

Institution: Lancaster University		
Unit of Assessment: 31, Theology and Religious Studies		
Title of case study: Influencing and Informing Policy and Practice regarding Uterus Transplantation and Other New Biomedical Technologies		
Period when the underpinning research was undertaken: 2013 to 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
John Appleby Laura O'Donovan Stephen Wilkinson Nicola Williams	Lecturer Research Associate Professor Senior Research Associate	September 2016 to present January 2019 to present January 2013 to present September 2014 to present
Period when the claimed impact occurred: January 2016 to December 2020		
Is this case study continued from a case study submitted in 2014? N		
1. Summary of the impact		
<p>Lancaster research on reproductive ethics has influenced and informed: (1) the UK Uterus Transplantation Programme; (2) the Nuffield Council on Bioethics (NCoB); and (3) Progress Educational Trust (PET). The influence on (1) led to specific changes in practice with the potential to extend the availability of uterine transplantation, ultimately leading to the creation of additional new human lives. The influence on (2) led to improvements in the language used by NCoB and shaped the content of its publications and its decisions about which work-packages to take forward. The influence on (3) improved PET's understanding of, and shaped its positions on, key bioethical issues. In addition, the team's work on transplantation ethics more broadly (i.e. beyond reproduction) has directly affected the content of Scottish organ transplantation law.</p>		
2. Underpinning research		
<p>Several new and emerging reproductive technologies have the potential to profoundly disrupt established social practices linked to human reproduction and parenting, as well as the concepts of relatedness and family. For example, gestation and pregnancy are already being affected by the use of new techniques such as non-invasive pre-natal testing and uterus transplants, and could be completely transformed by the uptake of future techniques, notably ectogenesis, which potentially allows fetuses to be developed wholly outside the human body. Similarly, new methods of creating eggs and sperm will enable us (if we so wish) to create children with two female or two male genetic parents, or who have multiple genetic parents, or perhaps no determinate genetic parents at all.</p> <p>Understanding the conceptual, cultural, ethical, legal, and social issues that this raises is of the utmost importance, and was the ambitious challenge that the Wellcome-funded research programme, <i>The Donation and Transfer of Human Reproductive Materials</i> (2013-2021) set itself [G1]. The Lancaster arm of the programme (administered jointly with King's College London) was led by Wilkinson. Appleby, O'Donovan, and Williams are, or have been, Lancaster-based researchers, working with and under Wilkinson's supervision. All of the research presented here is linked to the programme [G1]. Using methods of analysis from Philosophy and Law, the Lancaster team has sought to produce improved ways of thinking about ethical questions. Its findings usually take the form of novel analyses, arguments, concepts, or language - rather than categorical statements of what is or is not ethically acceptable - although often such findings nonetheless change people's thinking about practical ethical issues, as Section 4 explains. Some examples of the team's key research findings are as follows.</p> <p>(1) Williams demonstrates that the case for allowing healthy live volunteers (as opposed to only the recently deceased) to donate non-essential organs for <i>quality of life purposes</i> (i.e., not only for 'life saving' purposes) is stronger than commonly thought. One implication of this is that there is a good case, in certain circumstances, for permitting uterus donation from living donors (for example, from mothers to daughters) [G1,G2,R7].</p> <p>(2) Wilkinson & Williams show that arguments for publicly funding infertility treatments in general, and uterus transplants in particular, are better than is often supposed. They defend in</p>		

new ways the view that the unwanted absence of a uterus, in those who are legally and socially women, is a medical need meriting a response from health services [G1,R6].

(3) Wilkinson offers fresh insights into the importance and role of certain concepts and definitions. He refines or problematises key concepts, such as eugenics, germline modification, and the distinction between health and social aspects of infertility. This has practical implications for the language we use (for example, he has urged caution over the use of problematic expressions such as ‘artificial gametes’ and ‘eugenics’) and for how positions are framed and communicated [G1,R2,R4,R5,R6,R8].

