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INvestigational Study Into Transplantation of the Uterus (INSITU): a cross-sectional survey among women with uterine factor infertility in the UK assessing background, motivations and suitability

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ABSTRACT

Importance The study summarises the selection prescreen criteria currently used in the UK for a uterus transplant and highlights the number of women who are suitable to proceed.

Objectives To assess the demographics, motivations, reasons and suitability among women with absolute uterine factor infertility (AUFI) to undergo uterine transplantation (UTx).

Design A cross-sectional survey.

Setting An electronic questionnaire was sent via email to women with AUFI who had previously been referred to the UTx research team or approached the Womb Transplant UK Charity. The questions assessed suitability to undergo UTx based on demographic information, perceptions to adoption and surrogacy and reasons why UTx was preferable. Responses were assessed against the study selection criteria.

Participants Women with AUFI.

Results 210 women completed the questionnaire. The most common aetiology of AUFI in our cohort was Mayer-Rokitansky-Küster-Hauser (68%; n=143) whereas 29% (n=62) had previously undergone hysterectomy. 63% (n=132) of the cohort had previously considered adoption, 5% (n=11) had attempted it and 2 (1%) had successfully adopted. The most common reason cited to undergo UTx over adoption was to experience gestation (n=63; 53%), while 37% (n=44) wanted a biologically related child. 76% (n=160) of participants had previously considered surrogacy, 22 (10%) had attempted it and 2 (1%) had successfully become mothers using a surrogate. The most common reason to undergo UTx over surrogacy was to experience gestation (n=77; 54%). 15% (n=21) were concerned about the legal implications, 14% (n=20) identified the financial cost as a barrier and 8% (n=12) could not consider it due to religious reasons. On adhering to the selection criteria, 65 (31%) women were suitable to proceed with the trial.

Conclusion The study demonstrates that implementing commonly used selection criteria for a UTx led to an attrition rate of more than two-thirds of women who requested to initially undergo the process. As more studies present outcomes following UTx, critical assessment of the selection criteria currently used is warranted to ensure potential recipients are not being unnecessarily excluded.

Trial registration number NCT02388802.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study is the largest and most detailed screening analysis of women with absolute uterine factor infertility who have requested to be considered for uterine transplantation (UTx).
⇒ The findings highlight the most common reason to undergo UTx, over surrogacy and adoption, is to experience gestation.
⇒ The study cohort were women who had previously expressed an interest in UTx, and therefore, they were a group who remained highly motivated towards UTx.
⇒ The quantitative nature of the methodology did not allow for in-depth exploration of feelings or experiences with regard to the decision-making towards UTx.

INTRODUCTION

Uterine transplantation (UTx) is now considered a viable fertility restoring therapeutic intervention for women with absolute uterine factor infertility (AUFI),[1] where it is in the process of transitioning from research concept to clinical procedure.[2] Although it has been estimated that AUFI affects 1 in 500 women of childbearing age,[3] there are limited data regarding the potential demand

to undergo UTx within this population. Options for women with AUFI to acquire motherhood traditionally included only adoption and surrogacy.[4] A previous study in the UK demonstrated that 97.5% of women with AUFI would choose UTx over surrogacy and adoption, despite an awareness of the additional risks posed by UTx.[5] Likewise, when assessing the perceptions of women with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome specifically, almost two-thirds of women were motivated to undergo UTx.[6] A further questionnaire completed by 60 women with AUFI in France also determined that 58.3% would partake in a clinical trial in UTx.[7] These studies were undertaken more than 5 years ago, when data following UTx were limited, while the procedure was still considered a research concept. Following more than 90 cases and 49 livebirths after UTx,[8] it is likely perceptions towards UTx and subsequent demand will have changed.

Despite several published studies summarising case series or UTx research programmes, there is little known about how to screen and prioritise women with AUFI. Two studies have reported details of their selection processes. The first of which, was the Dallas UtErine Transplant Study, where a full selection process was described.[9] An initial prescreen assessment resulted in 179 potential recipients completing a questionnaire, of which 18 women were chosen by the principal investigator (PI) to proceed to the next stage; involving an extensive medical and psychological objective evaluation process.[9] Although the decision to proceed was based on meeting the selection criteria implemented for the trial, there was no further elaboration on the method used by the PI to prioritise which participants then progressed for further assessment. In a separate study based in Germany, 108 women were screened, 15 of whom progressed for further evaluation. Similarly, apart from meeting the selection criteria and having a potential living donor, no explanation was provided regarding how recipients were prioritised for the latter stage of the process.

