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Position statement on the provision and procurement of human eggs for stem cell research.


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Abstract
The nature of compensation for women who donate eggs (oocytes) for research remains a contentious issue internationally. This position paper lays out the arguments for, and discusses the arrangements in which, a modest payment might be ethically justifiable.
Introduction
In 2006, the International Society for Stem Cell Research (ISSCR) published Guidelines for the Conduct of Human Embryonic Stem Cell Research (ISSCR, 2006: www.isscr.org). The task force grappled with the issue of financial consideration for eggs (oocytes) used in such research, finally recommending that local stem cell research and ethics review committees, where allowed by law, might determine the nature of compensation, ensuring that it does not constitute an undue inducement (Daley et al., 2007). At the 2009 ISSCR Annual Meeting in Barcelona the Ethics and Public Policy Committee of the ISSCR hosted a debate on the ethics of payments (in cash or kind) to egg providers. This Position Paper is the culmination of the Committee’s discussions over the subsequent 36 months. In this document, the Committee formulates a view on the ethical acceptability, under certain specified and regulated conditions, of payments (in cash or in kind) to women providing eggs for stem cell research. The Committee’s view is that stem cell researchers should act to ensure that human eggs for research are sourced ethically.

There is an escalation in demand and a worldwide market for human eggs. Eggs are procured and provided in a number of combinations of circumstances: the purpose might be for research and/or for treatment; the providers might be IVF patients or women in the community (‘non-IVF patients’); there might be varied arrangements of exchange (for cash or for payment in kind or for no tangible return). Each of these circumstances raises major conceptual, ethical and socio-economic questions, many of which have been extensively debated elsewhere.

We do not engage directly or in detail with those debates, though we acknowledge their importance in providing a spring board for our discussions. Instead we lay out the progression of our argument through consideration of various stages of the debate. The stages we cover are: (i) current arrangements for providing eggs for research in exchange for payment; (ii) arguments identifying the scientific need for human eggs for research; (iii) whether there are ways of avoiding the use of human eggs in research; (iv) the need to recognise the contributions made by women providing eggs for research; (v) a consideration of the arguments against giving payments to those providing eggs; (vi) systematic responses to those concerns; (vii) our conclusions. Such a style, whilst affording brevity and clarity, does not allow for a nuanced discussion; however, the details of each position can be found in the literature cited and in the other publications of the authors listed here.

Clearly the terminology in this field is highly contestable and any particular choice of terms shifts the grounds of the debate in certain directions. Therefore, in Section 1 we clarify our use of key terms, to ensure consistency with the position that we advocate here, rather than attempting to provide an uncontested lexicon.
I. Current arrangements for paying women who provide eggs for stem cell research:

There are three broad sets of arrangements under which women currently provide eggs for stem cell research in exchange for payment, in cash or kind, beyond reimbursement for actual expenses incurred:

i. the first is where women who are undergoing fertility treatment can provide a proportion of their eggs for research in exchange for reduced IVF fees; a scheme established in the UK refers to this as ‘egg sharing’ (Choudhary et al., 2012)(Haimes et al., 2012);

ii. the second arrangement is where women who are not undergoing fertility treatment are encouraged to provide eggs for research. Women are compensated for: the time and inconvenience associated with donation; their willingness to accept some risk, and for out of pocket expenses. In other words, the compensation is not for the eggs but rather for undergoing the processes involved in providing those eggs. This is legally permitted in some parts of the USA (though state laws are variable and in some cases unclear). In 2009, New York State’s stem cell board voted to permit its funded researchers to give compensation, beyond direct expenses, to women who provide their eggs directly and solely to research. The board argued that: compensation of amounts up to $5,000 was reasonable; amounts between $5,000 and $10,000 required sufficient justification, and amounts over $10,000 were prohibited. The deliberations behind this decision, and the procedural mechanisms required by the State to protect the rights and welfare of egg providers are laid out in Roxland (2012). In the UK in 2011 the Human Fertilisation and Embryology Authority (HFEA) conducted a review of their gamete donation policies and raised the existing one-off payment from £250 to £750, to cover expenses and loss of earnings, to women providing eggs for treatment or research, as well as continuing the egg sharing scheme (HFEA Press Release, Oct 19, 2011, www.hfea.gov.uk). A month before the HFEA announcement the UK-based Nuffield Council on Bioethics had suggested introducing a pilot scheme offering payment to women providing eggs for research (Nuffield Council on Bioethics, 2011). Compensation beyond out of pocket expenses is not permitted in many other countries, such as Australia and most European countries.

