Uterine Transplantation

Plain language summary

A uterine transplant, or womb transplant, is a potential treatment for women who cannot become pregnant or carry pregnancy due to either not having a womb, or having a womb that is not functional. This problem affects one in 500 women. In these cases, women currently have the options of adoption or surrogacy. These are associated with legal, cultural, ethical and religious implications that may not be acceptable to some women.

Womb transplants have been performed all over the world, with more than 60 cases carried out so far. At least 14 babies have been born as a result, demonstrating that womb transplants can work. While it offers various advantages over adoption and surrogacy, the process is associated with significant risks, including multiple major surgeries and the need to take medications that help to dampen the immune system to prevent rejection of the womb, and there is a 30% risk of the transplant being unsuccessful.

Although the number of transplants to date is still relatively small, the number being performed globally is growing, and provides an opportunity to learn from the experience gained so far. This paper looks at the issues that have been encountered and may arise at each step of the process and proposes a framework for the future. However, long term follow-up of cases will be essential to draw reliable conclusions.

1. Background

Uterine transplantation (UTx) is a potential therapeutic intervention for women with absolute uterine factor infertility (AUFI), a condition that affects one in 500 women of childbearing age. AUFI refers to women with infertility secondary to the absence of a uterus or the presence of one that is anatomically or physiologically dysfunctional. The traditional routes to motherhood for women with AUFI include adoption or surrogacy, which to many are acceptable options. However, not only are these options associated with complex legal, financial, cultural, ethical and religious factors, but they do not allow the experience of pregnancy. UTx provides an opportunity to overcome some of these issues while giving women with AUFI the opportunity to conceive and experience pregnancy themselves.

At the time of writing this paper, more than 60 procedures have been performed worldwide, and at least 14 offspring have been born as a result. Following the development of the International Society of Uterine Transplantation (ISUTx) and the establishment of teams performing the procedure globally, it is anticipated that UTx will transition from research concept to clinical care in the future.

The purpose of this Scientific Impact Paper is to summarise the pertinent published literature on UTx and to propose a framework for establishing a sustainable UTx programme in the UK. The data presented herein refers to the 35 cases published in peer-reviewed journals to date. This includes cases that have been performed in Saudi Arabia, Turkey, Sweden, Xian (China), Czech Republic, Cleveland (USA), Dallas (USA), Germany and India.
2. Alternatives to uterine transplantation

Reproductive planning is a dynamic process that focuses on each individual’s values, which may be influenced by social or cultural norms, in the context of the resources available to them. Women with AUFI traditionally remained childless or considered the option of adoption or surrogacy.

There are pros and cons to adoption and surrogacy, therefore it is important for women with AUFI to ensure they are well informed about their options. For adoption, in the UK, women can gain information through government websites, and for surrogacy, the HFEA (Human Fertility and Embryology Authority) has signposted sources to obtain information (Surrogacy UK, Brilliant Beginnings, Childlessness overcome through surrogacy [COTS]).

While adoption and surrogacy are often suitable options for women with AUFI to become mothers, they do not resolve the anatomical issue underlying the cause of infertility. Women born with AUFI will therefore never experience menstruation, which to some women is part of being female and has been shown to contribute to gender identity. Adoption and surrogacy also do not facilitate the experience of pregnancy, which has been demonstrated to be the primary motivator in 63% of women with AUFI who request UTx. While UTx is associated with significantly greater physical risk, including multiple major surgeries and the necessity to take immunosuppression while the graft is in situ, it is acceptable to all major religions. As such, although there is no direct alternative to UTx, it is essential that consideration is given to adoption and surrogacy in the counselling process for UTx. This ensures the consent process is fully informed, and the additional risks associated with UTx can be appropriately considered in the context of the perceived individualised benefits.

3. Potential recipients

Potential recipients to undergo UTx are women of reproductive age with AUFI, the causes of which may be congenital or acquired, as summarised in Appendix I. The majority of cases have been performed for Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome (n = 32; 91.4%); two cases were performed following hysterectomy (one after postpartum haemorrhage, one after cervical cancer), and one case in a woman with Asherman syndrome who underwent preparatory hysterectomy at the time of UTx.

