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Abstract

Randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation (TOPS)

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Objectives: To determine the acceptability, efficacy and costs of medical termination of pregnancy (MTOP) compared with surgical termination of pregnancy (STOP) at less than 14 weeks' gestation, and to understand women's decision-making processes and experiences when accessing the termination service.
Design: A partially randomised preference trial and economic evaluation with follow-up at 2 weeks and 3 months.
Setting: The Royal Victoria Infirmary, Newcastle upon Tyne, UK.
Participants: Women accepted for termination of pregnancy (TOP) under the relevant Acts of Parliament with pregnancies < 14 weeks' gestation on the day of abortion. A further group of women attending contraception and sexual health clinics participated in a discrete choice experiment (DCE).
Interventions: STOP: all women ≥ 6 weeks' and < 14 weeks' gestation were primed with misoprostol 400 μg 2 hours before the procedure. STOP was performed under general anaesthesia using vacuum aspiration. MTOP: all women < 14 weeks' gestation were given mifepristone 200 mg orally, returning 36–48 hours later for misoprostol.
Outcome measures: Main outcome measure was acceptability of TOP method. Secondary outcome measures included strength of preference by willingness to pay (WTP); distress, using the Impact of Event Scale (IES); anxiety and depression; satisfaction with care; experience of care; frequency and extent of symptoms including self-assessment of pain; clinical effectiveness; and complications. A DCE was used to identify attributes that shape women's preferences for abortion services.
Results: The trial recruited 1877 women, 349 in the randomised arms and 1528 in the preference arms. Of those in the preference arms, 54% chose MTOP. At 2 weeks after the procedure more women having STOP would choose the same method again in the future. Acceptability of MTOP declined with increasing gestational age. The difference in acceptability between STOP and MTOP persisted at 3 months. At 2 weeks after TOP, women in the preference arms were prepared to pay more to have their preferred option. There was no difference in anxiety or depression scores in women having MTOP or STOP. However, women randomised to MTOP had higher scores on subscales of the IES at both 2 weeks and 3 months. There was no difference in IES scores between MTOP and STOP in the preference arm. Women were more likely to be satisfied overall and with technical and interpersonal aspects of care if they had STOP rather than MTOP. Experience of care scores were lower after MTOP in both randomised and preference arms. During admission women undergoing MTOP had more symptoms and reported higher mean pain scores, and after discharge reported more nausea and diarrhoea. There were no differences in time taken to return to work between groups; around 90% had returned to work and normal activity by 2 weeks. Rates of unplanned or emergency admissions were higher after MTOP than after STOP. Overall complication rates were also higher after MTOP, although this only achieved statistical significance in the preference arm. Overall, STOP cost more than MTOP due to higher inpatient standard costs. Even though complication rates were higher with MTOP, it was still more cost-effective. DCE identified three attributes with an almost equal impact on women's preferences: provision of

counselling, number of days delay to the procedure, and possibility of an overnight stay.
Conclusions: MTOP was associated with more negative experiences of care and lower acceptability. Acceptability of MTOP declined with increasing gestational age. MTOP was less costly but also less effective than STOP. The majority of women choosing MTOP were satisfied with their care and found the procedure acceptable.

Recommendations for further research:
An audit of provision of MTOP and STOP in England and Wales is urgently required. Further studies exploring the barriers to offering women the choice of method of TOP are needed, together with research on the acceptability and effectiveness of (1) MTOP and manual VA in pregnancies below 9 weeks' gestation and (2) MTOP and dilatation and evacuation after 14 weeks' gestation.
Trial registration: Current Controlled Trials ISRCTN07823656.

Contents

List of abbreviations

ANOVA	analysis of variance
BNF	*British National Formulary*
CI	confidence interval
CoSH	contraception and sexual health
DCE	discrete choice experiment
EPDS	Edinburgh Postnatal Depression Scales
GCSE	General Certificate of Secondary Education
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
HTA	Health Technology Assessment
ICER	incremental cost-effectiveness ratio
IES	Impact of Event Scale
MRS	marginal rate of substitution
MTOP	medical termination of pregnancy
NICE	National Institute of Health and Clinical Excellence
PM	preference medical
PS	preference surgical
QALY	quality-adjusted life-year
RCOG	Royal College of Obstetricians and Gynaecologists
RM	randomised medical
RPC	retained products of conception
RS	randomised surgical
RVI	Royal Victoria Infirmary
SAE	serious adverse event
SD	standard deviation
STOP	surgical termination of pregnancy
TOP(s)	termination of pregnancy(s)
VA	vacuum aspiration
VAS	visual analogue scale
WTP	willingness to pay

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Note

Gestational ages are reported in weeks + days, e.g. 9^{+1} indicates 9 weeks and 1 day.

Executive summary

Objectives

To determine the acceptability, efficacy and costs of medical termination of pregnancy (MTOP) compared with surgical termination of pregnancy (STOP) at less than 14 weeks' gestation, and to understand women's decision-making processes and experiences when accessing the termination service and taking part in the trial.

Design

A partially randomised preference trial and economic evaluation with follow-up at 2 weeks and 3 months.

Setting

The Royal Victoria Infirmary, Newcastle upon Tyne, UK, a large tertiary unit providing both MTOP and STOP up to 20 weeks' gestation to women throughout the north-east of England. The termination service is nurse practitioner-led and undertakes around 1800 terminations per year.

Participants

Participants were women accepted for termination of pregnancy (TOP) under clause C of the Human Fertilisation and Embryology Act (1990) amendment of the Abortion Act (1967) with pregnancies less than 14 weeks' gestation (based on ultrasound) on the day of abortion. A further group of women attending contraception and sexual health clinics in Newcastle upon Tyne participated in a discrete choice experiment.

Interventions

Surgical termination of pregnancy

All women ≥ 6 weeks' and < 14 weeks' gestation were primed with misoprostol 400 µg 2 hours prior to the procedure. All STOP procedures were performed under general anaesthesia using vacuum aspiration (VA) by two consultants each on a dedicated operating list.

Medical termination of pregnancy

All women < 14 weeks' gestation were given mifepristone 200 mg orally. They returned 36–48 hours later to the gynaecological day-case ward for prostaglandins (detailed below).

1. Women ≤ 9 weeks' gestation were given misoprostol 800 µg vaginally, followed 4 hours later by misoprostol 400 µg if no abortion had occurred. Subsequently if abortion did not occur by 1630–1700 and there was no excessive bleeding, women were discharged home with 2-week follow-up scan review.
2. Women ≥ 9^{+1} weeks' gestation were given misoprostol 800 µg vaginally followed by misoprostol 400 µg every 3 hours up to a maximum of four doses. If by midnight no abortion had occurred, mifepristone 200 mg orally was administered followed by gemeprost 1 mg vaginally 3-hourly from 0800 up to a maximum of five doses. If abortion had not occurred by 0800 the following morning, STOP was arranged.

Main outcome measures

The main outcome measure was acceptability determined by responses to the question: 'If you ever have another termination of pregnancy, would you opt for the same method?'

Secondary outcome measures included strength of preference by willingness to pay (WTP) using the payment card method; distress using the Impact of Event Scale (IES); anxiety and depression using the Hospital Anxiety and Depression Scale (HADS); satisfaction with care using a 5-point Likert scale; experience of care using a semantic differential rating scale; frequency and extent of symptoms including self-assessment of pain using a visual analogue scale; clinical effectiveness using unplanned/emergency admission requiring an overnight stay and complications.

A discrete choice experiment was used to identify key factors (attributes) that shape women's preferences for abortion services.

Results

The trial recruited 1877 women: 349 in the randomised arms and 1528 in the preference arms. Of those in the preference arms, 54% chose MTOP. When questioned 2 weeks after the procedure more women having STOP would choose the same method again in the future {adjusted difference 24.9% [95% confidence interval (CI) 15.8 to 34.9%] in the randomised arm and 15.9% [95% CI 12.2 to 19.6%] in the preference arm}. Acceptability of MTOP declined with increasing gestational age. The difference in acceptability between STOP and MTOP persisted at 3 months.

There was no difference in the maximum amount women were willing to pay for their preferred method prior to the procedure. At 2 weeks after TOP, women in the preference arms were prepared to pay more to have their preferred option, but there was no difference in the mean maximum WTP values between MTOP and STOP in the randomised or preference arms.

There were no differences in anxiety or depression between women having MTOP and STOP as measured by HADS. However, women randomised to MTOP had higher scores on the intrusion subscale of the IES at 2 weeks and both the intrusion and avoidance subscales at 3 months. There was no difference in IES scores between the MTOP and STOP groups in the preference arms.

Women were more likely to be satisfied overall and with the technical and interpersonal aspects of care if they had STOP rather than MTOP whether in the preference arms or randomised arms.

Experience of care as determined by median semantic differential scores were lower after MTOP in both randomised and preference groups. MTOP was felt to be more unpleasant, more disagreeable, harder and more painful while STOP was felt to be milder, more agreeable, faster and safer.

During admission women undergoing MTOP had more symptoms and reported higher mean pain scores. Compared with women having STOP, more women having MTOP reported nausea and diarrhoea after discharge. There were no differences in time taken to return to work between groups; around 90% of women had returned to work and normal activity by 2 weeks.

Rates of unplanned or emergency admissions were higher after MTOP than STOP (4.2% versus 0.7% respectively). Overall complication rates were also higher after MTOP (5.0% versus 2.6% respectively), although this difference only achieved statistical significance in the preference arm.

The overall cost of STOP was greater than MTOP (£498 versus £287 respectively) due to higher inpatient standard costs. Even though complication rates were higher with MTOP, the medical procedure was more cost-effective based on the measure of effectiveness used (successful completion of TOP on the day of admission).

A discrete choice experiment identified three service attributes that had an almost equal impact on women's preferences: the provision of counselling, the number of days delay to the procedure and the possibility of the need for an overnight stay. Women would be prepared to wait approximately one extra day to ensure access to post-termination counselling and to avoid an overnight stay following a termination.

Qualitative substudy

Women wanted quick access to abortion, but were concerned about what professionals thought of them. Women also found accessing the service via family planning clinics easier than via general practitioner surgeries. Once in the hospital service, quick assessment and treatment was important to them.

Women participated in the trial because by helping others they were able to feel compensated in some way for the unpleasant experience of undergoing termination. Some felt a general ethical obligation to help while others gained different levels of personal benefit; some women found talking about their experiences cathartic.

Some women found the concept of letting the computer 'choose' difficult to understand. For those with a strong pre-existing preference the trial design meant that women could still benefit by both choosing which method they preferred and participate in the trial to help others.

Conclusions

MTOP was associated with more negative experiences of care and lower acceptability. Acceptability of MTOP declined with increasing gestational age. MTOP was less costly, but also less effective than STOP. Women value the option to choose their preferred abortion method. However, the majority of women choosing MTOP were satisfied with their care and found the procedure acceptable, suggesting that a patient-centred abortion service should offer the choice of medical or surgical abortion up to 14 weeks of pregnancy.

Recommendations for further research

An audit of provision of MTOP and STOP in England and Wales is urgently required. Further studies exploring the barriers to offering women the choice of method of TOP are needed, together with research on the acceptability and effectiveness of (1) MTOP and manual VA in pregnancies below 9 weeks' gestation and (2) MTOP and dilatation and evacuation after 14 weeks' gestation.

Trial registration

This trial is registered as ISRCTN07823656.

Chapter 1
Introduction

Scientific background

Unwanted pregnancy is a major health issue: worldwide an estimated 53 million abortions are performed each year, resulting in up to 100,000 maternal deaths.[1] In 2007 nearly 200,000 pregnancy terminations were performed in England and Wales, of which 38% were performed in NHS hospitals and 50% in approved independent sector locations under NHS contract. The majority of abortions are performed before 13 weeks of pregnancy (90%) and by surgical methods (65%).[2] In 2000, 64 of 194 (33%) units with facilities for termination of pregnancy (TOP) before 13 weeks provided both medical and surgical methods, while among the 130 units with only one method available, surgical termination of pregnancy (STOP) was the only option in 79%.[3] Prior to 14 weeks' gestation surgical termination can be performed by vacuum aspiration (VA). This procedure, performed under general anaesthesia, has been the method of choice since the 1960s; VA is currently used in 57% of abortions performed prior to 10 weeks' gestation and 89% of those performed at 10–12 weeks' gestation.[4] The technique is safe and efficacious; major complications (uterine perforation, pelvic sepsis and haemorrhage requiring blood transfusion) occur in 0.2–0.9% of cases.[5–7] However, up to 5% of women return to hospital with post-abortion symptoms, of whom 50–65% require surgical evacuation for retained products.[6,7] Complication rates increase with gestation,[5–8] with incomplete abortion reported in up to 12% of cases ≥ 12 weeks' gestation.[7] Cervical preparation with prostaglandins facilitates cervical dilatation and reduces complications.[9] If the woman is under 18 years of age or at > 10 weeks' gestation, misoprostol 400 µg vaginally 3 hours prior to surgery is recommended.[9]

Medical abortion using mifepristone, an anti-progesterone, and prostaglandins has been available since the 1980s. For abortions at up to 63 days' gestation, evidence suggests that mifepristone (200 mg orally) followed 36–48 hours later by either gemeprost (1 mg vaginally) or misoprostol (800 µg vaginally) are equally safe and effective, with 94–97% of women achieving complete abortion.[10–13] Because of much lower costs, 72% of units use misoprostol.[3] Complete abortion rates with single-dose mifepristone/misoprostol fall from 98.5% at ≤ 49 days' gestation to 96.7% at 50–63 days,[12] but are much lower after 63 days.[14] For women at 49–63 days, if abortion has not occurred 4 hours after administration of misoprostol, a second dose (400 µg vaginally or orally) may be administered.[9] Between 64 and 91 days' gestation, efficacy is increased if the initial dose of misoprostol is followed by repeated doses of 400 µg.[15] However, even using up to a maximum of five further doses, the need for surgical evacuation increased from 0.9% at 9–10 weeks to 7.9% at 12–13 weeks.[15]

A Cochrane systematic review of medical versus surgical methods of first-trimester TOP identified only six relevant trials, mostly with small numbers.[16] Prostaglandins used alone seemed to be less effective and more painful compared with surgical abortion; only two trials of mifepristone/prostaglandins were included.[17,18] The review suggested there was inadequate evidence to comment on the acceptability and side effects of medical versus surgical abortions and called for trials to address the efficacy of currently used methods and women's preferences. This Cochrane review included the only partially randomised preference trial of medical and surgical TOP between 10 and 13 weeks.[18] Side effects (vomiting, diarrhoea and abdominal pain) were higher in the medical group, although there was no difference in the rates of major complications up to 8 weeks after the procedure. Subsequent to the review there has been one further partially randomised trial of medical versus surgical methods at < 64 days' gestation.[13,19] In addition to suggesting that surgical abortion had higher success rates, this study proposed that more women were satisfied with a surgical procedure.[13]

Available evidence suggests that 17–85% of women requesting first-trimester TOP have a preference for either a medical or surgical procedure.[16–18,20] The most common reason cited for preferring medical termination of pregnancy (MTOP) is the avoidance of surgery and/or anaesthesia.[16,21] The large variation in reported preference rates may be

explained by factors such as gestational age, prior experience and time to access the procedure.[16,20–22] Preference for STOP appears to increase with gestational age;[17,18] early in pregnancy women appear to perceive the medical procedure as easier and more natural, while later it is perceived as more stressful (related to concerns about pain and seeing the fetus).[20–22] If a woman has a preference for one method she is unlikely to be enrolled in a randomised trial or she may refuse the allocated method.[21] To represent the full range of service users, randomised trials need to include preference arms.

Service users' evaluations of the care they have received are clearly important in the context of current initiatives to develop a more patient-centred NHS. Patient satisfaction with their care is the most commonly used indicator in research on patient evaluations,[23] but definitions of satisfaction vary, and different measures incorporate different dimensions of the construct, such as adequacy, suitability and acceptability. A common problem with satisfaction measures is that they exhibit ceiling effects, i.e. most patients report being satisfied, and distinctions between care of different quality are often not observed. This is likely to be a particular problem in areas such as TOP, where patients are widely observed to experience a sense of relief after the procedure. Most studies of women's views about TOP have reported procedure acceptability; typically women have been asked whether they would opt for the same method in the future or recommend the method to a friend.[16,21,24] Data from randomised trials indicate that acceptability of both methods before 9 weeks' gestation is high (63–92%), with 2–36% of women randomised to STOP preferring a medical procedure in future and 22–37% of women randomised to MTOP preferring STOP.[16,18] Where women have a preference for one method, typically ≥90% would choose the same method in the future.[17,20–22,24] Acceptability may be lower at later gestations; in the only randomised trial of abortion methods at 10–13 weeks' gestation, more women opted for VA again than medical abortion (79% versus 70% respectively).[18] However, response rates were low (< 50%). The results reported above are based on the 'single question with a binary outcome' approach to assessing acceptability. Such measures are simple to collect and report, but provide limited information, particularly about why respondents hold the views they do. One supplementary approach is to ask respondents to rate specific features of their care, thereby providing information about the reasons underlying acceptability judgements. Using a semantic differential rating scale, Henshaw *et al*.[17] identified that in randomised women, medical abortion rated lower on six of the bipolar adjectives with pain showing by far the largest difference. VA was also rated less painful in women allocated according to preference.

The psychological effects of TOP have recently been reviewed.[25] The authors concluded that TOP rarely causes immediate or lasting negative psychological consequences in healthy women. Indeed several studies reported positive outcomes such as relief.[25] Henshaw *et al*.[17] performed a partially randomised preference trial of TOP at < 9 weeks' gestation and found no differences in depression, anxiety or low self-esteem 2 weeks after the procedure[26] nor, in a much smaller number, 2 years later.[27] Whether MTOP is associated with more adverse psychological consequences after 9 weeks' gestation is not known.

Although many studies have reported the outcomes of first-trimester TOP, very few have randomised the method of abortion, and only one has included women beyond 9 weeks of pregnancy, despite the fact that this group constitutes over 40% of TOPs.[18] There is a need for a partially randomised preference trial comparing VA with current methods of medical abortion. In addition to patient acceptability, the trial needs to determine the clinical effectiveness and cost-effectiveness of the two methods.

There is a clear policy impetus to understand, qualitatively, women's preferences for medical or surgical TOP and the decision-making processes that lead both to these preferences and to encounters with health services. The personal and political sensitivities that surround TOP have important consequences for research in the field. The most important of these is resistance to inquiry into decision-making and action where this may threaten the moral viability of the woman's decisions. This means that although TOP is one of the most common procedures in the UK, little work has been done that will contribute to robust understanding of preferences for types of procedures. Instead, the objective of much research in the field has been aimed at understanding decision-making on termination in relation to promoting access or reducing delays in referral to clinical services. Recently, this approach has led to an important qualitative study in the UK. In this study, Kumar *et al*.[28,29] have shown that most women prefer *not* to discuss their decision with clinicians, but prefer instead to receive information and prompt referral. Unease about discussing

personal aspects of termination has also been registered among professionals, especially nurses and midwives (this may also explain the paucity of social science research in the field).[30] Factors affecting the choice of method of termination are already known to be highly complex.[31] The problem of decision-making and preferences around termination is, therefore, quite unlike any other arena of clinical research, especially other areas where approaches to shared decision-making have become prominent in recent years.[32]

The intensive investigation of the experiences and preferences women had within the trial provided a point of departure for the qualitative substudy. This drew on data collected within the economic substudy of strength of preferences, and was an optional final phase of the trial experienced by a subgroup of 30 women. Qualitative substudies within trials tend to be used either as initial (reconnaissance) studies to assist in decision-making about instrument design, study organisation and recruitment; or as formative process evaluations of ongoing work.[33] In the present study, we intended to take a different tack, using the qualitative investigation as a means of illuminating women's responses to (1) the experience of participating in the trial and (2) their perspectives on the results of the economic study of strength of preference. Directly focusing on these topics will provide useful data, but will also indirectly open up earlier decision-making processes and questions of access to investigation. A key problem in qualitative studies of personally sensitive experiences and actions is that of the participant being forced to construct an account that provides a justification for action in the face of anticipated moral judgements by an external authority;[34] this makes for bias in accounts. We have adopted an approach to study design and data collection that was explicitly intended to move the focus of participants' accounts away from personal justification towards a wider explanatory perspective. We did this by asking participants to act as lay interpreters of data collected elsewhere in the study (see Chapter 3, Discrete choice experiment) and focused on the preferences and action of 'notional others',[35] using this interpretive function as a starting point for their own accounts. This approach meant that its design and application did not risk confounding recruitment and retention of participants, or other data collection, where these were already likely to be a challenge.

Chapter 2
Methods

Design

This was a partially randomised controlled preference trial comparing MTOP and STOP at less than 14 weeks' gestation. The principal outcome was acceptability of termination method as determined by preference for a future method of termination. This design ensured the inclusion of women who had a prior procedure preference (preference group) and those who did not (randomised group), and therefore reflects the population of a normal clinical setting. A substantial qualitative component was utilised to gather information about women's motives for joining the trial, their personal experiences of seeking termination and their decision-making process. Data collected using 'strength of preference' and the model developed from conjoint economic analysis were used as the focus to obtain women's perspectives. The study was approved by the Newcastle and North Tyneside Research Ethics Committee 2 (Reference 05/Q0906/38).

Participants

Participants were women accepted for TOP under clause C of the Human Fertilisation and Embryology Act (1990) amendment of the Abortion Act (1967) with pregnancies < 14 weeks' gestation (based on ultrasound assessment of fetal size) at the time of abortion between 18 July 2005 and 31 January 2008 (31 months).

Inclusion criteria

1. Women who had an unwanted pregnancy of < 14 weeks' gestation.
2. Women who were able to give written consent.
3. Women < 16 years of age who were deemed Fraser competent[36] by the nurse practitioner and had a parent or legal guardian present who was also willing to give written consent.

Exclusion criteria

1. Women with a pre-existing medical disorder that was an indication for either MTOP or STOP.
2. Non-English-speaking women (apart from French, Mandarin, Cantonese, Bengali, Urdu and Arabic) due to limited availability of interpreters.
3. Previous participation in the trial.
4. Current participation in a 'drug'-related trial.
5. Lack of availability of either MTOP or STOP within 10 days of outpatient assessment.

Setting

The trial was conducted at the Royal Victoria Infirmary (RVI), Newcastle upon Tyne, UK. The hospital is a large tertiary unit that provides both medical and surgical TOP up to 20 weeks' gestation to women throughout the north-east of England. The unit undertakes around 1800 terminations per year. The termination service has undergone continual development over the last 15 years in response to the needs of the women who access it. Women referred from primary care (general practice or sexual and reproductive health clinics) are seen by one of three nurse practitioners in assessment clinics which run 5 days per week. Towards the end of the trial, because of increasing referrals to the service, additional clinics were started on one evening and on a Saturday morning.

Recruitment

All women being referred to the TOP service were given an information leaflet by their referring health professional. The leaflet contained information about abortion services at the RVI as well as an explanation of medical and surgical TOP and common complications. When women arrived in the outpatient clinic they were given a patient information sheet about the Newcastle upon Tyne TOPS study and asked to read it before seeing the nurse practitioner. Women at < 14 weeks' gestation who were accepted for TOP had the two methods of abortion explained. The nurse practitioner emphasised that there was no evidence that one method was superior to the other, that women, therefore, had a choice of method and that research was being conducted into women's preferences for abortion method. Women

interested in participating were immediately referred to the research nurse in an adjacent room. The research nurse explained the study, answered any questions and, where appropriate, took written consent.

Within a few months of starting the trial, it became obvious that fewer recruited women than expected were prepared to have their method of abortion determined by randomisation. The potential factors contributing to this were extensively discussed by both the Trial Management Group and Trial Steering Committee, and changes to the recruitment procedure were proposed to try to increase recruitment to the randomised arm. An action plan was agreed and after approval by Newcastle and North Tyneside Research Ethics Committee, the following changes were implemented from 7 August 2006:

1. The information leaflet about the service at the RVI (Appendix 1) was amended to indicate that there was no medical evidence that one method of TOP was 'better' than the other and that research was being undertaken into women's preferences on abortion method. The amended leaflet was sent to all referring general practices and sexual and reproductive health clinics with a covering letter to encourage professionals to give this to referred women.
2. The research patient information sheet was amended to emphasise the value of randomisation and to better explain the process.
3. The dialogue used by the nurse practitioners when introducing the trial was standardised.

Randomisation

Participants with no preference, and willing to be allocated a procedure at random, were randomised using a purpose-designed computer system with web-based access for trial personnel (PowerTrial). All randomised allocations of procedure were performed by the research nurse and the allocation was concealed from the research nurse and participant until recruitment to the randomised arm had been completed; data entry of specific relevant information on the randomisation page of the database confirmed eligibility and allowed procedure assignment to take place. Allocation to medical or surgical arms was by a random sequence utilising a block size of 4. Randomisation was stratified according to gestation (< 9 weeks and 9–14 weeks) and for previous TOP.

Participants with a preference for MTOP or STOP were assigned to their method of preference. Thus there were four groups of participants in the trial:

1. randomised surgical (RS)
2. randomised medical (RM)
3. preference surgical (PS)
4. preference medical (PM).

Interventions

Surgical termination procedure

Women randomised to, or with a preference for, STOP were admitted to the gynaecological day unit on the morning of the procedure. All women were primed with misoprostol 400 µg vaginally at least 2 hours prior to the anticipated time of STOP. All STOP procedures were performed under general anaesthesia. Gestational age was confirmed on the operating table prior to cervical dilatation by ultrasound measurement of fetal crown–rump length or biparietal diameter or by pelvic examination. Following cervical dilatation with graded Hegar dilators, VA was performed using an aspiration curette size (in mm) equivalent to the gestational age (in weeks). A 12-mm aspiration curette was used for all VA procedures ≥ 12 weeks' gestation. Virtually all STOP procedures were performed by two consultant gynaecologists each of whom had a weekly dedicated operating list. In the absence of excessive bleeding or other problems, women were discharged 1–2 hours after the procedure. In line with the recommendations of the Royal College of Obstetricians and Gynaecologists (RCOG),[9] STOP was only performed after 6 weeks' gestation because of the higher failure rate at very early gestations. The appointment for STOP was timed in line with this recommendation.

Medical termination procedure

Women undergoing MTOP were given mifepristone 200 mg orally and observed for 1–2 hours on the gynaecology ward. In the absence of vomiting they were allowed home, to return to the ward at 0800 36–48 hours later.

Women ≤ 9 weeks' gestation were given misoprostol 800 µg vaginally. A further dose of misoprostol 400 µg was given 4 hours later, vaginally or orally (depending on vaginal bleeding), if no abortion had occurred.[9] Subsequently, if abortion did not occur and bleeding was not excessive, women were routinely discharged between 1630 and 1700, with an appointment for outpatient review 2 weeks later. At the time of the review all women underwent an

ultrasound scan to exclude an ongoing pregnancy or retained products of conception (RPC).

Women ≥9^{+1} weeks' gestation were given misoprostol 800 µg vaginally followed by misoprostol 400 µg every 3 hours up to a maximum of four doses if no abortion had occurred. If abortion had not occurred by midnight a further dose of mifepristone 200 mg orally was administered followed by gemeprost 1 mg vaginally 3-hourly from 0800 up to a maximum of five doses. If abortion had still not occurred by 0800 the following morning, MTOP was deemed to have failed and STOP arranged. In all cases expelled products were examined to confirm they were complete; if there was any doubt, an ultrasound scan was performed. Cases where the placenta was retained after expulsion of the fetus (confirmed by ultrasound examination and/or speculum examination) without significant bleeding were managed with a further dose of misoprostol 400 µg vaginally. Failure to pass the placenta after a further 3–4 hours was managed with surgical evacuation of RPC. Uterotonic agents were not used routinely during TOP procedures.

All women were given doxycycline 100 mg orally twice daily for 7 days, commencing on the day before or the day of the procedure. All women undergoing STOP were given metronidazole 1 g rectally at the time of the abortion.[9] Pain relief was available for all women, comprising paracetamol 1 g orally, diclofenac 75 mg orally or pethidine 100 mg intramuscularly.[9] Non-sensitised rhesus D-negative women were given anti-D immunoglobulin 1250 iu intramuscularly prior to discharge from hospital.

Objectives

The aim of this partially randomised preference trial was to determine the acceptability, efficacy and costs of medical compared with surgical TOP at < 14 weeks' gestation. There was also a need to understand women's decision-making processes and experiences when accessing the termination service and taking part in research.

Primary objective

The primary objective was to determine acceptability as revealed by preference for future TOP method at 2 weeks post procedure in women randomised to medical or surgical TOP.

Null hypothesis

The null hypothesis was 'In women without prior preference, medical and surgical terminations are equally acceptable'.

Secondary objectives

The secondary objectives were to compare surgical and medical procedures by assessing:

1. strength of preference
2. psychological sequelae
3. satisfaction with care
4. experiences of care
5. frequency and severity of procedure-related symptoms
6. clinical effectiveness
7. costs and cost-effectiveness.

Qualitative substudy

The aim of the substudy was to better understand the foundations of women's preferences and decision-making about method of termination. The objectives were:

1. to identify, describe and understand women's motives for joining the trial and their experiences of participation in it
2. to identify, describe and understand women's personal experiences of seeking termination and decision-making about method of termination
3. to identify, describe and understand women's perspectives on data collected on 'strength of preference' and the model developed from conjoint economic analysis.

