT as a safe method for reliable sex determination in the early stages of pregnancy may provide those who want to select the sex of their next child with an easy alternative on which the law has no grip. As, in most countries, the ban on sex selection applies only in the context of assisted reproduction, it does not specify anything about sex-selective abortion. Pointing to this legislative lacuna, the recent Council of Europe reports on sex selection calls for additional legal measures to close this gap \( (\text{Council of Europe, 2011}) \). However, that may not be easy, as it might readily interfere with women’s rights to ask for an abortion on ‘social grounds’. One option that has been proposed is the withholding of test results that would provide information about fetal sex, at least for so long as an abortion would still be legally possible. However, both ethically and (in many countries also) legally, this would be difficult to maintain as the prospective parents would have a right to this information. Moreover, it is not morally acceptable to systematically treat pregnant women as suspects in this regard.

**Conclusion: Two Views**

As in its earlier document, the Task Force is divided about the issue of sex selection for non-medical reasons. One view is that these reasons will often reflect discriminatory attitudes or stereotyping views, and that allowing the practice is fundamentally at odds with a human rights perspective based on the equality between the sexes. In this view, sticking to the present ban will send a clear and consistent message to society that selecting the sex of one’s offspring is morally wrong, also including the abortion variant on which the law admittedly has no grip.

The other view is that as sex selection is not inherently sexist, the deontological underpinning of the present ban is unconvincing. This means that the issue should be decided on the basis of evidence that sex selection for non-medical reasons would lead to serious harm affecting the children who would be born as a result, or affecting society as a whole. As the latter seems unlikely in Western countries and as concerns about harmful consequences for children are speculative, the present categorical ban is difficult to justify. Moreover, the developments described in this document change the impact of the ban from largely symbolic to effectively restricting reproductive choice and may have the unintended and morally adverse effect of contributing to sex-selective abortions as a result of forbidding all forms of sex selection for non-medical reasons prior to pregnancy. Together, these arguments seem to require a revision of the current legislation, allowing sex selection for non-medical reasons under conditions that take account of societal concerns about the possible impact of the practice.

A possible approach has been suggested by the Human Fertilisation & Embryology Authority in its 2003 report on options for regulating...
sex selection: allowing (preconception) sex selection in a trial setting involving proper pretreatment implications counselling and serious monitoring of all relevant aspects. Such a trial ‘would permit an assessment to be made of the extent and profile of demand for this service, and controlled follow-up of families involved, including the effects of selection on the subsequent treatment and long-term psychological development of the children’ (HFEA, 2003). As a matter of caution, it would be advisable to use ‘family balancing’ as a condition for access to this trial, with the aim of neutralizing the most important potential dangers and disadvantages of unrestricted sex selection (Pennings, 1996).

**Recommendations**

(i) Sex selection should be allowed in principle if aimed at avoiding offspring health risks. This not only includes sex selection to avoid the birth of a child with a sex-linked disorder such as haemophilia or Duchenne muscular dystrophy, but (depending on the proportionality of the procedure) also to reduce the chances of having a child affected by a disorder with an unequal sex-incidence, and for avoiding transgenerational health risks.

(ii) Centres offering flow sorting should commit themselves to careful monitoring and follow-up in order to provide data for assessing the longer term safety of the technology. As part of informed consent, prospective parents should be clearly informed that safety data are still limited and that sperm sorting through flow cytometry is not yet an established technology. In cases where the technology is not used as a preselection step for IVF/PGD, prospective parents should be well informed about the limited reliability of the technique.

(iii) The advent of NIPT may become an easy alternative route for those wanting sex selection for non-medical reasons. As sex-selective abortion is a morally more problematic method for sex selection than the methods that in most countries are not allowed for this purpose, this should be a concern for professionals and policy-makers, precisely because this alternative route would be difficult to regulate or control.

(iv) If the present ban on sex selection for non-medical reasons is to be maintained, clarification is needed as to whether it applies to fulfilling parental requests for additional selection in the context of a medically indicated IVF/PGD (or PGS) procedure. Depending on the precise wording of the ban in different countries, additional selection (not involving any extra procedures or use of techniques) may or may not be against the letter of the law. Professionals need to know what the legal position is with regard to answering such requests.

(v) If the arguments against a categorical ban are found convincing, there would still be a need for setting conditions defining the responsible use of sex selection for non-medical reasons. A cautious approach would be to allow preconception sex selection for family balancing in a setting designed to gain further data about all relevant aspects. The family-balancing requirement could be set at having at least one or at least more than one child of the non-requested sex in the household. Under the same family-balancing condition, professionals should then also be allowed to fulfill requests for additional sex selection after PGD or PGS, in cases where there are embryos of both sexes and in which the choice between those embryos is not fully determined by medical criteria.

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**Conflict of interest**

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**References**