In the UK, there are both living donor and deceased donor UTx programmes. The first living donor case was performed in the UK in 2023, with the commencement of embryo transfers anticipated in 2024.[10] The INvestigational Study Into Transplantation of the Uterus (INSITU) is a clinical trial involving a cohort of 10 women, who will undergo UTx using donation following brainstem death.[11] The selection process entails multiple stages, including an initial prescreen, which involves the completion of a detailed questionnaire assessing the key background information required to determine suitability to proceed, in line with the selection criteria for the study. The aim of this study is to summarise the prescreen process for the INSITU study, including the women's demographics, reasons for considering UTx over adoption and surrogacy and assess their suitability to advance in the process.

METHODOLOGY

Study design

Recruitment commenced from a population of women with AUFI. This included women who either contacted Womb Transplant UK (registered charity number 1138559) or were referred to the UK UTx research team, for consideration for UTx over an 8-year period between 1 November 2011 and 1 November 2019. The research was advertised on the Womb Transplant UK website. Potential participants were sent a consent form, a participant information leaflet (online supplemental appendix 1) and a screening questionnaire (online supplemental appendix 2) via email between 1 May 2019 and 1 November 2019. The questionnaire ascertained suitability to partake in the study by eliciting key demographic information before determining background medical, surgical, psychiatric, obstetric, gynaecological and social history. Further questions assessed perceptions to adoption and surrogacy and reasons why UTx was preferable. Following receipt of the signed consent form and a completed questionnaire, each application was assessed, using implementation of the selection criteria, as displayed in figure 1, to determine absolute suitability to proceed. The selection criteria were decided and agreed on, following an international symposium on UTx hosted by our team, in London on 12 June 2015. It was attended by UTx specialists from a variety of disciplines, including gynaecological and transplant surgeons, psychologists, ethicists, reproductive medicine specialists, early pregnancy specialists and specialists in novel imaging modalities, from the UK, Sweden and the USA. The purpose of the symposium was to discuss, critique and verify the protocols planned for use in the INSITU study, in light of the wealth of knowledge gleaned from animal studies and the human data ascertained from the cases undertaken by the Swedish team. The applications of the women who fulfilled the selection criteria were subsequently scored, using the scoring system in table 1, which was agreed on at the aforementioned symposium, to facilitate prioritisation of those most suitable to undergo the process. The applications were then ranked, with the highest ten scoring respondents invited to enrol in the main part of the INSITU study.

Data analysis

SPSS V.24 software (SPSS) was used for analysis. Descriptive statistical analysis was described as mean±SD or median±range.

Patient involvement

This study was developed as a direct response to demand from women who contacted Womb Transplant UK to enquire about the possibility of UTx. A number of women were consulted in the creation of participant information leaflets and the questionnaire to help refine content and terminology. The questionnaire was further piloted among a sample of women with AUFI to assess understanding and readability.

Inclusion	Exclusion
• Female • Age – 25-38 (<40 if oocytes cryopreserved <38 years) • AUFI • Normal length vagina • BMI <30 kg/m^2 • American Society of Anaesthesiologists grade I • Psychological criteria met • HFEA criteria for IVF met • Eligible for NHS treatment • Speak fluent English	• Unsuccessful oocyte retrieval • Previous multiple/significant surgeries • Skin graft or intestinal neovagina • Severe endometriosis • Cancer patients <5 years in remission • Previous living childbirth or adopted child or child born by surrogacy • HIV positive • Hepatitis B and/or Hepatitis C positive

Figure 1 Inclusion and exclusion criteria for potential recipients in INSITU study. AUFI, Absolute uterine factor infertility; BMI, Body mass index; HFEA, Human fertilisation and embryology authority; INSITU, INvestigational Study Into Transplantation of the Uterus; IVF, In vitro fertilisation; NHS; National health service.

RESULTS

Participant selection

A total of 962 women had previously expressed an interest in UTx or had been referred to the research team over the designated time period and were subsequently contacted to participate. A total of 210 women responded, consented and returned the questionnaire, resulting in a response rate of 21.8%. The demographics of the cohort are summarised in table 2. Among the cohort, 175 (83.3%) were UK residents, who lived a mean distance of 137±106 miles from the host hospital. The mean body mass index (BMI) was 25.5±7.7 kg/m^2. The majority of women were either married or in a relationship (n=195; 93%), the mean duration of which was 5.6±4.5 years.