(4) Wilkinson provides a novel framework for the ethics of non-invasive pre-natal testing (NiPT), Public Health Pluralism, which reconciles the conflict between purely public health rationales for NiPT (which are sometimes accused of being ‘eugenic’) and the opposite position that delivering autonomy and choice is the only ethically acceptable goal of NiPT [G1,R5].

(5) Appleby offers arguments suggesting that the ‘14-day rule’, which imposes a time limit on embryo research, is difficult to defend in its present form and that governments should seriously consider extending this to 28 days [G1,R1].

(6) O’Donovan, Wilkinson, & Williams build on and move beyond earlier work on *reproductive donation* to provide a new framework for deciding which organs/tissues should be within the scope of opt-out systems for posthumous donation, such as those recently introduced in the UK [G1,G2,R3,R9].

3. References to the research

[R1] Appleby, J, Bredenoord, A (2018) ‘Should the 14-day rule for embryo research become the 28-day rule?’ *EMBO Molecular Medicine* <https://doi.org/10.15252/emmm.201809437>

[R2] Golombok S, Scott R, Appleby J, Richards M, Wilkinson S (eds.) (2016) *Regulating reproductive donation* Cambridge: Cambridge University Press. Held at HEI.

[R3] O’Donovan L, Williams NJ, Wilkinson S (2019) ‘Ethical and policy issues raised by uterus transplants’ *British Medical Bulletin*, vol. 131, no. 1, 19-28 <https://doi.org/10.1093/bmb/ldz022>

[R4] Scott R, Wilkinson S (2017) ‘Germline Genetic Modification and Identity: the mitochondrial and nuclear genomes’ *Oxford Journal of Legal Studies*, vol. 37, no. 4, 886-915 <https://doi.org/10.1093/ojls/gqx012>

[R5] Wilkinson S (2015) ‘Prenatal screening, reproductive choice, and public health’ *Bioethics*, vol. 29, no. 1, 26-35 <https://doi.org/10.1111/bioe.12121>

[R6] Wilkinson S, Williams N (2016) ‘Should uterus transplants be publicly funded?’ *Journal of Medical Ethics* vol. 42, no. 9, 559-565 <http://dx.doi.org/10.1136/medethics-2015-102999>

[R7] Williams N (2016) ‘Should deceased donation be morally preferred in uterine transplantation trials?’ *Bioethics*, vol. 30, no. 6, 415-424 <https://doi.org/10.1111/bioe.12247>

[R8] Wrigley A, Wilkinson S, Appleby J (2015) ‘Mitochondrial replacement: ethics and identity’ *Bioethics*, vol. 29, no. 9, 631-638 <https://doi.org/10.1111/bioe.12187>

[R9] Williams, N, O’Donovan, L, Wilkinson, S (2019) ‘England’s Opt-Out Policy Consultation – Excluded Organs and Tissues’, *Journal of Medical Ethics Blog*, <https://blogs.bmj.com/medical-ethics/2019/07/10/englands-opt-out-policy-consultation-excluded-organs-and-tissues/>

Peer Reviewed Grants:

[G1] Wilkinson S (Lancaster PI); *The Donation and Transfer of Human Reproductive Materials*; Wellcome Senior Investigator Award: (2013 to 2021) GBP526,936.

[G2] Williams, N. *Quality of Life Transplantation: Philosophical and Policy Questions*; Leverhulme Early Career Fellowship: (2019 to 2022) GBP90,881.

[R2-R9] supported by the highly competitive **[G1]**. **[R3,R9]** also supported by competitive **[G2]**. All items above subject to peer review from funders, journals, and/or book publishers.

4. Details of the impact

Influencing and informing the UK Uterus Transplantation (UTx) Programme

From 2016, Wilkinson, Williams, & O’Donovan developed a highly productive working relationship with the leaders of Womb Transplant UK; this group includes the principal investigator for the Imperial College NHS Trust trial on uterine transplantation, the only operative trial of its kind in the UK. The relationship is a vehicle through which Lancaster research influences and informs ethical thinking and decision-making in practice [S1].