iii. the third arrangement might be called egg selling where a specific price is paid for each egg or batch of eggs. This paper does not cover these arrangements as we regard them as ethically distinguishable from egg sharing and from compensation for the donation process. Commercial transactions involving a substantial payment or reward for eggs are ethically highly controversial. In the UK, the Nuffield Council on Bioethics
(2011) rejected arrangements involving the sale and purchase of eggs whilst advocating the pilot scheme mentioned in (ii) above; this suggests that they also distinguish between compensation for providing eggs and egg selling.

The focus of this paper is to discuss those arrangements in which a modest payment, where efforts are made to avoid undue inducements (in cash or kind) might be ethically justifiable. For example, the HFEA payment of £750 was set at a level to avoid ‘attracting those who are merely financially motivated’.

II. The scientific need for human eggs in stem cell research

It is argued that human eggs are needed for stem cell research in a number of areas: to improve somatic cell nuclear transfer (SCNT) techniques; to thereby advance SCNT applications; to better understand early human development, and to assist stem cell research more widely. There is also competition for eggs for research on the causes and prevention of mitochondrial diseases; to improve fertility treatment, and to assist recognition of, and thereby avoid, fetal abnormalities. The use of eggs in stem cell research involves either direct research on, and with, eggs, or to create embryos; those embryos might then be used to derive stem cell lines. As early as 2005 stem cell researchers identified the need for fresh, healthy eggs rather than using eggs that had failed to fertilize (Stojkovic et al., 2005).

There are, therefore, various circumstances where scientific objectives rely on the creation of human embryos from eggs provided for research. However, stem cell researchers continue to note the shortage of human eggs for research (Noggle et al., 2011). Assuming that human embryonic stem cell research, and research into infertility and mitochondrial disease, is thought desirable, it is clear that there is a shortage of human eggs for use in research and that many more eggs will be needed.

III: Are there ways to avoid using human eggs in stem cell research?

It might be argued that other routes can be followed to achieve the same knowledge and therapeutic potentials identified above, obviating the need for research on eggs and thus for women to provide their eggs for stem cell research. However, a brief review of the main arguments suggests that this is not the case.

i. The derivation of human embryonic stem cell lines can be achieved using human embryos in excess of reproductive need from fertility programs. However, this does not provide the genetic compatibility offered by using SCNT embryos; also there are considerable ethical
challenges in using excess embryos from reproductive programs (Haines and Taylor, 2009, 2011a).

ii. The need for SCNT, and embryo-derived human pluripotent stem cells, has been questioned in light of the development of induced pluripotent stem cells (iPSCs), especially for the purpose of disease modelling or cell replacement. However, studies are highlighting the epigenetic differences between SCNT-derived embryonic stem cells and iPSCs, as well as genetic changes in iPSC lines, leading to concerns about the generation of abnormalities in iPSCs (Gore et al., 2011; Hussein et al., 2011; Kim et al., 2010). While these findings are unlikely to detract from the critical role of iPSCs in disease modelling, caution will be needed in their application to cellular replacement approaches. A strong consensus exists in the scientific community that research on SCNT-derived stem cells should continue while the full potential and safety implications of iPSCs and direct reprogramming are being explored.

iii. In the UK it was argued during parliamentary debates on the 2008 Human Fertilisation and Embryology Act that creating admixed human embryos (human-animal embryos) using eggs from cows would avoid the need to ask women to provide human eggs for research. However, no research of that kind has been published so this does not appear to be a viable alternative to using human eggs, despite the regulation being in place to allow it.