Medical history

MRKH accounted for more than two-thirds of the aetiology of AUFI (n=143; 68%). A total of 118 (83%) women had isolated uterovaginal hypoplasia (type I), whereas 25 (17%) had additional associated urological, ovarian or skeletal conditions (type II). Sixty-two (30%) women had previously undergone a hysterectomy. Thirty (48%) were performed for cancer, with cervical being the most common primary (n=22; 35%), followed by uterine (n=5; 8%), ovarian (n=2; 3%) and bowel (n=1; 2%). Thirty-two (52%) women had prior hysterectomy for benign indications, with the most common cause due to obstetric haemorrhage (n=13; 21%). Other indications included endometriosis/adenomyosis (n=8; 13%), dysfunctional uterine bleeding/fibroids (n=6; 10%), pelvic inflammatory disease (n=2; 3%), pelvic organ prolapse (n=1;2%), trauma (n=1;2%) and for a benign ovarian cyst (n=1;2%). Two (1%) applicants were male-to-female transgender women, two (1%) had severe Asherman's syndrome and one (0.5%) had complete androgen insensitivity syndrome.

Of the 143 women with MRKH, 70 (49%) had not previously undergone treatment to optimise vaginal length. A total of 58 (41%) women had previously used dilator therapy, whereas 15 (10%) underwent surgical intervention after unsuccessful dilator treatment. Six women underwent laparoscopic Vecchietti procedure, whereas five had a neovagina created using bowel (n=2), buccal mucosa (n=1), peritoneum (n=1) or perineal skin (n=1). Four women did not specify the surgical method used.

Other than their cause of AUFI, 47 (22%) women had relevant previous medical history, the specific conditions of which are summarised in table 3. In addition, 17 women (8%) reported congenital kidney abnormalities, the most common of which was unilateral renal agenesis (n=14; 82.4%). One woman had a pelvic kidney, another had a duplex kidney and one had a horseshoe kidney. Furthermore, 30 (14%) of the cohort reported previous mental health issues, the most commonly reported diagnosis was depression (n=14; 9%), 6 women (3%) had a diagnosis of anxiety and a further 5 (2%) reported mixed depression and anxiety. Much smaller proportions of women reported prior diagnoses of post-traumatic stress disorder (n=2; 1%), gender dysphoria (n=2; 1%), cyclothymia (n=1; 0.5%), body dysmorphic disorder (n=1; 0.5%), an eating disorder (n=1; 1%), borderline personality disorder (n=2; 1%) attention deficit hyperactivity disorder (n=1; 0.5%) and psychosis (n=1; 0.5%).

Table 1 Scoring system used to select recipients to proceed

Criteria		Score
Age	36–40	0
	24–36	1
BMI	25–30	0
	<25	1
Medical history	Mild chronic disease	0
	No medical problems	1
Allergies	Multiple drug allergies	0
	Single drug allergy or NKDA	1
Previous surgery	Previous total abdominal hysterectomy	0
	Previous subtotal hysterectomy	1
	No previous major abdomino-pelvic surgery	3
IVF score	No cryopreserved oocytes	0
	Previous cryopreserved oocytes 36–38	1
	Previous cryopreserved oocytes <36 years	3
Alcohol intake	>14 units/week	0
	<14 units/week	1
Smoking	Ex-smoker+smoker	0
	Non-smoker	1
Relationship duration	Single	0
	<1 year	1
	1–2 years	2
	>3 years	3
Role in raising awareness	No role	0
	Local/national fundraising events/social media involvement	1
Adherence and commitment	<1 year	0
	1–2 years	1
	3–4 years	2
	>5 years	3

BMI, body mass index; IVF, In-vitro Fertilisation; NKDA, no known drug allergies.

Reproductive history

Twenty-one (10%) women reported a previous pregnancy, which resulted in either a miscarriage or termination of pregnancy. Overall, 33 (16%) women were parous. Four women (2%) previously had a stillbirth, where a caesarean hysterectomy was performed for treatment of massive obstetric haemorrhage. There were 28 (13%) women who had previously cryopreserved embryos at a mean age of 28 years. The mean number of embryos stored was 6.5±5.1.

Motivations towards UTx

With regard to adoption, 132 (63%) women had previously considered it as an option, 11 (5%) had formally attempted it and 2 (1%) had successfully adopted. Of the 119 women who provided reasons for wishing to undergo UTx rather than pursue adoption, the most common reason was to experience gestation (n=63; 53%), followed by wanting a biologically related child (n=44; 37%). Figure 2 summarises the reasons for wishing to undergo UTx over adoption.

Over two-thirds (n=160; 76%) of women had previously considered surrogacy, 22 (10%) attempted it and 2 (1%) had successfully used a surrogate. Of those who gave a reason for wishing to undergo UTx over surrogacy (n=143), as summarised in figure 2, the most common reason was to experience gestation (n=77; 54%), whereas 21 women (15%) were concerned about the legal implications, 20 (14%) identified financial costs and 10 (7%) reported lack of trust over the surrogate as a barrier. Overall, 11 (8%) women stated an interest in surrogacy, should they be unsuccessful in their pursuit of undergoing a UTx.