Data collection

Baseline demographic data, including medical history and method of any previous termination, level of education, occupation and income, was collected by the nurse practitioner or research nurse from all participants. Contact details, including where possible mobile telephone numbers and availability, were also collected. All participants were invited to return for an outpatient assessment 2 weeks after the procedure and all assessments were undertaken in a hospital or community clinic. Outcome data were collected at 2 weeks (by structured interview and/or questionnaire) and at 3 months (by questionnaire) after the procedure (*Table 1*). For women who did not attend their 2-week follow-up visit, collection

TABLE 1 *Table of events*

	Visit 1 (baseline)	Visit 2 (TOP)	Visit 3 (post TOP)	
	Up to –2 weeks	0	+2 weeks	+3 months
Inclusion/exclusion screening	✗			
Written informed consent	✗			
Randomisation if applicable	✗			
Reason for preference if applicable	✗			
Demography + baseline data	✗			
Medical history	✗			
Concomitant medication	✗		✗	
Ultrasound	✗			
Strength of preference[a]	✗		✗	
Termination procedure		✗		
Visual analogue scale		✗		
Physical progress			✗	
Acceptability			✗	✗
Satisfaction with care			✗	✗
Experience of care			✗	✗
Impact of Events Scale			✗	✗
Hospital Anxiety and Depression Scale			✗	
Consent for qualitative interview[b]			✗	

a Only determined prior to procedure in the preference group.
b Qualitative interviews to be completed prior to 3-month time point.

of outcome data, as previously agreed, was undertaken via telephone interview, mobile text message and postal- or web-based questionnaire. All follow-up contacts and telephone interviews were conducted by a research nurse.

After the trial commenced, the distributions of the time it took women to respond to the questions asked at the 2-week and 3-month follow-ups were established. In view of these distributions, the Trial Management Group decided only to use responses (referred to as 'timely responses') if the date they were provided was within 4 weeks of the intended time after the procedure, i.e. 2-week data were accepted if it was provided within 42 days of TOP, and 3-month data were accepted if it was provided within 60–120 days after TOP.

Outcome measures

Acceptability

This was determined at 2 weeks and 3 months after the procedure by responses to the closed question 'If you ever have another termination of pregnancy, would you opt for the same method?' This simple question has been used in previous preference trials of TOP,[17,18] and has the advantage of being easily determined by telephone, questionnaire or text message.

Strength of preference

Willingness to pay (WTP) was used as a measure of strength of preference for medical or surgical TOP. This technique is being increasingly used in health technology assessment[37] and has been used previously for assessing strength of preference for abortion method.[27,38] An instrument was designed in order to frame a hypothetical scenario where women imagined that they had been offered their non-preferred method and that they had to pay an additional amount of money from their own income to obtain their preferred method. The economic theory underlying this design is part of welfare economic theory, which posits that individuals will choose their preferred set of goods (in this case, type of termination) from the total set of goods available subject to each set incurring some cost that must be met from some

fixed budget/income. Therefore, assuming full information, i.e. individuals know all the costs, the maximum amount that someone states they would be 'willing to pay' to get a new set indicates whether that set is preferred to the other. This is because this amount implies an opportunity cost, i.e. assuming that their current set was the preferred one, paying this extra amount must entail the loss of something that they wanted. This amount also entails a *strength of preference* to the extent that the greater the amount stated, the greater the opportunity cost, i.e. the more that the individual is willing to give up *ceteris paribus*. The bigger the income, the greater the amount of goods can be afforded. Therefore, observing a correlation between income and WTP is a useful test of validity.

Interviews were conducted using the payment card method,[39] with all women in the preference arm at baseline (following recruitment to the study) prior to admission for the procedure. Women were asked to state their maximum WTP amount for the termination method they had chosen. Interviews were also conducted on all women in both the randomised and preference arms at 2 weeks after the procedure when they were asked to state their maximum WTP amount to receive their preferred option at a future date. In order to avoid arbitrary units (and to encourage elicitation of the maximum amount) an approach was used that presented actual amounts in order. Mean WTP for each TOP method was estimated by calculating the sample mean for women in the randomised and preference arms. There are potential sources of bias with WTP elicitation. For example, stating zero might be due to a misunderstanding or suspicion that the scenario is not hypothetical or the assumption that it is the price that is wanted. Mean WTP was therefore also calculated excluding zero payers. A comparison was then made between mean WTP for MTOP and STOP (stratified by method to which women were randomised) and between randomised and preference arms to test the hypothesis that women who already have a preference (indicated by actual choice of procedure) will have a stronger subsequent preference (indicated by stated WTP for hypothetical future procedure). Finally, the validity of women's responses was tested by examining the correlation between stated WTP and level of income.

Distress, anxiety and depression

Distress was measured using the Impact of Event Scale (IES) at 2 weeks and 3 months after the procedure. This 15-item scale, with subscales for intrusion and avoidance, measures subjective distress to a specific event (in this case TOP),[40] and is most likely to detect a difference in actual experience of having one procedure rather than another. Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) at 2 weeks and 3 months after the procedure. This is a widely used 14-item self-report scale designed for medical patients.[41] Depression is the main problem service providers have been concerned about.[25] Both the IES and HADS have been used in women after TOP.[25–27]

Satisfaction with care

The methodological pitfalls of measuring satisfaction with care have been reviewed.[42] Women were asked to rate the quality of care during the termination and the counselling and support after the procedure using a 5-point Likert scale (from excellent to poor) at 2 weeks and 3 months after the procedure. Measures in which patients are asked to rate the quality aspects of their care show greater response variability than measures which seek direct ratings of satisfaction[43] and are better predictors of whether patients will return to the same doctor in the future.[43] For analysis we distinguished those who rated their care as excellent from the remainder as this provided better discrimination.[44] Ratings of care were supplemented by information on satisfaction with care from the qualitative substudy.

Experience of care

To provide information about the reasons underlying acceptability judgements, we used a semantic differential rating technique administered at 2 weeks and 3 months post procedure. This instrument used a pair of opposite adjectives (e.g. painless–painful) as end points on a graphic Likert scale. Women were asked to indicate their experience by placing a mark on the scale. Twelve bipolar adjectives were used, scored along an evaluation dimension representing a positive or negative attitude ranging from 3 to –3. Rating scores are quick and easy to complete and have been used previously to measure attitude towards TOP.[17,45]

Frequency and extent of symptoms

The incidence of nausea, vomiting, diarrhoea, dizziness and abdominal pain on the day of the procedure was recorded as well as an assessment of

the severity of pain, using a 10-cm visual analogue scale (VAS), and analgesic use. Symptoms after discharge were ascertained at the 2-week follow-up contact by the research nurse. These included the duration and severity of vaginal bleeding and pain as well as the length of time off work and time taken to return to normal activity.[18]

Medication use was recorded at baseline and at the time of the termination procedure by abstraction from the medical notes. Women were also asked about concomitant medications at the 2-week follow-up contact.

Clinical effectiveness

Previous studies have used a variety of measures of clinical effectiveness, but emphasis has been placed on failed TOP (with an ongoing viable pregnancy), incomplete abortion and presumed pelvic infection. Based on our proposed sample size (see below), the precision with which differences in each of these complications could be detected was limited. Hence a combined measure of clinical effectiveness that captures unplanned time spent in hospital, a key outcome for women, was used.

Unplanned or emergency admission was defined as (1) any unplanned admission requiring an overnight stay on the day of TOP or (2) emergency admission requiring an overnight stay after discharge from hospital following the primary procedure. Women were asked to report any attendances at their general practitioner (GP) surgery or hospital and any admissions at 2 weeks and 3 months after the procedure to ensure that all data on adverse outcomes were collected. The indication for referral and subsequent management were abstracted from the hospital or primary care notes. It was assumed that this outcome would capture all women with significant procedure-related morbidity due to (1) incomplete abortion, missed abortion or ongoing pregnancy (all of which require surgical evacuation) and (2) pelvic infection without RPC. Further, there is evidence to suggest that women who experience a failed TOP (requiring surgical evacuation) or excessive pain and or bleeding that results in admission are more likely to classify the experience as unsatisfactory[46] and to opt not to have the same procedure again in the future.[24,46]

Total procedure-related complications were also compared. A complication was defined by any of the following:

1. Haemorrhage: estimated blood loss > 500 ml.[47]
2. Incomplete abortion: products of conception passed, but clinical or ultrasound evidence of RPC.[15]
3. Failed TOP: no products of conception passed and cardiac activity present on ultrasound.[15]
4. Suspected pelvic infection (in the absence of RPC): based on the clinician's assessment [abnormal vaginal bleeding ± abdominal pain with uterine tenderness ± pyrexia (temperature ≥ 37.5°C)] and treatment (prescription of antibiotics).[48]

Sample size

The sample size was determined by the main comparison of acceptability (as assessed by the proportion of women who would opt for the same TOP method again) between women randomised to medical or surgical TOP. Assuming the acceptability of medical termination to be 75%,[17,18,20] responses from 335 women in each randomised arm were needed to detect a difference in acceptability of 10% (i.e. from 75% to 85%) with a significance level of 5% and power of 90%. This difference in the level of acceptability between MTOP and STOP was deemed important for both consumers and providers; a similar difference was sought by Ashok *et al*.[18] in their large randomised comparison of abortion methods.

Based on the sample size calculation we therefore needed primary outcome data on 670 women randomised to medical or surgical TOP at < 14 weeks' gestation. In order to achieve this number we calculated that:

- 1116 women would need to be randomised (assuming primary outcome data would not be available from 40% of women)
- 2232 women would need to be recruited (assuming 50% of women agreeing to participate in the study would have a preference for medical or surgical TOP)
- 3188 women would need to be approached (assuming 30% of women accepted for TOP would decline involvement in the study).

All three assumptions were based on the experience from our earlier pilot trial conducted at the RVI involving women requesting TOP at 9–13 weeks' gestation. For reasons detailed in Kumar *et al*.[28] we believed that our assumption of 60% follow-up was conservative. Previous trials conducted in the UK

had reported that 54%[17] and 82%[18] of recruited women undergoing TOP at < 9 weeks and 9–13 weeks, respectively, were prepared to have their method of TOP determined by randomisation. Thus our estimate that 50% of women agreeing to follow-up would be prepared to be randomised was also thought to be conservative. The proportions of women accepted for TOP who agreed to join these two prior randomised preference trials were not reported. Data from non-randomised studies conducted in the UK suggested that 87–92% of similar women were prepared to participate in studies involving follow-up (including psychological questionnaires) after TOP, suggesting that our assumption of 70% (based on the pilot study) was realistic.

Statistical methods

The study was designed to ensure the inclusion of women who had a prior procedure preference. Participants with a preference for either medical or surgical termination could choose one or the other (preference groups). Participants with no preference, who were willing to be allocated a procedure at random (randomised groups), were randomised using a computer system. The analysis strategy was similar to that used in a partially randomised preference trial of treatment for depression.[49] All data analysis was on an intention-to-treat basis, according to the inclusion/exclusion criteria.

The partially randomised preference design allows the following questions to be investigated:

1. Are the women who choose a procedure different from those who are randomised to one?
2. Which TOP procedure is more acceptable and effective?
3. Do women allocated to procedure of their choice fare better than those who are randomised?

Women effectively chose to be in one of three groups: preference for MTOP (PM), preference for STOP (PS) or randomised to either (RM or RS). Therefore, question 1 was answered by comparing the distributions of baseline variables between these three groups to see if there were any differences. Overall tests for equality of the three groups was carried out (chi-squared for comparison of proportions or ANOVA for comparison of means), and if there was a statistically significant difference between them, comparisons were made firstly between the two preference arms and then between combined preference versus combined randomised arms.

According to the original protocol, the primary comparisons for question 2 should have been carried out between the randomised arms of the study. However, from an early stage in data collection it was clear that there would be far too few women willing to be randomised for analysis to be definitive, so primary comparisons were carried out between women in the preference arms of the trial. The main comparison of the primary outcome was between the two preference arms at 2 weeks, and then at 3 months. This was then repeated for the two randomised arms, and then for the combined preference arms compared with the combined randomised arms (to answer question 3).

Acceptability (proportions willing to have the same termination procedure again) was compared via binomial regression including key baseline variables as covariates in the model (previous TOP, previous live birth, mother's age, educational level and gestation at TOP). However, the comparisons of the randomised groups did not adjust for these covariates: multivariate models would not converge because of the smaller sample size, but the groups are likely to be balanced on these covariates via the random allocation. Possible interactions between intervention and gestation, and intervention and past history of TOP were considered. These possible interactions are illustrated by plotting the proportion finding the procedure acceptable by gestation in weeks using a Lowess smoother for the two intervention groups. Where there was a statistically significant interaction, the difference in acceptability between intervention groups was estimated at three gestational age epochs.

The secondary outcomes were compared between the two preference arms, then between the two randomised arms, and then for combined preference arms compared with combined randomised arms. Mean ratings on the psychological scales were compared by multiple linear regression while adjusting for the key baseline variables listed above. Satisfaction with care was collected on a 5-point scale (poor to excellent), but was recoded as whether or not the women assessed their care as 'excellent': the trial arms were compared using binary regression adjusting for key baseline variables.

For other binary variables (e.g. occurrence of symptoms in the days after the termination, whether women had returned to work/normal activities at 2 weeks) unadjusted comparisons were made between trial arms with 95% confidence limit (CI) for the differences. Similar unadjusted comparisons were made between trial arms to compare the mean VAS pain scores (with 95% CI). The distributions of the semantic differential scales (7-point scales), strength of bleeding scale (5-point scale) and time to return to work and normal activity (in days) were compared between groups via Mann–Whitney tests. All analyses were done using STATA, version 8.[50]

Costs and cost-effectiveness analysis

Cost data relating to NHS resource use (both primary and secondary care) were collected following established methods[51] up to 3 months post TOP. This included data relating to the initial procedure, hospital stay, follow-up care as inpatients, any additional interventions and outpatient appointments. Data relating to GP consultations and referrals/admission to other secondary care units were collected using the postal questionnaire and, if agreed previously, by telephone.

For the costing exercise the resource quantities used and the unit cost (of the resource) for each method of TOP were determined. The total cost of each TOP method is the sum of the products of the quantity of units and unit cost. Obtaining data on resource use and the unit costs of each resource item was sometimes difficult given that some information was either not routinely collected or not accessible. For such costs, assumptions guided by expert clinical opinion were used.

Total individual cost was estimated as the sum of standard and individual-level costs.

1. *Standard costs* do not vary by individual patient and were reported in two parts: initial clinic attendance (which is assumed to be the same for both methods of TOP); and TOP procedure costs (which are assumed to vary only by procedure and not by patient).
2. *Individual-level costs* are informed by individual-level data. The number of patients who consumed at least one unit of resource was determined and the mean number of units calculated by dividing the total number of units by the sample size. Total mean individual cost was calculated as the sum of the product of the unit cost and the mean number of units.

Strictly, staff costs could vary per individual, but as actual staff times were not collected per individual they are included in standard costs. For consistency, staff costs are reported, as with all other costs, in the form of a marginal cost, i.e. the extra cost that would be incurred to buy another unit of the item. Staff costs for the TOP procedure were estimated by taking the total staffing cost from the NHS Trust attributed to the ward and then estimating the proportion of bed days for TOP out of all procedures carried out on that ward. All drug costs were taken from the *British National Formulary*, No. 55, and refer to the price per unit actually administered (as opposed to purchased). The mean cost of an overnight stay was provided by the local NHS Trust and includes overheads. Evacuation of RPC was assumed to cost the same as STOP.

Overheads were assumed to be 28% in accordance with the local NHS Trust. Staff unit costs were expressed per minute (calculated by multiplying annual salary by the duration of the time assumed to be spent per TOP patient divided by the total possible patient contact time). Total patient contact time was estimated from 42 weeks per year at 37.5 hours per week and assuming 0.7 of that time to be spent on patient contact.[52] The following salaries were used: nurse practitioner, £48,102.83; outpatient nurse, £18,098.00; and phlebotomist, £16,294.48.

A cost-effectiveness analysis was undertaken using standard methods whereby the average incremental cost-effectiveness ratio (ICER) was estimated as mean change in cost divided by mean change in effectiveness.[51] Cost was estimated as total NHS cost (as above). The measure of effectiveness was number of successful TOPs, where success was defined as completion of the TOP without an unplanned overnight stay and without any of the pre-specified complications. A 95% CI was estimated using bootstrapping in order to deal with the problem of a ratio of two variables (i.e. cost and effectiveness).[53]

Discrete choice experiment

In order to identify key factors that shape women's preferences for termination services, a discrete choice experiment (DCE) was conducted. This technique measures the strength of an individual's

preference for various attributes of a clinical intervention,[54] and has been used successfully in research relating to the provision of services for women.[55]

The sampling frame for this part of the study was non-pregnant women attending contraception and sexual health (CoSH) clinics in Newcastle upon Tyne, UK. This sampling strategy was chosen as it reduced the research burden on the main trial sample and did not interfere with the process whereby pregnant women in the trial formed and stated preferences (for medical or surgical termination). Further, results from a non-pregnant sample might be less influenced by immediate emotional responses.

Women attending three CoSH clinics in Newcastle upon Tyne (The Flat, Graingerville and Armstrong Road) were given a patient information sheet about the DCE study by the receptionist and were asked to read it before seeing the doctor or nurse practitioner. Those women who expressed an interest in participating were referred to the research nurse, who explained the study, answered any questions and, where appropriate, took written consent.

DCE design and attributes

A DCE is characterised by a number of attributes that are used to describe a particular aspect of a choice, in this case alternative means of receiving health care. A provisional list of attributes was selected based on a review of the relevant literature and after seeking expert opinion from medical and nursing practitioners working in the field. These attributes were then shown to a small sample of non-pregnant women ($n = 8$) to ensure they were consistent with their views. The final attributes used in the TOP DCE are shown in *Table 2*. They cover aspects of the process and outcome that occur before the termination takes place (waiting time), during the termination (being awake, need for painkillers, and the possibility of an overnight stay), and after the termination (the provision of counselling). The explanations/definitions of each attribute that were shown to respondents in preparation for the DCE are shown in the right-hand column of *Table 2*.

Table 3 shows that each of the five attributes was assigned two levels, producing a total of 32 (2^5) possible combinations of attributes, hereafter referred to as 'termination scenarios'. As this is too many scenarios to be considered by any one respondent, an orthogonal fractional factorial design[56] was used to reduce the number of scenarios to 16.

In order to be able to present respondents with a set of choices between two scenarios (A and B), the 16 scenarios generated by the orthogonal design were designated as Choice A. These 16 scenarios were then 'rolled over', i.e. the attribute levels in the original 16 combinations were changed so that an attribute that was coded as level 0 in the Choice A scenarios became level 1 for the Choice B scenarios. The 16 additional scenarios to be used as Choice B were then randomly allocated to each of the original 16 scenarios (Choice A) to produce 16 (A or B) choice sets. *Table 4* shows an example of a choice set, in which respondents had to indicate a choice of A, B, or neither ('refused').

Based on prior research,[54] a sample size of 100 women was judged to provide precise parameter estimates with the number of attributes and choices used.

Econometric analysis

DCEs draw upon Lancaster's economic theory of value[57] and random utility theory.[58] Equation 1 shows that the latent utility U_{iq} for the ith alternative (termination scenario) for the individual q is made up of two components:

$$U_{iq} + V_{iq} = \varepsilon_{iq} \quad [1]$$

where $V_{iq} = \alpha + \beta 1X1 + \beta 2X2 + \beta 3X3 + \beta 4X4 + \beta 5X5 + \beta 6X6$ and is the deterministic or explainable part of utility, and where iq is the random component that represents the unobservable influences that affect utility. V_{iq} is a linear function of the attribute levels characterising termination care (X1 to X6), where the coefficients $\beta 1$ to $\beta 6$ are estimated in the model and α is a constant term that detects any unobservable influences affecting individual's choices. The unobservable influences are assumed not to be related in any systematic way with the observed effects thus collapsing all such influences into iq.[59] Assuming the error term to be Gumbel distributed produces a multinomial logit model.[60]

For purposes of the analysis the data were coded using effects codes[61] (shown in *Table 3*). When using effects codes the sign of the coefficient indicates which of the attribute levels is preferred. Thus, a negative result for the attribute of being conscious

TABLE 2 *Discrete choice experiment: attribute definitions*

Attribute	Explanation
Will I be conscious during the termination process?	For some types of termination of pregnancy you will be unconscious, which means that you will be asleep and you will not see the fetus (this is what the baby is called from 8 weeks of pregnancy until birth). For other types of termination of pregnancy you will stay awake during the procedure and pass the pregnancy very much like a miscarriage. You might see the fetus. If the procedure occurs early in the pregnancy, it will be difficult to recognise the fetus
Will I be given counselling after the termination?	After the procedure you will be given a contact number to ring after discharge in case you want to talk to a trained counsellor about the way you are feeling. This will give you an opportunity to talk in confidence with someone who will listen carefully without judgement, so that you can be supported to find how to resolve the issues that are making you feel the way that you do
How many days would I wait from my initial appointment to having the termination?	Your initial appointment to request a termination would be with your GP or a family planning clinic. An appointment to have the termination will then be made with the clinic that does the termination. The time between the initial appointment and having the termination is how long you would wait
Will I need painkillers?	You might experience tummy pain. This can happen just before or after the termination. The pain feels like the pain many women experience at the beginning of their monthly period. If you do not need painkillers, this means that you have no or little pain. If you do need painkillers, this means that you do have pain, but most women only need tablets, although sometimes women need something stronger, e.g. an injection
Will I have to stay overnight in hospital after the termination?	If the pregnancy is no more than 9 weeks, you will go home the same day. Where a drug is used to cause the termination and if the pregnancy is over 9 weeks, you might have to stay overnight. This is because it might take up to 15 hours for the drug to work

TABLE 3 *Discrete choice experiment: characteristic descriptions and levels*

Attribute	Levels (effects code used in analysis)
Will the woman be conscious during the termination process?	Yes (1) No (–1)
Will the women be offered post-termination counselling?	Yes (1) No (–1)
What will be the number of days delay from the initial appointment to procedure?	7 days (1) 14 days (–1)
Will analgesics be required for pain relief?	Yes (1) No (–1)
Will the procedure involve an overnight stay in hospital?	Yes (1) No (–1)

TABLE 4 *Discrete choice experiment: example of a choice card*

Attribute	Choice A	Choice B
Will I be conscious during the termination process?	Yes	No
Will I be given counselling after the termination?	Yes	No
How many days would I wait from my initial appointment to having the termination?	7 days	7 days
Will I need painkillers?	Yes	No
Will I have to stay overnight in hospital after the termination?	Yes	Yes

would indicate that the preferred level is the one coded as –1, i.e. the woman prefers not to be conscious.

The trade-offs that women would make between termination attributes was determined by calculating the marginal rate of substitution (MRS). For a linearly additive model, the MRS between two attributes is the ratio of the coefficients of those two attributes.[60]

Qualitative substudy

We used a model of preference developed from the DCE as the basis for a semi-structured interview. A conventional model of qualitative analysis was used.[62] The analytic product of this work was: (1) a comparative model of preferences and their normative constraints, and (2) a model of contextual features that affect decision-making about TOP.

Inclusion and exclusion criteria for the substudy were the same as the trial. The sample recruited to the substudy was neither intended to be statistically representative nor to be a maximum variation sample; sampling was purposive and sequential in order to achieve maximum variation and representation from each arm of the trial. We expected a high rate of refusal to join the substudy and of attrition among those who did. This meant that although inclusion and exclusion criteria were the same as for the main trial, the sample entering the qualitative substudy was highly selected. The aim was to recruit 32 women, eight from each arm (i.e. PM, PS, RM and RS).

Women entering the trial between December 2006 and September 2007 were provided with a patient information sheet about the substudy on discharge after their procedure. At the 2-week follow-up, research nurses asked women if they had read the information and would like to participate in the substudy. Those who agreed to be interviewed provided their contact details (mostly mobile telephone numbers). With their verbal consent, the researcher sent a letter to provide written details of the interview date and place (with a map provided where needed) and contact numbers for the interviewee to ring if necessary. The researcher also used text messaging to send reminders, confirm appointments and provide directions.

Data collection

Participants were given a choice of three locations to hold the interview: 10 chose to be interviewed at home, seven at the hospital and 13 at the research institute where the researcher was based. Women were interviewed at a mean of 10 (range 6–16) weeks after the procedure. The women were asked to sign a consent form stating that they had read the information sheet, had had the opportunity to ask questions and had voluntarily agreed to take part in the study. The interview covered women's experience of entering and participating in the trial and their understanding of the trial. They also gave accounts of their experience of referral pathways into the service and clinical trial and their experiences of termination and its outcome. The duration of the interviews averaged 50 (range 27–64) minutes. Interviews were recorded using a digital recorder and were transcribed by an experienced medical secretary who removed identifying personal details. All transcripts were then edited for accuracy.

Data analysis

Anonymised transcripts formed the formal data for qualitative analysis. Following the conventional model of constant comparative analysis of a transcribed data set,[62] transcripts were interpreted iteratively, identifying and elaborating themes within participants' accounts. Thematic analysis was facilitated by QSR NVIVO 7 software. Descriptive and factual themes (or nodes) arose out of the topic

TABLE 5 *Qualitative analysis: analytic themes/nodes*

Parent node	Child node	Description
Trial participation	Feelings about participating	Feelings about being a trial participant
	Understanding about the research	What participants understood about the research, e.g. its purpose and the benefits
	Information and data collection	What participants thought of the information and data collection procedures
	Reasons for taking part	The reasons that participants gave for taking part in the trial and substudy
	Benefits from participating	How they personally benefited by participating
	Any concerns	Any doubts, fears or anxieties about participating
Experiences of the different stages		Narrative accounts of the different stages
	Discovery	Experience of finding out about the pregnancy
	Referral	Experience of referral services; issues of access, etc.
	Assessment	Experience at the TOP and trial assessment clinic
	Procedure	Experience of undergoing the procedure
	Discharge	Experience of discharge from the hospital
	Post-TOP health care	Experience of health care after the procedure
Decision-making	Having the TOP	How participants came to a decision to have a TOP
	Random or preference	How participants came to a decision about which arm of the trial to join
	Surgical or medical	How participants came to a decision on method of termination
	Having a choice	Participants' thoughts on the importance of patient choice
	TOP at home	Participants' thoughts on having the procedure at home
	Local anaesthetic	What participants thought of having a local anaesthetic
	Outcome	Satisfaction and future preference
Significant others		The influence of partners, next of kin, friends, work colleagues, etc. in decision-making
	Male partner	The influence of their reproductive partner in their decision-making
Experiences of health care		Narrative accounts of particular aspects of their experience
	Health-care professionals	Experience of treatment by health-care professionals
	Clinic layout and privacy	Waiting and visitor areas, toileting facilities and private space
	Practical issues	Concerns about travel, child care, hospital directions, appointments rather than with patient care
	Counselling	Personal experiences of counselling
	Waiting time	Personal experiences of waiting
Meanings and attitudes to TOP		More specific attitudes to TOP that include perception of the fetus and their relationship to it. Includes others' perceptions of abortion
Women's preferences		Women's responses to the results of the DCE: views and preferences
	Being unconscious	
	Counselling	
	Waiting time	
	Overnight stay	
	Painkillers	

TABLE 5 *Qualitative analysis: analytic themes/nodes (continued)*

Parent node	Child node	Description
	Additional features	Any features to be considered in addition to those in the DCE
Social background		Employment, household and other contextual information about participants' circumstances
Medical history		References to episodes of illness previous to TOP; compares past experiences of health care
Symptoms and side effects		Includes sickness, vomiting, pain, bleeding, dizziness, tiredness, loss of appetite
Thoughts and reflections		Additional thoughts and reflections, e.g. about emotional reaction, coping, reproductive future
Employment issues		The impact of pregnancy and TOP on paid employment, e.g. application for time off
Information sources		Identification of lay sources of information for decision-making on TOP, e.g. internet
Other influences		Additional influences to decision-making, e.g. religion, chance encounters, previous TOP
Implications for patient care		References suggesting scope for improvements in patient care

guide while referential nodes were drawn from the literature review and analytical questions arising from reading and interrogating the data. Themes were indexed and searches for discrete instances of codeable items of speech were undertaken in both cumulative comparisons (i.e. between interviews in the same arm of the trial) and condition comparisons (i.e. across interviews gathered from different arms of the trial). A coding frame of 46 parent and child nodes was created[63] (*Table 5*) and the nodes were checked for consistency under each theme. Each interview was also coded as a case with attributes, e.g. age, education and income for base data information. Interviewees' responses to the DCE were also coded as case attributes for an analysis of their preferences. In order to guard against the fragmentation of data through this 'code and retrieve' method of data analysis, fieldwork notes summarising the main points were written after each interview by the research associate, and individual interviews were examined as whole documents by the trial coinvestigator responsible for the substudy. Comparisons across the interviews within individual nodes were then carried out and the data collated and analysed thematically under headings such as Trial Participation, Decision-making, Significant Others and Experiences of Health Care.

Chapter 3
Results

Participant flow

Between 18 July 2005 and 31 January 2008, 4406 women were seen by the abortion service requesting TOP; 1324 women were ineligible for the study (*Table 6*). Of the 3082 eligible women with a viable pregnancy < 14 weeks' gestation, 634 (20.6%) were not approached because of logistic problems (*Table 7*) and 41 women (1.3%) were not referred to the research nurse by the nurse practitioner because of complex psychological or social problems.

Of the 2407 suitable women approached by the research nurse, 530 (22%) declined to take part in the study and 1877 were enrolled. Of these, 349 women agreed to be randomised and 1528 women were enrolled in the preference arms, of whom 705 (46%) preferred STOP and 823 (54%) preferred MTOP (*Figure 1*). Twenty-two women (1.2%) enrolled in the trial were recruited with the aid of an interpreter, the biggest group speaking Mandarin ($n = 11$).

