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Ethical issues in uterine transplantation

Julian J. Koplin[1,2], Evie Kendal[3,*]

[1]Melbourne Law School, University of Melbourne, Parkville, Australia
[2]Biomedical Ethics Research Group, Murdoch Children's Research Institute, Parkville, Australia
[3]Deakin School of Medicine and Alfred Deakin Institute, Deakin University, Melbourne, Australia

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Corresponding author: Julian J. Koplin
Melbourne Law School, University of Melbourne, 185 Pelham St., Carlton VIC 3053, Australia
E-mail: koplinj@unimelb.edu.au
*Current affiliation: Faculty of Health, Arts and Design, Swinburne University of Technology, Hawthorn, Australia

Despite a recent surge of bioethical attention, ethical analysis of uterine transplantation is still in its early stages, and many of the key ethical issues remain underexamined and unresolved. In this paper, we briefly review some key ethical issues associated with uterine transplantation (beyond those associated with organ transplantation more generally). We structure our discussion in terms of Beauchamp and Childress' four principles of biomedical ethics: beneficence, non-maleficence, autonomy, and justice. Our review highlights some ethical questions that require further bioethical attention before uterine transplantation can be fully embraced as a potential treatment for absolute uterine factor infertility. We close by arguing that the costs and benefits of uterine transplantation need to be considered in the context of other possible treatments for absolute uterine factor infertility and alternative methods of family creation.

Keywords: Organ transplantation; Medical ethics; Pregnancy; Infertility; Bioethics; Allocation

WHY UTERINE TRANSPLANTATION POSES ETHICAL CHALLENGES

Compared to other forms of organ transplantation, uterus transplantation (UTx) has a short history. The procedure was first performed in 2000—though in this case, the transplanted uterus ultimately deteriorated and had to be removed [1]. The first live birth from a transplanted uterus was achieved as recently as 2014 [2]. Today, uterine transplantation is on the cusp of becoming an established clinical practice for the treatment of absolute uterine factor infertility (AUFI) [3]. There is a real and pressing need to think through the ethical issues in uterine transplantation—and to do so now, before uterine transplantation moves from its clinical research phase to become standard clinical practice.

Current ethical frameworks for UTx are based largely on existing guidelines for solid organ transplantation [4]. However, UTx differs from other forms of organ transplantation in several important respects. For example, uterus transplants are temporary (the transplanted uterus is removed after the recipient has completed their family plans), and unlike other organ transplants, they are not life-saving, life-extending, nor directly life-enhancing; the transplant provides no direct health benefits to the recipient [5]. There are also some specific risks associated with the transplant, particularly in light of its reproductive purpose, that are not seen in other organ transplants, for example, risks that immunosuppression will affect fertility and/or pregnancy outcome [6]. Questions of transplant eligibility are also more complex in UTx than other forms of organ transplantation. For example, there is ongoing controversy regarding whether transgender women and others who are genetically XY ought to be eligible for UTx [7].

Despite a recent surge of bioethical attention, ethical

HIGHLIGHTS

- Uterine transplantation is an emerging area of fertility medicine.
- Ethical principles guiding other organ transplants may not apply to uterine transplants.
- Uterine transplants pose challenges for allocation, informed consent, and safety.

analysis of UTx is still in its early stages, and many of the key ethical issues remain underexamined and unresolved. In this paper, we briefly review some key ethical issues associated with UTx (Table 1). We structure our discussion in terms of Beauchamp and Childress' four principles of biomedical ethics: beneficence, non-maleficence, autonomy, and justice (Table 2) [8]. Our review highlights some ethical questions that require further bioethical attention before UTx can be fully embraced as a potential treatment for AUFI, focusing especially on issues beyond those associated with transplantation more generally (Table 3 for a comparison). We close by arguing that the costs and benefits of UTx need to be considered in the context of other possible treatments for AUFI and methods of family creation. In doing so, we make the point that there are moral reasons to continue to develop and make available alternatives to UTx, even as the procedure becomes safer and more widely available.