iv. Immune ‘matched’ stem cells for research might be gained by forming an embryo from human gamete(s) derived only from one person (without using SCNT). However, this procedure has so far only been successfully carried out by parthenogenesis using human eggs, thus not obviating the need for eggs to be provided (Kim et al., 2007; Revazova et al., 2007). The in vitro creation of human gametes for use in fertilization, SCNT, or other ways to derive hESC lines, raises its own ethical issues and for some might be more contentious than SCNT; even people who accept SCNT might object to the formation of embryos in this way.

This suggests that stem cell research using human eggs is scientifically justified, despite, or alongside, other research being conducted on other techniques.

**IV: Reasons to recognise the contribution of women who provide eggs for research**

It has been argued that women’s labor in providing eggs for research, and the risks that this might entail, have gone unrecognised (Daley and Solbakk, 2011). The process of providing eggs is arduous, potentially physically risky, and time consuming: women have to undergo a precise, self-administered, drug regime to
stimulate their ovaries; this process is risky as hyper-stimulation can occur; the long term effects of ovarian stimulation are unknown; the process of egg retrieval can be very painful. Throughout the process women have to organise their daily lives to ensure the medication is administered at the correct intervals and they have to attend a series of hospital appointments to monitor their progress.

This section identifies additional burdens for different groups of women who might provide eggs for research.

i. **Donation of eggs in the course of IVF treatment**: It has been argued that women undergoing IVF do not encounter additional dangers when providing eggs for research since their treatment necessarily entails all the above labor and risks. However, findings from a UK study of the donation of fresh embryos for hESC research revealed useful insights into IVF patients’ views about the use of their eggs in research. These patients regarded their eggs as a key resource for achieving a pregnancy so success in producing a good number of eggs during treatment was regarded as the first step towards getting pregnant. Therefore, whilst the use of eggs in research is less morally contentious than embryos, eggs are seen as being extremely precious. Giving away any of those eggs to research is seen as putting their chances of pregnancy at risk; this might explain why a scheme asking women to provide two eggs to research, without compensation, if 12 or more eggs were produced was not very successful and was replaced by an egg sharing scheme (see Section I(i)). Most of the IVF women interviewed would prefer not to provide eggs to SCNT research until they had achieved a pregnancy, even though the research itself was regarded as important (Haimes and Taylor, 2009). This suggests that even women not encountering additional physical risks (to those faced in routine IVF treatment) to give their eggs, should still be compensated for the potential risks to their chances of pregnancy. A study of the egg providers’ experiences of the UK egg sharing scheme, in which IVF patients provide 50% of their eggs in one cycle (if 6 or more eggs are produced) suggests that these women are prepared to risk their chances of pregnancy in one cycle only because the compensation provided means that they can afford an additional cycle of IVF, thereby giving them an additional chance of success (Haimes et al., 2012).

ii. **Donation of eggs outside of IVF treatment**: Women not undergoing IVF treatment will lose time from work or other responsibilities and will experience major disruption of their daily lives. These alone are enough to justify some sort of compensation; the physical risks encountered reinforce this claim (Nuffield Council on Bioethics, 2011). The Chair of the UK’s HFEA argued that the increase in 2011 in compensation for egg donors (see Section I) was a ‘fair reflection of the effort, the time and the pain’ involved in providing eggs (Jardine, Oct 19, 2011: www.bbc.co.uk/news/health-15356148). Anecdotal evidence indicates that
many women not undergoing IVF treatment are willing to provide eggs for research, but most do not proceed when they are told more about the time involved and the invasiveness of egg collection (Skene, 2010), a view confirmed by Egli et al. (2011).