A total of 76 women (4.0%) did not attend for the abortion procedure: 58 (3.8%) in the preference

TABLE 6 *Reasons for ineligibility*

Reason	Number (%)
Gestation > 14 weeks (at time of TOP)	523 (39.5)
Undecided about abortion decision (referred to counsellor)	273 (20.6)
Non-supported foreign language	137 (10.3)
Miscarriage	118 (8.9)
Previous participant in trial	92 (6.9)
Decision to continue with pregnancy	48 (3.6)
Under 16 years unaccompanied	41 (3.1)
Requirement for medical review	23 (1.7)
Not pregnant	20 (1.5)
Medical indication for TOP method	18 (1.4)
TOP declined by nurse practitioner	12 (0.9)
Unable to give consent	10 (0.8)
Other	9 (0.7)
Total	1324 (100)

TABLE 7 *Logistic reasons for not approaching suitable women*

Reason	Number (%)
Lack of TOP availability within 10 days	329 (51.9)
Research nurse not available	182 (28.7)
Database problem	79 (12.5)
No room available for research nurse in clinic	24 (3.8)
Evening clinic	10 (1.6)
Other	10 (1.6)
Total	634 (100)

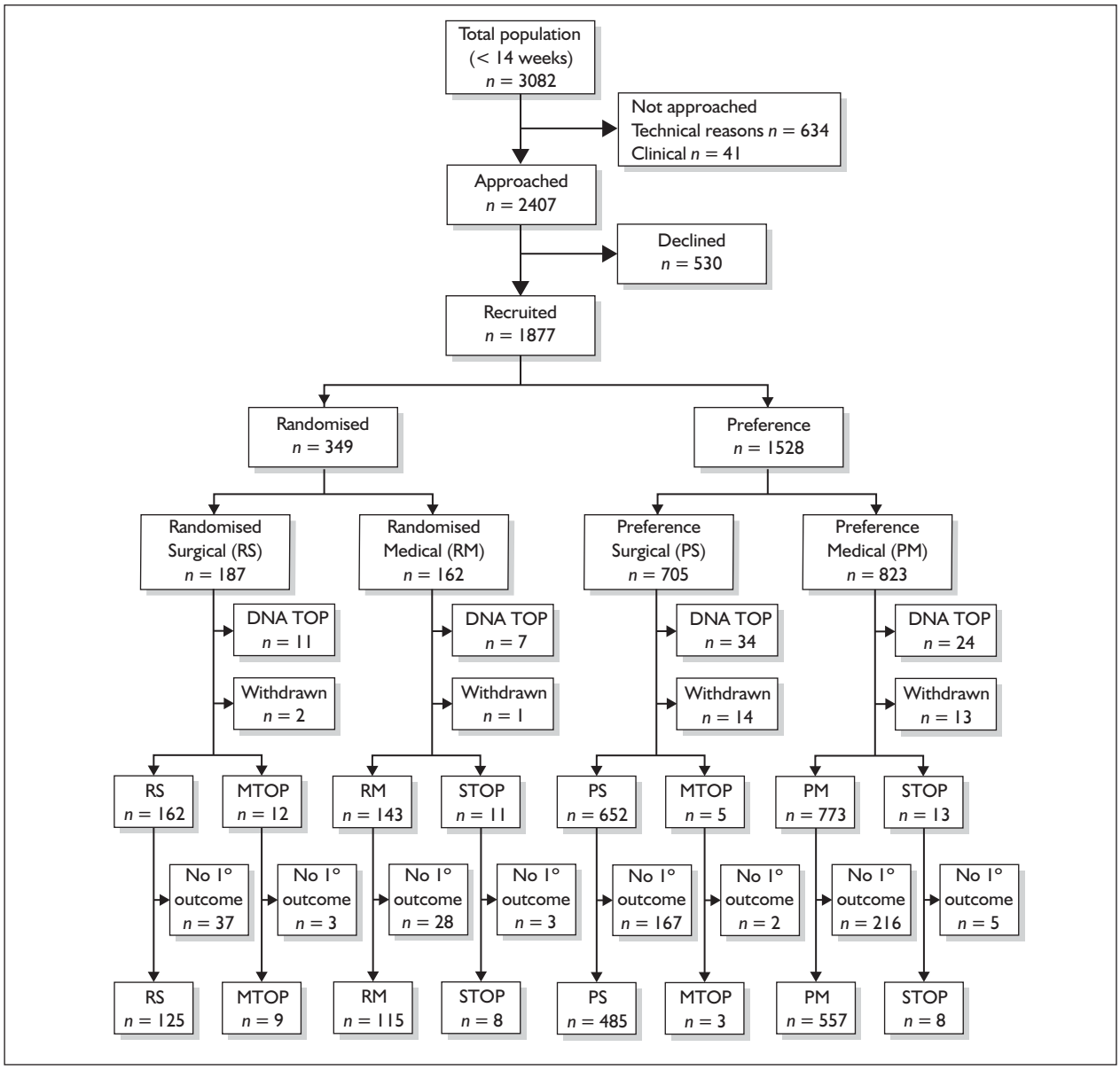

FIGURE 1 *Newcastle upon Tyne TOPS recruitment process.*

arm and 18 (5.2%) in the randomised arm. A further 30 women (1.6%) were withdrawn from the study: 27 (1.8%) in the preference arm and 3 (0.9%) in the randomised arm. The reasons for withdrawal are shown in *Table 8*. Thirteen women (1.6%) in the PM group subsequently underwent STOP and five women (0.7%) in the PS group subsequently underwent MTOP. Eleven women (7.0%) randomised to a medical procedure subsequently had STOP and 12 women (6.4%) randomised to a surgical procedure subsequently had MTOP. In most cases this followed a request from the participant, presumably reflecting a change in preference.

Primary outcome data at 2 weeks post abortion were collected from 1310 (70%) women: 755 (58%) by telephone questionnaire, 279 (21%) by postal questionnaire, 170 (13%) by questionnaire administered at the time of the follow-up clinic attendance, 53 (4%) by web-based questionnaire and 53 (4%) by text messaging. Satisfaction and experiences of care scales were completed by 1175 and 1173 women, respectively, while IES and HADS were completed by 773 and 775 women respectively. Acceptability data at 3 months post abortion were available from 436 women, mostly (n = 383) from postal questionnaires. However, only 403 (21%) responses were collected between 60 and 120 days.

TABLE 8 *Reasons for withdrawal from trial*

Reason for withdrawal	RS	RM	PS	PM	Total (number of women)
Withdrew consent to data use	0	0	0	1	1
Withdrew consent to study continuation	1	1	7	9	18
Adverse event	0	0	1	0	1
>15 weeks' gestation on day of TOP	0	0	1	0	1
Extrauterine pregnancy	0	0	1	0	1
Method indicated	1	0	1	0	2
Miscarried prior to any intervention	0	0	3	3	6
Total	2	1	14	13	30

Recruitment

Two research nurses and a midwife were responsible for recruitment during the trial. *Table 9* shows that there was little difference in their recruitment rates to the preference and randomised arms of the trial. However, there were some differences between the health professionals who undertook the initial clinical assessment and introduced the research nurse (*Table 10*). Nurse practitioner 1 had a higher proportion of randomised women than nurse practitioners 2 and 3.

Recruitment rates before and after the change in recruitment strategy are shown in *Table 11*. Although recruitment to the randomised arm increased slightly after 7 August 2006, this increase was not statistically significant. The slightly higher rate was not sufficient to recruit the planned numbers to the randomised arm of the trial.

Stated reason(s) for choice of method in preference arm

A total of 1516 (99%) women in the preference arm gave a reason for their preference. Of these, 232 (15%) stated two reasons. Reasons were grouped into seven broad categories (*Table 12*). The most frequently cited reason related to awareness during the procedure; 479 (32%) women who preferred MTOP wanted to be awake/avoid a general anaesthetic, while 213 (14%) who preferred STOP wanted to be asleep. A desire not to pass and see the fetus was the principal reason in a further 114 (8%) of women who preferred STOP. Prior personal experience of TOP or miscarriage/labour was the primary reason stated by 161 (11%) of women, with almost half preferring STOP. Temporal reasons were reported by 240 (16%) women, with those who wanted the minimum number of visits/length of stay predominantly choosing STOP, while a shorter time to MTOP was important for some women. Of the remaining reasons, 156 (10%) related to one procedure (mostly MTOP) being perceived as 'easier', 'less traumatic' or being associated with fewer complications/side effects.

Baseline comparisons

Table 13 shows comparisons of the baseline characteristics of women who chose each allocation method. There were small but statistically significant differences between the three groups on a number of these variables. *Figures 2 and 3* illustrate the distribution of mother's age and gestational age at recruitment in the preference groups, and between randomised and preference groups. There was a statistically significant difference in the mean mothers' ages in the three groups; while there was no difference between the preference arms, mean age was higher in the preference arms compared with the randomised arms by 1.2 years. Within the preference arms, the mean gestational age at recruitment (as determined by ultrasound) was 6 days longer for those women choosing STOP over MTOP. There was no significant difference in mean gestational age between the randomised and preference arms.

There was no significant difference in the proportion of women having a previous TOP between the three groups. Previous live-birth status was not recorded in 330 women. Further analysis indicated that this related to one nurse practitioner who had assumed leaving the field blank was the same as recording no prior live

TABLE 9 *Recruitment rates: research nurses*

Research nurse/midwife	*n*	Preference (%)	Randomised (%)
1	1085	81.9	18.1
2	465	80.7	19.4
3	327	80.7	19.3
Total	1877	81.4	18.6

TABLE 10 *Recruitment rates: nurse practitioners and other health professionals*

Health professional	*n*	Preference (%)	Randomised (%)
NP1	814	78.5	21.5
NP2	502	82.7	17.3
NP3	366	85.2	14.8
Others[a]	195	83.0	16.9
Total	1,877	82.4	17.6

NP, nurse practitioner.
a Refers to one nurse practitioner who started late in the trial and two doctors who undertook a small number of clinics because of organisational needs.

TABLE 11 *Recruitment rates before and after strategy change*

	n	Preference (%)	Randomised (%)
Before	634	82.5	17.5
After	1243	80.9	19.2
Total	1877	81.4	18.6

birth. It was therefore assumed that these women had no previous live births. The percentage of women who had had previous live births did not differ significantly between the randomised and preference arms. However, in the preference arms there were a higher proportion of women (6%) in the surgical group who had had one or more previous live births.

The percentage of women who smoked did not differ significantly between the preference and randomised arms. However, there were more (7%) smokers in the surgical group of the preference arm than the medical group. There was little difference in educational attainment between the preference and randomised arms of the trial, but within the preference arms 7% more women were only educated up to GCSE level in the surgical group compared with the medical group.

The primary outcome (acceptability at 2 weeks after termination) was available on 74% of women who entered the trial. A further analysis was undertaken to determine whether those women who provided data on the primary outcome were typical of all women who had entered the trial. *Table 14* shows the results of comparing baseline characteristics for those providing and not providing primary outcome data. It can be seen that any differences are small, the only statistically significant difference being that those on whom the primary outcome was available smoked slightly less.

Primary outcome: acceptability

Two weeks after termination

The results of the crude and unadjusted comparisons of acceptability between trial arms are shown in *Table 15*. There was a clear difference in

TABLE 12 *Stated reason(s) for preferred method of termination*

Category	Stated reason for preference	Reason 1	Reason 2	Medical	Surgical
Procedural	Fear of general anaesthesia/desire to be awake	479	0	479	0
	Desire to be asleep	213	1	1	213
	Fear of needles	15	11	22	4
	Dislike of taking tablets	14	7	0	21
	MTOP more 'natural'	17	12	29	0
Fetus	Desire not to see/pass fetus	114	5	0	119
Experience	Personal experience (of TOP or miscarriage/labour)	161	6	86	81
	Other people's experience	40	21	31	30
Time/stay	Minimum time in hospital	89	28	33	84
	Minimum visits to hospital	87	10	6	91
	Time to wait for procedure	64	14	56	22
Perceived 'ease'/risk	'Easier'/'better' emotionally or psychologically	76	38	74	40
	Fewer side effects/risks/complications	36	35	50	21
	Less violent/'barbaric'/'traumatic'	44	20	51	13
Pain	Less painful	33	10	5	38
Other	Gestation	20	9	20	9
	Contraception (wanted IUCD/implant)	8	1	0	9
	Other (e.g. confidentiality)	6	4	8	2
Total		1516	232		

IUCD, intrauterine contraceptive device.

TABLE 13 *Comparison of baseline characteristics of women who chose each TOP allocation method*

	Preference		Randomised	
	Medical (n = 786)	Surgical (n = 657)	(n = 328)	p-value[a]
Mean age (years)	24.3 (SD 6.3)	24.9 (SD 6.2)	23.3 (SD 5.7)	0.001
Mean gestational age (days)	57.4 (SD 12.6)	62.8 (SD 13.5)	59.7 (SD 13.0)	< 0.001
No previous TOP[b] (%)	77	75	79	0.35
No previous live birth[c] (%)	75	68	72	0.04
Smoke[d] (%)	39	47	41	0.02
Alcohol[d] (%)	74	72	73	0.53
Drug use[d] (%)	4	4	2	0.06
Education up to GCSE level[d] (%)	52	58	56	0.04
Support at home[d] (%)	31	30	26	0.21
Chlamydia				0.51
Negative (%)	73	76	72	
Positive (%)	5	5	5	
Unknown (%)	22	19	23	

GCSE, General Certificate of Secondary Education; SD, standard deviation.
a p-values from ANOVA or chi-squared tests.
b n = 65 unrecorded observations.
c n = 330 unrecorded observations assumed to be no previous live birth.
d n = 9–18 unrecorded observations for these variables.

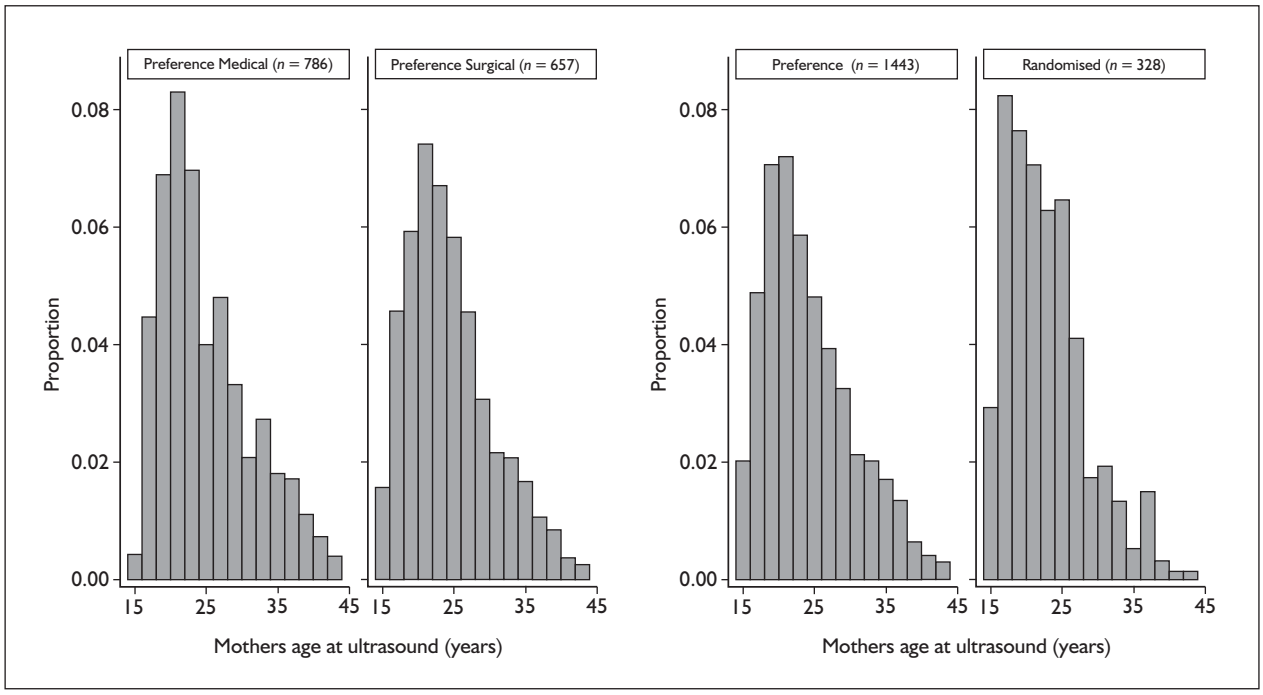

FIGURE 2 *Distribution of mothers' ages (compared within preference arms and between combined preference and randomised arms).*

acceptability between STOP and MTOP: women in the surgical arms were more likely to opt to have the same method again compared with those having a medical termination (either within the preference or randomised arms). Women in the preference arms were slightly more likely to regard their TOP method as acceptable compared with randomised women.

For women in the preference arms the interaction between past TOP and preference arm was not statistically significant. There was a significant interaction between gestation and preference arm. This is illustrated in *Figure 4a* which shows the smoothed proportions in the two arms by gestational age. The difference in acceptability between preference arms increased with gestation, so the model estimated these differences at three different gestational ages, assuming a linear trend in gestation. However, for the comparisons of randomised arms, and the comparison of preference to randomised arms, there was no

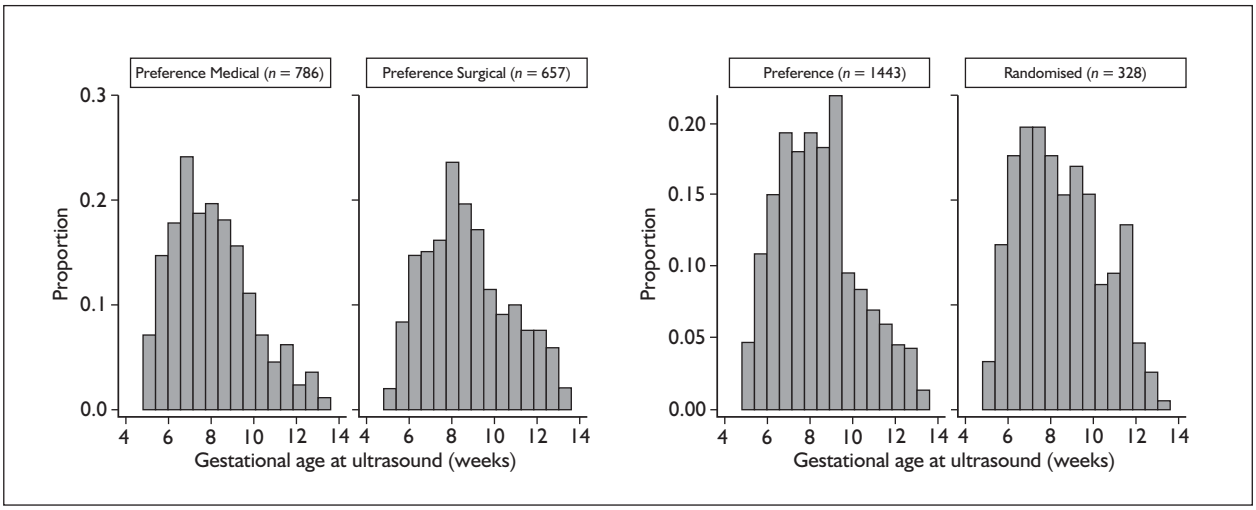

FIGURE 3 *Distribution of gestational ages (at ultrasound compared within preference arms and between combined preference and randomised arms).*

TABLE 14 *Comparison of baseline characteristics of women for whom outcome was available or missing*

	Primary outcome		
	Available (*n* = 1310)	**Missing (*n* = 461)**	***p*-value[a]**
Mean age (years)	24.5 (SD 6.2)	24.0 (SD 6.1)	0.11
Mean gestational age (days)	59.5 (SD 13.2)	60.7 (SD 13.2)	0.09
No previous TOP[b] (%)	77	75	0.35
No previous live birth[c] (%)	72	72	0.87
Smoke[d] (%)	41	47	0.02
Alcohol[d] (%)	73	75	0.45
Drug use[d] (%)	3	5	0.22
Education up to GCSE level[d] (%)	54	59	0.08
Support at home[d] (%)	29	31	0.4

GCSE, General Certificate of Secondary Education; SD, standard deviation.
a *p*-values from *t*-tests or chi-squared tests.
b *n* = 65 unrecorded observations.
c *n* = 330 unrecorded observations assumed to be no previous live birth.
d *n* = 9–18 unrecorded observations for these variables.

statistically significant interaction between trial arm and gestation (*Figure 4b*). The difference in acceptability was, therefore, estimated across all gestational ages.

Three months after termination

The crude and unadjusted comparisons of acceptability between trial arms at 3 months are shown in *Table 16*. The interactions between past TOP and trial arm, and between trial arm and gestational age were not statistically significant. Therefore, all comparisons were made across all gestations. There was still a clear difference in acceptability between STOP and MTOP at 3 months after the procedure; women in the surgical arms were more likely to opt to have the same method again (either within preference or within randomised arms). Women in the preference arms were slightly more likely to regard their TOP method as acceptable, but this difference was not statistically significant.

TABLE 15 *Acceptability of procedure at 2 weeks after termination (i.e. percentage that would opt for same method again)*

PS (*n* = 488)	96.5%	Crude difference 15.7% (95% CI 12.0 to 19.2)
PM (*n* = 565)	80.9%	Adjusted difference[a] Overall 15.9% (95% CI 12.2 to 19.6) At 6 weeks 9.8% (95% CI 4.2 to 15.4) At 9 weeks 17.6% (95% CI 13.4 to 21.8) At 12 weeks 25.4% (95% CI 16.6 to 34.1)
RS (*n* = 134)	94.0%	Crude difference 24.9% (95% CI 15.8 to 34.9)
RM (*n* = 123)	69.1%	
Preference combined (*n* = 1052)	88.1%	Crude difference 6.0% (95% CI 0.9 to 11.1)
Randomised combined (*n* = 257)	82.1%	Adjusted difference 8.2% (95% CI 2.9 to 13.4)

a Adjusted differences are estimated from a binary regression model adjusting for key baseline factors.

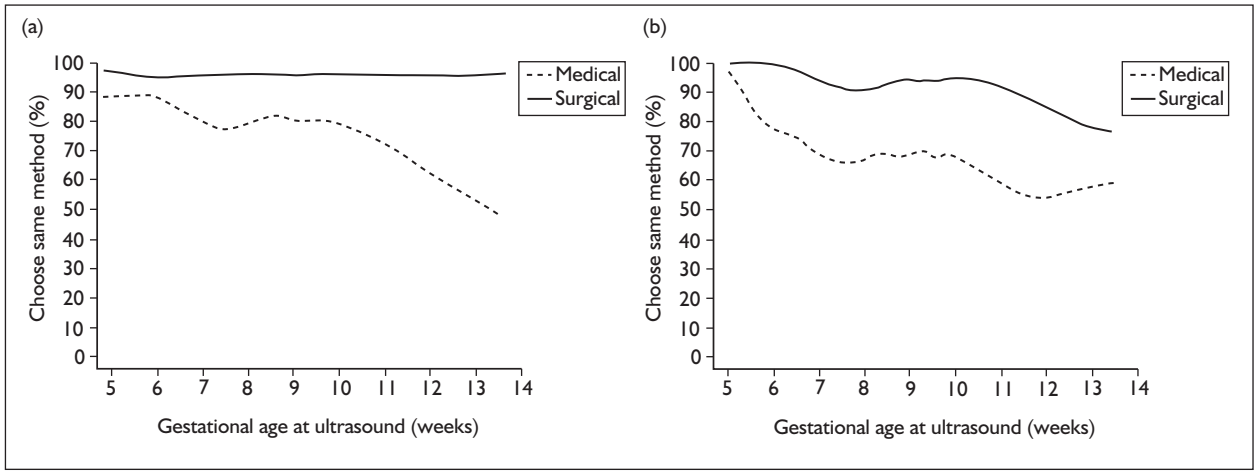

FIGURE 4 *Acceptability by gestation at 2 weeks post termination: (a) comparing preference arms; and (b) comparing randomised arms.*

Comparisons between results at 2 weeks and 3 months after termination

Characteristics of those who provided information

Far fewer women provided timely information on acceptability at 3 months post termination compared with that at 2 weeks. The subgroup of women who responded at 2 weeks was considered and split into those who did and did not respond at 3 months. It was found that those women who failed to respond at 3 months tended to be slightly younger (mean age 24.2 versus 25.1; $p = 0.03$) and less well educated [57% versus 46% educated to General Certificate of Secondary Education (GSCE) or less; $p < 0.001$). There was no significant difference between responders and non-responders on gestational age and numbers of previous terminations.

Changes in acceptability between 2 weeks and 3 months

There were only 382 women for whom timely information on acceptability was available at both 2 weeks and 3 months after TOP. Only 7% of responses had changed over time, and these are shown in *Table 17*. Overall, the proportion willing to have the same method again had reduced from 87.3% to 85.1%, a difference of 2.2% (95% CI –0.6 to 4.9).

Willingness to pay

A total of 1389 (91%) women in the preference arm completed the WTP scenario (761 requesting MTOP and 628 requesting STOP); 397 (28.6%) recorded zero (zero WTP group), while 93.8% of respondents were willing to pay up to £1000. There was no statistically significant difference in the mean WTP between women with a preference for MTOP compared to those with a preference for STOP whether or not zero payers were included (*Table 18*).

A total of 132 (37.5%) women in the randomised group completed the WTP scenario at 2 weeks, although 19 failed to state their choice of TOP method; 59 women (45.0%) recorded zero (zero WTP group), while 97.7% of respondents were willing to pay up to £1000. There was no

TABLE 16 *Acceptability of procedure at 3 months after termination (i.e. percentage that would opt for same method again)*

PS ($n = 135$)	95.6%	Crude difference 16.6% (95% CI 9.8 to 23.4)
PM ($n = 190$)	79.0%	Adjusted difference[a] 14.7% (95% CI 8.6 to 20.8)
RS ($n = 42$)	95.2%	Crude difference 25.8% (95% CI 9.4 to 42.2)
RM ($n = 36$)	69.4%	
Preference combined ($n = 325$)	85.9%	Crude difference 2.5% (95% CI –6.6 to 11.6)
Randomised combined ($n = 78$)	83.3%	Adjusted difference[a] 2.8% (95% CI –6.2 to 11.8)

a Adjusted differences are estimated from a binary regression model adjusting for key baseline factors.

TABLE 17a *Comparison between acceptability at 2 weeks and 3 months after termination: all arms combined*

	3 months: yes	3 months: no
2 weeks: yes	318	19
2 weeks: no	7	38

TABLE 17b *Comparison between acceptability at 2 weeks and 3 months after termination: separately by trial arm*

	PM		PS		RM		RS	
	3 months: yes	3 months: no	3 months: yes	3 months: no	3 months: yes	3 months: no	3 months: yes	3 months: no
2 weeks: yes	136	13	122	2	23	3	37	1
2 weeks: no	4	26	2	4	1	7	0	1

statistically significant difference in the mean WTP between women with a future preference for MTOP compared to those with a future preference for STOP whether or not zero payers were included (*Table 19*).

Table 20 shows the mean WTP for a future TOP according to method of TOP to which women were randomised. Again there were no statistically significant differences between the groups. However, it is worth noting that WTP for switching choice of TOP method was consistently greater than the amount women were willing to pay to have the same method again; the differences for women randomised to MTOP were of borderline statistical significance.

A total of 549 (35.9%) women in the preference group completed the WTP scenario at 2 weeks (300 from the preference MTOP group and 249 from the preference STOP group), although 31 failed to state their choice of TOP method; 140 women (25.5%) recorded zero (zero WTP group), while 96.7% of respondents were willing to pay up to £1000. There was no difference in the mean WTP between women with a future preference for MTOP compared to those with a future preference for STOP whether or not zero payers were included (*Table 21*).

Table 22 shows the mean WTP for a future TOP according to the method of original preference. There were no statistically significant differences between the groups. As in the randomised group, WTP for switching choice was greater than the amount women were willing to pay to have the same TOP method again.

TABLE 18 *Mean WTP for requested TOP method in preference group*

	Medical	Surgical	*p*-value	95% CI for mean difference
Including zero payers				
n	761	628		
Mean WTP (£)	372.70 (SD 778.61)	431.85 (SD 855.23)	0.51	–113.12 to 55.96
Excluding zero payers				
n	538	454		
Mean WTP (£)	527.18 (SD 881.13)	597.36 (SD 955.65)	0.23	–184.72 to 44.38

SD, standard deviation.

TABLE 19 *Mean WTP for a future TOP method in randomised group*

	Medical	Surgical	*p*-value	95% CI for mean difference
Including zero payers				
n	49	73		
Mean WTP (£)	192.86 (SD 248.23)	215.55 (SD 616.17)	0.81	–206.41 to 161.03
Excluding zero payers				
n	32	35		
Mean WTP (£)	295.31 (SD 253.33)	449.57 (SD 834.09)	0.32	–461.07 to 152.55

SD, standard deviation.

TABLE 20 *Mean WTP for a future TOP according to original randomised group*

Method of termination	Mean WTP (£) for future TOP preference		*p*-value	95% CI for mean difference
Including zero payers				
Medical	Medical (*n* = 42) 179.76 (SD 197.42)	Surgical (*n* = 19) 482.63 (SD 1127.83)	0.09	–659.33 to 53.59
Surgical	Medical (*n* = 7) 271.43 (SD 467.13)	Surgical (*n* = 54) 121.57 (SD 221.82)	0.15	–57.27 to 356.97
Excluding zero payers				
Medical	Medical (*n* = 28) 269.64 (SD 184.52)	Surgical (*n* = 12) 764.17 (SD 1358.96)	0.06	–1016.65 to 27.61
Surgical	Medical (*n* = 4) 475.00 (SD 554.53)	Surgical (*n* = 54) 285.43 (SD 263.90)	0.28	–160.04 to 539.17

SD, standard deviation.

TABLE 21 *Mean WTP for future TOP method in preference group*

	Medical	Surgical	*p*-value	95% CI for mean difference
Including zero payers				
n	227	291		
Mean WTP (£)	328.90 (SD 409.37)	357.47 (SD 538.12)	0.51	–113.12 to 55.97
Excluding zero payers				
n	177	211		
Mean WTP (£)	421.81 (SD 419.26)	493.01 (SD 576.85)	0.17	–173.62 to 31.22

SD, standard deviation.

