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The stem cell debate continues: the buying and selling of eggs for research

F Baylis, C McLeod

Now that stem cell scientists are clamouring for human eggs for cloning-based stem cell research, there is vigorous debate about the ethics of paying women for their eggs. Generally speaking, some claim that women should be paid a fair wage for their reproductive labour or tissues, while others argue against the further commodification of reproductive labour or tissues and worry about voluntariness among potential egg providers. Siding mainly with those who believe that women should be financially compensated for providing eggs for research, the new stem cell guidelines of the International Society for Stem Cell Research (ISSCR) legitimise both reimbursement of direct expenses and financial compensation for many women who supply eggs for research. In this paper, the authors do not attempt to resolve the thorny issue of whether payment for eggs used in human embryonic stem cell research is ethically legitimate. Rather, they want to show specifically that the ISSCR recommended payment practices are deeply flawed and, more generally, that all payment schemes that aim to avoid undue inducement of women risk the global exploitation of economically disadvantaged women.

In December 2006, the International Society for Stem Cell Research (ISSCR)—a scientific membership organisation for stem cell scientists, laboratories and biotechnology companies—released its *Guidelines for the conduct of human embryonic stem cell research* (hereafter the ISSCR Guidelines).¹ One of the ethically controversial issues addressed therein is financial compensation for women who provide eggs used to create research embryos for stem cell science. Significantly, this issue is one of the few on which authors of the ISSCR Guidelines did not readily agree.² Some argued that altruism alone should motivate women to provide eggs for research and that even reimbursement of direct expenses could result in abuse. Others insisted that it would be both unfair and exploitative to have women bear the potential harms of hormonal stimulation and surgical egg retrieval without financial compensation.

In the end, the authors of the ISSCR Guidelines agreed to the following: “Except when specifically authorised by the SCRO (Stem Cell Research Oversight) process, no reimbursement of direct expenses or financial considerations of any kind may be provided for donating

embryos or gametes that have been generated in the course of clinical treatment and are in excess of clinical need or deemed of insufficient quality for clinical use” (11.5a).¹ Here, the ISSCR Guidelines essentially take a *prohibitive* stance towards paying women in fertility treatment for their eggs (ie, payment is not permitted unless specifically authorised). This interpretation is consistent with the language that the Guidelines use to describe these women: they are egg *donors*. In sharp contrast, women whose eggs are collected outside of treatment are egg *providers*, and paying them is permitted. The Guidelines suggest that researchers should follow local practice regarding reimbursement for research participation and use the usual local research ethics review process to “ensure that reimbursement of direct expenses or financial considerations of any kind do not constitute an undue inducement” (11.5b).¹ Here, the Guidelines take a *permissive* stance towards paying women outside of treatment to provide eggs for research (ie, payment is permitted, provided there is no undue inducement). By permitting reimbursement of direct expenses and other financial compensation for eggs for stem cell research from

some women, and some women only, the ISSCR Guidelines distinguish themselves on two counts from other guidelines and laws that prohibit payment for eggs:¹ the ISSCR Guidelines allow payment for eggs and also create two classes of payees. Presumably, the purpose of allowing some payments is, in part at least, to increase the number of women who provide eggs for stem cell research.

In this paper, we critically examine the ISSCR strategy for recruiting women as egg providers for stem cell research. First, we consider the presumed global shortage of eggs available to create embryos for stem cell research using somatic cell nuclear transfer technology (hereafter called cloning technology).ⁱⁱ We accept that altruistic giving is unlikely to provide the hoped-for number of eggs for cloning-based stem cell research. But, at the same time, we question whether cloning research is necessary to the development of safe and effective stem cell therapeutics and therefore whether a recruitment strategy for egg providers with payment as an incentive is necessary to the pursuit of stem cell research and therapeutics.

Second, we review the different stances in the ISSCR Guidelines with respect to paying women according to whether their eggs are collected during or outside the course of clinical treatment. We discuss possible reasons for the difference and find each of these reasons wanting.