Specific mechanisms for impact included: (a) discussing Lancaster research findings with Womb Transplant UK at workshops and conferences and in private communications; (b) joint work on papers for clinical audiences. While (b) is, in one sense, a clinical research output, the co-design processes and communications from which these papers result are a freestanding pathway to impact, with Lancaster ethics research feeding into the thinking of the larger multidisciplinary team (comprising approximately 8 clinicians) and the outcomes of that feeding in turn into papers for clinical audiences. As Womb Transplant UK colleagues state: *“The collaboration ... has changed our perceptions of some of the ethical challenges raised by uterus transplantation ... Working together on the papers has provided an additional route through which Prof Wilkinson’s ... team have been able to influence and inform us, not only as co-authors, but as practising clinicians and scientists, in relation to ethical and professional standards. In some instances ... practices and policies have been adapted as a result of this”* [S1].

Two particular areas of influence are worthy of note. For each, the impact at the time of writing is predominantly on clinicians’ thinking about ethics and policies. Within a few years however, major tangible downstream effects are also expected to benefit service users, including the treatment of otherwise untreated infertility, leading to the creation of new lives and the extension of services to those who may not otherwise have received them.

First, the Lancaster team’s research concerning the ethics of using living, as opposed to only deceased, donors encouraged the UK UTx team to expand their programme to include living donors (e.g., to include living mother to daughter donation) [G1,R3,R7].

They write: *“our team were focussing solely on deceased donor uterine transplantation. However, Dr Nicola Williams’ work ... exploring the ethical challenges raised by the different donor models, encouraged us to think much more positively about the use of living donor models. This work, in combination with evolution of the surgical technique which reduced donor risk, contributed greatly towards our decision to commence a living donor uterine transplant programme”* [S1]. Since deceased uterine donation is logistically challenging (e.g. because most potential donors die unpredictably in sub-optimal donation environments, because mainstream lifesaving organs – hearts, livers and kidneys – must always take priority, and because of the need to obtain familial approval) the decision to open up the programme to living donors has *“the capacity make uterus transplants available to many more women in the UK and could ultimately lead to hundreds of new lives created which would not otherwise exist”* [S1]. These effects are expected to start in the near future, with Womb Transplant UK reporting that *“the first living donor uterine transplant case in the UK was planned to be undertaken on Sunday 22nd March 2020”* but had to be cancelled due to the COVID-19 pandemic [S1]. Once we move beyond the COVID-19 pandemic, a resumption of this living donation programme is envisaged.

A second influence is the Lancaster team’s work on access to UTx services: in particular, on questions concerning public funding, and the inclusion of transgender women in future programmes. The focus of research here has been on providing arguments for the (often contested) view that infertility in general, and the absence of a uterus in particular, are (for those who are legally and socially women) genuine medical needs meriting a response from public health services [G1,R2,R3,R6]. Regarding public funding, the Womb Transplant UK team state that *“work from the Prof Wilkinson and Dr Williams ... which strongly supports public funding for UTx has greatly improved our awareness of the essential ethical constructs present, and has enhanced our capacity to lobby government and other stakeholders, such as the NHS”* [S1]. The inclusion of transgender women in the UTx programme will not be technically feasible for several years. Work presented at Lancaster ethics workshops and discussions with the team however influenced Womb Transplant UK’s attitudes and ethical thinking and led them to view their inclusion in future programmes more positively [S1,S2].

Influencing and informing the work of the Nuffield Council on Bioethics (NCoB)

NCoB is an independent advisory body, funded by the Nuffield Foundation, Wellcome, and the Medical Research Council. It examines and reports on “ethical issues raised by developments in biological and medical research in order to advise policymakers and stimulate debate” and acts

“to ensure that clear, rational and well-founded ethical arguments are brought to bear on important policy issues” [S3].