3.1 Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome

MRKH has an incidence of 1 in 5000 women. It arises due to incomplete development of the Müllerian ducts, which manifests with congenital absence of the uterus and fallopian tubes, along with variable degrees of vaginal shortening. Therapeutic intervention is often required to optimise vaginal diameter and depth to enable sexual function. Various methods exist including dilator therapy, the Vecchietti procedure or the creation of a surgically created vagina, referred to as a neovagina, using skin, peritoneum or intestine. Women with MRKH generally have normally functioning ovaries with an associated normal hormone profile, making them ideal candidates for UTx. A study assessing perceptions to UTx among women with MRKH showed that almost two-thirds of participants were motivated to undergo the procedure, with a full understanding of the potential risks involved.

Specific preoperative considerations are required for women planned for UTx. A normally functioning and normal length vagina is considered requisite for some teams, which excludes women who have a neovagina. The surface of the vagina is composed of stratified squamous epithelium, which as a protective mechanism desquamates into the vaginal lumen, concomitantly removing adherent microorganisms. Vaginal epithelium also contributes to the innate immune response by facilitating the recognition of pathogens and stimulating the production of antimicrobial peptides and
proinflammatory cytokines. These immunomodulatory mechanisms contribute to the maintenance of a commensal microbiome, which provides a suitable physiological environment to prevent infection and maintain physiological conditions for pregnancy. The second global UTx case was performed in a recipient with an intestinal neovagina, where despite multiple miscarriages, a live birth was yet to be achieved. Furthermore, in the Swedish case series, the only woman to have not given birth following successful UTx, who also suffered at least five miscarriages, had a skin neovagina.

Women with atypical MRKH, specifically those with renal abnormalities, also require consideration. Those with pelvic kidneys cannot be considered, owing to the structural hindrance during implantation. Caution should also be taken in those with unilateral renal agenesis, which affects around a quarter of cases, owing to the more than two-fold increased risk of hypertensive disorders in pregnancy including pre-eclampsia. In a Swedish cohort who underwent UTx, three had unilateral kidney agenesis, and all three developed a hypertensive disorder during pregnancy that necessitated early delivery.

3.2 Hysterectomy

Reasons for hysterectomy in the reproductive age group include benign gynaecological disease, gynaecological cancer (such as cervical cancer) or severe postpartum haemorrhage. Caution is required in women having UTx following previous cancer diagnoses, because of the potential risk of recurrence, as a consequence of the necessity for immunosuppression postoperatively. In kidney transplantation, a history of previous cancer is associated with a 30% increased risk of death in the recipient. Moreover, across all solid organ transplants, a meta-analysis found that all-cause mortality, cancer-specific mortality and the risk of developing a new primary malignancy was greater in those with a pre-transplant diagnosis of cancer, when compared with recipients with no pre-transplant malignancy. As such, additional counselling is required for these women, and it is prudent to allow a period of at least years in remission, before being considered for UTx. While no meaningful conclusion can be taken from a single case, the single UTx case performed in a woman with a previous diagnosis of cancer, which in this case was of the cervix, has achieved two live births, and following completion hysterectomy, there has been no recurrence or new diagnosis of cancer reported.

3.3 Asherman syndrome

Asherman syndrome remains the main cause of AUFI where the uterus is present, but dysfunctional, affecting up to 1.5% of women of reproductive age. Characterised by the formation of adhesions inside the uterus and/or the cervix, this condition can cause amenorrhoea, recurrent miscarriage and infertility. Fertility restoration can be achieved using hysteroscopic adhesiolysis, although high rates of infertility, miscarriage, poor implantation and abnormal placentation remain. Performing UTx for Asherman syndrome should be reserved for severe cases, where all other treatment options have been exhausted.

3.4 Male to female transgender women

Male to female transgender women are considered the same as cisgender women. Under the Equality Act (2010), individuals who are proposing to undergo, currently undergoing, or have undergone a process of gender reassignment cannot be subjected to discrimination on the basis of this characteristic alone. Subsequently, if UTx becomes a treatment option for women with AUFI, based on EU and UK legislation it will, in the absence of the provision of compelling justification, be legally impermissible not to perform UTx in transgender women, because of their gender identity. There are, however, a number of anatomical, psychosocial, physiological, fertility and obstetric considerations...
that question the feasibility and require further research before UTx can be performed as part of
gender reassignment.\textsuperscript{18}

\textbf{3.5 Other causes}

Other less common causes of AUFI include severe or complex congenital uterine anomalies, radiotherapy damage and complete androgen insensitivity syndrome. Owing to the complex nature of these conditions, the role of UTx in these cases is at present unclear.