TABLE 22 *Mean WTP for a future TOP method according to original preference group*

Method of termination	Mean WTP (£) for future TOP preference		*p*-value	95% CI for mean difference
Including zero payers				
Medical	Medical (*n* = 225) 321.16 (SD 408.56)	Surgical (*n* = 65) 408.56 (SD 474.16)	0.15	–31.44 to 203.60
Surgical	Medical (*n* = 2) 750.00 (SD 353.55)	Surgical (*n* = 54) 391.53 (SD 551.42)	0.36	–412.25 to 1129.19
Excluding zero payers				
Medical	Medical (*n* = 175) 418.06 (SD 419.32)	Surgical (*n* = 33) 470.91 (SD 580.58)	0.53	–220.55, 114.85
Surgical	Medical (*n* = 2) 750.00 (SD 353.55)	Surgical (*n* = 178) 497.11 (SD 577.71)	0.54	–556.33, 1062.11

SD, standard deviation.

Mean WTP for a future TOP was £341.80 [standard deviation (SD) 478.35] in the preference arm ($n = 549$) compared with £225.84 (SD 546.90) in the randomised arm ($n = 131$). This difference was statistically significant (mean £115.96; 95% CI 21.99 to 209.940; $p = 0.016$). *Table 23* compares mean WTP for future TOP according to preferred method in the two trial arms. Women in the preference arm showed a consistently higher WTP for their choice of next TOP: for women preferring a future MTOP, those in the preference arm were prepared to pay an extra £136.04 (95% CI 16.33 to 255.75; $p = 0.026$); for women preferring a future STOP, those in the preference arm were prepared to pay an extra £141.93 (95% CI –0.82 to 284.67; $p = 0.051$).

Table 24 shows the mean WTP in each income band in the two arms of the trial. In both arms there were statistically significant differences between mean WTP in the different income groups [$p < 0.0001$ analysis of variance (ANOVA)]. There was a correlation between WTP and income in the preference arm (correlation coefficient 0.194, $p < 0.0001$) but not in the randomised arm.

Psychological rating scales at 2 weeks and 3 months after admission

The differences in the mean scores on the psychological rating scales between pairs of trial arms are shown in *Table 25*. Differences between groups were consistently small. The only statistically significant differences at either time point were a higher score in the IES intrusion subscale at 2 weeks after MTOP compared with STOP in both preference and randomised comparisons. At 3 months after termination, both avoidance and intrusion subscales of the IES were higher in the medical compared with the surgical arm in those women who had been randomised. These comparisons were not statistically significant in the preference arms.

TABLE 23 *Mean WTP for future TOP method according to preferred method (in preference and randomised arms)*

Future preferred TOP method	Trial arm	*n*	Mean WTP (£)
Medical	Preference	227	328.90 (SD 409.36)
	Randomised	49	192.86 (SD 248.23)
Surgical	Preference	291	357.47 (SD 538.12)
	Randomised	73	215.55 (SD 616.17)

SD, standard deviation.

TABLE 24 *Relationship between stated income and WTP for future TOP method*

Stated income	*n*	Mean (£)
Preference arm		
£0	150	248.80 (SD 380.30)
< £10,000	206	301.94 (SD 362.82)
£10,000–£19,999	136	467.94 (SD 671.34)
£20,000–£30,000	43	347.44 (SD 370.00)
> £30,000	14	682.14 (SD 610.68)
Total	549	341.80 (SD 478.34)
Randomised arm		
£0	41	124.39 (222.39)
< £10,000	35	318.28 (550.74)
£10,000–£19,999	29	137.93 (175.66)
£20,000–£30,000	15	181.67 (340.23)
> £30,000	5	1240.00 (2110.21)
Total	125	233.32 (558.64)

SD, standard deviation.

Satisfaction with care

This was reported on a 5-point scale (excellent to poor) and is summarised as the proportion of women who rated aspects of their care as excellent. *Table 26* shows the comparisons of these percentages across trial arms. Women were more likely to be satisfied overall and with technical and interpersonal aspects of care if they had a surgical rather than medical termination. This was found in comparisons within preference arms and within randomised arms. There was no difference in satisfaction with waiting when comparing both within preference arms and randomised arms. None of the differences in satisfaction with care between combined preference and randomised arms were statistically significant.

Experience of care: semantic differential scales

Women rated their experience on 12 different scales defined by pairs of opposite adjectives. Scores could vary between –3 (most 'negative') to +3 (most 'positive'). The distribution of these scores is compared between the two preference arms at 2 weeks after termination in *Figure 5*. The distributions were similar shapes in both arms for some scales (e.g. predominantly positive scores for 'Dangerous–Safe' indicating that most women found both procedures very safe), but quite different for other scales, e.g. Painful–Painless scores were predominantly negative ('painful') for women in the medical arm and predominantly positive ('painless') in the surgical arm.

Table 27 summarises these distributions by reporting the median scores for each pair of trial arms compared at 2 weeks. There was a significant difference in the distribution of scores between the two preference arms on all scales, and for all but one scale when the randomised arms were compared. In all cases, the experience of care had more responses towards the negative end of the scale in the medical compared with the surgical arms. No significant differences were found between the combined preference and randomised arms.

The information at 2 weeks after TOP was sought via postal questionnaires, clinic visits, telephone calls and online completion. Approximately half of the women provided information over the telephone and in these cases only six of the scales were used: these are the scales with the larger sample size. However, the nurses collecting information over the telephone found that women quite often requested clarification of the meaning of the 'Passive–Active' scale. For this semantic differential scale the distribution of responses was quite different (*Figure 6*) for women where responses were obtained by telephone compared with other routes. This was not the case for other scales. These results must, therefore, be interpreted with considerable caution, as they suggest that some women used the scale differently if they had the chance to clarify issues with researchers.

Table 28 compares the median semantic differential scores for the two preference arms at 3 months after termination. Although far fewer completed the questionnaire at this time point, the patterns are similar to those at 2 weeks. Those experiencing a surgical termination rated their experience of care more highly than those having a medical termination on all scales.

There was some interest in how the experience of care scores had changed between 2 weeks and 3 months for those women who had responded on both occasions. The distributions of the differences are shown in *Figure 7*. A positive difference indicates that the experience was less 'positive' at 3 months than at 2 weeks. It can be seen that while many women gave the same or very similar scores on the two occasions, others changed their scores

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TABLE 25a *Comparison of mean scores on psychological rating scales between trial arms: 2 weeks after termination*

Psychological rating scale	Preference					Randomised				Preference vs randomised		
	Medical[a]	Surgical[b]		Difference	95% CI	Medical[c]	Surgical[d]	Crude difference	Crude 95% CI		P–R	95% CI
IES avoidance	16.6	17.4	Crude	–0.9	–2.5 to 0.7	16.9	15.3	1.5	–1.7 to 4.8	Crude	0.9	–0.9 to 2.7
			Adjusted	–0.2	–2.1 to 1.7					Adjusted	1.1	–0.9 to 3.2
IES intrusive	15.1	13.4	Crude	1.6	0.0 to 3.2	16.2	12.0	4.2[e]	0.9 to 7.5	Crude	0.2	–1.6 to 2.1
			Adjusted	2.7[e]	0.8 to 4.6					Adjusted	0.5	–1.6 to 2.6
IES total	31.6	30.9	Crude	0.8	–2.1 to 3.7	33.0	27.3	5.7	–0.2 to 11.6	Crude	1.1	–2.2 to 4.4
			Adjusted	2.5	–0.9 to 5.9					Adjusted	1.6	–2.1 to 5.3
HAD depression	4.4	4.5	Crude	–0.1	–0.7 to 0.4	4.5	4.5	0.1	–1.3 to 1.4	Crude	–0.1	–0.7 to 0.6
			Adjusted	0.0	–0.7 to 0.7					Adjusted	0.2	–0.5 to 1.0
HAD anxiety	6.2	6.5	Crude	–0.3	–1.0 to 0.4	7.0	5.9	1.1	–0.5 to 2.6	Crude	–0.1	–0.9 to 0.8
			Adjusted	0.0	–0.9 to 0.8					Adjusted	0.4	–0.5 to 1.3

a IES $n = 318$, HAD $n = 325$.
b IES $n = 276$, HAD $n = 281$.
c IES $n = 71$, HAD $n = 72$.
d IES $n = 71$, HAD $n = 71$.
e Difference statistically significant at the 5% level.

TABLE 25b *Comparison of mean scores on psychological rating scales between trial arms: 3 months after termination*

Psychological rating scale	Preference					Randomised				Preference vs randomised		
	Medical[a]	Surgical[b]		Difference	95% CI	Medical[c]	Surgical[d]	Crude difference	Crude 95% CI		P–R	95% CI
IES avoidance	13.8	15.4	Crude	–1.6	–4.0 to 0.8	18.1	12.7	5.5[e]	0.5 to 10.5	Crude	–0.8	–3.6 to 1.9
			Adjusted	–1.3	–4.2 to 1.6					Adjusted	0.2	–2.9 to 3.3
IES intrusive	11.8	11.0	Crude	0.8	–1.3 to 2.9	14.5	9.8	4.7[e]	0.6 to 8.9	Crude	–0.6	–2.9 to 1.8
			Adjusted	2.3	–0.2 to 4.8					Adjusted	0.8	–1.8 to 3.5
IES TOTAL	25.5	26.3	Crude	–0.8	–4.8 to 3.2	32.6	22.4	10.2[e]	1.9 to 18.5	Crude	–1.4	–5.9 to 3.1
			Adjusted	1.0	–3.8 to 5.7					Adjusted	1.0	–4.1 to 6.1
HAD depression	3.3	3.8	Crude	–0.5	–1.2 to 0.2	4.1	3.0	1.1	–0.5 to 2.6	Crude	–0.1	–0.9 to 0.7
			Adjusted	–0.1	–1.0 to 0.8					Adjusted	0.0	–0.9 to 0.9
HAD anxiety	5.9	6.0	Crude	–0.1	–1.1 to 0.9	7.0	5.2	1.8	–0.3 to 4.0	Crude	–0.1	–1.2 to 1.1
			Adjusted	0.2	–1.0 to 1.4					Adjusted	0.2	–1.1 to 1.5

a IES $n = 184$, HAD $n = 183$.
b IES $n = 128$, HAD $n = 127$.
c IES $n = 35$, HAD $n = 35$.
d IES $n = 39$, HAD $n = 40$.
e Difference statistically significant at the 5% level.

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TABLE 26a *Comparison of satisfaction scores between trial arms (percentage rating aspects of care as excellent): 2 weeks after termination*

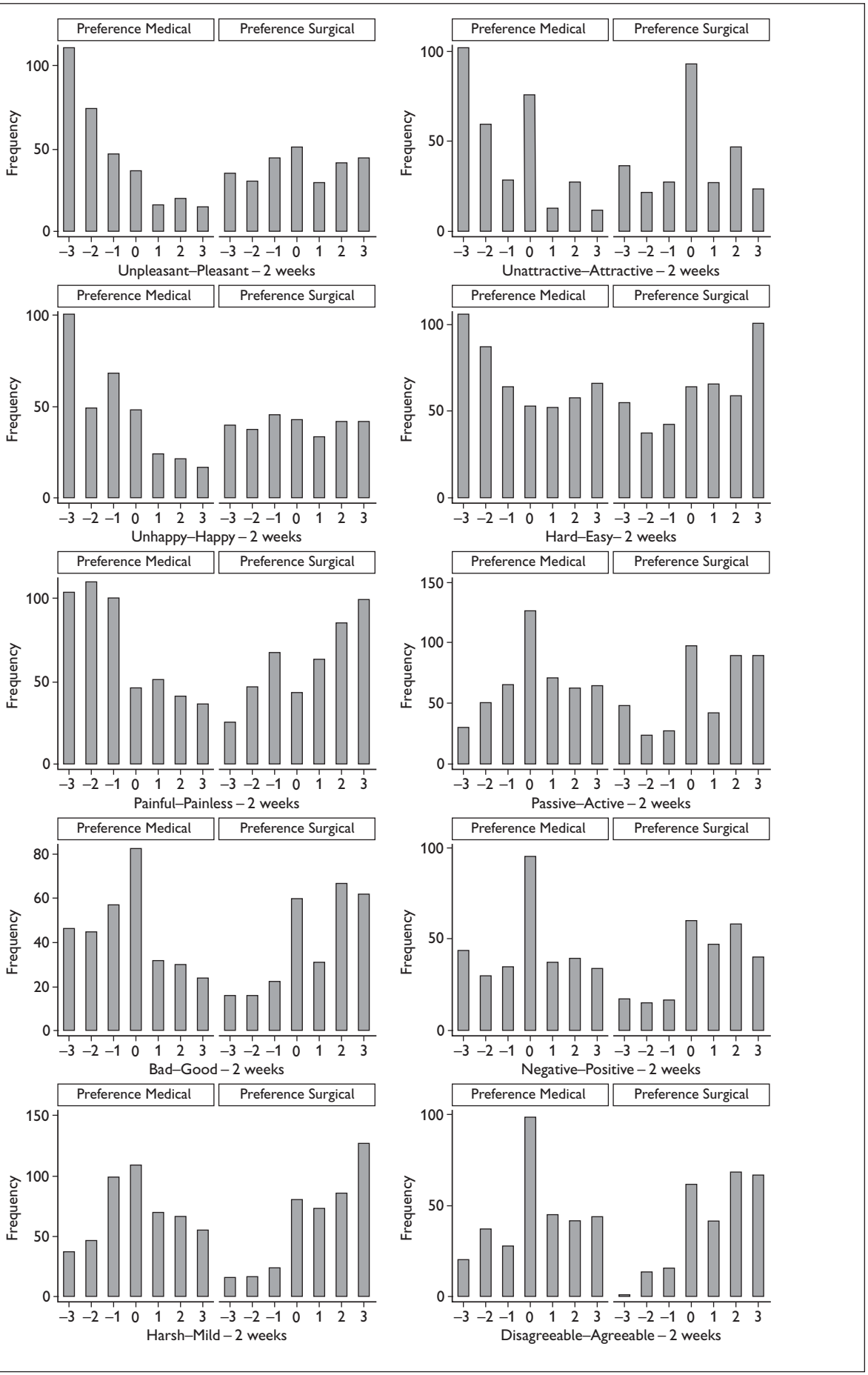
	Preference					Randomised				Preference vs randomised		
Satisfaction scores	**Medical (*n* = 492)**	**Surgical (*n* = 429)**		**Difference**	**95% CI**	**Medical (*n* = 112)**	**Surgical (*n* = 113)**	**Crude difference**	**Crude 95% CI**		**P–R**	**95% CI**
Overall	40.2	60.8	Crude	–20.7[a]	–27.0 to –14.3	43.8	61.1	–17.3[a]	–30.2 to –4.5	Crude	–2.7	–9.9 to 4.6
			Adjusted	–21.3[a]	–27.8 to –14.8					Adjusted	–2.7	–10.0 to 4.7
Technical	47.2	60.8	Crude	–13.7[a]	–20.1 to –7.3	51.8	62.8	–11.0	–23.9 to 1.8	Crude	–3.8	–11.0 to 3.4
			Adjusted	–13.7[a]	–20.2 to –7.1					Adjusted	–6.0	–12.9 to 1.7
Interpersonal	52.6	67.6	Crude	–15.0[a]	–21.2 to –8.7	62.5	69.9	–7.4	–19.7 to 4.9	Crude	–6.6	–13.6 to 0.3
			Adjusted	–15.1[a]	–21.5 to –8.7					Adjusted	–8.2[a]	–15.2 to –1.2
Waiting	36.4	35.5	Crude	0.9	–5.3 to 7.1	32.1	34.5	–2.4	–14.7 to 10.0	Crude	2.6	–4.3 to 9.5
			Adjusted	–0.3	–6.6 to 7.0					Adjusted	1.7	–5.3 to 8.6

a Difference statistically significant at the 5% level.

TABLE 26b *Comparison of satisfaction scores between trial arms (percentage rating aspects of care as excellent): 3 months after termination*

	Preference					Randomised				Preference vs randomised		
Satisfaction scores	**Medical (*n* = 192)**	**Surgical (*n* = 132)**		**Difference**	**95% CI**	**Medical (*n* = 36)**	**Surgical (*n* = 42)**	**Crude difference**	**Crude 95% CI**		**P–R**	**95% CI**
Overall	27.1	50.0	Crude	–22.9[a]	–33.5 to –12.3	25.0	50.0	–25.0[a]	–45.7 to –4.3	Crude	–2.0	–14.0 to 10.0
			Adjusted	–23.4[a]	–34.0 to –12.9					Adjusted	–0.3	–12.1 to 11.6
Technical	31.7	56.1	Crude	–25.3[a]	–36.0 to –14.6	41.7	47.6	–6.0	–28.0 to 16.1	Crude	–3.8	–16.1 to 8.4
			Adjusted	–25.6[a]	–36.4 to –14.8					Adjusted	–3.5	–15.8 to 9.0
Interpersonal	41.2	58.3	Crude	–17.2[a]	–28.1 to –6.3	41.7	66.7	–25.0[a]	–46.5 to –3.5	Crude	–7.0	–19.3 to 5.3
			Adjusted	–17.4[a]	–28.5 to –6.4					Adjusted	–7.7	–20.1 to 4.7
Waiting	35.4	32.8	Crude	3.0	–7.9 to 13.1	25.0	35.7	–10.7	–31.0 to 9.5	Crude	3.6	–7.9 to 15.1
			Adjusted	0.2	–10.5 to 10.8					Adjusted	3.5	–8.0 to 14.9

a Difference statistically significant at the 5% level.


Preference Medical
Preference Surgical
Frequency
Unpleasant–Pleasant – 2 weeks
Unattractive–Attractive – 2 weeks
Unhappy–Happy – 2 weeks
Hard–Easy– 2 weeks
Painful–Painless – 2 weeks
Passive–Active – 2 weeks
Bad–Good – 2 weeks
Negative–Positive – 2 weeks
Harsh–Mild – 2 weeks
Disagreeable–Agreeable – 2 weeks

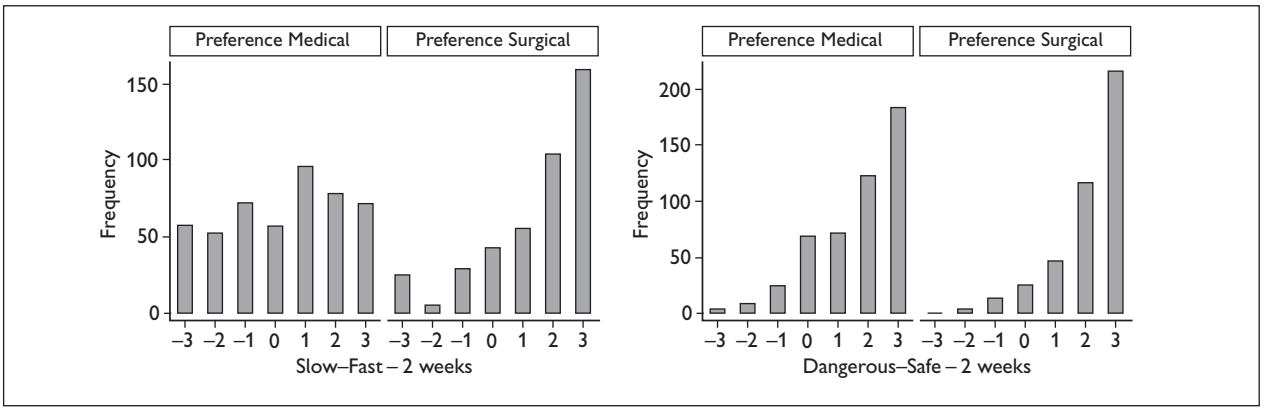


FIGURE 5 *Comparison of semantic differential score distributions (between preference arms at 2 weeks).*

considerably (in both directions). One scale which had fewer women reporting the same score on both occasions was 'Passive–Active'; this may be due to the fact that data were collected by telephone on 49% of women at 2 weeks, but on only 1% at 3 months, and the distribution of responses varied with the data collection method.

Symptoms during admission and 2 weeks after termination

Women were questioned about symptoms and pain they experienced during admission, and then again at 2 weeks after the procedure. The results are shown in *Table 29*. During admission, in the preference arms, there was a statistically significant difference for all symptoms, with a higher percentage of women reporting symptoms and higher mean pain scores during MTOP than STOP. The differences were largest for nausea, vomiting and pain. The same differences were seen in the randomised arm with the exception of dizziness (where only one woman reported this symptom in the medical group). There were no significant differences in symptoms between the preference and randomised arms during admission.

At the 2-week follow-up the only significant difference between the preference arms was the percentage of women reporting diarrhoea, which was again higher in the MTOP group. In the randomised arms more women reported nausea and diarrhoea after medical termination. There were no significant differences between the two combined arms (preference and randomised) at 2-week follow-up.

Table 30 shows the amount of bleeding experienced after discharge as reported at the 2-week follow-up. Compared with STOP, women had more bleeding after a medical procedure in both the preference and randomised arms. The difference in the distribution of amount of bleeding in the preference arms is illustrated in *Figure 8*. There was no significant difference in the amount of bleeding between women in the randomised and preference arms.

Time taken to return to work and normal activity

There were 255 unemployed women who were not included in the analysis of time taken to return to work. *Table 31* shows that there were no differences in the distributions between groups undergoing medical and surgical termination in either the preference or the randomised arms. However, there was a significant difference between preference and randomised arms, with slightly more women returning to work immediately in the randomised arm (*Figure 9*).

Table 32 shows that the time taken to return to normal activity was very similar to time taken to return to work, with no significant differences in the distributions between medical and surgical groups in either arm. Again, the difference in distribution between the randomised and preference arms was statistically significant, with more women in the randomised arm reporting an immediate return to normal activity (*Figure 10*).

There were no differences in percentage of women returning to work and normal activity by 2 weeks

TABLE 27 *Comparison of median semantic differential scores between trial arms at 2 weeks (number of women in parentheses)*

	Preference			Randomised			Combined		
Semantic differential	**Medical**	**Surgical**	***p*-value[a]**	**Medical**	**Surgical**	***p*-value[a]**	**Preference**	**Random**	***p*-value[a]**
Unpleasant–Pleasant	–2 (320)	0 (274)	<0.001	–2 (72)	0 (68)	<0.001	–1 (594)	–1 (140)	0.66
Disagreeable–Attractive	–2 (317)	0 (272)	<0.001	–2 (71)	0 (67)	<0.001	0 (589)	0 (138)	0.96
Sad–Happy	–1 (324)	0 (278)	<0.001	–1 (72)	0 (72)	<0.001	–1 (602)	0 (144)	0.15
Hard–Easy	–1 (485)	1 (424)	<0.001	–1 (111)	1 (111)	<0.001	0 (909)	0 (222)	0.42
Painful–Painless	–1 (487)	1 (428)	<0.001	–1 (112)	1 (112)	<0.001	0 (915)	0 (224)	0.45
Passive–Active	0 (467)	1 (415)	<0.001	0 (108)	0 (107)	0.88	0 (882)	0 (215)	0.24
Bad–Good	0 (317)	1 (274)	<0.001	0 (72)	1 (69)	<0.001	0 (591)	0 (141)	0.83
Negative–Positive	0 (314)	1 (276)	<0.001	0 (72)	2 (67)	<0.001	0 (590)	1 (139)	0.85
Harsh–Mild	0 (482)	2 (420)	<0.001	0 (110)	1 (110)	<0.001	1 (902)	1 (220)	0.80
Disagreeable–Agreeable	0 (315)	2 (271)	<0.001	0 (72)	1 (69)	<0.001	1 (586)	0 (141)	0.24
Slow–Fast	1 (486)	2 (427)	<0.001	0 (111)	2 (111)	<0.001	1 (913)	1 (222)	0.57
Dangerous–Safe	2 (487)	3 (426)	<0.001	2 (110)	3 (111)	0.003	2 (913)	2 (221)	0.99

a *p*-value from Mann–Whitney test.

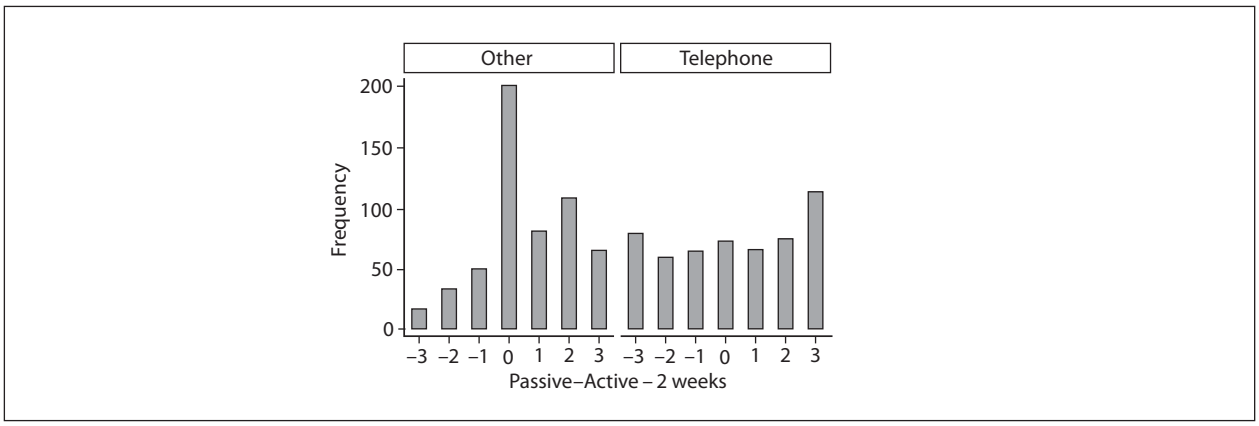


FIGURE 6 *Comparison of responses on the 'Passive–Active' scale (obtained over the telephone or by other routes).*

between medical and surgical groups in the preference arm, or between the preference and randomised arms (*Table 33*).

Clinical effectiveness

Unplanned or emergency admission

A total of 63 women had a procedure-related admission (*Table 34*). In 16 cases this was 'planned', i.e. anticipated, and in most cases this was because of a lack of support/supervision at home for the night after the TOP; 33 women had an unplanned admission on the day of the TOP. In most cases this was an overnight stay because of late passage of products of conception, symptoms or complications. Six women were readmitted as an emergency after their initial discharge, mostly because of RPC.

Table 35 shows a comparison of planned and unplanned admissions/overnight stays in the two arms of the trial. There were no differences in planned admissions between women undergoing MTOP and STOP. However, more women having an MTOP had an unplanned admission. This difference was statistically significant in both the randomised and preference arms.

Complications

All women who entered into the trial have been included in the reporting of complications. A total of 72 women experienced complications as a result of the termination, including one woman who was also categorised as a serious adverse event (SAE). Eleven of the women who experienced complications subsequently withdrew from the trial.

A breakdown of complications by trial arm is given in *Table 36*. In the preference group the percentage of women experiencing complications was 2.4% higher in the group undergoing MTOP. This pattern was also seen in the randomised arms, but the difference was not statistically significant.

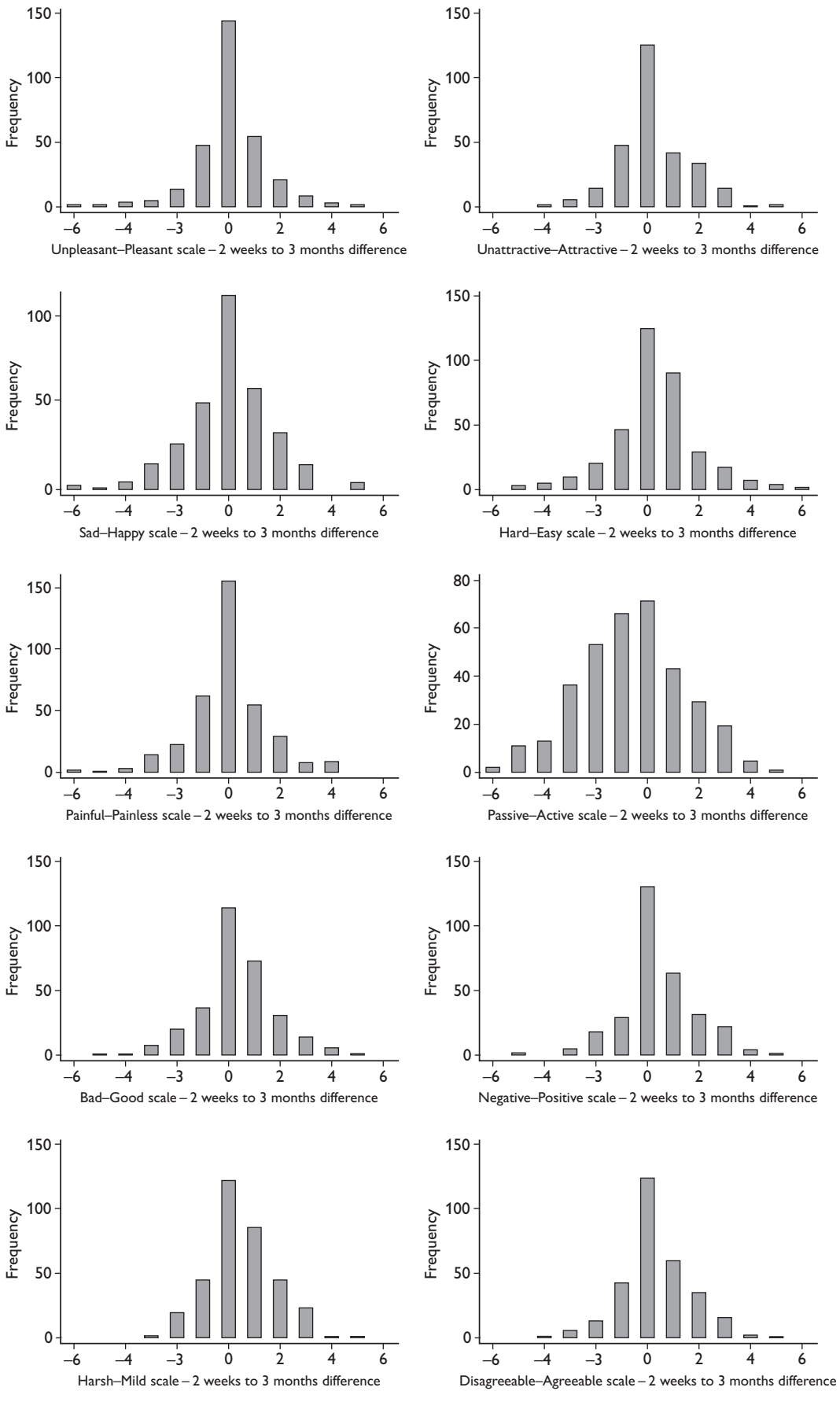
Table 37 provides a detailed list of complications. A total of 48 women had a clinical diagnosis of RPC, two associated with haemorrhage; 28 presented as an emergency after discharge from hospital (with vaginal bleeding with or without abdominal pain), four had RPC diagnosed at the 2-week outpatient review and 16 were kept in hospital overnight because of failure to pass 'complete' products. Of the 48 women with suspected RPC, 34 had an evacuation under general anaesthesia (26 in the emergency admission group and 8 in the overnight stay group), eight had products of conception removed from the cervix/vagina (with a subsequent scan suggesting no additional intrauterine products of conception), four were managed medically (with misoprostol) and two were managed expectantly. In those cases managed medically or expectantly an ultrasound scan subsequently showed no intrauterine products of conception.