V: Ethical concerns about ‘rewarding’ women for providing eggs for research

We now briefly outline the ethical concerns commonly raised about compensating women for providing eggs for stem cell research and in the next section proffer counterpoints:

(1) Concerns specific to women in IVF treatment programs

i. It is argued that offering rewards for providing eggs might compromise women’s autonomy, especially if recruitment starts early in the fertility treatment process. This is thought to inhibit women’s ability to make a free choice (give informed consent) because they may discount or overlook the potential risks and burdens through their desire to have a child and therefore to access more affordable treatment (Hyun, 2006; Skene, 2009).

ii. It is also argued that poorer women might be vulnerable to exploitation, as they might give up much wanted eggs in order to access treatment they cannot otherwise afford.

iii. There might be a conflict of interest for IVF practitioners if they advocate compensation for patients providing eggs as this could be seen as encouraging provision and therefore as promoting the practitioner’s broader research interests over the interests of their patients (particularly if points (i) and (ii) above are thought to hold sway).

iv. It has been argued that resources that are available for fertility treatment should not be allocated to non-fertility research. Under the principle of ‘just participant selection’ (Ballantyne and de Lacey, 2008), eggs obtained for research into fertility should be obtained only from women in fertility programs and their eggs should be used only for such research. Eggs for other types of research, such as drug development, should be obtained only from volunteers with a family interest in the medical condition for which the drug is being developed. Therefore it might be argued that compensation for providing eggs might encourage this ‘diversion’ of eggs from fertility research towards non-fertility research.

(2) Concerns relating to women who are not undertaking IVF treatment

i. Where women are not undertaking fertility treatment, it is argued, on the same grounds of autonomy and informed consent, that it is inappropriate to encourage them (through the offer of rewards) to take significant risks
(such as ovarian hyper-stimulation syndrome and the long-term effects of any form of stimulation) solely for the purpose of research.

(3) Concerns about the exploitation of vulnerable women

i. There might be exploitation of impoverished women if there are economic inequalities either within a country, or across national borders (Widdows, 2009). Such exploitation might occur either through the ‘cross-border trade’ in eggs or through the movement of scientists to exploit regulatory conditions more favourable to their research (Haines and Taylor, 2011b).

(4) Wider concerns about commodification and altruism:

There is a concern that practices in egg provision and procurement might affect broader values in other areas of research.

i. One concern is that eggs might be commodified by this practice and that this might set a precedent for the commodification of other body parts. It is argued that the best scheme for the provision of eggs and other bodily material for research is an altruistic system of donation.

ii. Another concern is that compensating women for providing eggs could create an unfortunate precedent in countries where payment for blood, tissues and organs is the exception (Isasi and Knoppers, 2007; Nuffield Council on Bioethics, 2011) thereby undermining long established and widely accepted systems of non-remunerative donation practices.

iii. Rewarding women who provide eggs for research diminishes the moral value of altruistic donation. It might deter women who would donate their eggs altruistically but not provide eggs for reward.

VI: Responses to these ethical concerns

We acknowledge the importance of these concerns and make the following responses.

(1) Concerns specific to women in IVF treatment programs

i. Offering women in fertility treatment programs a reward for providing some of their eggs for research is ethically justifiable to compensate them for their willingness to accept added anxiety and some risk of reduced chances of pregnancy (see Section IV (i)).

ii. This is not a payment for the eggs themselves as women will be entitled to the compensation even if no eggs are collected or the eggs collected are
not suitable for the research. (However, IVF patients would not be entitled to compensation if they changed their minds about providing eggs for research and decide to keep all their eggs for their own treatment, since this means that their chances of success in achieving a pregnancy will not, after all, have been compromised by the research (see Section VI (i)). This is the agreement in the HFEA-licensed egg sharing scheme in the UK).

iii. Women’s autonomy will not be compromised if researchers take proper care to ensure that women are fully informed. Consent processes are not always ideal but every effort should be made to ensure the consent process is optimised for the local community and that the entire egg donation process, including the risks, are adequately considered. Competent adult women can decide for themselves whether to provide their eggs for research, as long as they are properly informed (Haimes et al., 2012). Recruitment systems can also be designed to avoid pressure on women to provide their eggs for research, such as a scheme that is based on women taking the initiative to come forward to provide eggs (as in the UK egg sharing scheme), rather than being put in the position of having to respond to direct requests for eggs from clinicians supervising their IVF treatment.