\section{4. Potential donors}

The majority of UTx cases performed so far have been undertaken using living donors ($n = 27; 77.1\%$), while the remaining used deceased donors ($n = 8; 22.9\%$). In the cases where the parity of the donor was known ($n = 33$), the majority have been multiparous ($n = 30; 90.9\%$) while three were nulliparous ($9.1\%$).

\textbf{4.1 Living donors}

Logistically, given the diverse array of multidisciplinary expertise required, planning an elective surgery using living donors is more straightforward than the on-call arrangement needed in the context of deceased donation. Routine investigations for all solid organ transplant apply to all UTx donors, including microbiological screening to prevent transmitted infection such as HIV, hepatitis B and C, cytomegalovirus, Epstein Barr Virus, syphilis, toxoplasma, and human T-cell lymphotropic virus. The use of living donors allows greater time for investigation, which at a minimum should include a cervical smear/HPV testing, tests to exclude STIs (chlamydia, gonorrhoea and trichomoniasis) and a vaginal culture to exclude \textit{Candida} species and bacterial vaginosis. A transvaginal ultrasound scan (TVS) should also be undertaken to exclude structural abnormalities, and magnetic resonance angiography (MRA) or computed tomography angiography (CTA) to provide information about vessel morphology, calibre and patency.

The majority of living donors used so far have been related ($n = 19/26; 69.2\%$), with 16 (53.8\%) being mothers of the recipients, while eight (30.8\%) were unrelated. While the use of first-degree relatives may provide immunological benefit,\textsuperscript{21} the use of older donors is associated with other risk factors. Significantly, increasing age correlates with risk of atherosclerotic change in the pelvic arteries, which may result in an insufficient quality organ for implantation.\textsuperscript{22} Moreover, even before macroscopic or histological evidence of atherosclerosis is evident, increasing age has been shown to cause arterial inflammation,\textsuperscript{23} which may increase the likelihood of post-transplant graft vasculopathy.\textsuperscript{24} In addition, increasing donor age, irrespective of recipient age, increases the rate of acute allograft rejection in other solid organ transplants.\textsuperscript{25}

With 14 live births now achieved using living donors, the feasibility of the procedure using this donor type is difficult to refute. However, the major disadvantage in living donors is the potential donor risk. Regarding donor surgical morbidity in the cases performed so far, as per the Clavien Dindo classification of surgical complications, four (11.4\%) donors suffered grade IIIb complications. Two donors suffered ureteric injuries which were repaired intraoperatively during the retrieval,\textsuperscript{26,27} while one donor re-presented postoperatively with a uretovaginal fistula.\textsuperscript{28} The other grade IIIb complication was vaginal cuff dehiscence which subsequently required surgical repair.\textsuperscript{29} Six (17.1\%) donors suffered grade I–II complications including wound infection, bladder hypotonia,\textsuperscript{28} urinary tract infection (UTI), constipation, leg/buttock pain and depression.\textsuperscript{29} Extensive multidisciplinary counselling is therefore essential, with thorough explanation of the potential risks, to ensure that all donors can give informed consent, in the absence of undue pressure or coercion.
4.2 Deceased donors

The use of deceased donors ultimately negates donor risk, and allows a more radical dissection, which enables greater calibre vessels to be taken, theoretically reducing the risk of graft thrombosis. This was theorised following animal research, where smaller vessel anastomoses, such as the uterine vessels, resulted in gradual vessel thrombosis. Subsequent studies utilising larger vessel patch techniques substantiated the concept, following successful UTx and pregnancies in both small and large animal models.

In the human model, the uterine graft has successfully been retrieved as part of a multiorgan retrieval with no adverse impact upon other organs retrieved. The uterus has been retrieved before the lifesaving organs in some cases, and after in others. Appropriate preoperative investigation of the donor can still be undertaken, with TVS, GUM screen and cervical cytology/HPV testing being expedited to ensure results are available within the pre-retrieval period. In this time the donor can be physiologically optimised while other retrieval teams perform their preliminary investigations.

Donation of the uterus in the UK is currently dependent upon the donor having consented for organ donation, and in addition requires donor family consent. Initial studies in the United States indicated a poor potential uptake from donor families, with as few as 6% of families agreeing to procurement of the uterus. However, a more recent European study highlighted that donation of the uterus was readily accepted, with no refusals (n = 14) and no negative impact on the donation of other organs.