Figure 3 outlines the process of systematic exclusion after implementing the selection criteria. In total, 65 (31%) applicants were deemed suitable to proceed with the trial. A total of 145 (69%) women were excluded for the following reasons: 56 (27%) were <24 years or >38 years, 16 (7%) had a BMI>30 kg/m^2, 26 (12%) were not UK residents, 3 (1%) were not fluent in English, 1 (0.5%) was assigned male at birth, 17 (8%) already had living children, 2 (1%) had a significant medical history or was <5 years in remission from cancer, 6 (3%) had a skin intestinal or unspecified neovagina, 5 (2%) had a history of premature ovarian insufficiency or no functioning ovaries, 1 (0.5%) had a history of recreational drug use and 12 (6%) were current smokers.

DISCUSSION

The data presented here contain the largest and most detailed screening analysis of women with AUFI who have requested to be considered for UTx. It demonstrates the characteristics of such women, highlights their suitability and provides novel insight into their perceptions of UTx, with respect to alternative options to acquire motherhood.

The most common aetiology of AUFI in this cohort was MRKH syndrome. This is consistent with the UTx screening process in Germany, where among 46 potential recipients, congenital AUFI or MRKH accounted for 85% of the cohort.[12] However, in both the Dallas and Cleveland UTx programmes, the predominant cause of AUFI among potential recipients, was prior hysterectomy, which was seen in 63% and 64% of women, respectively.[9] Considering, 50%–73% of the hysterectomies were undertaken for benign indications, this is reflective of different clinical practices between Europe and the USA. In our own cohort, only 62 (29%) women underwent prior hysterectomy, of which 30% were undertaken for

Table 2 Basic demographic information of potential uterine transplant recipients

			Number (n)	%
Age (years)	20–29		65	31
	30–39		108	51
	40–49		34	16
	50–59		3	1
Body mass index (kg/m^2)	<18.4	Underweight	4	2
	18.5–24.4	Normal	104	50
	25–29.9	Overweight	59	28
	30–34.9	Obesity I	27	13
	35–39.9	Obesity II	3	2
	>40	Obesity III	10	5
Ethnicity	White		142	68
	Asian		23	11
	Black		8	4
	Mixed		1	0
	Other		9	4
	Would rather not say		27	13
Language	English		172	82
	Non-English but fluent in English		33	16
	Non-English but not fluent in English		5	2
Employment status	Employed full/part time		186	89
	Self-employed		2	1
	Housewife		11	5
	Unemployed		6	3
	Student		5	2
Relationship status	Single		12	6
	In a relationship		123	59
	Married		72	34
	Divorced		3	1
Smoking status	Never smoked		152	72
	Ex-smoker		29	14
	Current smoker		29	14
Alcohol intake (units per week)	0		114	54
	≤14		95	45
	>14		1	1

benign gynaecological reasons, compared with 14% due to gynaecological cancer. Cause of AUFI is an important consideration in UTx. Women with MRKH are ideal candidates to undergo UTx, as surgery is rarely needed in the diagnosis of such women. As such, there may be less pelvic adhesions and surgical complexity compared with other causes of AUFI such as after hysterectomy or following radiotherapy.

The majority of women with MRKH in our cohort (83%) had isolated uterovaginal hypoplasia; type 1 MRKH, whereas only 17% of women accounted for type 2 MRKH. Previous data have shown that women with type 1 constitute approximately 44% of all MRKH cases compared with 56% of type 2.[13] This suggests within our own cohort, women with type 1 are more likely to consider UTx than type 2. This is unsurprising given that women with atypical MRKH are more likely to have concomitant medical issues that may preclude them from undergoing UTx, such as significant renal/urological manifestations, observed in approximately 28%–34% of women with MRKH.[14–16] For example, among the 17% of women diagnosed with a pelvic kidney,[15] many would be considered unsuitable for UTx, should the anatomical deviation cause structural hindrance during implantation.