BENEFICENCE AND NON-MALEFICENCE

The principles of beneficence and non-maleficence are directly relevant to the task of deciding whether or where the benefits of UTx are great enough to outweigh the risks. This task is currently relevant to achieving equipoise in clinical research. It will remain relevant as UTx transitions to standard clinical practice. Some facets of this task are relatively tractable. Current and future clinical research can help us quantify both the medical risks of UTx and the prospects of a "successful" transplant—which by some definitions refers only to transplants that result in a live birth. However, the weighing of risks and benefits is more complex for UTx than for other forms of organ transplantation. UTx also includes risks that do not parallel risks in other forms of organ transplantation. For example, there is an increased risk that recipients will experience disappointment even in the case of a successful transplant given that nervous innervation is not currently possible and many sensations associated with pregnancy would therefore be absent [9]. This disappointment might also impact the early experience of parenthood. Unlike

Table 2. Principles of biomedical ethics

Principle of biomedical ethics	
Beneficence	An ethical duty to help others and promote good for society
Non-maleficence	An ethical duty to avoid harming or injuring patients
Respect for autonomy	An ethical duty to ensure patients' decisions are informed and voluntary.
Justice	An ethical duty to ensure the risks and benefits of treatments are distributed fairly

Table 1. Ethical issues in UTx

Ethical concern	Example
Risks vs. benefits	• Do the benefits of UTx outweigh the risks? • How can we balance risks and benefits for donors versus recipients? • How can we balance risks and benefits for prospective mothers and future children?
Eligibility	• To whom should UTx be available? For example, should transplant uteruses be available to transgender women, gay couples, and/or women who are already mothers? • What health conditions might disqualify a person from being a donor or recipient of UTx?
Prioritization and funding	• Which recipients (if any) should have the greatest priority for a uterus transplant? • Should UTx be publicly funded? • Are there alternatives for family creation that should be prioritized or also made available?
Autonomous decision-making	• Would women's decision to undergo UTx generally be autonomous? • How can we best protect autonomy in the context of UTx?

UTx, uterus transplantation.

Table 3. Comparison of ethical issues in UTx and solid organ transplantation

Ethical principle	Issues seen in many forms of solid organ transplantation	Issues that may be unique to UTx
Respect for autonomy	Recognised need to protect donors/donor families and recipients from interpersonal coercion and pressure	Unclear whether the cultural significance of reproduction poses additional threats to autonomy (in terms of social or family pressure to donate or accept a uterus for transplant).
Beneficence & non-maleficence	Harms and benefits of organ transplantation are balanced under existing criteria for medical suitability for transplantation e.g., predicted survival time, ability to recover from surgery, matching, etc.	UTx carries unique benefits (which are not lifesaving nor life-sustaining) and unique risks (e.g., to resulting children) because it is a special type of transplant intended to assist in family creation.
Justice	Existing organ allocation principles aim to promote fairness/justice e.g., organs allocated according to medical urgency and not financial ability to pay.	Existing allocation principles do not neatly extend to UTx, e.g., medical urgency.

UTx, uterus transplantation.

other forms of organ transplantation, UTx carries risks to parties other than the recipients—specifically the resulting children, who would be subjected to immunosuppressive therapy while in utero [10]. Precisely how we should weigh the risks to future children is a difficult philosophical question. It turns, inter alia, on the non-identity problem; i.e., the problem of weighing harms to children when the child in question would not have been brought into existence had a different course of action been followed instead. While the non-identity problem has received much attention in bioethics more generally [11], its significance to UTx remains underexplored.