A potential drawback to using deceased donors is the associated systemic brain-death inflammation that may influence organ quality. The risk of fungal infection may also be greater, owing to potential contamination of the sterile vessels from organisms within the non-sterile vaginal cuff, as exemplified by the unsuccessful UTx from a deceased donor after brain death in Cleveland, which resulted in hysterectomy because of candida vasculitis within the uterine vessels.

The first successful live birth following UTx using a deceased donor was achieved in Brazil in 2017, demonstrating the feasibility of using this donor type. However, further long term follow-up and cases are required before accurate comparison of efficacy between donor types can be undertaken.

5. Surgical considerations for the recipient

UTx entails transplantation of the uterus, including cervix, a cuff of vagina, the surrounding ligamentous and connective tissues, as well as the major blood vessels supplying and draining the uterus. The majority of donor surgeries performed so far have used the laparotomy approach, while the use of minimally invasive surgical techniques have been proposed, and recently implemented (robot-assisted = 1, laparoscopy = 4). While unpublished, several further cases have been performed, highlighting that the transition toward utilising minimally invasive retrieval techniques is already in progress.

With regards to graft survival, of the 35 cases reported in detail so far, 28.6% (n = 10) have required emergency hysterectomy, mostly because of graft thrombosis (n = 6; 60%), due to infective causes (pelvic bacterial infection/abscess), n = 1; candidal vasculitis of the arterial anastomosis, n = 1; herpes simplex infection of the graft (n = 1) and 10% (n = 1) because of graft ischaemia of unspecified aetiology. Postoperatively, 70% (n = 7) of emergency hysterectomies occurred within 0–15 days, 20% (n = 2) occurred during months 3–4 and 10% (n = 1) during month seven. With regard to donor type, graft survival among cases using living donors was 73.1% (6/9), whereas in deceased donors it was 66.6% (28/35). Five (14.3%) women have had completion hysterectomies after successful pregnancies; and 20 (57.1%) continue to have functioning grafts.
successful UTx procedures have resulted in menstruation without the need for supplementary hormone therapy (n = 25).

In addition to the graft failures, surgical complications in UTx recipients so far, as per the Clavien Dindo classification, have included six (17.1%) grade IIIb complications including vaginal cuff dehiscence (n = 1), a vesicovaginal fistula (n = 1), vaginal stenosis requiring stenting (n = 4). Four (11.4%) recipients suffered grade I–II complications, including UTIs (n = 2), and postoperative pleural effusions (n = 2).

6. Immunological considerations

Rejection can be defined as destruction of the donor graft by the host’s immune response, activated against the graft’s alloantigens because of a difference in donor-recipient genes. In UTx, the immune response of the recipient towards the implanted graft can be just as deleterious as the host response in other transplanted organs. As for all solid organ transplants, it is essential the burden of immunosuppressive medications is offset by an improvement in quality of life. As such, the minimum number of immunosuppressive agents should be used at the smallest dose possible, while avoiding the use of steroids where possible. In UTx cases performed so far, tacrolimus has predominantly been the agent of choice, initially in combination with mycophenolate mofetil (MMF), with or without the addition of prednisolone. MMF is later stopped in anticipation of embryo transfer, owing to its teratogenic nature, where it is usually replaced with azathioprine.

While symptoms of rejection include abdominal pain, fever or vaginal discharge/bleeding, such symptoms would only become apparent once rejection had been firmly established. A preliminary grading system for uterine allograft rejection was proposed following a study on baboons, which concluded that cervical biopsies were a consistent and achievable method of detecting rejection in the graft. In the available data from human cases to date there have been 16 episodes of rejection (10/35; 28.6%). Fourteen episodes were proven on histology, using cervical biopsies, while two were diagnosed following the presentation of symptoms suggestive of rejection in the context of raised serum lymphocyte subpopulations. The majority of episodes of rejection were successfully managed with a 3-day course of intravenous methylprednisolone (13/16; 81%), although three episodes (19%) required the addition of antithymocyte globulin. The majority of the histologically proven cases of rejection (12/14; 86%) were mild or moderate, while two (15%) were severe.

A unique advantage of UTx over other solid organ transplants is that it is ephemeral, and once the woman’s family is complete, the graft can be removed, allowing the cessation of immunosuppression. Given that immunosuppression-associated morbidity such as cancer, diabetes and nephrotoxicity is dose and duration dependant, the anticipated implications in UTx are expected to be less than in lifelong organ transplants, although long term data following UTx are required.