Table 3 Other medical history of women seeking uterine transplantation

	Number (n)	%
Asthma	14	6
Hypothyroidism	10	4
Premature ovarian insufficiency	7	3
Fibromyalgia	3	2
Epilepsy	2	1
Hypermobility	2	1
Glaucoma	1	0.5
Previous pancreatitis	1	0.5
Degenerative disc disease	1	0.5
Lymphoedema (legs)	1	0.5
Leukaemia (in remission)	1	0.5
Rheumatoid arthritis	1	0.5
Osteopenia	1	0.5
Ulcerative colitis	1	0.5
Anaemia	1	0.5
Hypertension	1	0.5
Type 2 diabetes	1	0.5
Migraine	1	0.5
Irritable bowel syndrome	1	0.5
Joint hypermobility	1	0.5

Furthermore, 23%–28% of women with MRKH have unilateral renal agenesis,[15 17] which is associated with an approximate 35% risk of hypertensive disorders in pregnancy, including pre-eclampsia.[18 19] While the presence of unilateral kidney agenesis requires consideration,[20] and warrants additional obstetric counselling, if the renal function is entirely normal, it is reasonable for such women to still be considered for UTx. Women with type 1 may be associated with superior reproductive potential compared with type 2, as demonstrated by an increased number of follicles and mature oocytes retrieved.[21] Furthermore, they require fewer days of stimulation with gonadotrophins, produce more embryos and experience similar pregnancy rates when data was analysed in surrogate pregnancies.[21]

Another consideration in women with MRKH is that they have varying degrees of vaginal shortening, often requiring treatment to optimise diameter and depth, to enable adequate sexual function. Vaginal restoration techniques include conservative dilator therapy or surgical intervention using either the Vecchietti procedure, or the creation of a neovagina into the rectovesical space lined with skin, peritoneum or intestine.[22] The structure of the vaginal microbiome is associated with various clinical and reproductive implications essential to the process of UTx, whereby a dysbiotic microbiome can impact pregnancy and live birth rates, as well as risk of miscarriage and preterm birth.[23] As such, it is vital that consideration of the technique used to acquire vaginal length in women with congenital forms of AUFI is given in the preoperative assessment process, as it may directly impact outcomes. This is exemplified by the reported UTx case performed in Turkey, where the recipient was a 21-year-old woman with MRKH who had previously undergone intestinal vaginoplasty for vaginal reconstruction.[24] This case was adversely impacted by 13 unsuccessful embryo transfers, 5 miscarriages and while a live birth was eventually achieved 9 years later, this was at 28 weeks' gestation following preterm prelabour rupture of membranes (PPROM) at 19 weeks' gestation.[24] The team attributed the aetiology of these poor reproductive outcomes to venous outflow obstruction, which was treated with an open vascular revision. However, as there were two further unsuccessful embryo transfers, and the subsequent PPROM at 19 weeks' gestation, it seems plausible an ongoing issue remained. While data evaluating the vaginal microbiome in sigmoid neovaginas remain scarce, data can be extrapolated from studies assessing the microbiome of sigmoid neovaginas in transgender women. Such neovaginas have been shown to have a similar microflora to that of normal bowel, containing many facultative anaerobe species.[25] In the absence of a lactobacilli-rich microflora, it is unsurprising that such dysbiotic microbiomes result in a more alkaline environment, which contrasts with the acidic environment established in normal vaginal microbiomes. There is a wealth of data demonstrating that dysbiotic microbiomes result in poor reproductive outcomes including miscarriage, recurrent implantation failure and preterm, PPROM, as seen in this case.[23]

Uterus transplant recipients are at increased risk of cancer post-transplant,[26 27] owing to immunosuppression associated burden secondary to induced physiological impairment to destroy neoplastic cells. Moreover, immunosuppression may also enhance the growth of pre-existing dormant cancer cells, as recipients with a pretransplant history of cancer have a 30% increased rate of overall death, compared with those without.[28] This has been reaffirmed by a meta-analysis which established that all-cause mortality, cancer-specific mortality and risk of new primary malignancy was higher in recipients with a pretransplant diagnosis of cancer.[29] Cervical cancer specifically is five times more likely following kidney transplant, compared with the general population.[30] This is of particular relevance in this cohort, as the primary cancer in the vast majority of cases was the cervix (n=22; 73%). The greatest increased mortality is in the first 5 years following cancer diagnosis.[28] As such, many UTx teams have stipulated selection criteria that preclude performing UTx until at least 5 years following the diagnosis of cancer.[31 32] The recurrence risk also appears to be greater for more aggressive cancers, such as sarcoma.[33] As such, it may be prudent for women with previous hysterectomy for uterine sarcoma to be cancer free for longer periods before consideration for UTx, or instead, surrogacy or adoption should be advised if acceptable to the woman.