The benefits of UTx also differ in kind to the benefits of other kinds of organ transplants. As noted above, UTx is neither lifesaving nor life-sustaining. Admittedly, some other forms of organ transplantation, such as hand transplantation or corneal transplantation, are also life-enhancing rather than lifesaving, so UTx is not unprecedented in this respect. However, UTx is life-enhancing in a very particular way. Not only does UTx provide a means for persons with AUFI to become parents, its ultimate goals include helping women become visibly pregnant, emotionally pregnant, and socially recognized as pregnant [10]. It is these goals that distinguish UTx not only from other forms of organ transplantation, but also from other means of achieving parenthood in the context of AUFI, such as adoption or surrogacy. Exactly what kind of value should be attached to gestation remains an open philosophical question. So too does the question of what degree or kinds of risk ought to be accepted in pursuit of this goal.

AUTONOMY

Taken at face value, the principle of autonomy provides moral reason to facilitate UTx. Making UTx available promotes women's ability to "shape their families according to their own values and preferences" by providing additional reproductive options for some women [12]. The ability to shape one's life according to one's values is a central facet of autonomy. Accordingly, we can promote autonomy by making UTx available.

This view, however, elides some difficult questions about how best to respect and promote autonomy in the context of UTx. In the case of both recipients and living donors, there is at least some risk that external pressures, such as coercion or pressure from family members to pursue UTx, or interpersonal pressures to donate one's uterus, might render consent less than fully voluntary [13]. At the same time, it might be asked whether broader social factors—specifically, pro-natalist ideology and associated social pressures—might pose a threat to autonomous consent. Pronatalism is associated with increased social pressures to have genetically related children, which could significantly influence a woman's decision to pursue UTx or to donate their own uterus to a daughter, another family member or loved one, or even a stranger. Many feminists describe pronatalism as an oppressive social force [14]. In pronatalist societies, it might be asked whether (many) women's participation in UTx would be less than fully voluntary even if they are not additionally subjected to interpersonal coercion or pressure. Whether these diffused social pressures pose a challenge for informed consent to UTx—and, if so, how this challenge can best be addressed—remains an important and an un-

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der-explored ethical question. Furthermore, the question of whether UTx poses any unique challenges compared to other methods of family creation, including through other assisted reproductive technologies, warrants further ethical evaluation as the option becomes more widely available.

JUSTICE

Justice is most obviously relevant to the allocation of organs for transplant. While justice issues are already under discussion in relation to UTx research trials, there is not yet any consensus regarding who should be able to participate. Inclusion and exclusion criteria vary internationally. For example, Swedish criteria explicitly require recipients to live in a stable couple relationship; UK criteria do not. Conversely, UK criteria, exclude recipients who have previous children, including children who have been adopted or born via surrogacy arrangements, while Swedish criteria appear to focus only on biological parenthood [15]. These inconsistencies point towards the ethical complexity of developing inclusion and exclusion criteria for UTx clinical trials, and the associated difficulty of working out who should be eligible (or prioritized) for a transplant in the event UTx becomes standard clinical practice.

These questions about who should be eligible or prioritized for a transplant are familiar from other forms of organ transplantation. However, many of the established principles for organ allocation do not map neatly to the context of UTx. There are no more or less "urgent" cases of infertility; a "sickest first" allocation principle does not seem to extend to UTx; and prognosis and quality of life gains are more difficult to quantify for UTx transplants than transplants that serve a direct medical need. When it comes to eligibility, some particular points of controversy are whether UTx should be offered to women who are genetically XY, women in same-sex relationships (where the other party does not have AUFI), and women who are already mothers [5,7,15]. It might further be asked whether UTx should be made available to men (either publicly or privately) on the grounds that they, too, lack a functional uterus and are in this sense subject to AUFI [13].

Justice concerns are also relevant to the question of whether UTx ought to be publicly funded. Notably, in many jurisdictions, public resources are already used to fund assisted reproductive technologies aimed at overcoming infertility; accordingly, it is not a stretch to think that public funding might also be used to achieve the same goal via UTx. However, it might be argued that public funding for UTx is inappropriate, given that there are alternative means for people with AUFI to achieve social (and in some cases also genetic) parenthood—specifically, adoption and surrogacy. Notably, UTx is currently much more expensive than either adoption or surrogacy. It might therefore be asked whether the state ought to fund UTx in contexts where cheaper alternatives are available [16]. While similar objections are sometimes levelled at publicly-funded *in vitro* fertilization programs (on the basis such interventions are not aimed at improving health so much as meeting a desire to have biological children), recent evidence suggests there is widespread support for at least some public expenditure to address infertility [17].