Artificial Gametes and Human Embryo Culture

Wilkinson presented at a 2016 horizon-scanning workshop, organised by NCoB to inform decisions on the direction of its future work. He presented ideas from his team’s ongoing and published research on: the importance of judiciously selecting appropriate concepts, definitions, and language when discussing this topic; eugenics and the concept of germline genetic modification; and the over-geneticisation of the concept of family [G1,R1,R2,R4,R5,R6,R8]. One direct effect of this (solely down to Wilkinson’s input) is that NCoB changed its language, “*dropping the term ‘artificial gametes’ from all subsequent communications, for example in its annual horizon scanning infographic*” (which now uses Wilkinson’s preferred terminology, ‘in vitro derived gametes’) [S3,S6a,S6b]. Wilkinson argued that, while artificial gametes constitute a fascinating new case study, the underlying bioethical issues raised are not as novel as is often thought. This led to a second effect: that NCoB discontinued its work on ‘artificial gametes’ as a discrete work-package, instead refocussing on the related issue of developments in extended embryo culture [S3]. This led, in turn, to further NCoB work on the latter, culminating in its 2017 report Human Embryo Culture [S6c]. That report “*helped to encourage and focus broader discussions among researchers, funders and policy makers about whether the time had arrived to review the existing statutory limits for human embryo culture*” [S3].

Non-Invasive Pre-Natal Testing (NIPT)

Wilkinson was one of six consultants commissioned to review an early draft of NCoB’s 2017 report, Non-Invasive Prenatal Testing: ethical issues [S3,S6d]. His input, based on his work on the Public Health Pluralist Framework for NIPT [R5], resulted in “*changes to the way eugenics is described and referred to in the report, and influenced sections on autonomous decision making, the role of organisations that provide support to women undergoing screening, and fetal sex determination*” [S3]. Three of his publications are cited in the report [S6d]. Professional standards, guidelines or training are being updated as a result of it, notably those of the Royal College of Obstetricians and Gynaecologists (RCOG) [S3,S6e].

Egg Freezing

Under UK Law, women who make use of ‘social’ egg freezing can only have their eggs stored for 10 years, after which they must be used or destroyed. (‘Social’ in this context means ‘not as a response to the immediate prospect of fertility loss due to a medical condition’, such as cancer.) Appleby’s work (and collaborative work with Wilkinson) [G1,R1,R2] helped NCoB to argue against this legal time limit in its 2020 briefing note Egg Freezing in the UK [S6f]. The research was used “*significantly to influence and shape the issues, content, and conclusions*” and “*made a valuable contribution that has positively influenced and informed the content*”, supporting the conclusion that “*there are few arguments against increasing storage limits for social egg freezing*” [S4]. NCoB has subsequently been contacted by the Department of Health and Social Care to discuss possible policy change and sees the briefing note as having as having “*an important contribution to make in future debate and potential legislative change*” [S4].

Influencing and informing the work of Progress Education Trust (PET)

PET is a UK charity that “advances public understanding of science, law and ethics in the fields of human genetics, assisted reproduction, embryology and stem cell research” [S5]. Since 2014, the Lancaster team has had a close working relationship with PET and provides advice on specific issues. According to the Director, “*the work of Professor Wilkinson and his team has informed and improved PET’s understanding of key bioethical issues such as: Mitochondrial Donation; Uterine transplants; The extension of the 14-day Rule on embryo research; Genome editing*”. The team’s “*work has also been used in the preparation the Director’s media appearances for example, BBC Radio 4’s Today programme*”. PET is frequently involved in “*high level policy discussions with the Human Fertilisation and Embryology Authority (HFEA), the Department of Health and Social Care (DHSC), Wellcome policy team and the World Health Organisation and others on the legal, ethical, and societal implications of assisted reproduction technologies. The work produced by Professor Wilkinson and his team has influenced and consolidated PET’s thinking which is then in turn shared in these discussions or consultation responses*” [G1,R1,R2,R3,R4,R6,R7,R8,S5].