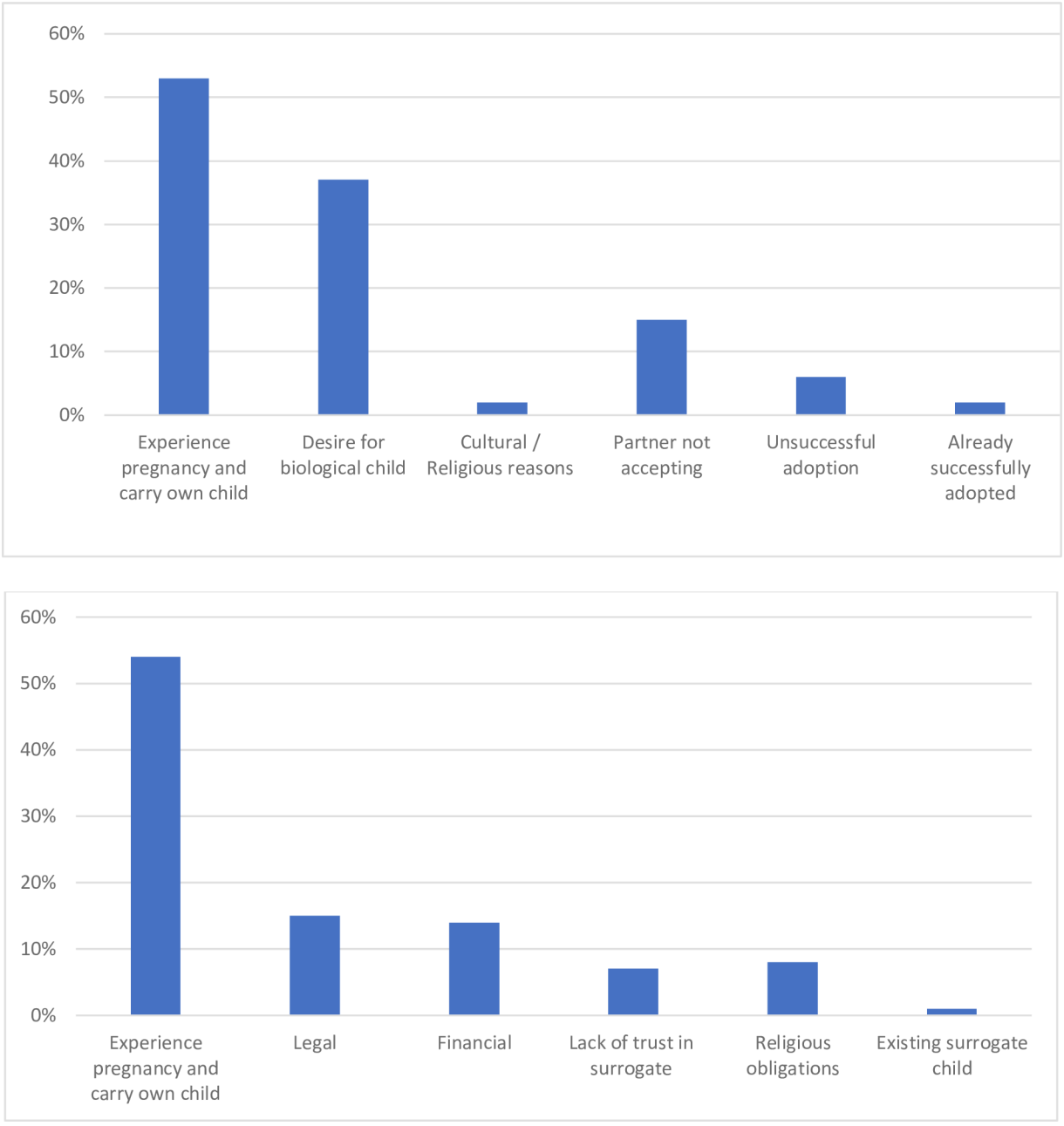

Figure 2 Reasons attributed to preference of uterine transplantation over adoption (top) and surrogacy (bottom).

As this cohort was self-selected, it is inappropriate to generalise perceptions of UTx, over adoption and surrogacy to the general population. However, our findings highlight the predominant reason women with AUFI choose to undergo UTx is to experience gestation. Furthermore, legal issues associated with surrogacy were cited as the primary motivating factor to undergo UTx in 15% of our cohort. The vast majority of those (n=19; 90%) lived in the UK. Such findings may be attributed to the fact that surrogacy arrangements are not currently legally enforceable in the UK, thus placing couples relying on this method, in a legally precarious position. The economic implications of surrogacy were also cited by 14% as reasons to undergo UTx. UK legislation states that only reasonable expenses can be paid towards the surrogate, and anything that exceeds this amount needs authorisation by the Court. The average cost of undergoing surrogacy in the UK was shown in a recent cross-sectional study to be approximately £25 000.[34] However, these costs noticeably vary between counties, with median costs of £120 000 reported in the USA.[34] That said, UTx may represent a similarly, if not more costly alternative to surrogacy. Moreover, it is unlikely such a procedure will be funded by insurance companies, and it is currently unknown whether or not the National Health Service (NHS) would fund this programme through NHS England, as a highly specialised service. It is, therefore, likely that UTx will necessitate self-funding, which will be prohibitive for most women.