iv. With regard to other equity issues, it is true that rewards may be more attractive for women of limited means than for wealthy women. However, the objection that this makes the rewards inequitable, and may lead poorer women to take more risks, may be met by noting that some of these women will not be able to get fertility treatment without a scheme of this kind. As long as their choice is free and informed, and as long as the terms are fair, compensation schemes can actually increase access to such treatment for women whose economic conditions would otherwise disallow it (Haimes et al., 2012). It is unrealistic and unfair to require them to wait for state funding schemes for fertility treatment to be changed. Nonetheless, policy debates on how to facilitate wider access to fertility treatment should continue.

v. Potential conflicts of interest for practitioners in fertility treatment (who might want to treat women successfully but also participate in research) could be minimised by applying the ‘principle of separation’. This is an arrangement in which those who recruit tissue providers, and/or inform them of the research risks and benefits, are separate from the personnel who have the role of caring for women in treatment programs.

vi. The question of ‘just participant selection’ in the area of egg provision for research (whether or not for reward) raises the wider question of who makes, or should make, the decision about the appropriate use of eggs. Ongoing studies are investigating egg providers’ preferences for the possible research uses of their eggs and we regard these studies as a vital component in this debate. If most women who provide eggs for research want those eggs to be used only in research on infertility, those
wishes should inform the development of future policies on the provision of eggs for research.

(2) Concerns relating to women who are not undertaking IVF treatment

i. Women who are not receiving IVF treatment are being compensated for undergoing the procedures involved, rather than for the eggs themselves. As with women undergoing IVF, they will receive strong ethical protection against exposure to reduced autonomy, undue risks, and exploitation, by robust procedures ensuring voluntary participation, fully informed consent and rigorous ethical oversight. Competent adult women will be able to decide for themselves if they wish to provide eggs under such conditions.

ii. Other healthy people who participate in medical research, including sperm donors, commonly receive some payment and it is inconsistent to exclude egg provision from this established compensation system.

(3) Concerns about the exploitation of potentially vulnerable women

i. It is presumptuous to assume that poorer women are not able to make their own decisions about whether they wish to take health risks in exchange for rewards. Some women may have limited life opportunities available to them, because of background injustices affecting their lives, but that does not preclude them from making a rational and informed decision about which opportunities are preferable.

ii. However, it is the proper role of ethics and law to protect groups and individuals in situations in which they might become vulnerable. The suggestions, in points iii-vi below and in the Conclusions, for monitoring the effective functioning of protective measures must be taken seriously by all parties concerned and be subject to regular review and investigation (Isasi and Knoppers, 2007).

iii. Possible exploitation of other ‘vulnerable’ women can be addressed by the requirement of oversight of all research involving the use of human eggs by independent ethics committees. This should include, as a minimum requirement, periodic monitoring to identify any disparate level of contribution by women who are vulnerable for any reasons within areas of traditional concern about voluntariness, such as poverty, race, or mental condition.

iv. Concerns about research tourism and the welfare of women in impoverished countries can be met by requiring researchers and ethics committees to follow robust and internationally-accepted principles of ethics in the receipt and brokerage of tissue to be used in research. Again, ongoing monitoring should alert both researchers and ethics committees to possible abuse.

v. Researchers who import human eggs for use in research should be required, as part of the procedure for obtaining ethical approval for their
project in their own country, to ensure that imported eggs are obtained by a process that would meet the ethical requirements within their own country.

vi. To reduce the risk that some countries might have lower ethical requirements in dealings with their own citizens, international ethics bodies could be encouraged to stimulate discussion in other countries about the issues identified here.