Effects on Scotland's new opt-out organ donation system

O'Donovan, Wilkinson, & Williams used published and ongoing research [G1,G2,R3,R9] to provide written evidence to a Scottish Government consultation in 2020; this sought “views on which parts of the body should be listed in regulations as exempt from deemed authorisation and in what circumstances” [S7]. In September 2020, an analysis of the consultation responses highlighted two key recommendations (below) from the Lancaster submission. In both cases, just “one respondent” made these points [S8].

(1) A full paragraph of the Government's analysis discusses the Lancaster proposal that “the ‘face’ could be removed from Group 2 and instead placed in Group 1” [S8,s.25]. What this change would mean is that the donation and transplantation of the face, *or any part of it*, would be excluded from deemed authorisation (presumed consent) in all circumstances; in other words, active explicit consent, either from the deceased person during their lifetime or from their close family after death, would be needed. This is in contrast to the original proposal, that parts of faces could be used without explicit consent in some circumstances [S7].

(2) Another whole paragraph discusses a “potential difficulty”, pointed out by the Lancaster team, “particularly related to a face transplant, in making sure that legal definition [*sic*] relating to tissues are not over-specified ... that the consulted definition for a ‘face’ did not capture all of the parts which may be included in a transplant” [S8,s.27].

The actual regulations were published in November 2020 [S9]. These differ from the draft regulations originally proposed in ways that align precisely with the Lancaster recommendations.

(1) The face is now listed in Group 1, as recommended, along with sexual and reproductive tissues, the brain, spinal cord, and trachea. The face had previously been proposed for listing in Group 2 alongside the finger, foot, forearm, hand, lower leg, thigh, toe, upper arm. (2) The legal definition of ‘face’ in the regulations has changed and is now less narrow and restrictive in line with Lancaster recommendations. Asked about the role of the consultation in deciding on the final content of the regulations, the then Minister for Public Health, Sport and Wellbeing stated “*[m]ost of the responses came from experts in the field ... who were able to help us shape the regulations ... Engagement, particularly with that expert group, helped to shape the bill and the secondary legislation*” [S10].

O'Donovan, Wilkinson, & Williams' work has informed and improved organ donation law and policy in Scotland. As a result, explicit consent will always be required before parts of the faces of the deceased can be used for transplantation purposes, and a more practicable, comprehensive, and accurate definition of ‘face’ has been incorporated into Scottish regulation.

5. Sources to corroborate the impact

[S1] Testimonial from the leaders of the UK Uterus Transplantation (UTx) Programme (2020)

[S2] Jones, BP, Williams, NJ, Saso, S, Thum, M-Y, Quiroga, I, Yazbek, J, Wilkinson, S, Ghaem Maghami, S, Thomas, P, Smith, JR. Uterine transplantation in transgender women. *BJOG* 2019; 126: 152– 156 <https://doi.org/10.1111/1471-0528.15482>

[S3] Testimonial from the Assistant Director of the Nuffield Council on Bioethics (2020)

[S4] Testimonial from the Senior Research Officer of the Nuffield Council on Bioethics (2020)

[S5] Testimonial from the Director of the Progress Educational Trust (2021)

[S6] Nuffield Council on Bioethics publications: [S6a] What's on the Horizon for Bioethics? (2019); [S6b] What's on the Horizon for Bioethics? (2020); [S6c] Human Embryo Culture (2017); [S6d] Non-Invasive Prenatal Testing: ethical issues (2017); [S6e] Non-invasive prenatal testing is starting to get the attention it deserves (2019); [S6f] Egg Freezing in the UK (2020)

[S7] Consultation on the draft content of the Human Tissue (Authorisation) (Scotland) Regulations: Response 1044683196 (2020)

[S8] Human Tissue (Authorisation) (Scotland) Regulations 2020: consultation analysis

[S9] The Human Tissue (Excepted Body Parts) (Scotland) Regulations 2020

[S10] Health and Sport Committee of the Scottish Parliament, Official Report, 27 October 2020