Third, we show how the stipulated requirement that there be “no undue inducement” of women who provide eggs generated outside of clinical treatment amounts (perhaps unwittingly) to endorsement of a policy according to which some women are paid less for their eggs than other women. Such endorsement is inevitable, because “undue inducement” is context-dependent. For example, on average, a payment that would not amount to “undue inducement” for egg providers from Eastern Europe would be substantially lower than any such payment to women from wealthier nations, such as Britain or the USA. A similar worry exists about payment to economically disadvantaged women in wealthy countries compared with payment to economically advantaged women in these same countries. We conclude that the

ⁱExamples of these guidelines and laws are the National Research Council guidelines³ and laws in Massachusetts, Connecticut, Indiana, Maryland,⁴ California,⁵ France,⁶ South Korea⁷ and Canada.⁸

ⁱⁱHuman cloning involves the insertion of nuclear DNA from a human somatic cell into an enucleated human egg, which is then activated so that it starts dividing, becoming an embryo from which stem cell lines can be derived.

ISSCR Guidelines are unfair to, and potentially exploitative of, women.

CLAMOURING FOR EGGS

Debate regarding payment for human eggs for stem cell research is broiling, especially in jurisdictions where payment is prohibited. Among the staunchest advocates for paying egg providersⁱⁱⁱ are stem cell scientists who want to create (human) research embryos using cloning technology, from which they hope to derive personalised stem cell lines. The keen interest in devising a system of financial compensation for egg providers stems from the current experience of not having enough women who altruistically supply eggs for this research. For example, Robert Lanza of Advanced Cell Technology Inc, in Alameda, California (USA), reports that he has only had one woman donate eggs for stem cell research, after having spent more than a year looking for donors and having placed about 100 advertisements.⁹ In addition, Kevin Eggan of the Harvard Stem Cell Institute says that he has been looking for altruistic egg donors for nearly 8 months without success.⁹

By contrast, the success in getting eggs for embryo research from women in fertility clinics has been a little better (at least in the UK), but apparently the numbers are still too low. For example, the Human Fertilisation and Embryology Authority (HFEA), an independent regulatory body that licenses fertility clinics and embryo research in the UK, reports that in 2003, 64 eggs were donated to embryo research from women in fertility treatment. In 2004, the number of eggs donated by this cohort of women was 53.¹⁰ However, researchers say that these numbers are not nearly high enough for cloning-based stem cell research. In February 2007, the HFEA amended its policy on altruistic egg donation so that women could be financially compensated or receive benefits in kind for donating eggs to research. Women who provide eggs for research that are collected outside the course of clinical treatment can now claim up to £250 in reasonable, proven expenses, including loss of earnings, and women who provide eggs for research collected during the course of clinical treatment can receive a reduced rate on treatment. (Previously, a reduced rate was available only to women who donated eggs for treatment.)^{11–13} In September 2007, the HFEA allowed that the benefit in kind to women who provide eggs for research during the course of

fertility treatment could be as high as £1 500. The Medical Research Council (MRC) awarded the North East England Stem Cell Institute in Newcastle a research grant that included £150 000 to subsidise in vitro fertilisation (IVF) treatment and £760 000 for research costs. The MRC agreed to pay £1 500 towards the £3 000 cost of one IVF cycle to every woman who agreed to provide half of her eggs for cloning-based stem cell research.¹⁴ The MRC agreed to the payment scheme because alternative approaches for getting eggs for this type of research have failed.

A crucial underlying assumption in the debate about the need for eggs for cloning-based stem cell research is that the research is necessary for the development of safe and effective stem cell therapies. An oft-cited reason for this type of stem cell research is the need to develop personalised stem cell lines for transplantation into patients, in order to avoid the potential harms of immune rejection. Yet the benefit of personalised stem cell lines is questionable, because the risk of immune rejection with embryonic stem cells has yet to be confirmed.^{15–16} In fact, evidence suggests that tissues derived from stem cells are less likely to provoke host immune rejection than other transplantable tissues.^{17–18} If, however, the evidence did eventually confirm a significant risk of immune rejection, cloning-based stem cell research would not be the only (and might not be the best) solution to this problem. Alternatives, suggested by Jamie Thomson, include "... banking cell lines with defined major histocompatibility complex backgrounds or genetically manipulating ES [embryonic stem] cells to reduce or actively combat immune rejection."¹⁹

More recently, Snyder and Loring offered a more comprehensive critique of cloning-based stem cell research. They briefly described the putative benefits of this research, and then dismissed each benefit in turn, thereby suggesting that, at best, the need for cloning-based stem cell research is uncertain:

[t]he theoretical usefulness of SCNT [cloning technology] is threefold: to make graft material that is genetically and immunologically matched to prospective transplant recipients, to make more representative in vitro models of poorly understood human diseases (for testing drugs or unraveling pathophysiological mechanisms), and to provide an alternative method for making stem-cell lines that does not involve the use of fertilized oocytes. [But as Snyder and Loring readily admit, each of these] ... specific indications for SCNT ... remain

uncertain. In fact, concern about the need for patient-specific cell lines is now being tempered by the recognition that stem-like cells may actually be less immunogenic than was initially presumed. There may also be simpler ways to make models of disease—for example, from blastocysts with diseases identified through preimplantation genetic diagnosis. And there may be other ways of circumventing the moral concern about the destruction of embryos in the creation of stem-cell lines (eg, the dedifferentiation of somatic cells).²⁰

These cautionary remarks are consistent with the views of Austin Smith, a prominent stem cell researcher in the UK. According to Smith, cloning research "has limited potential and adds little to scientific understanding of human biology".²¹ Statements like these suggest that the need for—and thus the "chronic" shortage of—eggs for cloning-based stem cell research may be overstated. But even if scientists agree that there is no pressing need for cloning-based stem cell research, they might still argue that there is a chronic shortage of eggs, because eggs are needed to create research embryos using IVF. One could reasonably counter this objection to our skepticism about an egg shortage, however, by noting that there is an alternative source of IVF embryos for research: namely, cryopreserved embryos remaining after fertility treatment.^{22–23} As noted above, the number of such embryos donated to research does not satisfy the research need for embryos. But this problem, such as it is, does not justify payment for eggs to create research embryos. Consider the following analogy. At present, there is a chronic shortage of solid organs for transplantation. In most jurisdictions, however, we have not tried to solve this problem by introducing a system of payment for solid organs. Rather, we continue to develop strategies to encourage altruistic donation. Arguably, we should do the same with respect to the need for IVF embryos for stem cell research, and develop strategies to encourage the altruistic donation of IVF embryos that are in excess of clinical need. Indeed, some have suggested that increasing public debate and discussion about embryonic stem cell research could motivate women to donate their frozen embryos to stem cell research.^{22–24}

EGG DONORS VERSUS EGG PROVIDERS

As outlined above, the ISSCR Guidelines treat the selling of eggs to researchers differently depending on whether the eggs are "generated in the course of

ⁱⁱⁱ For obvious reasons, we follow the ISSCR Guidelines in using the term "providers" rather than "donors" when there is payment involved.

clinical treatment" or not (11.5a). More specifically, the ISSCR Guidelines include different prescriptions for these two scenarios. For women who donate eggs collected during treatment, payment is not the norm, but rather requires specific authorisation. In contrast, women who are not in treatment are research participants and, as such, are to be financially compensated in a manner consistent with research compensation practices in effect in the relevant jurisdiction. The ISSCR Guidelines also refer to undue inducement with the second group of women but do not even mention this possibility when discussing payment for the first group (women who donate eggs during treatment). Presumably for this group, undue inducement would be a topic for discussion during an SCRO process initiated for the purpose of authorising an exception payment. Nonetheless, failure to name this concern explicitly for these women is surprising, especially given that elsewhere in the ISSCR Guidelines, there is evident concern about the coercion and exploitation of women undergoing fertility treatment who are asked to provide eggs for stem cell research. Consider in particular this directive: "Wherever possible, the treating physician or infertility clinician should not also be the investigator who is proposing to perform research on the donated materials" (11.4).¹ The worry here is with the potential harms of coercion and exploitation.

The ISSCR Guidelines themselves do not explain the different directives about financial compensation for women who provide eggs for stem cell research, depending upon whether the eggs are collected during or outside of treatment. The thought, however, seems to be that women who are not fertility patients would not otherwise bear the burdens of time and inconvenience, or the potential harms of superovulation and egg retrieval. Since they experience these potential burdens and harms solely by virtue of their participation in research, they should be eligible for financial compensation, just as healthy volunteers for other types of research would be eligible for compensation.