(4) Wider concerns about commodification and altruism

i. Unlike the practice of ‘egg selling’, the compensations envisioned in this report do not constitute a ‘commodification’ of eggs (Caulfield and Ogbogu, 2012); they are not a payment for the eggs themselves (for example, the UK egg sharing scheme is not based on a price per egg). The suggestion is that compensation should be paid for participating in the whole process, so that women will be entitled to receive the reward whether or not eggs are produced or suitable for research.

ii. Compensation for providing eggs need not be a precedent for procurement of blood, tissue and organs for research. Peripheral blood may be donated for research but this is a minor procedure with few risks, so it is appropriate that it should be uncompensated, if that is the norm in any particular country. The same is arguably true of other tissue that may be donated by a living person for research. However, solid organs like kidneys cannot lawfully be removed from a living person for research (only for treatment), so there is no question of anyone being paid for providing a solid organ for research.

iii. The moral value of altruistic donation need not be undermined by compensating some women who provide eggs for research. Altruistic donation could be maintained for women who do not wish to receive anything for donating eggs or other tissue (Isasi and Knoppers, 2007; Nuffield Council on Bioethics, 2011).

VII: Conclusions

It is evident from the above that the research demand for eggs is part of a larger global market for human tissue. Anything that is said about eggs therefore has the potential to impact on wider debates about the provision and procurement of other tissue and organs for research and also on debates about the therapeutic uses of human tissue. However, those debates, whilst overlapping, also have their distinctive considerations and it would be irresponsible to make too glib a cross-over from one area to another. Therefore, whilst acknowledging that potential for overlap, we confine our comments here to reiterating our views on the role of payments in egg provision for stem cell research.
For the reasons given above, our position is:

(1) Paying (in cash or kind) women for providing eggs for research is ethically justifiable as a means of compensating them for their time, inconvenience, willingness to accept some risks and as a reimbursement for out-of-pocket expenses. This is not a payment for the eggs themselves.

(2) We repeat our view, stated at the end of Section I, and in agreement with the ISSCR Guidelines (2006), that efforts should be made to avoid payments becoming undue inducements. We would regard such levels of payment as constituting ‘egg selling’, a practice we reject in Section I (iii).

(3) The ISSCR is an international organisation and given the wide socio-economic variations across its member countries, it would be inappropriate to specify actual payment amounts. However, we endorse the view that payments for providing eggs for research should be limited, even if higher amounts may be paid where eggs are provided for treatment purposes. For example, the U.K.’s HFEA limit of £750 is well below the payments obtainable elsewhere in the world for providing eggs for treatment purposes. (We would also welcome research on whether payments for eggs for treatment purposes constitute undue inducements).

(4) Fertility clinics and research centres that collect eggs should establish systems for collecting and, where possible, publishing, data around the procurement and provision of eggs for research, including information on: eggs providers’ motivations and preferences; who applies to be an egg provider; who is rejected and why, and, long term tracking of egg providers’ health.

(5) Independent ethics committees should ensure that the informed consent documentation includes amongst other things (ISSCR Guidelines, 2006): full information about the risks involved; a statement that women need not participate, and, a statement that women can withdraw from the research at any time until the eggs are actually used in research, without detriment to their treatment. Ongoing monitoring of consent should ensure that the documentation is effective when applied in actual everyday practices.

(6) The roles of treating women undergoing fertility treatment and recruiting egg providers for research should be separated.

(7) Stem cell researchers, as an additional interest group, have an obligation of prudent stewardship of this scarce resource (London et al., 2010) and should act to ensure that the tissue that they work on has been ethically sourced. This applies especially where the tissue is imported from another country for use in research, bearing in mind the ethical issues that have been highlighted in this paper.
(8) National regulatory bodies must ensure that the ethical dangers of cross-border trade are avoided or minimised.

(9) International ethics bodies should encourage discussion in other countries about the issues in this paper.

These conclusions should be reviewed in the light of the analysis of the views and values of egg providers themselves and the reports of different public bodies dealing with the ethics of medical and health related research.

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