7. Fertility considerations

During UTx, while the fallopian tubes are usually retrieved as part of the graft to facilitate uterine manipulation, they are subsequently removed post implantation, to reduce future risk of ectopic pregnancy. As such, prior to UTx, the creation and cryopreservation of embryos is a requisite. Not only does this guarantee the availability of embryos postoperatively but reduces risk when compared with performing egg collections after UTx, when anatomy may be distorted and there is increased risk of infection following the introduction of immunosuppression. Following the development of vitrification techniques, the success rates of using vitrified embryos are now similar to using fresh embryos, which minimises any potential negative impact of cryopreservation on embryo quality.
Multiple gestation would be particularly problematic following UTx, where the additional associated risks including preterm labour, miscarriage, pre-eclampsia and gestational diabetes would greatly potentiate antenatal risk. Consequently, single embryo transfer should always be implemented following UTx. In early cases, \(^{52}\) embryo transfer was initially delayed until at least 12 months postoperatively, as per standard solid organ transplant guidance. \(^{53}\) However, in more recent cases, \(^{29}\) a period of six months has been adopted. This allows sufficient time for surgical healing and stabilisation of the immunosuppression regime. In anticipation for embryo transfer, it is essential to review medications that may be unsafe for pregnancy. Potentially teratogenic immunosuppression, such as MMF, \(^{47}\) should be stopped a minimum of six weeks prior to embryo transfer, and can be replaced by a different agent, such as azathioprine.

### 8. Obstetric considerations

While there is currently a paucity of data published on pregnancy outcomes, the data from the first six pregnancies following UTx demonstrated that 50% (n = 3) developed hypertensive disorders of pregnancy necessitating early delivery between 31 and 35 weeks of gestation. \(^{12}\) It could be argued that this may be a consequence of in vitro fertilisation (IVF), \(^{54}\) or the transplant of postmenopausal uteri, with an inherently less elastic vasculature. \(^{55}\) It should be noted that all three women had unilateral kidney agenesis, while those without kidney abnormalities remained normotensive. \(^{13}\) While the three offspring born following pregnancies complicated by pre-eclampsia were appropriate weights for gestational age, the risk–benefit ratio in women with unilateral renal agenesis is clearly increased. This has resulted in such women initially being excluded from certain research studies, \(^{56}\) although some teams continue to include them. \(^{28}\)

### 9. Psychological considerations

Not only does AUFI result in an inability to conceive, but it can also result in significant psychological sequelae. More than a third of infertile women develop severe symptoms of depression and have also been shown to have a two-fold increased risk of suicide. \(^{57}\) The inability to bear children affects the perception of infertile women’s femininity while it also negatively impacts their quality of life. \(^{58}\) Owing to the interrelationship between infertility and psychological wellbeing, specialist psychological evaluation, counselling and follow-up is required in UTx for the recipients and, where applicable, the donors.

Psychological aspects of UTx for recipients \(^{59,60}\) and donors \(^{61}\) have been published assessing a number of factors including psychological wellbeing, relationships, managing childlessness, relationship with the donor, and knowledge about associated risks. Participants, as well as their partners, did not report any psychological issues at baseline, nor following the procedure, despite adverse events, such as episodes of rejection, which were confirmed quantitively using SF-36 and Fertility Quality of Life (FertiQoL), the Hospital Anxiety and Depression Scale (HADS) and Dyadic Adjustment Scale (DAS) questionnaires. Many recipients expressed relief by the onset of menstruation following UTx, as it not only demonstrated graft function but made them feel like every other woman. There was no recorded significant impact following UTx upon sexual desire or satisfaction.

Regarding psychological outcomes in donors, semi-structured interviews in combination with questionnaires including the Psychological General Well-Being Index (PDWB), DAS, HADS and SF-36 were used in the selection process. Two donors experienced a deviation from their baseline quality of life scores (SF-36), one of which coincided chronologically with the donor suffering complication with a uretovaginal fistula in addition to the graft loss in the recipient, her daughter. Overall there was no mean significant change in quality of life across donors between baseline and 12 months and over the same timeframe there was a reduction in HADS score. No donors reported feelings of regret, even in
those who experienced complication or whose recipients suffered graft loss. All donors returned to their preoperative social and physical activities. These findings resonate with the positive psychosocial outcomes demonstrated following lifesaving solid organ donation.\textsuperscript{62,63}