Presumably no similar financial obligation exists towards women who are infertility patients and who elect to provide eggs for research, because they independently agree to all that egg collection involves; they do so for their own benefit in the hope of establishing a pregnancy. Without their participation in research (ie, without a decision to provide eggs for research), they would still have the time investment, inconvenience and potential harms just mentioned. So they

have done nothing specific to earn financial compensation. For this reason, no payment need be provided to women in fertility treatment. And presumably, exception payments "authorized by the SCRO process" need only be sought when there is a perceived need for payment as a motivating factor (11.5a).¹

A second possible explanation for the ISSCR position is a utilitarian desire to minimise potential harm to women by not encouraging those who are at greatest risk of harm—that is, female infertility patients—to assume this risk for financial compensation. On this view, the potential harm to infertility patients who provide eggs to stem cell researchers is greater than the potential harm to healthy volunteers (women who are not in clinical treatment). With both groups of women, there are the initial potential physical harms associated with superovulation and egg retrieval. With infertility patients, however, there are additional potential psychological and physical harms if they do not become pregnant in the cycle in which they sold eggs for research. To explain: female infertility patients are producing eggs, first and foremost, for their own reproductive use. If they do not become pregnant after having sold some of their eggs for research (particularly if those eggs were deemed suitable for transfer), and they attribute their failed treatment to their decision to sell some of their eggs, then they could experience psychological harm. In addition, if they decide to undergo additional superovulation and egg retrievals in the hope of achieving a pregnancy, they could experience additional physical harms. These additional harms do not apply to women who provide eggs for research that are collected outside the course of treatment.

A third possible reason for the ISSCR policy difference on payment for eggs is a concern about the greater potential harm of undue inducement with paying infertility patients. Fertility treatment is expensive and, for some, cost-prohibitive. The only way to access IVF might be to agree in advance to sell some of one's eggs for research.

While these reasons for the ISSCR policy difference seem plausible, they do not amount to a principled defense of a fair policy. Women who provide eggs collected in treatment are not so unlike women who provide eggs collected outside of treatment that there ought to be different guidelines with respect to paying for their eggs.

First, while it is certainly true that infertility patients accept the potential harms of superovulation and egg retrieval for their own benefit, their decision to

assume these potential harms also benefits researchers who are provided with some of the eggs. More generally, the fact that infertility patients accept certain potential harms irrespective of whether they are benefiting researchers or are financially compensated is irrelevant to whether they should be compensated. Consider the following analogy. Writers who would write even if the public did not appreciate their work and would not pay for their writings are nonetheless still entitled to make money from their work. One does not lose a legitimate right to compensation by virtue of a willingness to act without compensation.

Second, one could argue that the greater potential physical and psychological harms to infertility patients of offering up their eggs entitles them to at least as much financial compensation as is available to women who are not in treatment. Usually, forms of labour that involve serious potential harms are compensated favourably because of the harm. To expand on the potential harms for infertility patients of providing eggs for stem cell researchers, consider that to maximise the chance of pregnancy, all eggs produced in one cycle of IVF should be exposed to sperm to obtain a maximum number of fertilised eggs (assuming that with responsible ovarian stimulation, women would not produce an inordinate number of eggs per cycle). Eggs that do not fertilise (and otherwise would be discarded) would become eligible for research, as would fertilised eggs deemed unsuitable for transfer (and thus for freezing) for morphological, biological or genetic reasons. If there were still more fertilised eggs suitable for transfer than could reasonably be transferred in one cycle, then these remaining embryos should be frozen for later use in possible future cycles. Freezing these embryos allows women to avoid having to go through superovulation and egg retrieval again. When a woman's treatment does not follow this path, her chances of success with IVF are reduced and her chances of realising the potential harms are increased.²⁵ Included among such women would be those who provide eggs for stem cell research.

A recent report from the Institute of Medicine (commissioned by the California Institute for Regenerative Medicine) minimises the potential harms of superovulation and describes egg retrieval as a "remarkably safe procedure".²⁶ But many would insist that the potential harms of ovarian hyperstimulation syndrome (OHSS), as a consequence of superovulation therapy, are not insignificant (although, with proper monitoring, they can be minimised).^{24, 27} For

example, mild, short-term OHSS is characterised by fluid accumulation, rapid weight gain and abdominal distension and discomfort. More severe forms of OHSS are accompanied by nausea, vomiting, diarrhoea and respiratory difficulty. At its most severe, OHSS requires hospitalisation and can be life threatening; complications include renal failure, adult respiratory distress syndrome, haemorrhage from ovarian rupture, and thromboembolism.^{27–29} At the 2006 meeting of the European Society for Human Reproduction and Embryology, six deaths from OHSS were reported.³⁰ By comparison, potential long-term harms of superovulation are less well documented. Two studies, however, suggest a link between superovulation and ovarian cancer.^{31–33}