Fifteen women experienced haemorrhage during their initial admission (including the SAE case), of whom four received a blood transfusion. Eleven women were suspected of intrauterine infection, five with evidence of RPC. All were admitted as an emergency with vaginal bleeding with or without abdominal pain. Two women had a failed MTOP; one had a subsequent STOP and the other had a subsequent successful MTOP. One woman had a failed STOP; products of conception were not identified at operation and a subsequent ultrasound scan showed a viable pregnancy. The

TABLE 28 *Comparison of median semantic differential scores between preference arms at 3 months*[a]

	Preference			Randomised			Combined		
Semantic differential	**Medical (*n* = 191)**	**Surgical (*n* = 132)**	***p*-value**[b]	**Medical (*n* = 36)**	**Surgical (*n* = 42)**	***p*-value**[b]	**Preference (*n* = 322)**	**Random (*n* = 78)**	***p*-value**[b]
Unpleasant–Pleasant	–2	0	< 0.001	–2	0	< 0.001	–1	–1	0.78
Disagreeable–Attractive	–1	0	< 0.001	–2	0	< 0.001	–1	–1	0.34
Sad–Happy	–1.5	0	< 0.001	–1.5	0	0.007	–1	–1	0.82
Hard–Easy	–1	0	0.002	–2	1	< 0.001	–1	0	0.74
Painful–Painless	–1	1	< 0.001	–1	0.5	< 0.001	–1	–1	0.90
Passive–Active	0	0	0.005	0	0	0.370	0	0	0.91
Bad–Good	–1	1	< 0.001	–1	1	< 0.001	0	0	0.55
Negative–Positive	0	1	< 0.001	0	1	< 0.001	0	0	0.52
Harsh–Mild	0	1	< 0.001	–1	0.5	< 0.001	0	0	0.66
Disagreeable–Agreeable	0	1	< 0.001	0	1	0.002	0	0	0.53
Slow–Fast	0	2	< 0.001	0	1	0.002	1	1	0.28
Dangerous–Safe	2	2	0.002	2	2	0.018	2	2	0.88

a Up to 13 extra missing values for some scales in the preference arms and up to three in the randomised arms.
b *p*-value from Mann–Whitney test.



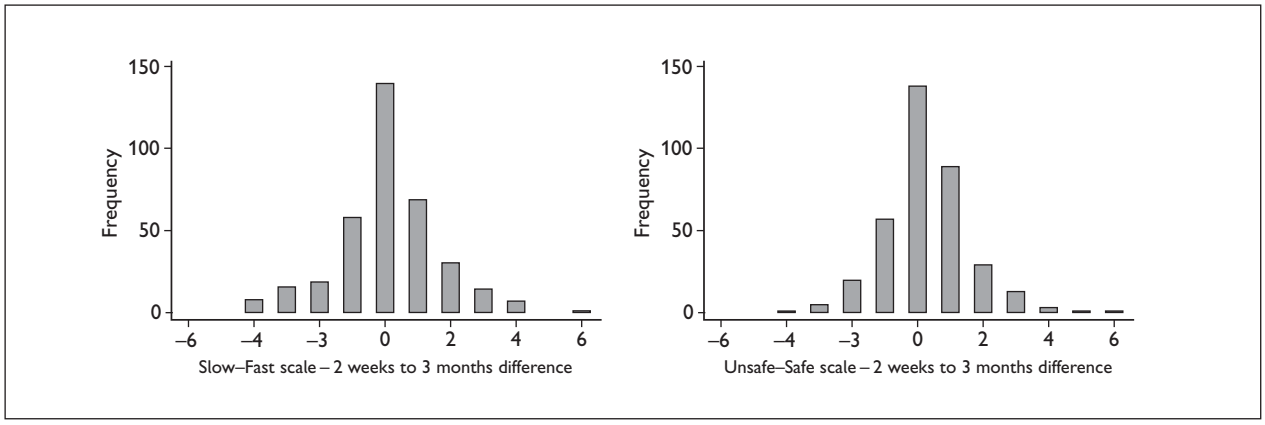


FIGURE 7 *Differences on semantic differential scales between 2 weeks and 3 months after TOP (preference arms only). Note that a positive difference indicates that the experience was less 'positive' at 3 months than at 2 weeks.*

woman subsequently underwent a successful STOP. There were three cases of uterine trauma: two cervical lacerations at STOP that required suturing and one uterine perforation (see SAE below).

It might be expected that women experiencing complications may find the method of TOP less acceptable. *Table 38* shows the acceptability (would women opt for the same method again) at 2 weeks and 3 months after the procedure for those who had and had not experienced a complication. Acceptability was much lower for those women experiencing a complication. The difference is even greater at 3 months than 2 weeks, though based on far fewer responses. In fact, of the 21 women who gave a timely response on both occasions, seven said 'yes' both times, seven said 'no' both times, and seven changed their response from 'yes' to 'no'.

Serious adverse events

There was one SAE during the trial. A 29-year-old women who had previously had a loop electrosurgical excision procedure was admitted for STOP at 9^{+3} weeks of pregnancy (preference arm). She received misoprostol (400 µg) to prime the cervix. At operation the cervix could not be dilated and a decision was made to convert to MTOP. Mifepristone (200 mg) was given and the patient returned 2 days later for misoprostol (800 µg vaginally). She received a further three doses of misoprostol (400 µg) orally that day and then five doses of gemeprost (1 mg vaginally) the following day without passage of products of conception. The patient opted to go home and return for a second attempt at STOP 2 days later. At operation the cervix was dilated sufficiently to allow a 9-mm suction curettage. Following evacuation of products of conception there was significant haemorrhage. Laparoscopy confirmed a haemoperitoneum and at laparotomy the cervix was found to be almost completely separated from the uterine body. A hysterectomy was performed and a small defect in the bladder was repaired. The patient was transfused 2 units of blood. Postoperatively a ureteric injury was suspected because of a watery vaginal loss and confirmed with an intravenous urogram. The patient was taken back to theatre 3 days after the initial laparotomy where a cystoscopy and retrograde pyelogram identified a right uretero-peritoneal leak. A further laparotomy was therefore performed and the right ureter reimplanted. Subsequent postoperative progress was uneventful.

Costs

Standard costs

Clinic attendance costs are shown in *Table 39*. These were assumed to be the same for women having MTOP and STOP. The additional standard costs for MTOP and STOP are shown in *Tables 40* and *41*. The total standard costs for MTOP and STOP were £261.37 and £489.91 respectively.

Individual-level unit costs

Individual-level unit costs and resource usage based on method of TOP and in the two arms of the trial are shown in Appendices 3 and 4 respectively.

Total cost

Total costs for each TOP method and for women assigned to the randomised and preference arms

DOI: 10.3310/hta13530

TABLE 29 *Symptoms experienced during and after TOP*

	Preference					Randomised					Preference vs randomised	
Symptom	***n*[a]**	**Medical**	**Surgical**	**Difference**	**95% CI**	***n*[b]**	**Medical**	**Surgical**	**Difference**	**95% CI**	**Difference**	**95% CI**
During admission for TOP												
Nausea (%)	1251	16.5	4.0	12.5[c]	9.3 to 15.7	284	20.9	3.3	17.6[c]	10.1 to 25.0	–0.8	–4.9 to 3.3
Dizziness (%)	1261	4.3	1.4	2.9[c]	1.1 to 4.7	285	0.8	2.6	–1.9	–4.8 to 1.1	1.2	–0.6 to 3.0
Diarrhoea (%)	1418	3.1	0.3	2.8[c]	1.5 to 4.1	320	5.3	0.6	4.7[c]	1.0 to 8.5	–1.0	–2.9 to 1.0
Vomiting (%)	1420	18.2	2.2	16.0[c]	13.1 to 18.9	325	23.7	2.3	21.4[c]	14.3 to 28.5	–1.5	–5.4 to 2.5
Mean VAS pain score	1322	47.2	22.3	25.0[c]	22.4 to 27.5	298	51.0	22.9	28.1[c]	22.7 to 33.5	0.1	–3.3 to 3.5
During 2 weeks after TOP												
Nausea (%)	910	13.2	10.1	3.0	–1.1 to 7.2	222	19.3	8.8	10.4[c]	1.3 to 19.5	–2.2	–7.2 to 2.8
Dizziness (%)	905	14.0	12.7	1.3	–3.2 to 5.7	220	18.7	15.0	3.6	–6.3 to 13.5	–3.4	–8.9 to 2.0
Diarrhoea (%)	906	11.0	6.6	4.4[c]	0.7 to 8.1	220	18.7	5.3	13.4[c]	4.9 to 21.8	–2.9	–7.5 to 1.8
Vomiting (%)	908	6.8	7.3	–0.5	–3.9 to 2.8	221	8.3	4.4	3.9	–2.5 to 10.4	0.7	–2.9 to 4.3
Still bleeding at 2 weeks (%)	884	22.4	21.6	0.8	–4.7 to 6.3	208	26.7	19.4	7.2	–4.1 to 18.6	–1.0	–7.4 to 5.3
Mean VAS pain score	511	36.8	37.0	–0.2	–4.2 to 3.9	115	39.1	38.1	1.0	–7.9 to 10.0	–1.9	–6.5 to 3.0

VAS, visual analogue scale.
a Number of women responding to this question in preference arms.
b Number of women responding to this question in randomised arms.
c Difference statistically significant at the 5% level.

TABLE 30 *Bleeding after discharge (as reported at 2-week follow-up)*

		Bleeding since discharge					
		Excessive (%)	**Heavy (%)**	**Moderate (%)**	**Minimal (%)**	**None (%)**	***p*-value[a]**
Preference	Medical	3.6	36.7	45.0	13.4	1.4	<0.001
	Surgical	2.1	18.1	42.2	32.8	4.8	
Randomised	Medical	5.3	37.2	36.3	19.5	1.8	<0.001
	Surgical	0.0	20.0	35.7	38.3	6.1	
Combined	Preference	2.9	28.1	43.7	22.4	3.0	0.162
	Randomised	2.6	28.5	36.0	29.0	4.0	

a *p*-value from Mann–Whitney test.

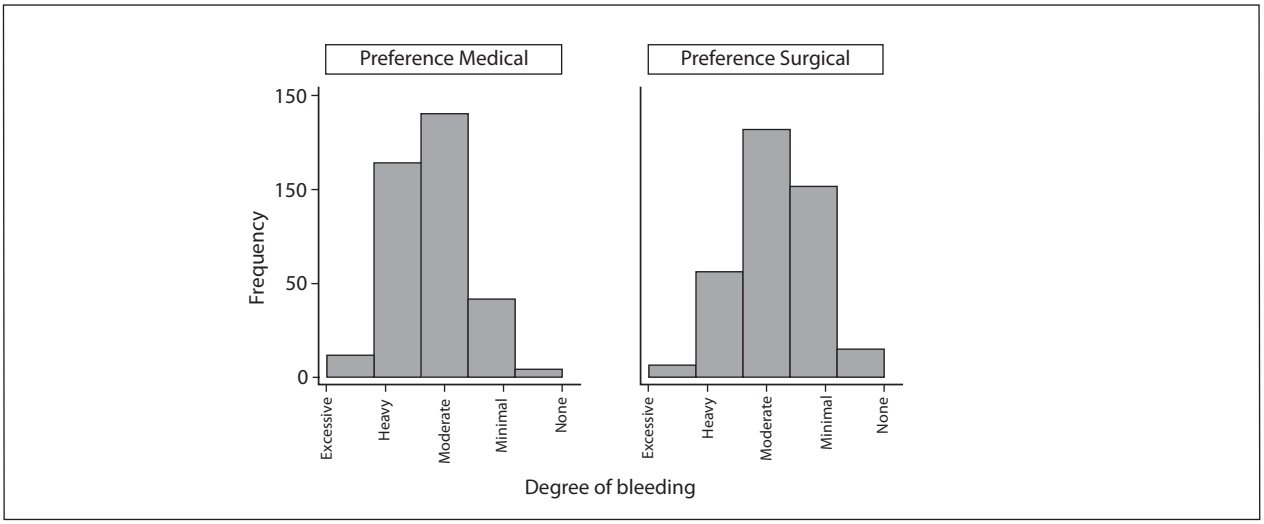


FIGURE 8 *Amount of vaginal bleeding after TOP as reported at 2 weeks.*

TABLE 31 *Distribution of time (days) taken to return to work between trial groups*

		n	**Median**	**Range**	***p*-value[a]**
Preference	Medical	323	4	0–63	0.484
	Surgical	256	3	0–33	
Randomised	Medical	80	3	1–23	0.940
	Surgical	69	3	0–47	
Combined	Preference	579	3	0–63	0.034
	Randomised	149	3	0–47	

a *p*-value from Mann–Whitney test.

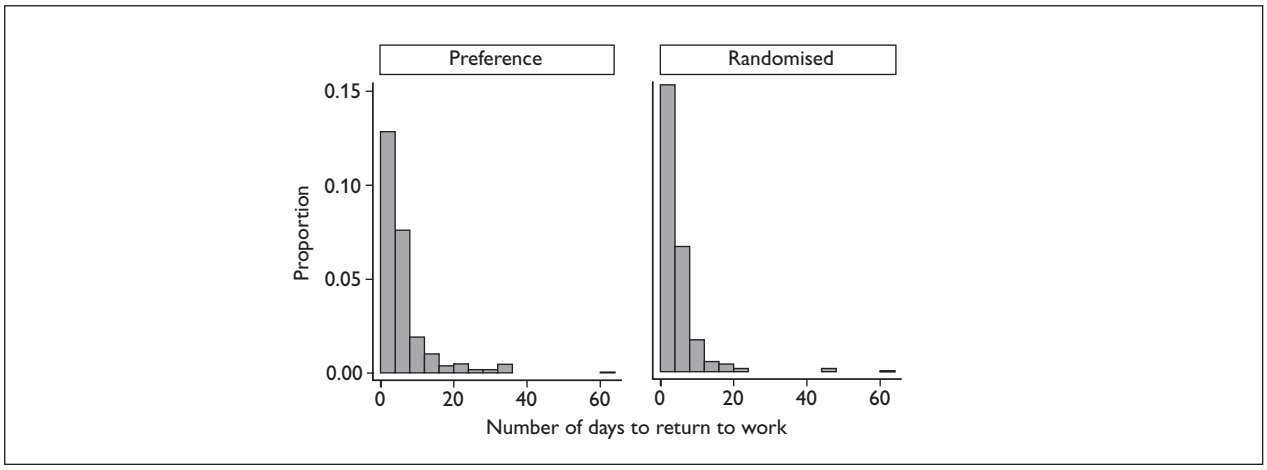


FIGURE 9 *Distribution of days taken to return to work.*

TABLE 32 *Distribution of time (days) taken to return to normal activity*

		n	Median	Range	*p*-value[a]
Preference	Medical	443	3	0–63	0.128
	Surgical	387	3	0–37	
Randomised	Medical	101	3	0–32	0.298
	Surgical	106	2	0–18	
Trial arm	Preference	830	3	0–63	0.032
	Randomised	207	2	0–32	

a *p*-value from Mann–Whitney test.

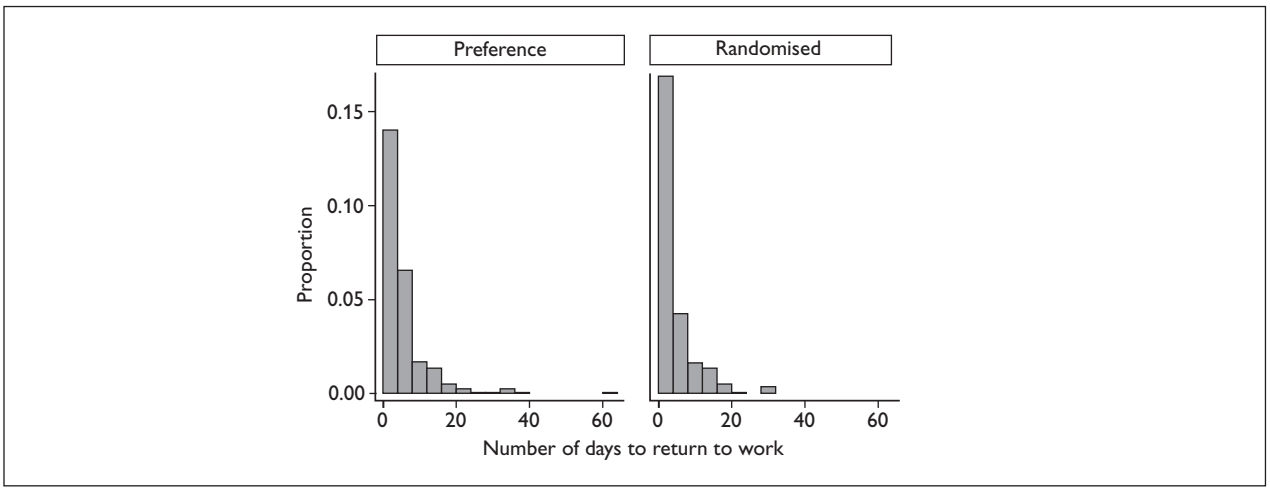


FIGURE 10 *Distribution of days taken to return to normal activity.*

TABLE 33 *Percentage of women who had returned to work/normal activity by 2-week follow-up between trial groups*

	Preference					Randomised					Preference vs randomised	
	n[a]	Medical	Surgical	Difference	95% CI	*n*[b]	Medical	Surgical	Difference	95% CI	Difference	95% CI
Returned to work	658	91.5	88.8	2.6	–2.0 to 7.3	174	91.3	86.6	4.7	–4.6 to 14.1	1.2	–4.0 to 6.4
Returned to normal activity	922	93.9	93.8	0.1	–3.0 to 3.2	224	93.7	95.6	–1.9	–7.8 to 4.0	–0.8	–4.2 to 2.5

a Number of women responding to this question in the preference arms.
b Number of women responding to this question in the randomised arms.

TABLE 34 *TOP-related admissions*

	Randomised		Preference	
Admissions	**Surgical**	**Medical**	**Surgical**	**Medical**
Planned overnight stay				
Social[a]	2	0	6	4
Cervical priming	1	0	2	0
Medical (non-gynaecological) problem	0	0	1	0
Total planned	3	0	9	4
Unplanned overnight stay (during initial admission)				
Complications	0	2	4	18
Retained products of conception		1	1	14
Haemorrhage		1	3	3
Failed MTOP				1
Aborted following day after additional cervagem	0	1	0	5
Products of conception passed late on day of admission	0	1	0	5
Moderate/heavy vaginal bleeding	0	0	0	4
Vomiting	0	0	0	1
Unplanned overnight stay (following emergency admission)[b]	0	0	2	4
Total unplanned	0	4	6	37

a No support at home.
b Indications for stay were infection ($n = 1$), RPC and evacuation of RPC ($n = 1$) in PS group, and RPC and evacuation of RPC ($n = 3$) or medical management ($n = 1$) in PM group.

TABLE 35 *Percentage of women experiencing a planned and unplanned admission*

Admissions		***n***	**Per cent (*n*) admitted**	**Difference (95% CI)**
Planned admissions				
Preference	Medical	823	0.5 (4)	–0.8 (–1.7 to 0.2)
	Surgical	705	1.3 (9)	
Randomised	Medical	162	0.0 (0)	–0.4 (–0.9 to 0.05)
	Surgical	187	0.4 (3)	
Unplanned admissions				
Preference	Medical	823	4.5 (37)	3.6 (2.1 to 5.2)
	Surgical	705	0.9 (6)	
Randomised	Medical	162	0.5 (4)	0.5 (0.01 to 1.0)
	Surgical	187	0.0 (0)	

TABLE 36 *Percentage of women experiencing complications*

		n	Per cent experiencing complications	Difference (95% CI)
Preference	Medical	823	5.1	2.4 (0.5 to 4.3)
	Surgical	705	2.7	
Randomised	Medical	162	4.3	2.2 (–1.6 to 5.9)
	Surgical	187	2.1	

TABLE 37 *Complications*

Complication	Frequency	Per cent
Haemorrhage[a]	14	19.4
Retained products of conception[b]	46	63.4
Infection	6	8.3
Failed	3	4.2
Uterine trauma	3	4.2
Total	72	100

a Three women also had other complications: two with RPC and one with RPC and infection.
b Five women also had infection.

TABLE 38 *Acceptability of procedure for those experiencing or not experiencing complications (at 2 weeks and 3 months after termination)*

Complications at 2 weeks		
No (*n* = 1252)	Acceptability 88.3%[a]	Crude difference 29.6% (95% CI 16.8 to 42.4)
Yes (*n* = 58)	Acceptability 58.6%	
Complications at 3 months		
No (*n* = 381)	Acceptability 88.5%	Crude difference 56.6% (95% CI 36.9 to 76.4)
Yes (*n* = 22)	Acceptability 31.8%	

a Percentage of women who would opt for the same method again.

are shown in *Table 42*. MTOP is cheaper than STOP primarily due to the lower standard costs.

Cost-effectiveness analysis

The ICERs in the two arms of the trial are shown in *Table 43*. To gain one more successful TOP (i.e. an uncomplicated TOP without the need for an unplanned admission) cost more with a surgical procedure in both arms of the trial.

Discrete choice experiment

A total of 310 women attending 58 CoSH clinics were approached by the research nurse (average of 5.3 per session, range 0–10). We recruited up to the point where 100 women agreed to participate; 210 declined to take part. The characteristics of the study group are shown in *Table 44*.

Table 45 shows the results from the regression analysis. Four of the five attributes had coefficients

TABLE 39 *Clinical attendance costs*

Category	Grade/source	Unit cost (£) 2007–8 prices	Quantity per individual	Cost (£) excluding overheads	Cost (£) including overheads
Staff					
Nurse practitioner	NHS Band 7	0.727	25	19.27	24.67
Outpatient nurse	NHS Band 3	0.274	25	7.25	9.28
Phlebotomist	NHS Band 2	0.246	15	3.73	4.76
Other inputs					
Ultrasound scan	NHS Trust	66.48	1	66.48	85.09
Chlamydia screen	NHS Trust	14.23	1	14.23	18.21
Full blood count	NHS Trust	2.35	1	2.35	3.00
Haemoglobinopathy screen	NHS Trust	18.58	1	18.58	23.79
Total					168.80

TABLE 40 *Additional costs for MTOP*

Category	Source	Unit cost (£) 2007–8 prices	Quantity per individual	Cost (£) excluding overheads	Cost (£) including overheads
Mifepristone	BNF	13.94	1	13.94	13.94
Staff (all)	NHS Trust	58.00	1	58.00	74.24
Misoprostol (800 μg)	BNF	0.67	1	0.67	0.67
Doxycycline (200 mg)[a]	BNF	3.72	1	3.72	3.72
Total					92.57

BNF, *British National Formulary*.
a Seven-day course.

TABLE 41 *Additional costs for STOP*

Category	Source	Unit cost (£) 2007–8 prices	Quantity per individual	Cost (£) excluding overheads	Cost (£) including overheads
Staff (excluding those involved in operation)	NHS Trust	58.00	0.843[a]	48.91	62.61
Misoprostol (400 μg)	BNF	0.33	1	0.33	0.33
Operation[b]	NHS Trust	9.92	20	198.35	198.35
Surgeon	MC5605	100,683	0.00021	20.98	26.85
Anaesthetist	MC5605	100,683	0.00021	20.98	26.85
Doxycycline (200 mg)[c]	BNF	3.72	1	3.72	3.72
Metronidazole (1 g)	BNF	2.40	1	2.40	2.40
Total					321.11

a Correction to allow for reduced mean length of time on ward compared with MTOP cases (380 min vs 451 min, $p < 0.001$).
b Cost per minute.
c Seven-day course.

TABLE 42 *Total costs for MTOP and STOP*

	Total costs (£)			
	Medical	**Surgical**	**Difference**	***p*-value**
Whole sample	287.78 (*n* = 940)	498.12 (*n* = 831)	210.34	0.00
Randomised arm	287.04 (*n* = 174)	496.71 (*n* = 174)	209.67	0.00
Preference arm	287.93 (*n* = 766)	498.48 (*n* = 657)	210.55	0.00

TABLE 43 *Incremental cost-effectiveness ratio (ICER)*

		Mean cost (£)	**Mean effect**	**ICER (£)**	**95% CI**
Preference arm	MTOP	287.93	0.97	12,959.10	6458.39 to 54,613.19
	STOP	498.48	0.99		
Randomised arm	MTOP	287.04	0.97	7979.60	4187.67 to 34,882.89
	STOP	496.71	1.00		

TABLE 44 *Characteristics of DCE study group (n = 100)*

Mean age (years)	25.1 (SD 7.9)
Stated income level (n)	
Zero	26
< £10,000	31
£10,000–£19,999	22
£20,000–£30,000	16
> £30,000	5
Marital status (n)	
Single no partner	20
Single with partner	65
Married/living with partner	15
Maximum level of educational qualification (n)	
No qualification	4
GCSE	11
A Levels	24
Degree	47
Higher degree	14

GCSE, General Certificate of Secondary Education; SD, standard deviation.

TABLE 45 *Regression results for the DCE*

Attribute (interpretation)	Coefficient	SE	z	*p*-value
Conscious (prefer to be unconscious)	–0.0999	0.0384	–2.6	0.009
Counselling (prefer access to counselling)	0.4298	0.0382	11.24	0.000
Days delay (prefer 7 days to 14 days)	0.4842	0.0384	12.62	0.000
Analgesics	–0.0409	0.0383	–1.07	0.286
Overnight stay (prefer no overnight stay)	–0.04424	0.0389	–11.37	0.000
Constant	0.00461	0.0380	0.12	0.904

SE, standard error.

TABLE 46 *Marginal rate of substitution*

Attribute gain	Additional days wait to termination for attribute gain
Conscious during termination	0.0999/0.4842 = 0.21
Counselling provided	0.4298/0.4842 = 0.89
Overnight stay avoided	0.4424/0.4842 = 0.91

that were statistically significantly different from zero; only the need for analgesics was not statistically significant. Based on the size of the regression coefficients, three attributes had an almost equal impact on women's preferences: the provision of counselling, the number of days' delay to the procedure and the possibility of the need for an overnight stay. Being conscious or not had a lesser impact on women's preferences.

We were also interested in the number of additional days that women were prepared to wait (trade-off or MRS between waiting and the other significant service attributes) for the termination procedure (*Table 46*). Women would be prepared to wait approximately one extra day to ensure access to post-termination counselling and to avoid an overnight stay following a termination.

Chapter 4

Qualitative substudy results

Recruitment

Of the 69 who were referred, 41 initially consented when contacted by the researcher and altogether 30 women from the PS ($n = 11$), PM ($n = 9$), RS ($n = 6$) and RM ($n = 4$) arms of the trial were interviewed. Of those who were not interviewed, 14 gave no reply, six declined, three hung up, one moved house, and six postponed or did not attend and did not reply or hung up on further telephone calls. Letters were written to two women who had not provided a telephone number. A further nine who had been referred were not followed up because numbers had been met in the respective arms of the trial. An interval of at least 5 weeks was given between the procedure and the interview date and no interviews were carried out more than 18 weeks after the procedure. Difficulties in recruitment in the random arms of the trial are reflected in the numbers recruited onto the substudy.

Interviewee and non-interviewee characteristics

The characteristics of the substudy group are shown in *Table 47*. The mean age of participants was 24.7 (range 16–38) years. Two-thirds ($n = 21$) were educated to A-level standard and above, and two-thirds were employed. Of the nine who were married and cohabiting, six had previous live births, while among the 20 who were single, five had previous live births. Five women had had a previous TOP. In comparison, the mean age of non-participants was 23.4 years. Two-fifths had educational qualifications of 'A' levels and above, and half were employed. Just under half had previous live births, but only one-sixth were married or cohabiting. Those who were interviewed thus tended to be older, more educated, in a long-term relationship, and more likely to be in paid work.

Of the women who opted for the preference arm of the trial, 4 of 20 were less than 9 weeks' gestation, compared with 7 of 10 in the randomised arm. Of 17 women who had a surgical termination, eight had live births, compared with 3 of 13 who had a medical termination. They also tended to be older (mean age 25.5 versus 23.7 years). Of the 30 women, two were asylum-seekers, two were British Asians, and two were economic migrants from Africa and the EU.

Experiences and understandings of the trial

Women's reasons and motivations for seeking TOP were not within the remit of this study, although they were sometimes revealed in the course of the interviews. Access to TOP is an important policy topic, and one about which there are significant political and moral debates, but in this study women tended to describe their experiences of seeking TOP in mainly procedural terms.