### 10. Opinion

- Although still under investigation, with only 14 live births worldwide, UTx offers the possibility of an alternative option for women with AUFI to acquire motherhood.
- UTx allows the experience of pregnancy, is not constrained by the legal or religious issues associated with surrogacy and appears to be readily accepted by women with AUFI.
- UTx is associated with significant morbidity, including three/four major surgeries (UTx, caesarean section/s and hysterectomy to remove the transplant) and the risks associated with transient immunosuppression. Moreover, in the cases performed so far almost 30% of grafts have been removed due to complications. As such, recipients must be highly motivated, with excellent support networks and have access to appropriate psychological services and be fully informed of the potential risks involved.
- With regards to living donors, more than 30 procedures have now been performed, resulting in 14 live births so far, with transition into clinical practice expected in the future. The use of living donors necessitates considering the significant potential risk to the donor, and priority must be given to putting in measures to minimise such risks.
- Despite one successful live birth being achieved, the use of deceased donors continues to remain a research concept with further cases needed, including extensive follow-up, before comparisons between the efficacy of each donor type can be evaluated.
- Prior to commencing a clinical programme in UTx, experience in animal and human cadaveric models should be undertaken, and initial cases mentored by teams with experience in performing UTx.
- Membership with the ISUTx is advised, and attendance at their annual meetings recommended, to refine and collaborate on research, as well as reflect and learn from cases performed.
- All cases should be registered with the international registry to enable performance and safety monitoring, including appropriate follow-up of donors, recipients and offspring.

### References


**Appendix I Causes of absolute uterine factor infertility (AUFI)**

<table>
<thead>
<tr>
<th>Uterus present</th>
<th>Uterus absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asherman syndrome</td>
<td></td>
</tr>
<tr>
<td>• Fibroids</td>
<td></td>
</tr>
<tr>
<td>• Severe adenomyosis</td>
<td></td>
</tr>
<tr>
<td>• Uterine malformation</td>
<td></td>
</tr>
<tr>
<td>• Pelvic irradiation</td>
<td></td>
</tr>
<tr>
<td>• Hysterectomy</td>
<td></td>
</tr>
<tr>
<td>• Obstetric haemorrhage</td>
<td></td>
</tr>
<tr>
<td>• Benign cause</td>
<td></td>
</tr>
<tr>
<td>• Cancer</td>
<td></td>
</tr>
<tr>
<td>• Congenital</td>
<td></td>
</tr>
<tr>
<td>• Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome</td>
<td></td>
</tr>
<tr>
<td>• Complete androgen insensitivity syndrome (CAIS)</td>
<td></td>
</tr>
<tr>
<td>• Male to female transgender</td>
<td></td>
</tr>
</tbody>
</table>
This Scientific Impact Paper was produced on behalf of the Royal College of Obstetricians and Gynaecologists by:

Mr BP Jones MRCOG, London; Mr S Saso MRCOG, London; Mr JM Yazbek MRCOG, London; Dr M-Y Thum MRCOG, London; Miss I Quiroga FRCS, The Oxford Transplant Centre, Oxford University Hospitals NHS Trust; Dr S Ghaem-Maghami MRCOG, London; and Mr JR Smith FRCOG, London

and peer reviewed by:

XXXX

The Scientific Advisory Committee lead reviewer was: Dr N Potdar FRCOG, Leicester.

The chair of the Scientific Advisory Committee was: Professor MD Kilby FRCOG, Birmingham.

All RCOG guidance developers are asked to declare any conflicts of interest. A statement summarising any conflicts of interest for this Scientific Impact Paper is available from: https://www.rcog.org.uk/en/guidelinesresearch-services/guidelines/sipXX/.

The final version is the responsibility of the Scientific Advisory Committee of the RCOG.

The paper will be considered for update 3 years after publication, with an intermediate assessment of the need to update 2 years after publication.

DISCLAIMER

The Royal College of Obstetricians and Gynaecologists produces guidelines as an educational aid to good clinical practice. They present recognised methods and techniques of clinical practice, based on published evidence, for consideration by obstetricians and gynaecologists and other relevant health professionals. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor or other attendant in the light of clinical data presented by the patient and the diagnostic and treatment options available.

This means that RCOG Guidelines are unlike protocols or guidelines issued by employers, as they are not intended to be prescriptive directions defining a single course of management. Departure from the local prescriptive protocols or guidelines should be fully documented in the patient’s case notes at the time the relevant decision is taken.