Third, while we certainly believe that undue inducement is a worry for women undergoing fertility treatment, we do not accept that the risk of it is necessarily higher for them than for women who provide eggs collected outside of clinical treatment (it may or may not be higher). Offers of money amount to undue inducement when they are enough to get people to “discount [any] risks to themselves and to make decisions they will later regret” (p262).³⁴ With women seeking IVF, the concern about offering them money for their eggs in exchange for a reduced rate on treatment is that their psychological need to get pregnant will trump any concern about potential harms (ie, the potential physical and psychological harms of IVF). Supposedly, the same sort of problem does not arise, at least not with the same frequency, in the context of offering money to women for eggs collected outside of treatment. But this line of reasoning is problematic for two reasons. First, it presumes a level of desperation among women seeking fertility treatment that is not borne out by the relevant psychological literature; the literature does not show that these women are so obsessed with getting pregnant that they would simply ignore potential harms to themselves.³⁵ Second, desires that motivate women outside the course of clinical treatment to sell their eggs could be just as intense and overwhelming as a desire to get pregnant after a long period of infertility. Examples include desires to avoid a crushing credit-card debt, to pay tuition or pay off student loans, to feed and clothe one’s children and to be able to pay for medical treatment for oneself or a loved one. On average, then, undue inducement could be the same for the two groups of women.

We have shown that different assumptions about payment for eggs in the ISSCR Guidelines are unfair. In any scheme in which women benefit finan-

cially from providing eggs to stem cell researchers, women should benefit equally regardless of whether their eggs are collected inside or outside of fertility treatment.

NO UNDUCE INDUCEMENT

Several years ago, Donna Dickenson anticipated the increased demand for eggs because of stem cell research involving cloning.^{36–37} She predicted that there would be an acute risk of exploitation, since there would be little concern about the genetic traits of the women providing the eggs for cloning research. According to Dickenson, one could reasonably anticipate women of the southern hemisphere being targeted as egg providers: “Enucleated eggs have no genetic content ... race therefore does not matter: [the] enucleated egg [of a woman from the south] can still be used in stem cell technologies and therapeutic cloning” (p60).³⁶

With the introduction of the ISSCR Guidelines as proposed international best practice for stem cell research, Dickenson’s concerns about an unregulated trade in human eggs and the likely exploitation of some women take on added urgency.³⁸ To explain, the ISSCR Guidelines do not propose a fee schedule for egg production, but simply preclude payments that would constitute undue inducement for women who provide eggs outside the course of treatment. This move seems reasonable insofar as undue inducement is not about the amount of the payment, but about the gap between the payment offered for eggs and payments otherwise available to women for goods and services they might be able to provide in the marketplace. The problem, however, is that in wanting to avoid undue inducements, the Guidelines in effect legitimise paying some women substantially less for their eggs than other women, based solely on geography and the local economy. Consider the following: consistent with national ethics guidelines, women in the United States who provide eggs for therapeutic use are routinely paid US\$4 000 to US\$5 000 per cycle.^{39–40} For the sake of argument, let us assume that this payment, and a similar payment for eggs for stem cell research, to these women does not amount to undue inducement. What about offering the same payments to women from poorer nations? Surely the women would be unduly induced by these offers, given the local economy. People have already expressed concerns, understandably, about the undue inducement of women from Eastern Europe who are paid a mere £250 (approximately US\$500) to provide eggs for therapeutic purposes.⁴¹ It would

appear, therefore, that to avoid undue inducement, as required by the ISSCR Guidelines, one would have to insist that women from poorer nations be paid considerably less for their eggs than women from wealthier nations (or insist that all women be paid the same low amount, an unlikely scenario and an ethically troublesome one, as suggested below).