Of the 30 women in the substudy, 23 approached their family doctor in the first instance to arrange for a termination. At the first point of contact with primary care to seek TOP, most women did not describe explicit obstacles to referral. Only one participant encountered a doctor who declined to refer her for TOP on grounds of conscience. However, 10 of 30 did experience difficulties that they characterised as related to being adequately informed about the treatment options available to them. Information available to them in primary care was variable: some general practices provided written information, while others referred women to information available at the hospital.

Women's response to uneven provision of information varied. Some were dissatisfied, but others felt that they were not in a position to process detailed information about referral and treatment options because of its psychosocial impact on them. For example, one participant told us that:

> I don't think I could have dealt with knowing everything there and then…because I didn't want to have the information that day. I just, I was having enough problems dealing with everything, I didn't want to have it in black and white in front of me (5132 RS).

It is now well established that women seeking help for reproductive health problems have a

TABLE 47 *Substudy group characteristics*

Characteristic	MTOP (*n* = 13)	STOP (*n* = 17)	All (*n* = 30)
Age			
21 and below	6	3	9 (30%)
22–30	6	12	18 (60%)
Over 30	1	2	3 (10%)
Education			
GCSE	4	5	9 (30%)
A level	5	5	10 (33%)
First degree	3	4	7 (23%)
Higher degree	1	3	4 (13%)
Income			
Unassigned	1	0	1 (3%)
Nil	0	6	6 (20%)
< £10,000	7	2	9 (30%)
£10,000–£20,000	4	6	10 (33%)
> £20,000	1	3	4 (13%)
Partner status			
Unassigned	1	0	1 (3%)
Single	9	11	20 (67%)
Cohabiting	0	5	5 (17%)
Married	3	1	4 (13%)
Gestation			
6–8 weeks	6	5	11 (37%)
9–11 weeks	6	11	17 (57%)
12–14 weeks	1	1	2 (7%)
Previous live births			
Unassigned	1	0	1 (3%)
0	9	9	18 (60%)
1	0	5	5 (17%)
2 or more	3	3	6 (20%)
Previous TOP			
Yes	2	3	5 (17%)
No	11	14	25 (83%)

GCSE, General Certificate of Secondary Education.

preference to consult female professionals,[64] and in this study participants indicated that encounters with male doctors took on a greater formality, while their female counterparts seemed to be more empathic. Women seemed also to experience greater satisfaction with services provided by family planning clinics. Seven women initially sought TOP through a family planning clinic. Two of the women who had initially sought TOP through general practice subsequently moved on to a family planning clinic, one because she was uncertain about whether TOP was appropriate, and the other because of change in area of residence. Onward referral to the hospital service from family planning clinic could be accomplished swiftly and without complication. However, referral

from general practice imposed a further burden on women, who had to take on additional co-ordinating work to chase up appointments and referrals with local administrative staff.

Because of their area of residence, four women had a choice of hospital. Their decisions were based mainly on the earliest appointment available rather than distance, and one was advised by the family planning clinic to have it at the RVI because they were uncertain about how many weeks pregnant she was and her local hospital had stricter limits on gestational age. The normal waiting time between referral and appointment at the hospital was 14 days, with around 7 days between assessment and the actual procedure. The shortest waiting time recorded was 2 days between seeking TOP and hospital assessment, with a further 2-day wait for the procedure. However, 11 of 30 women waited more than 14 days to be referred, and one (an asylum-seeker) waited more than 21 days. Delays for women occurred at the referral stage, with pregnancy testing sometimes holding up a referral. However, two women started the medical procedure at their first visit to the RVI after they were assessed. In some cases delays were due to women being unable to keep an appointment or requiring counselling before the procedure. Once women were referred to the hospital, some had trouble locating the clinic and were reluctant to ask for directions, suggesting a degree of stigma attached to attending the TOP clinic. The assessment clinic could be a busy place; two women felt that there were a lot of people to see in one day, and for another two the clinic felt rushed as one was 'bundled off in different directions'.

The literature suggests that women's decisions to seek TOP are pragmatic ones[65] and that women prefer rapid access to services characterised by supportive non-judgemental staff. We cannot make confident claims about participants' reasons for seeking TOP, but qualitative data suggest that empathic service provision in primary care was preferred by them. In this case, women's accounts of help-seeking were largely procedural, and factors that shaped this were primarily related to organisational processes.

Experiences of trial participation itself were dominated by accounts of (1) the clinical procedure and its contexts and (2) data collection. Like participants in other clinical trials,[66] participants in the TOPS trial accounted for their involvement through the notion of 'helping' in some way. They made reference to the benefits of medical research and women's experiences that triggered the desire to help. They also reflected on abortion as an unpalatable and painful experience that was somehow compensated for by research participation. All except one of the women made references to the idea of 'helping' in some form or other as their reason for being involved. Altruistic involvement was the most common feature of accounts of motivation and half of the participants in the substudy described their involvement in this way. For example, one younger respondent said that:

> I just feel though…as though it is a good thing because if it helps other people that's why when I was talking to me family about it they were saying 'Ah but what you doing it for?' and I was, like, well if it's going to benefit somebody else then, well, that's all that matters really (3618 RS).

Eight women expressed their reason for volunteering as having to do with the important role of research as contributing to knowledge. Other women asserted an ethical obligation to help:

> With a study like that I mean it, it…there's only certain people obviously that are suitable to take part in a study like that, people that are pregnant and are having a termination and you know a lot of people I think wouldn't be prepared to talk about it and wouldn't be prepared to participate in this study and since I, you know, I felt OK about it then I thought well you know, I should, I should do it (4062 PS).

Other women reflected on the pain of their experiences and their empathy with women in the same position as being the trigger for volunteering:

> It's a horrible situation where you are going into something that you don't know anything about and you don't even know which method would be best for you, so I think it would be better if people did know which would be better so (4564 RM).

Because this was a partial preference trial, participants had three possible pathways through it. They could (1) choose (prefer) STOP, (2) choose (prefer) MTOP, or (3) choose to be allocated to one of the randomised arms of the trial. At enrolment into the trial the question of randomisation posed a problem for participants. Some women had difficulty deciding a preference:

> When I was sitting in the room with, like, the lady and she was saying we can do it for you on the computer and just pick a random if you want to be part of that study and things, I was just kind like 'Urgh! I don't know, I don't know' but I eventually picked medical (4304 PM).

On the other hand, the process of randomisation was also described as a solution to problems of decision:

> About each, er, each method and what it involves and I just thought there was so many pros and cons of each one that I really couldn't decide which one would be better for me and then when I was told about the, the research that you were doing I just thought it would be better seeing as I couldn't personally decide anyway 'cos I just thought each method had good and bad points, I just thought it would be better to do the research (4564 RM).

Although women who had a preference should not have entered the randomisation arms of the trial, they often sought to oblige staff by offering to do so:

> I asked the researcher, I said 'Well you know, can I do the random thing, and then if it comes up as a surgical can I change my mind?' and she went 'No, if you've got a preference that's the one you've got to have'… Because I'd already stated that I had a preference she couldn't just put me in the random thing because she already knew that I already had a preference (4336 PM).

Participation in follow-up data collection meant that women had to revisit what they perceived as an essentially private experience. Some women had the opportunity to come back into the hospital for the 2-week follow-up. The contingencies of everyday health care meant that the circumstances in which this took place were not always ideal:

> Er, and then there was another girl there as well and she sort of said 'You know, will you do it together'? and I've never met this girl and we both said 'No' and then she put me in the same room where I'd had all my scan and everything, which was really unpleasant and I think if I'd been prepared for that it would have been OK but I'd been expecting to see T, in the cosy room you know (4062 PS).

More than one-third ($n = 13$) thought that the questions they had to answer were easy. However, there were some difficulties with the length of the questionnaire and the scale questions:

> Some things I didn't really understand like, just the, er, when they have numbers like from zero and then going up.
>
> *Interviewer*: It's a scale isn't it?
>
> Yeah and it's like, some of the words don't really make sense, and for me I would have to elaborate or write something underneath, because it doesn't.
>
> *Interviewer*: Did you do that though?
>
> Em, on some of them, yeah, because I just thought it just doesn't make sense (4760 RM).

A small number of participants attributed benefits to participating in the study that either stemmed from feeling that they were 'not alone' in their experience or because they found the experience in some way cathartic. More generally, women were appreciative of approaches to informed consent that enabled understanding and provided opportunities for questions to be asked. However, there are some indications that the time scale of recruitment and maintaining the right balance of information are issues to be addressed in future research.

It is unsurprising that women's accounts of their understanding of the research itself centred on decision-making between MTOP and STOP. However, they referred mainly to the study providing some objective evaluation of the two procedures, rather than discovering women's subjective preferences. Over one-third of the women referred to finding out women's preference for a particular method, with one interviewee referring to statistical approaches. One-third of the women spoke about the research in terms of effectiveness, that is, which method was 'best' or 'better', which method was 'best in the long term', and which was safer. However, participants also referred to the improvement of services for women, focusing on improving care during and after the procedure, making women more 'comfortable' and reducing the 'emotional strain' of the procedure. A small number of participants also referred to the trial more specifically as being able to assist in women's choices:

> I guess you're trying to, er, trying to see whether it actually has an impact on people physically and psychologically to do the kind of well being after the event depending on which, which method they go for because I suppose the NHS the medical, er, the medical way would actually be cheaper, more efficient and if it doesn't have, you know, any poorer implications compared to the surgical method then that's going to be something that is possibly advocated more and you use that to help people make decisions I suppose (4648 PS).

Participants framed the benefits of involvement in the trial in altruistic terms, but also saw a cathartic effect in talking about their experiences. Only three participants did not describe such a benefit from being involved in the trial.

Decision-making and preferences

This study was not concerned with the processes which led women to seek a termination in the first place. However, because it was a partial preference trial, the means by which women decided on their preferences were important. The substudy interviews provided accounts of how past experiences of both childbirth and surgical procedures shaped women's decision-making. In deciding between medical and surgical procedures, only a few women in the substudy referred to advice from professionals as an influencing factor in making their choice.

Similarly, four women in the substudy were concerned about what was involved in the surgical procedure. In their accounts of surgery, the women used terms such as 'dangerous', 'risky', 'brutal', 'horrific', 'serious', 'harsh' and 'invasive'. A participant in the PS arm of the trial referred to it as 'being under the knife' but felt that it needed to be called something else 'as it didn't require any stitches'. A participant in the RM arm of the trial, on the other hand, referred to the 'tools and things' that had to be used in the procedure. Another PS participant had to put aside the idea of 'flushing away something that would be human', or it would have changed her mind about having a surgical termination. Concerns about general anaesthesia may have led some women to enter the PM arm of the trial, either because of assessment of 'potential' risks or previous experiences. Other women spoke of a more general fear of surgery – not knowing what to expect, and how their bodies would react. Three women described anxiety about injections, in the form of a 'fear of needles', and two of these opted for medical termination. A participant in the PM arm of the trial described this anxiety thus:

> I was a bit scared of the surgical thing. I just thought I didn't want to be put to sleep, I didn't like the idea of the needles, I didn't like the idea of waking up and that, you know, that feeling of, kind of, well that's it over (4304 PM).

A small number of women in the substudy referred to the emotional trauma involved in the medical procedure; often these were linked particularly to the pain and the sight of the fetus. Four women who underwent a medical procedure would prefer to have a surgical procedure instead if the situation arose again. One RM participant was profoundly affected by seeing the expelled fetus:

> But now looking back to it, I would go with the surgical one. I think you're going to get pain with each one so I think, you know, whether I got the same amount of pain with that one would just be very unlucky really but, you know, I'd know what to expect but with the surgical one. There's no chance that I'd see the fetus so that would be what would be, what would sway me towards that one if I had to do it again (4564 RM).

However, other women saw MTOP as offering greater control and confidentiality. Importantly, they saw MTOP as procedurally easier. For example:

> And I think at the end of the day it was quicker for me and quicker for them at the hospital just to do the tablets, it was easier, you weren't having anaesthetic people and it wasn't an operating theatre or anything like that, you were just in a ward, with a bed, think it was easier (5042 PM).

Other women in the PM arm described this method as more 'natural', a view also taken by participants in other qualitative studies.[67,68]

The idea of 'control' was elaborated on in the interviews with women who tried to explain their reasons for choosing the medical procedure in spite of the drawbacks of the method. For example, one RM participant felt that being under an anaesthetic

was being 'detached' and therefore she preferred the medical method, where she could assume a degree of responsibility for what was happening. Another was anxious about 'not know[ing] what's going on' and not being 'in control'. A PM participant opted to both be in control and to be 'responsible'. 'I just wanted to see it through myself', she said.

The speed of the surgical procedure was acknowledged by 9 of 30 participants in the substudy. A number of women reflected on the fact that waiting for the medical process to happen was problematic. A PS participant said that:

> …the nurse talked me through it and said you have this and then, you know, you'll start to have pain and then you know the fetus might come out and then that might not happen and you might have to have more and then wait another few hours and then if it still doesn't happen then you can stay in overnight and then I was like 'Oh my God' that's just getting worse and worse and worse (3648 PS).

Other participants in the surgical arms were very clear that they wanted to be unconscious during the procedure. Rather than be in 'control' as women who preferred the medical option wished, they wanted instead to be 'completely oblivious' and not know that anything had happened. One said that she did not want to 'see it coming away'; another sought to avoid the experience of 'something coming out of me', and another was pleased that she didn't have to 'live through it'. Six women referred to the surgical procedure as offering them the advantage of it being 'done properly' all in one go and three were glad it did not involve a second visit. This sense of finality was also expressed in the following ways: wanting an 'end' to it, having it all to be 'fixed', 'done and dusted in one day', 'all over, gone'.

Women's perspectives on the conjoint analysis (DCE)

The novel component of this qualitative substudy was that it followed-up the DCE. It is important to note that this was not intended to 'verify' the results of the DCE by applying it to the actual study group, but was rather intended to develop a lay analysis of its results.

In the interview, women were shown a flash card describing the results of the DCE in summary form. The flash card showed the order of factors affecting preferences for MTOP or STOP. Interviewees were asked if they agreed or disagreed with the relative importance of these factors, and to give their reasons. They were also asked why they thought these features were ranked in this way, and whether there were other aspects of the experience that needed to be considered. The results of this process are interesting, but not conclusive. Some women distinguished between the ranking features according to their personal experience as opposed to what they would recommend on behalf of women in general. Others found it difficult to respond to the question or to retain a firm view.

Women's responses to these questions were collated and analysed according to how they would rank the features themselves (*Table 48*). The findings from this exercise differed significantly from the results of the DCE. While 'waiting time' was overall the most important (20 women ranked it in first place, while 7 ranked it in second place), counselling was considered the second most important feature (6 put this in first place and 11 in second place). 'Consciousness' was overall the third most important feature as six women put it in first place, and four women in second place. However, the choices of women in the sub-study appeared to be closely linked to their experience of the termination. For women who had had a medical termination, ten out of the 13 put waiting time as their top priority, while ten out of 17 who had had a surgical termination did so. As a medical termination can only be carried within a certain number of weeks of gestation, this may explain why timing was more significant to these women, particularly those with a specific preference for the procedure.

> I think it was good because I had a chance to go through the things in my head and be absolutely certain that was what I wanted to do (4062 PS).

However, 11 women felt that the waiting time was far too long, and for two of them the waiting was the worst part of the experience. They considered going to a private clinic to speed up the process. One said that:

> As soon as you find out you're pregnant you just want it over with. I would have quite happily gone in that day (5042 PM).

While for most women, a short waiting period was much preferred, the expectations and stresses

TABLE 48 *Top three factors influencing women's choice of method of TOP*

	Waiting time		Counselling		Consciousness	
Rank position	**1st**	**2nd**	**1st**	**2nd**	**1st**	**2nd**
PM	6	2	3	3	1	0
PS	4	5	2	5	5	0
RM	4	0	1	1	0	1
RS	6	0	0	2	0	3
Total	20	7	6	11	6	4

MTOP, *n* = 13; STOP, *n* = 17.

associated with it were subject to a number of different interpretations according to women's circumstances. One participant, who was ambivalent about having the termination in the first place, appreciated that the procedure was quick:

> Yeah, it was pretty quick, I was quite shocked at how quick it was actually…I thought it was a bit hurried but coming to think about it now it was better that way…'cos then you didn't have a chance to sit and think about it and worry about it (5002 PM).

Apart from gestational age, women's household living arrangements and experience of morning sickness could also be factors that affected their sense of urgency. For example:

> And that it, it seemed like forever 'cos by that stage I had really bad morning sickness and I just, I could hardly function [laughs]. It was horrible, er, and 'cos I live in a shared house with my sister and her friend and I didn't want to tell them about the pregnancy test, I was trying to hide it from them (4578 RS).

While being unconscious was more of an issue for those who had had a surgical termination, counselling appeared to be important to those who had had the medical procedure: 8 of 13 rated counselling in first and second place, while 9 of 17 in the surgical arm did so. This might be an indication of the level of distress that these women underwent. However, interviews provided a mixed view of counselling. Some women equated counselling with personal support that they were able to access from family and friends, while it was more specific for others. Access to counselling was uneven across the 30 women. Of the 15 women who elaborated on their views that counselling was important, equal numbers expressed the opinion that counselling was more important before, after, or both before and after the procedure. Among this group, 10 women had support from other sources, and of these, five did not think counselling was necessary. Six women felt they did need counselling. For example:

> I think you automatically look at what you've been through and think well it's like afterwards, when I think I could have done with seeing someone for once, er, I don't know, it's, I wouldn't like anyone to feel the way I felt and not be able to talk to anyone professionally about it. I mean family members, yeah, but they don't really understand if they haven't been through it (4552 PS).

Five women had experienced formal counselling. This compared counselling favourably to support from family and friends:

> Yeah, it was good to talk to someone out of the whole equation… It's not like friends and family and everyone was telling us to think things 'Oh just do what you want' and I didn't know what I wanted. So it was just nice to talk to someone out of the whole equation (3796 PS).

In contrast, five women in the surgical arm put 'being asleep or awake' in first place compared with only one in the medical arm. A participant in the PM arm described why she rated being asleep as more important than any of the other features:

> Er, you got a bit of a shock but you had to check to see what you passed and I got a bit of a shock… They said just leave it and we'll check it for you but I guess because I was at the point where I was absolutely desperate to

> pass something and so I didn't have to have the operation, er I, and it was quite large so you… not like you could not see it I guess (4400 PM).

When women were asked if they thought other features should be included in the list, 18 women had suggestions to make. Six women mentioned that a friendly and sensitive attitude of medical and nursing staff towards them was important. Four women suggested that information should be one of the features. Privacy was also referred to by two women, and post-TOP care and support by another two women.

Chapter 5
Discussion

Introduction

This trial sought to determine the acceptability, clinical effectiveness and cost of MTOP and STOP at less than 14 weeks of pregnancy. Despite poor recruitment to the randomised arm of the trial, the results show that, at 2 weeks after the procedure, women in the surgical arms were more likely to opt to have the same method again compared to women having MTOP. This difference in acceptability at 2 weeks was found to increase with gestational age at abortion and the greater acceptability of STOP persisted at 3 months. Women having MTOP were more likely to report symptoms during their admission and they had higher pain scores. Further, MTOP was associated with more unplanned emergency admissions and more complications. Consistent with these findings, women's experiences of care were generally more negative and they were less satisfied with MTOP. However, STOP was more costly due to much higher standard costs. Whether STOP would be considered cost-effective depends on the value placed on increased effectiveness for this increased cost. Despite these differences, many women chose MTOP and found the procedure acceptable.

Comparison with prior studies

Although the procedure for STOP is consistent in prior studies of abortion prior to 14 weeks, a number of different medical regimens have been employed; early randomised trials employed prostaglandins alone[1,69] or mifepristone alone.[70] A systematic review of medical methods for first-trimester abortion concluded that combined mifepristone and prostaglandins was more effective (in terms of achieving complete abortion) than prostaglandins or mifepristone alone.[71] Single-agent regimens are no longer recommended in the UK.[9] Therefore, in order to allow meaningful comparisons, studies quoted in the following discussion are limited to those in which MTOP was attempted using mifepristone followed by prostaglandins.

Trial design

The primary outcome (acceptability) and the design (partially randomised patient preference) of this trial were stipulated in the Health Technology Assessment (HTA) Commissioning Brief. Although a randomised clinical trial would be the most scientifically rigorous design for evaluating MTOP and STOP, it cannot deal with the post-randomisation effects of patient's preferences on treatment outcomes.[72] Participant preferences may affect compliance and motivation, introducing bias that affects the internal validity of a trial. Thus in the case of TOP, women randomised to their preferred procedure may be better motivated and report better outcomes, while women who do not receive their preferred method may be less motivated, may not report accurately during follow-up and may even drop out of the trial.[73] Effects of preference are likely to be more apparent where the outcome measure is subjective and self-reported by the patient. In addition patients' preferences may also have a 'therapeutic effect', similar to a placebo effect, directly influencing outcomes.[74] Where strong preferences exist, as appears likely with TOP method,[17,20] a large number of participants may refuse randomisation, adversely affecting the external validity of the trial and limiting the generalisability of the results.[72]

The approach taken to deal with women's preferences in this trial was to employ a partially randomised preference design. This design takes women's preferences into account in the allocation of TOP method, generating two groups of women in whom motivational factors should have been optimised by allowing them to choose their own method of TOP and two groups of randomised women in whom motivational factors should have been equalised. This allows the independent effect of women's preferences to be examined, thus providing information on the benefits of providing a choice.[75] A disadvantage of this design is that the outcome (acceptability) may be affected by uncontrolled confounders in the preference groups, which may bias the results.[76] An alternate approach would have been to use a fully randomised preference trial in which, after

consent and before randomisation, women's preferences were recorded and taken into account in the analysis.[77] Although a potential criticism of this design is that ignoring patients' preferences and proceeding with randomisation is unethical, this may not be the case if the treatments being offered are believed to be effective and patients give fully informed consent.[72] It is still unclear whether patient preferences significantly affect the validity of randomised trials. In a systematic review of predominantly partially randomised preference trials, King *et al*.[73] found that while preferences led to a substantial proportion of people refusing randomisation, there was little evidence that outcomes differed between randomised and preference groups across the trials. In contrast, a recent systematic review of eight fully randomised preference trials in musculoskeletal medicine found that, after adjustment for baseline scores and categorical variables of trial and treatment allocation, preferences were associated with treatment effects; patients who were randomised to their preferred treatment had a standardised effect size greater than that of those who were indifferent to the treatment assigned.[72] Perhaps surprisingly this review also showed that participants who did not receive their preference were more likely to return their first follow-up questionnaire, although overall response rates were similar.

Baseline characteristics

Comparison of the baseline characteristics revealed a number of differences between the three allocation groups. Within the preference groups, women opting for STOP were more advanced in their pregnancy and were more likely to smoke, to be educated up to GCSE level and to have had a prior live birth. However, the only difference between women in the randomised and preference groups was that mean age was slightly greater (1.2 years) in the preference arm, a difference similar to that reported in the systematic review of fully randomised patient preference trials.[72] No such differences in participant characteristics were reported in the two smaller partially randomised preference trials of TOP method conducted in the UK,[17,18] although Henshaw *et al*.[17] did find that women preferring STOP had a greater distance to travel to hospital. This parameter was not recorded in the present study.

Trial recruitment

Only 19% of women recruited to the study were prepared to have their method of termination randomly assigned. Changes to the written information given to women, emphasising the absence of evidence that one method was superior and the value of randomisation, failed to increase randomisation rates which remained much lower than in our pilot trial conducted in 2002; of the 284 suitable women at 9–13 weeks of pregnancy in the pilot, 49% were prepared to be randomised to MTOP or STOP. The achieved randomisation rate was also much lower than prior partially randomised trials of TOP method conducted in the UK, which reported randomisation rates of 54%[17] and 82%.[18]

We can speculate on the reasons for these differences. It is possible that knowledge of abortion methods, particularly MTOP, has increased over recent years. Certainly the availability and acceptance of MTOP, both in Newcastle upon Tyne and nationally, has increased dramatically; medical procedures accounted for 35% of all abortions in 2007[4] compared with only 12% in 2001 and 0% in 1991 (the year mifepristone was licensed in the UK).[5] With improved knowledge and an increasing emphasis on choice, stressed in the NHS literature on TOP supplied by the Trust, women in the current study may have felt more empowered to state a preference. The accounts of women participating in the qualitative substudy are informative in this context: decisions about mode of TOP were mainly founded on issues around control and on prior experiences (either personal or those of friends/relatives), some of which related to MTOP. Further, while some women may have agreed to randomisation to 'oblige' staff, most of the randomised women interviewed chose this option as a means of resolving their difficulties in deciding on a preferred method.

The problem of explaining the rationale and process of randomisation to participants in clinical trials is well known[78] and some of the women interviewed voiced difficulties understanding these concepts. We considered the possibility that personnel involved in patient assessment for TOP and trial recruitment could have influenced the proportion of women opting for randomisation. In both the previous studies conducted in Aberdeen,[17,18] (A Templeton, University of Aberdeen, 2008, personal communication) and in our pilot trial, medical staff were involved in both processes. In contrast, in the current study

women were predominantly assessed by nurse practitioners and all recruitment was undertaken by research nurses. The fact that recruitment rates were the same for each research nurse suggests that the process of recruitment was conducted in a consistent manner. However, randomisation rates were higher in women seen by one of the nurse practitioners, suggesting that despite attempts to standardise the dialogue about the trial, women's views on randomisation were influenced, albeit to a small degree, by the health professional who introduced the study. Although recruitment rates did not seem to be influenced by involvement of medical staff, the small number of women assessed by them precludes any firm conclusions.

Preferences

Slightly more than half (54%) of the women who expressed a preference opted for a medical procedure. It is difficult to draw meaningful comparisons with prior studies because of variations in study design and service/user attitudes to medical abortion. In a review of 12 studies of women at ≤9 weeks of pregnancy published prior to 1994, Winikoff[21] reported that 'in most trials' 60–70% of women chose medical abortion. In the partially randomised preference trial of Henshaw *et al*.[17] conducted in Aberdeen, 72 of 156 (46%) women at ≤9 weeks of pregnancy in the preference arm preferred MTOP, while in the subsequent trial from the same unit only 15 of 77 (19%) of women at 10–13 weeks of pregnancy preferred MTOP.

In order to better understand the reasons underlying women's choice of abortion method, we collected the reason(s) for procedure preference in all women in the preference arm immediately after recruitment. We attempted to group stated reasons into broad categories to facilitate interpretation and comparison with previous studies, but acknowledge this required several assumptions and resulted in an oversimplification of the data. Awareness during the procedure (which is closely linked to, but not synonymous with, a desire to avoid general anaesthesia) was cited by nearly 60% of women opting for MTOP. Previous studies have reported that 37–59% of women stated fear of anaesthesia or surgery as the reason for choosing MTOP at less than 9 weeks' gestation.[17,46] Ashok *et al*.[79] reported that 67% of women preferring MTOP at 10–13 weeks perceived being conscious/aware as an advantage of the method, while 78% saw avoiding anaesthesia as an advantage. In contrast, 27% of women opting for STOP stated they wanted to be unconscious/unaware of the procedure and a further 15% did not want to pass or see the fetus. A desire to be unconscious was deemed important/advantageous by 39% of women who opted for STOP in the study by Henshaw *et al*.,[17] but by 94% of those opting for STOP at 10–13 weeks.[79] All these prior studies also identified that women with a preference for MTOP perceived this as a more 'natural' procedure with fewer complications/psychological problems.[17,46,79] For a small proportion of women the avoidance of an additional visit and the greater likelihood of avoiding an overnight stay were important factors in choosing STOP.

The importance of 'control' during the abortion procedure was further emphasised and developed by the women who participated in the qualitative component of the study. Women who preferred STOP sought to control their exposure to the experience of the procedure (which was achieved with finality while they were unconscious). Opting for STOP ensured they would not see the fetus and were less likely to experience pain. In contrast, women who sought MTOP wanted to exercise a degree of control over the process itself. Awareness was seen as assuming responsibility for what was happening. Consistent with views of participants in other qualitative studies,[65] several of the women in the preference MTOP group described the MTOP procedure as more 'natural' in contrast to STOP which was perceived as 'harsh' and 'brutal'.

Strength of preference

We sought to gain more quantitative information about women's strength of preference by recording WTP. When assessed prior to TOP, the maximum amounts that women were prepared to pay to have their preferred option (rather than their less preferred option) were similar for the two methods (mean £373 for MTOP, mean £432 for STOP). At 2 weeks after abortion, women in the preference arm were prepared to pay more for their preferred option, but there were no differences in mean maximum WTP values for each method in the randomised arm (MTOP £193 versus STOP £216) or the preference arm (MTOP £329 versus STOP £357). Gibb *et al*.[38] are the only other group to compare strength of preference for abortion method by WTP. In their small study of 50 women there were no differences in mean WTP values between women preferring MTOP and STOP (both before and after abortion). Despite only two women being zero-payers, mean WTP values were lower

(MTOP £103, STOP £48) than those recorded in the present study. These values were also lower than the amount women were prepared to pay for their choice of TOP method in the study of Howie *et al*.[27] from the same unit (median £311, range £40–500).

The WTP method has been advocated as a way of eliciting public preferences for alternate health-care programmes.[80] We found the method simple and quick to administer, a key consideration in the present study in view of the large number of outcomes being collected. However, the method has several limitations. Convergent validity is low,[81] although other preference elicitation methods used in economic analyses, e.g. conjoint analyses and the various health status violation techniques, also have problems with consistency.[82] A further limitation is the extent to which WTP can be associated with 'ability to pay'.[83] Gibb *et al*.[38] found that WTP for TOP method was positively associated with social class and the importance women attached to having a choice, supporting the validity of the technique in this population. We found a correlation between stated WTP and women's income, providing some support for the internal validity of the measure in this study. Based on the present findings, and those of Howie *et al*.,[27] it can be concluded that the majority of women attach significant value to being able to choose their method of abortion. Further, while most women express a preference for abortion method, the strength of this preference, as assessed by the amount they are willing to pay to attain it, is similar for MTOP and STOP.