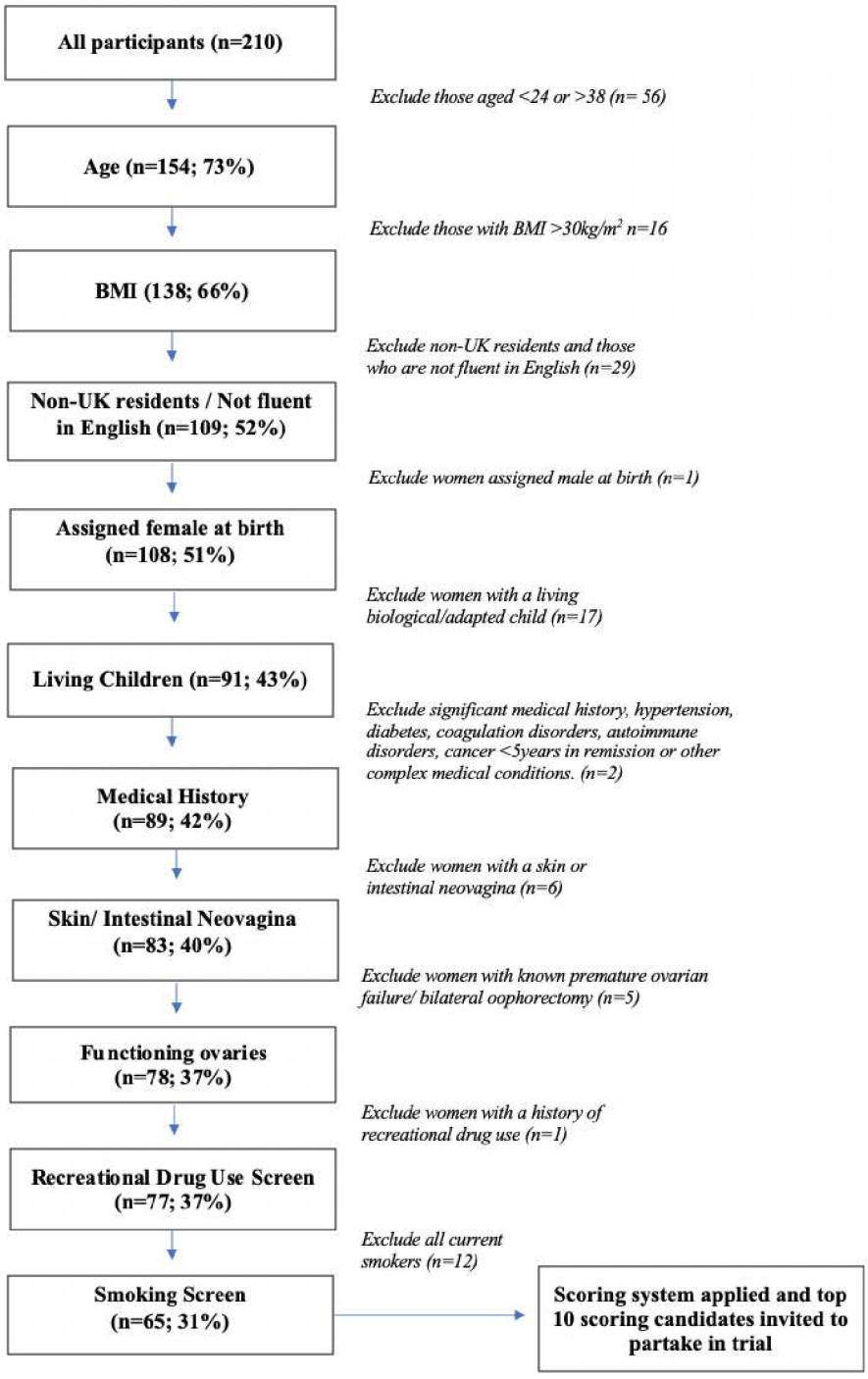

Figure 3 Flow chart summarising the process of systematic exclusion after implementing INSITU selection criteria. BMI, body mass index; INSITU, INvestigational Study Into Transplantation of the Uterus.