Furthermore, because the ISSCR Guidelines not only allow, but, as per the argument above, require unequal payments to women depending on their level of economic advantage, the Guidelines create an incentive for researchers to collect eggs from women who are economically disadvantaged. But if researchers disproportionately seek out these women, then they take unfair advantage of their economic state. In other words, they exploit them. We think the authors of the ISSCR Guidelines would agree with this analysis; in fact, they anticipated this problem of exploitation and included the following directive in response to it: “[t]here must be monitoring of recruitment practices to ensure that no vulnerable populations—for example, economically disadvantaged women—are disproportionately encouraged to participate as oocyte providers for research” (11.5bi).¹

Though we commend the authors for recognising the likely problem of disproportionate participation by, and exploitation of, economically disadvantaged women, we believe that a simple directive to monitor recruitment practices cannot possibly offer these women adequate protection from exploitation. There simply is no way to ensure, and no reason to expect, equitable participation in egg selling by rich and poor women. Are stem cell researchers in economically disadvantaged countries to refrain from recruiting nationals—women who are likely to be economically disadvantaged? What does it mean for these researchers not to encourage the disproportionate participation of economically disadvantaged women when all women in their country are situated in this way? And what about stem cell researchers in wealthy countries where there are many affluent women, but also many poor women? Are these researchers to track the socioeconomic status of all egg sellers and then endeavour to meet a certain quota for women in different economic strata? Or do these researchers only need to show that their recruitment strategies do not *purposely* target economically disadvantaged women and that any imbalance in participation between the rich and the poor is simply to be expected (ie, natural), given that wealthy women would hardly be

motivated to sell their eggs for stem cell research for what to them would be little money.

In cautioning researchers against undue inducement (at least for some women), the authors of the ISSCR Guidelines accept that the price of eggs for stem cell research will be a function of geography and will vary as the price of eggs for fertility treatment does now. Such inequality creates an incentive for researchers to obtain eggs from poor women more often than from wealthy women. Moreover, the ISSCR Guidelines do not do enough to prevent researchers from acting on this incentive—that is, from acting in a way that the authors themselves deem to be ethically problematic.

CONCLUSIONS

Since we do not accept unchallenged the claim that cloning-based stem cell research is necessary for the development of successful stem cell therapies, we are not sympathetic to the oft-repeated claim that there is a chronic shortage of eggs needed for cloning-based stem cell research. It follows that we are not inclined to look favourably upon payment schemes aimed at increasing the number of eggs available for this research. In our view, egg production and collection are potentially very harmful activities for women, and without clear evidence of significant potential benefit there is no favourable harm–benefit ratio that justifies asking women to assume the potential harms (for the sake of research or for any other end).

In addition to the potential physical and psychological harms of egg production and collection, there are the potential harms of undue inducement and of exploitation inherent in any system of payment for eggs. (Indeed, were it not for these potential harms, it would be relatively simple and, for some, uncontroversial to set a fair price for women's labour in producing eggs for research.) To avoid the potential harms of undue inducement and exploitation, some system other than the one outlined in the ISSCR Guidelines is needed. These Guidelines wrongly fail to specify that women ought to be treated equally regardless of whether their eggs are collected inside or outside of fertility treatment. In addition, the Guidelines fail to account for the tension that exists between the directive not to offer women financial compensation that would constitute undue inducement and the directive not to exploit economically disadvantaged women. In the contexts of both global science (where the mobility of researchers is not constrained) and global markets (where human cells and

tissues can be imported and exported, with or without profit), these directives cannot meaningfully coexist. To avoid unduly inducing women from poorer nations to undergo superovulation and egg retrieval, one would have to keep payments small; but in doing so, one creates the problem of these women being exploited. Yet by increasing payments to try to eliminate the exploitation, one reintroduces the problem of undue inducement.

In our view, the only straightforward way to avoid the harms of undue inducement and of exploitation is to have a system of altruistic donation (with compensation for direct, receipted expenses) and to accept that if women are not inclined to be selfless with their eggs and with the effort it takes to produce them, then eggs for stem cell research will be in short supply.ⁱⁱⁱⁱ

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Authors' affiliations

F Baylis, Novel Tech Ethics, Dalhousie University, Halifax, Nova Scotia, Canada
C McLeod, Department of Philosophy, University of Western Ontario, London, Canada

Correspondence to: Françoise Baylis, 1234 Le Marchant Street, Dalhousie University, Halifax, Nova Scotia, Canada B3H 3P7; francoise.baylis@dal.ca

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ⁱⁱⁱⁱ To be clear, with a system of altruistic donation that permits reimbursement for direct, receipted expenses (including such things as travel, accommodation and childcare and excluding such things as inconvenience, time, pain and discomfort), any inducement that might occur would not be undue. Such inducement would simply aim to ensure that a woman's altruistic decision to provide eggs for research did not result in personal financial loss.

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