Creinin[20] in his small randomised trial of MTOP and STOP sought to determine strength of preference using a VAS. Mean VAS scores were similar for those women in each group (STOP 93%, MTOP 63%) who found the method to which they were randomised acceptable (as determined by their choice for future abortion method). No other VAS data were presented. These results appear to support the conclusion of the present study that the strength of preference women have for their preferred method of TOP (whether that be the method chosen for their index abortion or for a future abortion) is similar for MTOP and STOP.

Service attributes

In an attempt to identify key factors that shape women's preferences for TOP services, we conducted a DCE in a sample of non-pregnant women attending a family planning clinic. The rationale for selecting this patient group was to ascertain the expectations and views of potential future users of TOP services. From the attributes considered, provision of counselling, procedural waiting time, need for overnight stay and consciousness during the procedure significantly shaped women's preferences. We were able to further develop this analysis in the substudy. The women interviewed prioritised waiting time above counselling and consciousness. The significance of waiting time was also emphasised by some women during their interviews. The high priority given by women to avoidance of an overnight stay supports the use of this measure of effectiveness in the trial.

It is reasonable to assume that waiting time was not relevant to women's choice of TOP method as the waiting times for MTOP and STOP after recruitment to the trial were very similar (usually less than 7 days and always less than 10 days). The RCOG standard for waiting time from first appointment with the referring doctor to the procedure is 3 weeks;[9] over the duration of the trial this standard was met in nearly 90% of pregnancies less than 14 weeks' gestation. However, in other units this standard is met in less than 50% of cases.[84] This study identified delays both before and after referral from primary care and the barriers faced by women seeking abortion; 82% of 140 GPs surveyed considered themselves 'broadly anti-abortion' and the authors emphasised the need to evaluate alternative approaches that bypass traditional gatekeepers to abortion care.[84] These barriers were also highlighted by some women participating in the substudy (see below). Availability of counselling is also unlikely to have impacted on women's preferences for TOP method. Women in the trial were not given routine follow-up appointments for counselling. Rather, in keeping with national guidance,[9] they were all given a contact telephone number to access a trained counsellor provided as part of the NHS service.

Acceptability

Acceptability was the primary outcome of the trial and we chose to assess this by determining the proportion of women who would opt to have the same procedure again. This measure was chosen for two reasons: (1) it was easy to collect, particularly using text messaging (perceived to be a novel means of optimising data collection in this participant group); and (2) virtually all previous

studies comparing MTOP and STOP had reported future choice as a measure of acceptability, allowing the results to be incorporated into existing evidence. At 2 weeks after the procedure, compared with women randomised to MTOP, women randomised to STOP were more likely to opt to have the same procedure again (69% versus 94% respectively). This finding is consistent with prior randomised trials: 74% versus 87% ($p < 0.001$) in the study of Henshaw *et al.*[17] in women ≤9 weeks' gestation, and 63% versus 92% ($p < 0.001$) in the study of Creinin[20] in women < 7 weeks' gestation. A smaller difference (70% versus 79%, $p < 0.001$) was reported by Ashok *et al.*[18] in women at 10–13 weeks of pregnancy, although the results from randomised and preference arms were combined. No differences were reported in the small trial of Rosen *et al.*[69]

In keeping with prior studies,[79] women in the preference arms were more likely to regard their chosen method as acceptable. Consistent with the results in the randomised arm, more women choosing STOP than MTOP opted to have the same procedure again (96.5% versus 80.9% respectively at 2 weeks), an effect maintained at 3 months (95.6% versus 79.0%). In contrast, Henshaw *et al.*[17] found no difference in acceptability between women who preferred STOP and those who preferred MTOP (90% versus 95%), although numbers were much smaller ($n = 156$). Results from prior prospective cohort studies comparing STOP and MTOP before 9 weeks' gestation have found conflicting results in terms of procedure acceptability. However, the extent to which women chose their method of abortion in these studies varied; in most of the earlier studies reporting high acceptability rates with MTOP, the procedure was not generally available and women themselves sought out access to medical abortion.[24] In more recent cohort studies where women had choice of abortion method, STOP has been found to be either as acceptable[85] or more acceptable[86] than MTOP.

Surgical TOP remained more acceptable to women in both arms of the trial at 3 months after the procedure. Only 26 of 382 (7%) women who provided responses at both time points changed their responses, of whom 16 (13 in PM and 3 in RM arms) would no longer opt for MTOP in the future. Howie *et al.*[27] reported 2-year follow-up data from 80% of the women participating in the partially randomised preference trial of Henshaw *et al.*[17] Of those women originally allocated to treatment according to preference, 89% in both the MTOP and STOP groups opted for the same procedure in future. In contrast, 64% of women randomised to MTOP, but 87% randomised to STOP opted for the same procedure (95% CI for difference in proportions –39 to –1, $p < 0.05$). These findings support the conclusion that more women regard STOP as acceptable.

Acceptability of MTOP declined as gestational age increased such that by 13 weeks' gestation only 50% of women opted to have MTOP again. In contrast, the acceptability of STOP remained high (> 90%) between 5 and 13 weeks. Studies on early MTOP have consistently shown that procedure failure and more pain and bleeding than expected are predictors of not choosing MTOP again.[24,87–89] The likelihood of each of these predictors increases with gestational age.[15,89] Of particular relevance is the increase in need for surgical evacuation following MTOP because of ongoing pregnancy or missed/incomplete abortion, which has been reported to increase from 0.9% at 9–10 weeks to 7.9% at 12–13 weeks of pregnancy.[15] Unsuccessful medical therapy has also been shown to reduce acceptability in a randomised trial of medical and surgical management of early pregnancy failure.[90] Although we did not undertake a detailed analysis of predictors of acceptability, we did confirm that acceptability at both 2 weeks and 3 months was reduced in women experiencing complications.

Semantic rating/satisfaction

To further assess women's experiences of the abortion procedure we used semantic differentials constructed using bipolar adjectival scales as end points on a graphic Likert scale. The instrument is easy to use and has been shown to be internally consistent and valid.[91,92] Rather than develop a new set of adjectival pairs, we utilised the 12 pairs employed by Henshaw *et al.*[17] and Ashok *et al.*[79,93] in their studies of the acceptability of MTOP and STOP. At both 2 weeks and 3 months after the procedure, MTOP was rated significantly lower on all 12 bipolar adjectives in the preference group and on 11 of 12 in the randomised group, clearly indicating that women rated their experiences of MTOP more negatively than their experiences of STOP: MTOP was felt to be more unpleasant, more disagreeable, harder and more painful, while STOP was felt to be milder, more agreeable, faster and safer. These experiential effects were greater than those reported by Henshaw *et al.*[17] who found that MTOP was rated lower on six of the 12 adjectives in their randomised arm but only on

one of the 12 in their preference groups (MTOP was more painful). However, the fewer significant differences may have been explained by the much smaller sample size in the Aberdeen study. Ashok *et al*.[93] analysed their data by totalling the scores for each adjectival pair to give an estimate of change in 'self-esteem' before and after abortion. More women randomised to MTOP at 10–13 weeks of pregnancy had a fall in 'self-esteem'.

Fewer women having MTOP rated their overall care as excellent. Again this result was consistent across both trial arms and at both time points. Women were less satisfied with the technical and interpersonal aspects of care, but not the waiting time for MTOP. Although satisfaction data were not reported in previous randomised trials, two cohort studies comparing MTOP and STOP have measured overall satisfaction with care; Slade *et al*.[86] found no difference in mean scores on the Satisfaction with Care Scale, but Jensen *et al*.,[24] using a 5-point scale, reported higher mean satisfaction scores with STOP. Taken together the results of the present study and those of most prior studies suggest that experiences of care are more negative and satisfaction lower with MTOP, likely contributing to the lower acceptability of medical abortion prior to 14 weeks of pregnancy.

Psychological outcome

Anxiety and depression, as assessed by HADS or Edinburgh Postnatal Depression Scales (EPDS), have consistently been shown to fall after abortion.[26,85,86,93] Consistent with prior randomised trials[26,93] and cohort studies[85,86,94,95] that have used HADS or EPDS as a means of screening for anxiety and depression, we found no difference in mean scores between women having MTOP and STOP. The proportion of 'clinical' cases of anxiety and depression during the first month after abortion (inferred, for example, by the proportion of women with HADS > 10) has also been found to be similar in women having MTOP and STOP (6–28% for anxiety and 2–10% for depression).[26,85,86,93] Interestingly, Ashok *et al*.,[93] in addition to the HADS, measured anxiety levels using a VAS before and after TOP at 10–13 weeks; women randomised to STOP were more anxious prior to the procedure, but less anxious following abortion than women randomised to MTOP. No such differences were recorded in the preference arm. Long-term follow-up studies of women having first-trimester abortion have generally found no evidence of an increased risk of anxiety or depression, but these studies have not differentiated between MTOP and STOP.[96–98]

The IES has been used for over 20 years as a measure of stress reactions after traumatic events.[40] The scale is based on the two common responses to stress: intrusion, involving unbidden thoughts and images, bad dreams and strong feelings related to the event; and avoidance, involving denial of thoughts and feelings related to the event.[40] Systematic review has shown that the two-scale structure is stable over different types of traumatic events (e.g. injury, illness and bereavement) and has convergent validity with observer-diagnosed post-traumatic stress disorder.[99] Compared with the mean IES scores reported here, Broen *et al*.[100] reported slightly lower mean scores on both subscales at 10 days after induced abortion (method not defined). Thereafter IES avoidance scores remained unchanged (at 8–10 points) at 6 months, 2 years and 5 years after TOP, while IES intrusion scores fell reaching a mean value of 3.6 points at 5 years. The proportion of IES intrusion 'cases' (defined as those with a score > 19) fell from 24% at 10 days to less than 5% at 2 and 5 years after TOP, while the proportion of IES avoidance cases increased slightly from 12% to 19%.[100] As emphasised by the authors, the IES is not a measure of post-traumatic stress disorder.[99] Rather, classification as a 'case' infers that the person suffers some degree of mental distress. Many women have avoidance symptoms after induced abortion and the incidence appears to be influenced by culture; Rue *et al*.[101] reported that 36% of American women reported three or more avoidance symptoms compared with only 3% of Russian women. The incidence of post-traumatic stress disorder in these populations, as determined by the Traumatic Stress Institute's Belief Scale, was 14% and 1% respectively.

Women randomised to MTOP had higher scores on both subscales at 3 months and on the intrusion subscale at 2 weeks after the procedure. No differences were evident between women opting for MTOP and STOP. The only study to compare IES scores after MTOP and STOP was reported by Slade *et al*;[86] in their study mean scores on the two subscales were almost identical to those reported here and were similar in the two TOP groups at 4 weeks post procedure. However, within the medical group, those women who had seen their fetus (56%) were more likely to experience intrusive events (nightmares, unwanted thoughts and images). Mean gestational age at MTOP was more advanced in the current study and it is possible that the difference in IES intrusion scores relates to a higher proportion of women seeing their fetus. One could speculate that women in the preference

group were less affected and/or better prepared for this eventuality.

Side effects

The procedure of MTOP was associated with more pain and more gastrointestinal symptoms than STOP. These results are in agreement with previous randomised trials and cohort studies.[12,17,20,86] The incidence of side effects during MTOP has varied substantially between different studies. For example, the proportion of women reporting vomiting and diarrhoea has varied between 0–49% and 0–43% respectively.[18,20,88,102] The incidence and severity of symptoms is influenced by the dose and route of administration of misoprostol;[88] gastrointestinal symptoms and fever are more common with oral administration.[88] We found that a similar proportion of women (~ 22%) having MTOP and STOP were still bleeding 2 weeks after the procedure, although more women in the MTOP group reported heavy blood loss. Duration of bleeding has consistently been reported to be longer after MTOP than STOP and longer after abortion at 10–13 weeks compared with abortion at ≤ 9 weeks.[16,18,20,24,86] Further, bleeding in excess of expectations (either in terms of amount or duration) has been reported more frequently after MTOP.[86] In their cohort study, Slade *et al*.[86] found that more women reported 'disruption of activities' after MTOP than STOP (44% versus 15% respectively); this could be explained as a consequences of differences in symptomatology. We sought to determine the impact of TOP by ascertaining when women returned to normal activities. There were no differences in this measure or the time taken to return to work between groups; reassuringly, around 90% of women had returned to normal activity/work by the 2-week follow-up.

Effectiveness

We chose to assess the overall clinical effectiveness of MTOP and STOP using unplanned/emergency admission requiring an overnight stay. We reasoned that this would capture all significant procedure-related morbidity. Feedback from women during our pilot trial also underscored that this was an important outcome for women; in addition to the disruption of domestic and work-related activities, a high proportion of women had not informed their partners or parents of their TOP, making unplanned overnight stay a significant problem.

Rates of unplanned or emergency admission were higher in the MTOP group in both the randomised and preference arms; overall 4.2% of women having MTOP had an unplanned overnight stay compared with 0.7% of women having STOP. Most of these admissions were overnight stays on the day of the MTOP procedure due to failure to achieve complete uterine evacuation. As the study had limited precision to estimate differences in specific complications, we reported the overall rate of complications that included haemorrhage, incomplete abortion, failed abortion and suspected pelvic infection. Complication rates were more common after MTOP, although this difference only achieved statistical significance when comparing preference arms. Overall 5.0% of women having MTOP experienced a complication compared with 2.6% of women having STOP.

Previous randomised trials have tended not to report complication rates, presumably because of the small numbers of women recruited. However, in their randomised preference trial of MTOP and STOP at 10–13 weeks' gestation, Ashok *et al*.[18] reported 'failure' rates within 8 weeks of abortion, i.e. failure to achieve complete uterine evacuation without the need for a second procedure [subsequent surgical (re)curettage or medical regimen]. In this study, 11 of 203 (5.4%) undergoing MTOP and 5 of 242 (2.1%) undergoing STOP had a failed TOP, a difference that was not statistically significant.

Several studies have reported single-unit comparative studies of MTOP and STOP. Jensen *et al*.[24] reported primary procedure failure (defined as the need for suction curettage) in 18% of 150 women having MTOP and 4.6% of 151 women having STOP at up to 9 weeks' gestation. The high 'failure' rates may partly reflect the MTOP regimen used (single dose of 400 µg misoprostol orally) and the fact that emergency curettage was not based on evidence of products of conception. In a study of 932 women undergoing abortion at ≤ 9 weeks of pregnancy, surgical curettage for 'presumed retained products of conception' and ongoing pregnancy was more common in women having MTOP than STOP (9.8% versus 5.5% respectively).[103] More women having MTOP were admitted overnight during their TOP (3.8% versus 0% respectively), but rates of presentation as an emergency were similar (9.0% versus 8.8% respectively). Rates of emergency admission with overnight stay were not reported. Hamoda *et al*.[104] reviewed 1927 consecutive cases of abortion at 9–13 weeks' gestation. Detailed analysis of 1076 cases of

MTOP was reported together with basic outcomes of 851 women having STOP. No statistical comparisons of the two methods were performed. In total 4.2% of MTOP cases required surgical evacuation: 1.9% for incomplete abortion, 0.5% for retained sac and 1.5% for continuing pregnancy; a further 0.4% of women required emergency curettage because of bleeding. Surgical evacuation rates increased from 2.7% at 64–70 days' gestation to 8.0% at 85–91 days. Haemorrhage (blood loss > 500 ml) occurred in eight women (0.8%) and suspected pelvic infection in 12 (1.1%). Repeat surgical evacuation, haemorrhage and suspected pelvic infection occurred in 0.8, 0.1 and 0.3% of STOP cases respectively.

Useful comparator data on complication rates also come from large prospective series of a single TOP method. Ashok *et al.*[12] reviewed 4132 consecutive cases of MTOP up to 9 weeks of pregnancy. In total 2.3% of cases required surgical evacuation: 1.6% for incomplete abortion, 0.3% for missed abortion and 0.3% for continuing pregnancy. Surgical intervention rates were not influenced by gestational age (comparing groups up to 49 days' and 50–63 days' gestation) or by the misoprostol regimen (comparing one or two doses of misoprostol), although continuing pregnancy rates were higher with the single-dose regimen (0.6% versus 0.1%). Rates of haemorrhage and infection were not reported. No woman experienced uterine trauma (cervical laceration or uterine perforation), although two women underwent laparoscopy (and one a subsequent laparotomy) for suspected perforation. Hakim-Elahi *et al.*[105] reviewed complications in 170,000 first-trimester STOPs performed in three New York clinics; repeat surgical evacuation was required in 0.4% of cases and sepsis/mild infection developed in 0.5%. Rates of cervical tear and uterine perforation amounted to only 0.01% each. No information was given on mean gestational age or the relationship between gestation and complication rates.

Thus the complication rates encountered in the present study were broadly in keeping with previous studies. Further, they support the overall conclusion that STOP is more effective than MTOP, being associated with lower failure rates (and hence lower rates of surgical evacuation) and lower rates of unplanned and emergency admission.

Costs and cost-effectiveness

The overall cost of STOP was greater than MTOP due to the higher inpatient standard costs, notably the operation (theatre), surgeon and anaesthetist costs, which accounted for 50% of the total cost of STOP. Thus even though complication rates (and costs) were higher with MTOP, the medical procedure was cheaper. STOP might still be cost-effective if the gain in effectiveness (measured here as avoidance of overnight stay) is worth paying for. The usefulness of this measure of cost-effectiveness depends on an understanding of the value of successfully completing TOP on the day of admission and thus avoiding unplanned or emergency overnight stay. The National Institute of Health and Clinical Excellence (NICE) sanctions new technologies according to an approximate threshold of £20,000–£30,000 per quality-adjusted life-year (QALY).[106] If this decision guide were to be applied to a choice between MTOP and STOP, at an ICER of about £8000 per QALY (randomised arm), each overnight stay avoided would have to be worth at least approximately one-quarter of a QALY (or the equivalent of about 3 months in full health).

The national tariffs for STOP and MTOP are £504 and £432 respectively.[107] Thus our costs for STOP approximate the tariff, but those for MTOP are substantially lower. We can speculate on the causes of this discrepancy. It may relate to differences in costing methods; national tariffs are derived from average costs over all NHS Trusts (over 300). Alternatively (or in addition), complication rates (and particularly surgical evacuation rates) related to MTOP may be lower in Newcastle upon Tyne than other units. However, even if this were the case, which seems unlikely in view of the comparability of complication rates with previous studies, this could not account for the differential cost.

There have been no recent studies of abortion costs from the UK. Creinin[20] in his randomised trial of abortion methods below 9 weeks' gestation estimated that STOP was 10% more expensive than MTOP. However, his assessment of resource use was limited to staff time and did not estimate actual monetary costs. Afable-Munsuz *et al.*[108] assessed costs of MTOP models from data gathered from a sample of 11 abortion care settings. The total episode cost for providing MTOP ranged from $252 to $460. In 2001–2 the average self-paying woman in the USA was charged $372 for STOP, but Grimes and Creinin[109] provide strong evidence that charges are below market value and that the genuine cost is 'several times higher'. The only cost-effectiveness study identified from a literature search of the last 10 years was also conducted in the USA and compared dilatation and evacuation and

MTOP in the second trimester.[110] STOP was found to be less costly and more effective than MTOP. However, standard costs are higher for second-trimester MTOP.

It is important to emphasise that the policy for abortion provision (that must be funded and resourced) is not necessarily to move from one method to another. Rather, based on the results of the present study, there is a strong argument for considering making both methods available and giving women the choice. The costs provided can help inform any policy defined by a mix of MTOP and STOP in a range anywhere from 0% MTOP to 100% MTOP, but which, in the context of choice, ideally reflects women's preferences. It is therefore up to the decision-maker to weigh up any gain from changing the mix against any loss from taking resources from other aspects of health-care provision.

Participants' experiences of involvement in the trial

One of the aims of the qualitative substudy was to better understand the factors that shape women's experiences of the health service contexts in which clinical trials are undertaken. In addition, we wished to identify those factors that promote and inhibit women's involvement in clinical trials on TOP.

Existing work on the ways that participants understand and enact their participation in clinical trials has tended to focus on older people participating in studies of the management of chronic illness, particularly cancer[111,112] and cardiovascular disease,[113] where the time horizons for consent, recruitment and trial participation are often extended over many months. This research has highlighted the difficulties that participants face in conceptualising and responding to randomisation processes and dealing with therapeutic misconception.[114,115] An important motive in such research has been the perceived need to better understand processes of informed consent with the hope of improving recruitment, and retention into trials.[116]

Research on participation in clinical trials of abortion differs in several important respects from research in other areas. First, participants tend to be young and are normally quite healthy. Second, although a clinical procedure is at issue, participation is not normally a matter of treatment. Third, the procedure itself is normally a single event and not a matter of management over an extended period. Finally, the time horizons in which women seek a termination, consent to enter a trial and undergo the procedure are highly compressed. Indeed, because these horizons are limited by the Abortion Act, timeliness of TOP is a matter of central importance. Qualitative research on experiences of participation in trials of TOP is limited – in a structured narrative review,[65] we identified 18 qualitative studies. Of these, only three were embedded in studies comparing MTOP and STOP and all were conducted in the USA in the 1990s, two relating to home administration of mifepristone.[65,117]

Our review[65] highlighted rapid access to services characterised by supportive non-judgemental staff appeared to characterise positive responses to TOP. Participants in the present study also sought rapid access to abortion services and were concerned about the ways that professionals evaluated them. Those attending family planning clinics experienced a smoother pathway to secondary care that required them to invest less work in negotiating and co-ordinating their own care. Once in the hospital service, rapid assessment and treatment was important to women. The accounts of participants in this trial fit well with qualitative and observational data from the wider literature: unobstructed entry into care, supportive professionals and quick access to TOP were important. Women responded negatively to problems that retarded or obstructed their rapid progress along the clinical pathway. We know that participants were under significant psychosocial pressure in the period that they negotiated access to TOP, but their accounts of this are largely procedural in form.

Like participants in other clinical trials,[66,118] participants in this trial accounted for their involvement through the notion of helping in some way; women's accounts of enrolling into the trial were organised through a set of ideas about altruism in which an unpleasant experience (TOP) was compensated by helping others through participation in research. For some this was framed as a general ethical obligation, but for others different levels of personal benefit were also described. Their accounts of the trial itself were dominated by the problem of allocation to an arm of the trial (which was itself an important component of negotiating preferences), in which the question of randomisation played a significant part. Letting the computer 'choose' the method of

TOP remained something that some participants found hard to understand. In combination with what seems a strong set of pre-existing preferences, this led to poor recruitment into the randomisation arm of the trial. This is because the partial preference trial design enabled women to construct their choice to participate in altruistic terms. It also meant that they could control what that altruistic choice meant in practice, by choosing the arm of the trial that represented the mode of TOP that they actually preferred.

Limitations of research

The main limitation of the study was the poor follow-up rates, particularly at 3 months after the procedure. By a combination of interview (at both hospital and community clinics), postal questionnaire, text messaging and web-based participant entry we were able to capture primary outcome data from 70% of participants, 10% more than we predicted. One of the major benefits of the purpose-designed computer system was the ability to collect data by text messaging and the internet. However, only 4% of participants utilised each of these approaches, with the majority of women (53%) preferring contact by telephone. As a result we were able to collect complete secondary outcome data from a minority of women. Methods of data collection were more limited at 3 months (being confined to postal, telephone or web-based questionnaires). This may account for the low rate of data collection at this time (21%). The difficulties obtaining follow-up data on women after abortion have been highlighted previously, with response rates typically between 60% and 75% within the 4 weeks after the procedure, falling to as low as 30% thereafter.[18,26,27,86,97,100]

Generalisability of results

Despite the high proportion of women who declined randomisation, we believe the results of the trial are generalisable. We acknowledge that some aspects of the abortion service offered in Newcastle upon Tyne may differ from those provided elsewhere in the UK. Women referred for abortion were assessed in a nurse-led abortion clinic rather than by a medical professional in a general gynaecological outpatient clinic. This system minimised delays and is popular with women and those making referrals.[119] We believe this aspect of service provision is very unlikely to have influenced the trial findings. While the procedures of MTOP and STOP followed national guidance,[3] virtually all STOPs were performed by two consultant gynaecologists. Rates of incomplete abortion, and by inference the associated morbidity, are influenced by the seniority of the surgeon as well as gestational age, ranging from 2% when the surgeon was a consultant to 12% with a senior house officer and from 0% at 5–6 weeks' gestation to 12% at 12–13 weeks' gestation.[7] It is therefore possible that incomplete abortion associated with STOP may be slightly lower in this trial than in other services.

Conclusions

In this randomised preference trial of medical and surgical abortion in pregnancies less than 14 weeks' gestation, MTOP was associated with more negative experiences of care and lower acceptability, as determined by fewer women opting for the same procedure in the future. The acceptability of MTOP declined with increasing gestational age. Although MTOP was less costly, it was less clinically effective than STOP, being associated with more unplanned admissions and more complications. The trial provides further evidence that women value the option to choose abortion method; over 80% of participants expressed a preference, of whom just over half opted for MTOP. The majority of those choosing MTOP were satisfied with their care and would choose the same method again in the future.

A large number of participants declined randomisation in this trial reflecting, at least in part, strong preferences about abortion method. While this generates concern about the external validity of the trial and the generalisability of the results, the anticipated impact on future patient outcomes also depends on the nature of the changes in clinical practice that are implemented in response to the trial results. If, as here, the results do not support the unambiguous superiority of one treatment over another, and there is evidence of strong preferences, then the policy response which best reflects all the study data would be to continue doing what was done in the trial, i.e. to offer patients choice. In these circumstances, we would argue that the generalisability of the overall conclusion drawn from the study data will be enhanced in comparison to that based upon a more traditional trial design.

Implications for health care

Provision of abortion care varies substantially across England and Wales; a national survey in 2000 found that, of those units with facilities for abortion before 13 weeks, only 32% of NHS units and 41% of specialised non-NHS units provided both MTOP and STOP.[120] Even fewer (21%) NHS units provided both methods after 13 weeks.[120] While provision of MTOP has increased since 2000,[2] there is increasing concern that access to STOP, particularly after 12 weeks of pregnancy, is declining.[121] This study provides persuasive evidence that a patient-centred abortion service should offer women the choice of medical or surgical termination up to 14 weeks' of pregnancy.

Surgical TOP was more costly than MTOP, but more effective (as determined by lower rates of unplanned overnight stay and emergency admissions). STOP might still therefore be cost-effective if this gain in effectiveness is felt to be worth paying for. The results of the DCE indicated that women felt that avoidance of overnight stay was an important service attribute. Another key attribute, also emphasised by many of the women interviewed, was waiting time. There is evidence of barriers to referral within primary care,[84] and similar concerns were identified by some of the women interviewed. As complication rates increase with gestational age at abortion,[2] it is important that women can access abortion services as quickly as possible; subsequent to completion of this trial a system of direct access has been introduced that allows women seeking abortion to refer themselves to the termination service.[122]

In order to make an informed choice about abortion method, women need high-quality information about their options. Evidence suggests that most leaflets from abortion services in England and Wales contain insufficient information to enable informed decision-making.[123] This study provides important information that should be incorporated into a national evidence-based decision-aid leaflet.[124]

Summary of key recommendations for practice

1. Patient-centred abortion services should offer women the choice of abortion method up to 14 weeks' of pregnancy.
2. In order to make an informed choice about abortion method, women need high-quality information about their options.
3. Abortion services should be accessible to women including direct access options. Where GPs are uncomfortable referring women for abortion, systems need to be in place to ensure they are redirected promptly.

Recommendations for future research

1. Audit of provision of MTOP and STOP in England and Wales: the last national survey of abortion provision was in 2000 and there is an urgent need to reaudit available NHS and specialised non-NHS services.
2. Exploration of barriers to offering women the choice of TOP method and ways of improving accessibility to TOP services. The Faculty of Family Planning and Reproductive Health have expressed concern regarding provision of STOP services, particularly after 12 weeks of pregnancy.[121] The barriers to development and maintenance of this service, particularly within the NHS sector, need exploring.
3. Comparison of MTOP and manual vacuum aspiration under local anaesthetic in pregnancies below 9 weeks' gestation: many women would prefer not to have MTOP, but also fear general anaesthesia. Manual vacuum aspiration is a safe and effective method of early abortion,[125] but has never been compared with MTOP in a UK population.
4. Comparison of MTOP and STOP after 14 weeks' gestation: surgical abortion after 14 weeks necessitates dilatation and evacuation. The only randomised trial comparing dilatation and evacuation with the currently recommended regimen for MTOP (mifepistone/misoprostol) was abandoned because of poor recruitment.[126] There is an urgent need to compare the acceptability and effectiveness of late abortion methods.

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Contributions of authors

First and final draft of report prepared by SC Robson. First draft of report (methods and results) prepared by T Kelly. Study design and statistical analysis prepared by D Howel. Design and analysis of DCE prepared by M Deverill. Design and discussion of psychological aspects prepared by J Hewison. Qualitative substudy (methods and results) prepared by MLS Lie. Statistical analysis prepared by E Stamp. Economic analysis prepared by N Armstrong.

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Appendix 1

Information pamphlet

The Newcastle Upon Tyne Hospitals NHS
NHS Trust

Termination of Pregnancy

Your Questions Answered (1)

Women's Services Directorate

What will happen at the hospital clinic?