Religious factors were responsible for 2% of the cohorts' motivation to undergo UTx over adoption. From a religious perspective, UTx itself is generally accepted by most major religions. In Islam, the transplantation of organs that do not carry genetic traits, such as the uterus is permissible. Moreover, the necessary use of IVF and embryo cryopreservation is acceptable,[35] but only if the gametes are from a lawfully married couple. In Judaism, the pursuit of a cure for infertility is seen as noble, given the centrality of children within the marital relationship. However, deceased organ donation is unacceptable in Jewish law, thereby UTx is restricted to the use of living donors. The currently adopted surgical technique uses prophylactic bilateral salpingectomy to reduce risk of ectopic pregnancy, necessitating the use of IVF. In Catholicism, whereas the transplantation of the uterus itself would be acceptable,[36] owing to the dissociation of husband and wife, the use of IVF is seen as immoral, thereby precluding those of fixed Catholic faith. While UTx may be acceptable if natural conception was possible

following UTx, given the high rates of tubal blockage seen in non-human primates following utero-tubal autotransplantation,[37] concerns would remain about future tubal patency and potential risk of ectopic pregnancy.

The selection criteria were carefully chosen for this study, initially based on the Indianapolis Consensus,[38] but with additional insight from the preliminary UTx outcomes in Sweden, which were shared at a multidisciplinary academic symposium in 2015.[31] The criteria were selected exclusively for this study, to minimise confounding variables and help accurately demonstrate outcomes following UTx. The scoring system was further discussed and approved at the meeting, which was attended by the leading specialists in the field across various disciplines, including gynaecology, transplantation, psychology and ethics, to ensure they prioritised the most suitable candidates, but remained fair and just. Whereas most criteria such as age, BMI, medical and surgical history, having stored embryos and not smoking or drinking excessively are easily justified, other criteria such as relationship duration, period of adherence to the procedure and raising awareness or fundraising for the charity provoked more discussion. They were eventually included to enhance the chance of selecting women who are stable, well supported and committed, and have had an extended period of time to consider this as an option. Undergoing UTx is not just physically, but psychologically challenging, as is the ultimate aim of undergoing the process; becoming parents.[39] As such, consideration of potential candidates in a holistic approach is fundamental, not just in the academic setting, but as the procedure eventually becomes a clinical procedure.

Following implementation of the selection criteria, 69% of women were excluded. While selection criteria can be used to minimise risk and optimise outcomes, where it is based primarily on value judgements, or are excessively more stringent than necessary, discrimination is encouraged.[40–42] Organ allocation in UTx, unlike life-saving solid organ transplants, will not be governed by clinical urgency or survival benefit.[43] As such, it is expected that age,[44] tissue matching and previous childbirth,[42 43] may impact prioritisation in the future, following the transition into clinical practice. Less stringent selection criteria should open up the possibility of UTx to many more women with AUFI, should it be demonstrated that safety and efficacy is not impacted.[45]

While this study is the largest and most detailed screening analysis of women with AUFI who have requested to be considered for UTx, it is not without its limitations. The study cohort were women who had previously expressed an interest in UTx, and therefore, they were a group who remained highly motivated towards UTx and as such, the findings cannot be extrapolated to all women with AUFI. The suboptimal response rate may be attributable to multiple reasons. First, most women who did not meet the criteria were responded to at the time of their initial contact, to enable them to readjust their reproductive aspirations and plans accordingly, and as such, knew they did not meet the criteria. Second, as women were being contacted up to 8–9 years previously, it is likely that UTx may not now be a suitable option or they may have already achieved their family using alternative means. Finally, the contact details supplied at their initial contact may not have been active, so many women may have been lost to follow-up.

CONCLUSION

This study summarises a detailed screening analysis of more than 200 women with AUFI who are interested in undergoing UTx. It demonstrates the characteristics of such women, and highlights that the majority who wish to undergo UTx in this cohort are those diagnosed with type I MRKH. This study also provides insight into the reasons why women would choose to undergo a procedure associated with significant physical risk, over other options to acquire motherhood, of which, the most common reason is to personally experience gestation. We also demonstrate that implementing commonly used selection criteria, led to an attrition rate of more than two-thirds of women who requested to initially undergo the process. As more studies present outcomes following UTx, critical assessment of the selection criteria currently used is warranted to ensure potential recipients are not being unnecessarily excluded, while maintaining those important to optimise success rates.

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Contributors BPJ conceived and wrote the manuscript and performed the analysis of the results. SV, LSK and IM helped write the manuscript and revised the final draft. SS and TB-M helped with data analysis and revised the final draft. JN, M-YT, CD-G, IQ, JY and JRS helped conceive the study, provided methodological support and revised the final draft.JRS is the guarantor for this paper and accepts full responsibility for the work and/or the conduct of the study.

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