This issue intersects with another issue flagged above in relation to beneficence and non-maleficence: what, precisely, is the significance of fulfilling the desire to have a (genetically-related) child via pregnancy, and to what extent do we as a society have an obligation to facilitate the realization of this desire? Like questions of beneficence and nonmaleficence, the question of whether UTx should be publicly funded turns partly on how we understand the value of facilitating pregnancy for women with AUFI.

ALTERNATIVES

As mentioned previously, there are multiple ways in which women with AUFI can become parents, including adoption and surrogacy. While adoption does not allow a couple to have a genetically related child, gestational surrogacy arrangements (whether altruistic or commercial) can precisely achieve this end. More speculatively, the development of ectogenesis technologies (e.g., artificial wombs) may eventually make it possible to gestate a child entirely outside any woman's body without any need for a human uterus [18].

Accordingly, the ethics of allowing/facilitating uterine transplantation (and how heavily we promote this option relative to the alternatives) cannot be considered in isolation from these alternative strategies for overcoming AUFI. These comparisons are most directly relevant to the application of the principle of clinical equipoise; when applying this principle, we need to consider whether the

balance of risks and benefits of UTx compares favorably to alternatives such as gestational surrogacy, at least in jurisdictions where this option is available [19]. But all-things-considered comparisons between allowing/facilitating uterine transplants are also relevant to broader issues of public policy.

For those interested in matters of public policy, it is important to think not only about whether UTx compares favourably to existing means of achieving parenthood, but also about whether there might be reason to make these alternatives more readily available than they currently are. As described above, UTx does impose some nontrivial burdens on health systems and women who undergo the transplant (and on live donors, where they are involved.) If we are willing to accept these costs to help women achieve parenthood in the context of UTx, it might also be appropriate to make commensurate efforts to help women achieve parenthood by other means [20]. The relative ease or difficulty of adopting a child depends on the policies and laws that have been enacted in one's jurisdiction. The availability of both altruistic and commercial surrogacy is also modifiable depending on the law in one's jurisdiction (including especially any laws that prohibit altruistic and/or commercial surrogacy), as well as the forms of support that are available to gestational mothers. The eventual development of ectogenesis (artificial womb) technologies might provide an entirely novel means for women with AUFI to become parents.

CONCLUSION

The lesson here is that ethical analysis of UTx should not be divorced from broader discussions about alternative means by which women with AUFI might become mothers. When deciding which options to allow and which to promote, we should consider the relative costs and benefits of each of the available options. When it comes to options that require further development before they can be made available, such as ectogenesis, we should take care that potentially valuable interventions for AUFI are not de-prioritized just because other alternatives are available. While UTx does provide one possible means of having a child, for many women (including those who wish to avoid the risks of UTx and/or pregnancy) the option of receiving a uterus transplant might be less than ideal.

The corollary is that in working out what role UTx should play as a treatment for AUFI, we will need to work out how UTx compares to other means of overcoming AUFI. It will be particularly important to consider the unique aspects of UTx relative to other alternatives—most notably, the opportunity not only to have a (genetically and socially) related child, but also to undergo pregnancy oneself. Precisely how we ought to value this unique feature of UTx is important for each of the four key principles of biomedical ethics described above: beneficence, non-maleficence, autonomy, and justice. It is the central question that policymakers, philosophers, ethicists, and social scientists interested in UTx will need to consider as UTx moves toward standard clinical practice.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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ORCID

Julian J. Koplin https://orcid.org/0000-0002-2752-7334
Evie Kendal https://orcid.org/0000-0002-8414-0427

Author Contributions

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