- You will be seen by a specialist nurse or doctor.
- They will take all your medical details, check your blood pressure and examine your abdomen (tummy).
- They will perform a scan through your abdomen to find out the size of the pregnancy. For this you need a full bladder.
- You will be asked if a swab can be taken from the neck of the womb (cervix) to see if there is an infection (chlamydia). This involves passing a speculum into the vagina (similar to having a smear).
- A blood sample will be taken to find out your blood group and to check you are not anaemic.
- You should be in the hospital clinic for no more than an hour.
- Remember; if your doctor has given you a letter please bring this to the clinic.
- You will be given a prescription for antibiotics to reduce the risk of infection. You should start these the day before the termination.

What methods of termination of pregnancy (abortion) are available?

Surgical

- Termination is undertaken by an operation under a general anaesthetic.
- You are admitted to the Day Unit (Ward 39) or the Gynaecology Ward (Ward 40) on the morning of operation.
- Before the operation it is necessary to insert some tablets (prostaglandin) into the vagina to prepare (soften) the cervix.
- A few hours later you will be taken to the operating theatre where an anaesthetic (injection) is given into the back of your hand.

- When you are asleep the cervix is gently opened and the pregnancy removed. The operation takes 5-10 minutes.

- Sometimes women experience crampy tummy pain just before or after the operation.

- Most women go home later the same day after they have recovered from the anaesthetic.

Medical

- You are admitted to the Gynaecology Ward (Ward 40).

- Termination is undertaken by tablets in two parts.

- The first part involves taking an oral tablet (Mifepristone) which helps prepare the womb by altering the hormone balance needed for the pregnancy to continue. This is usually given on the ward after you have been seen in the out-patient clinic. You can go home after taking this tablet.

- The second part involves coming into hospital 2 days later (at around 8.30 AM) when different tablets (prostaglandin) are inserted into the vagina. These stimulate the womb to expel the pregnancy.

- If the pregnancy is **less than nine weeks** size, abortion usually occurs within four hours of the tablets but if not, further prostaglandin tablets are given. You can go home 1-2 hours after passing the pregnancy providing you feel alright. There is a one in 10 chance that abortion does not occur before going home at 4.30 pm. This is not a problem but you may experience heavier bleeding and pain at home.

- If the pregnancy is **9 weeks or more**, further prostaglandin tablets are usually required. These are repeated until the pregnancy is passed. This may mean staying overnight. There is a 3-4 in 100 chance the tablets don't work in which case you would be offered a surgical termination.

- Prior to passing the pregnancy it is usual to experience vaginal bleeding and crampy tummy pain. This tends to be worse in pregnancies over 9 weeks. Most women only need simple pain killers, but stronger injections are available if needed.

Which is the 'best' method of termination?

- At present there is insufficient evidence to be certain whether one method of termination is preferable. More research is needed to find out which method is most acceptable to women.

- Some women, especially during medical termination, feel sick and have vomiting and diarrhoea.

- Overall 3-5 out of every 100 women will experience pain and/or bleeding after a medical or surgical termination requiring them to seek medical advice. In about half of these cases, the termination is not complete, and an operation is necessary to empty the womb.

- More serious problems (such as severe infection or bleeding and damage to the womb) are much less common (less than 1 in 100 women).

- **We need your help to find out which method of termination is most acceptable to women in order that we can improve our services.** A research study is being carried out at the Royal Victoria Infirmary to find out more about women's experiences of medical and surgical termination. You may be invited to take part. If so, this will be fully explained and it is up to you to decide whether or not to take part.

- The method of termination will be decided once you have spoken to the specialist nurse or doctor.
  It is helpful to keep an open mind until you have had the opportunity to discuss this.

What happens if I am undecided about the termination?

- The decision to terminate a pregnancy is always difficult. Some women remain undecided if this is the right option for them
- If you have doubts about whether to go through with the termination, it is important to share these with the specialist nurse or doctor
- Some women benefit from further counselling before they decide what to do. The important thing is to make the right decision and not feel rushed into doing something you really don't want to do.

What about future contraception?

- It is important to have effective contraception
- The specialist nurse or doctor will discuss future contraception with you and there are information leaflets available in the clinic.
- Whatever contraceptive method you choose, we will ensure this is prescribed before you go home.

If you wish to cancel your appointment or you think you may be late please ring the Out Patients Department on 0191 2825900

Version 4. Feb 2006
Information written by Professor S. Robson
Review date February 2008

Appendix 2

Protocol – A randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation

Protocol ID: TOP/SCR/002

Protocol version: 1

Date: 9 February 2005

EudraCT number: 2004-002920-17

1 Protocol contacts

Chief Investigator

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Statistician
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Trial Manager
Kathryn Oliver, Clinical Trials Unit, Centre for Health Services Research, University of Newcastle, 21 Claremont Place, Newcastle upon Tyne, NE2 4AA. Tel: 0191 222 7045 ext. 3816

2 Protocol signature page

2.1 Protocol authorisation signatories

Signature ..... Date .....

Denise Howel, Statistician

Signature ..... Date .....

Kathryn Oliver, Trial Manager

2.2 Chief investigator signature

I agree to comply with the study protocol, the principles of GCP and the appropriate reporting requirements.

Signature ..... Date .....

Professor Stephen Robson

3 Contents

4 Glossary

AE	Adverse Event
GA	General Anaesthetic
GCP	Good Clinical Practice
GP	General Practitioner
HADS	Hospital Anxiety and Depression Scale
HTA	Health Technology Assessment
IES	Impact of Events Scale
IMP	Investigational Medicinal Product
NHS	National Health Service
PM	Preference Medical
PS	Preference Surgical
RCOG	Royal College of Obstetricians and Gynaecologists
RM	Randomised Medical
RS	Randomised Surgical
RVI	Royal Victoria Infirmary
SAE	Serious Adverse Event
SUSAR	Serious Unexpected Suspected Adverse Reaction
TOP	Termination of Pregnancy
WTP	Willingness to Pay

5 Protocol summary

Full title	A randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation
Short title:	TOP study
Protocol version:	1
Protocol date:	9 February 2004
Chief investigator:	Professor Stephen Robson
Sponsor:	Department of Health, Research and Development, Health Technology Assessment Programme
Funder:	Department of Health, Research and Development, Health Technology Assessment Programme
Study design:	A partially randomised preference trial comparing surgical and medical termination of pregnancy up to 14 weeks' gestation. Follow-up will be conducted at 2 weeks and 3 months
Study intervention:	Surgical or medical termination of pregnancy
Objectives:	To determine differences in efficacy, acceptability and cost
Primary outcome	Acceptability, determined by preferred method of a future variable: termination
Study site:	Royal Victoria Infirmary, Newcastle upon Tyne
Study population:	2232 eligible women
Study duration:	3 years

6 Responsibilities

Sponsor

Department of Health, R&D, Health Technology Assessment Programme

Trial management

The following functions falling under the responsibility of the sponsor will be delegated to the Newcastle Clinical Trials Unit.

- Authorisation: including CTA request, research ethics committee opinion, notification of protocol amendments and the end of trial.
- GCP and conduct: including GCP arrangements, management of IMP (free of charge), emergency and safety procedures.
- Pharmacovigilance: including defining adverse events/reactions, reporting of SUSARs, notifying investigators of SUSARs, annual listings and safety report.

Trial conduct at site

Investigator responsibilities:

- Study conduct and the welfare of study subjects.
- Familiar with the use of the investigational medicinal product as described in the product information, administration according to the protocol and drug accountability.
- Compliance with the protocol, documentation of any protocol deviations and reporting of all serious adverse events.
- Screening and recruitment of subjects.
- All trial-related medical decisions.
- Provision of adequate medical care in the event of an adverse event.
- Obtaining site-specific assessment from local ethics committee:
  - Assistance will be provided by the CTU.
- Obtaining R&D approval from the appropriate Trust and abide by the policies of research governance.
- Compliance with the principles of GCP.
- Obtain written informed consent from participants prior to their participation.
- Qualified by education, training and experience to assume responsibility for the proper conduct of the trial and shall provide a current signed and dated curriculum vitae as evidence.
- Availability for study meetings and in the case of an audit.

- Maintenance of study documentation and compliance with reporting requests:
  - Maintaining a project file, including copies of study approval, list of subjects and their signed informed consent forms.
  - Documenting delegation of tasks to study personnel, e.g. co-investigators, research nurse.
  - Ensure data collected is accurate and complete.
  - Updating the CTU regarding the progress of the trial.
  - Ensure subject confidentiality is maintained during the project and archival period.
- Ensure archival of study documentation for a minimum of 12 years following the end of the study, unless local arrangements require a longer period.

7 Background

Unwanted pregnancy is a major health issue; worldwide an estimated 53 million abortions are performed each year, resulting in up to 100,000 maternal deaths.[1] In 2002 nearly 185,000 pregnancy terminations were performed in England and Wales of which 78% were funded by the NHS. The majority of abortions are performed before 13 weeks of pregnancy (87%) and by surgical methods (86%).[2] In 2000, 64 of 194 (33%) units with facilities for termination of pregnancy before 13 weeks provided both medical and surgical methods, while among the 130 units with only one method available, surgical termination of pregnancy was the only option in 79%.[3] Prior to 14 weeks' gestation surgical termination can be performed by vacuum aspiration (VA). This procedure, performed under general anaesthesia, has been the 'method of choice' since the 1960s; VA is currently used in 81% of abortions performed prior to 10 weeks' gestation and 92% of those performed at 10–12 weeks.[2] The technique is safe and efficacious; major complications (uterine perforation, pelvic sepsis and haemorrhage requiring blood transfusion) occur in 0.2–0.9% of cases.[2,4,5] However, up to 5% of women return to hospital with post-abortion symptoms, of which 50–65% require surgical evacuation for retained products.[4,5] Complication rates increase with gestation,[2,4–6] with incomplete abortion reported in up to 12% of cases ≥12 weeks.[5] Cervical preparation with prostaglandins facilitates cervical dilatation and reduces complications.[7] It is recommended, if the woman is under 18 years of age or at gestation > 10 weeks, using misoprostol 400 µg vaginally 3 hours prior to surgery.[7]

Medical abortion using mifepristone, an anti-progesterone, and prostaglandins has been available since the 1980s. For abortions up to 63 days' gestation, evidence suggests that mifepristone (200 mg orally) followed 36–48 hours later by either gemeprost (1 mg vaginally) or misoprostol (800 µg vaginally) are equally safe and effective, with 95–97.5% of women achieving complete abortion.[8–10] Because of much lower costs, 72% of units use misoprostol.[5] Complete abortion rates with single-dose mifepristone/misoprostol fall from 98.5% at ≤49 days to 96.7% at 50–63 days[10] but are much greater after 63 days.[11] For women at 49–63 days, if abortion has not occurred 4 hours after administration of misoprostol, a second dose (400 µg vaginally or orally) may be administered.[7] Between 64 and 91 days' gestation, efficacy is increased if the initial dose of misoprostol is followed by repeated doses of 400 µg.[12] However, even using up to a maximum of five further doses, the need for surgical evacuation increased from 0.9% at 9–10 weeks to 7.9% at 12–13 weeks.[12]

A Cochrane systematic review of medical versus surgical methods of first trimester termination of pregnancy identified only five relevant trials, mostly with small numbers.[13] Although the authors concluded that prostaglandins alone seemed to be less effective than surgical abortion, only one trial of mifepristone/prostaglandins was included.[14] The review suggested there was inadequate evidence to comment on the acceptability and side effects of medical versus surgical abortions. A partially randomised preference trial of medical and surgical termination of pregnancy between 10 and 13 weeks has subsequently been reported.[15] Side effects (vomiting, diarrhoea and abdominal pain) were higher in the medical group, although there was no difference in the rates of major complications up to 8 weeks.

Available evidence suggests that 17–85% of women requesting first-trimester termination of pregnancy have a preference for either a medical or surgical procedure.[13–16] The most common reason cited for preferring a medical termination of pregnancy is the avoidance of surgery and/or anaesthesia.[13,17] The large variation in reported preference rates may be explained by factors such as gestational age, prior experience and time to access the procedure.[13,16–18] Preference for surgical termination of pregnancy appears to increase with gestational age;[14,15] early in pregnancy women appear to perceive the medical procedure as easier and more natural while later it is perceived as more stressful (related to concerns about pain and

seeing the fetus).[16–18] If a woman has a preference for one method she is unlikely to be enrolled in a randomised trial or she may refuse the allocated method.[17] To represent the full range of service users, randomised trials need to include preference arms.

Service users' evaluations of the care they have received are clearly important in the context of current initiatives to develop a more patient-centred NHS. Patient satisfaction with their care is the most commonly used indicator in research on patient evaluations,[19] but definitions of satisfaction vary, and different measures incorporate different dimensions of the construct, such as adequacy, suitability and acceptability. A common problem with satisfaction measures is that they exhibit ceiling effects, i.e. most patients report being satisfied, and distinctions between care of different quality are often not observed. This is likely to be a particular problem in areas such as termination of pregnancy, where patients are widely observed to experience a sense of relief after the procedure. Most studies of women's views about termination of pregnancy have reported procedure acceptability; typically women have been asked whether they would opt for the same method in the future or recommend the method to a friend;[13,17,20] data from randomised trials indicate that acceptability of both methods before 9 weeks gestation is high (63–92%), with 2–36% of women randomised to surgical termination of pregnancy preferring a medical procedure in future and 22–37% of women randomised to medical termination of pregnancy preferring a surgical termination of pregnancy.[13,15] Where women have a preference for one method, typically ≥90% would choose the same method in the future.[14,16–18,20] Acceptability may be lower at later gestations; in the only randomised trial of abortion methods between 10 and 13 weeks, more women opted for VA again than medical abortion (79% versus 70% respectively).[15] However, response rates were low (< 50%). The results reported above are based on the 'single question with a binary outcome' approach to assessing acceptability. Such measures are simple to collect and report but provide limited information, particularly about why respondents hold the views they do. One supplementary approach is to ask respondents to rate specific features of their care thereby providing information about the reasons underlying acceptability judgements. Using a semantic differential rating scale, Henshaw *et al.*[14] identified that in randomised women, medical abortion rated lower on six of the bipolar adjectives, with pain showing by far the largest difference. Vacuum aspiration was also rated less painful in women allocated according to preference.

The psychological effects of termination of pregnancy have recently been reviewed.[21] The authors concluded that termination of pregnancy rarely causes immediate or lasting negative psychological consequences in healthy women. Indeed several studies reported positive outcomes such as relief.[21] Henshaw *et al.*[14] performed a partially randomised preference trial of termination of pregnancy < 9 weeks and found no differences in depression, anxiety or low self-esteem 2 weeks after the procedure[22] nor, in a much smaller number, 2 years later.[23] Whether medical termination of pregnancy is associated with more adverse psychological consequences after 9 weeks' gestation is not known.

Although many studies have reported the outcomes of first-trimester termination of pregnancy, very few have randomised the method of abortion, and only one has included women beyond 9 weeks of pregnancy, despite the fact this group constitutes over 40% of termination of pregnancies.[15]There is a need for a partially randomised preference trial comparing VA with current methods of medical abortion. In addition to patient acceptability the trial needs to determine the clinical and cost effectiveness of the two methods.

In 2002 a pilot randomised trial of medical versus surgical termination in women at ≥9 weeks' gestation was commenced at the Royal Victoria Infirmary (RVI)), Newcastle upon Tyne. Women not expressing a preference for one method were randomised to medical or surgical termination of pregnancy. All women were offered follow-up at 2 weeks post procedure. Due to limited availability of the research nurse, recruitment was only possible from selected clinics.

Of 408 women at 9–13 weeks, 284 (70%) were suitable and agreed to participate in research, of which 139 (49%) were prepared to be randomised to medical or surgical termination of pregnancy. Outcome data at 2 weeks was obtained in 75 (53%) and included emergency admission rates, psychological scales (Impact of Event Scale, Hospital Anxiety and Depression Scale) and satisfaction with care. The pilot study information has been used to inform recruitment and precision calculations for the proposed trial.

During the pilot study women were divided into two gestational age groups: 9–13 weeks and

14–20 weeks based on ultrasound. Methods of medical and surgical termination of pregnancy in the 9–13 week group were identical to those proposed in the present application. Psychological impact was measured using the Impact of Event Scale (IES) and Hospital Anxiety and Depression Scale (HADS). Clinical outcome was measured using blood loss (as determined by drop in haemoglobin), unplanned (emergency) admission and symptoms (pain, diarrhoea, vomiting and vaginal bleeding). A follow-up visit at the Royal Victoria Infirmary was arranged for all women in the trial and key outcomes collected at this point by clinical enquiry and questionnaire. Updated data on recruitment and follow-up (as at March 2004) indicated that for the 9–13 week group, data on IES at 2 weeks post procedure was available from a total of 65% of randomised women. Statistical analysis of the psychological and clinical data has not been undertaken.

There is some indication that the follow-up rate (using clinic visits and selected telephone contact) is lower in the surgical arm. This could be explained by women undergoing a surgical termination of pregnancy feeling less in need of reassurance about the termination of pregnancy outcome, and therefore being less willing to attend the follow-up visit. However, a 95% confidence interval for the difference in follow-up rates between arms is 2% to 31%, i.e. the data are consistent with either a difference of little or of real practical importance. Telephone follow-up was only used for the latter part of the pilot study, and we anticipate that we can obtain key outcome data in all arms for a greater proportion of women in future by offering a choice by way of place and method of follow-up.

There is a clear policy impetus to understand, qualitatively, women's preferences for medical or surgical termination of pregnancy and the decision-making processes that lead both to these preferences and to encounters with health services. The personal and political sensitivities that surround termination of pregnancy are now well established, and have important consequences for research in the field. The most important of these is resistance to inquiry into decision-making and action where this may threaten the moral viability of the woman's decisions. This means although termination of pregnancy is one of the most common surgical procedures in the UK, little work has been done that will contribute to robust understanding of preferences for types of procedures, and even less qualitative work that has investigated this problem. Instead, the objective of much research in the field has been aimed at understanding decision-making on termination in relation to promoting access or reducing delays in referral to clinical services. Recently, this approach has led to an important qualitative study in the UK. In this study, Kumar *et al*.[24,25] have shown that most women prefer *not* to discuss their decision with clinicians, but prefer instead to receive information and prompt referral. Unease about discussing personal aspects of termination has also been registered amongst professionals, especially nurses and midwives (this may also explain the paucity of social science research in the field).[26] Factors affecting the choice of method of termination are already known to be highly complex, and organised mainly in relation to social rather than clinical factors.[27] The problem of decision-making and preferences around termination is therefore quite unlike any other arena of clinical research, especially other areas where approaches to shared decision-making have become prominent in recent years.[28]

The personal and professional sensitivities around termination of pregnancy require a highly sensitive approach to research. In this trial of surgical versus medical termination, women's preferences and responses are being intensively investigated through measures of experiences of care; strength of preference; psychological outcomes; cost-effectiveness; satisfaction with care; and also by clinical measures of morbidity including experience of symptoms and emergency admission.

The intensive investigation of women's experiences and preferences within the trial provides a point of departure for the qualitative substudy. This will draw on data collected within the economic substudy of strength of preferences, and is an optional final phase of the trial experienced by a subgroup of 32 women. Qualitative substudies within trials tend to be used either as initial (reconnaissance) studies to assist in decision-making about instrument design, study organisation and recruitment; or as formative process evaluations of ongoing work.[29] In the present study, we intend to take a different tack, using the qualitative investigation as a means of illuminating women's responses to (1) the experience of participating in the trial, and (2) their perspectives on the results of the economic study of strength of preference. Directly focusing on these topics will provide useful data, but will also indirectly open up earlier decision-making processes and questions of access to investigation.

A key problem in qualitative studies of personally sensitive experiences and actions is that of the subject being forced to construct an account that provides a *justification* for action in the face of anticipated moral judgements by an external authority;[30] this makes for bias in accounts and we have adopted an approach to study design and data collection that is explicitly intended to move the focus of subjects' accounts away from personal justification towards a wider explanatory perspective. We will do this by asking subjects to act as lay interpreters of data collected elsewhere in the study (refer to conjoint analysis, section 15), focusing on the preferences and actions of 'notional others'[31] and to use this interpretive function as a starting point for their own accounts. This approach means that its design and application do not risk confounding recruitment and retention of subjects, or other data collection, where these are already likely to be a challenge.

8 Objectives

This is a non-commercial study to determine the acceptability, efficacy and cost of medical versus surgical termination of pregnancy.

Primary objectives

To determine the acceptability of medical and surgical termination procedures as determined by their preferred method for any future TOP.

Secondary objectives

To compare experiences of care, strength of preference, psychological impact, efficacy and cost-effectiveness of surgical versus medical termination.

Qualitative substudy

The aim of the substudy is to better understand the foundations of women's preferences and decision-making about method of termination. The objectives are:

1. to identify, describe and understand women's motives for joining the trial and their experiences of participation in it
2. to identify, describe and understand women's personal experiences of seeking termination and decision-making about method of termination
3. to identify, describe and understand women's perspectives on data collected on 'strength of preference' and the model developed from conjoint economic analysis.

9 Study design

This is a partially randomised controlled preference trial comparing two procedures for termination of pregnancy at less than 14 weeks' gestation. Termination can be performed surgically (the uterus is evacuated under general anaesthetic) or medically (tablets given to procure abortion); it is unclear which of these methods is more acceptable to women. This design ensures the inclusion of women who have a prior procedure preference (preference group) and those who do not (randomised group), and will therefore reflect the population of a normal clinical setting.

Primary outcome measures

The primary outcome variable is acceptability of the procedure at 2 weeks after the procedure; participants will be asked if they would have the same method of termination again.

Secondary outcome measures

A secondary comparison of acceptability of the procedure will also be determined at 3 months after the procedure. Additional secondary outcome variables are strength of preference for the procedure, measured after 2 weeks; experiences of care, psychological impact, efficacy and satisfaction with care, measured at 2 weeks and 3 months after the termination procedure.

Further analysis will be performed to explore the relationships between willingness to pay, satisfaction and acceptability measures.

In order to better understand women's decisions regarding termination of pregnancy the study will include a qualitative component. A conceptual model of preferences will be developed via conjoint analysis in a group of non-pregnant women, and then explored via interview in a sample of women who have participated in the trial 2 weeks after their termination procedure.

Table of events

Visit	1 (baseline)	2	3	
Time	**Up to –2 weeks**	**0**	**+2 weeks**	**+3 months**
Inclusion/exclusion screening	✗			
Written informed consent	✗			
Randomisation if applicable	✗			
Reason for preference if applicable	✗			
Demography	✗			
Medical history	✗			
Concomitant medication	✗			
Ultrasound	✗			
Strength of preference		✗[a]	✗	
Termination procedure		✗		
Adverse events		✗	✗	✗
Concomitant medication		✗	✗	✗
Acceptability			✗	✗
Satisfaction with care			✗	✗
Experience of care			✗	✗
Impact of Event Scale			✗	✗
Hospital Anxiety and Depression Scale			✗	✗
Quality of Life (EQ-5D)			✗	✗
Consent for qualitative substudy			✗	
Qualitative interview			✗	

a Only determined prior to procedure in the preference group.

The study involves up to three hospital visits; the third visit is currently only part of normal care for those patients where it is unclear if medical abortion has been complete or who are experiencing problems. However, the RCOG has recently recommended that all women should be offered a follow-up appointment within 2 weeks of abortion.[7]

Alternative methods of collecting the primary and secondary outcome data will be discussed at baseline to ensure maximum follow-up.

- The third visit can be performed in a community clinic (based within sexual and reproductive health services), rather than the hospital setting.
- If participants fail to attend the 2-week follow-up visit, contact and data collection will be attempted by telephone, followed by postal questionnaire (with an option to complete the questionnaire via the internet). Also if agreeable, a final option of text message will be used to elicit primary outcome data; text messaging may also be used for a visit reminder.
- 3-month follow-up data will be collected via postal or web-based questionnaire.

From month 10 of recruitment, 32 women (8 from each arm) will be invited to join the qualitative substudy during the 2-week follow-up visit. A convenient time will be arranged by the researcher to perform this interview.

Definition of end of study

The end of the study will be the last participant's final study contact, at 3-months follow-up.

10 Subject population

This is a single-site study and will be conducted at the RVI in Newcastle upon Tyne, a busy NHS unit which undertakes nearly 1300 terminations a year. A total of 2232 women requesting termination of pregnancy are required for inclusion into the study.

10.1 Inclusion criteria

- Women requesting and accepted for termination of pregnancy at less than 14 weeks' gestation (as determined by ultrasound).
- Women under 16 years of age will be approached where they are determined to be Gillick competent (by the clinical practitioner) and where a parent/legal representative is present.
- Ability to give written informed consent.

10.2 Exclusion criteria

- Pre-existing medical disorder which is an indication for either medical or surgical TOP.
- Non-English-speaking women (apart from French, Mandarin, Cantonese, Bengali, Urdu and Arabic) due to limited availability of interpreters.
- Previous participation in this trial.
- Current participation in a 'drug' related trial.

Substudy

This sample is neither intended to be statistically representative nor to be a maximum variation sample; sampling will be purposive and sequential. Every woman entering the trial in the period after 10 months recruitment will be invited to join the qualitative substudy at 2-week follow-up. We expect a high rate of refusal to join this substudy and of attrition amongst those who do. This means that although inclusion and exclusion criteria will be the same as those for the main trial, the sample entering the qualitative substudy will be highly selected.

11 Subject recruitment

At the time of referral, all women are provided with standard hospital information about the choices and risks of termination of pregnancy. This information leaflet explicitly states that there is no medical evidence that one method of termination is 'better' than the other and research is currently being conducted at the RVI to better inform this choice. For reasons of confidentiality the study information sheet will not be sent to women prior to their consultation visit.

The initial consultation at the unit involves acceptance for termination and discussion of choices and risks. A nurse practitioner will discuss the available options and risks of termination, and then those women eligible for the study will be approached for interest in the study. Interested women will then discuss the study in detail with a research nurse and discuss their preference options. Written study information will be provided, along with opportunity for questions and time to consider the study. Willing participants will sign a consent form along with the research nurse, and confirm their decision for randomisation or preference for a medical or surgical termination.

For those women less than 16 years of age (minor), a parent or legal representative shall also have the study explained and have opportunity to ask questions. The parent or legal representative will provide written consent at the same time as and in addition to the minor's consent. For the purposes of this study, a suitable legal representative would be a close relative: sibling (age > 16), aunt/uncle or grandparent.

Unaccompanied women, or accompanied women with unsuitable representatives, of less than 16 years will not be considered for the study.

12 Study interventions

12.1 General information

Termination of pregnancy (TOP) is the commonest gynaecological procedure. It can be performed surgically or medically as described in section 1 (Background).

Vaginal bleeding and mild abdominal pain are normal post surgical and medical procedure. Nausea, vomiting and diarrhoea may also be experienced. There is also a risk of infection. Pain relief and antibiotics are provided as part of normal care.[7] Occasionally abortion is incomplete and surgical evacuation is required. Major complications of surgical termination are rare, but include uterine perforation, pelvic sepsis and haemorrhage.

Misoprostol is widely used in the UK to induce medical abortion and in cervical preparation for surgical termination, even though this is an unlicensed indication. Therefore for the purposes of this study misoprostol will be treated as an investigational medicinal product (IMP).

The Summary of Product Characteristics for mifepristone is included in Appendix A. This will be prescribed and administered as per normal practice.

12.2 Use within the study

Misoprostol will be presented as 200-µg tablets, packaged and labelled as an IMP.

Surgical termination

Women will be admitted to the Surgical Day Unit where they will receive misoprostol 400 µg vaginally 3 hours prior to the estimated time of surgery.[7] Following induction of general anaesthesia and mechanical dilatation of the cervix, the uterus will be evacuated using vacuum aspiration with a 9–12 mm curette. In the absence of excessive bleeding or other problems, women will be discharged 1–2 hours after the procedure.

In line with RCOG recommendations,[7] surgical termination will only be performed after 6 weeks' gestation because of the high failure rate (relative risk 2.9) at very early gestations. The appointment for surgical termination will be timed in line with this recommendation.

Medical termination

At an initial appointment participants will be given mifepristone 200 mg orally on the gynaecological ward by the nursing staff. After 36–48 hours, they will be admitted to the gynaecological ward where they will receive misoprostol 800 µg vaginally at approximately 8.30 a.m. Following administration of misoprostol, participants will receive oral paracetamol (500 mg) plus dihydrocodeine (10 mg) or diclofenac (75 mg), or parental diamorphine (5 mg) as required and as per normal practice. At the time of the termination participants will receive rectal metronidazole (1 g), followed by oral doxycycline (200 mg) daily for 7 days, commencing on the day of the termination. In the absence of excessive bleeding, participants will be discharged 1–2 hours after passage of the uterine contents.

Subsequent management will depend on gestation period.

Less than 9 weeks

- If the contents of the uterus have not been passed 4 hours after misoprostol administration, a second dose of misoprostol (400 µg) will be administered vaginally or orally (depending on preference and amount of bleeding).[7]
- Subsequently, if abortion does not occur and bleeding is not excessive, women will be routinely discharged between 4.30 and 5.00 p.m. The abortion occurs at home and women return for follow-up after 2 weeks.

9–13 weeks

- If the contents of the uterus have not been passed 3 hours after misoprostol adminstration, further doses of misoprostol (400 µg) will be given vaginally (or orally if bleeding is heavy) at 3-hour intervals up to a maximum of four further doses.[7]
- If the contents are still not passed, an ultrasound scan will be performed. In cases of an ongoing pregnancy, missed or incomplete abortion, surgical evacuation will be performed.

13 Randomisation

Participants with a procedure preference will decide whether to opt for a medical or surgical termination. Participants with no preference, and willing to be allocated a procedure at random, will be randomised using a computer system with web-based access for trial personnel (PowerTrial). Randomisation will be stratified according to gestation (< 9 weeks and between 9 and 13 weeks) and for previous termination of pregnancy.

14 Study data

14.1 Data collection

Baseline demographic data, including medical history and method of any previous termination, education level, occupation and income, will be collected by the nurse practitioner or research nurse for all participants. Contact details (including where possible mobile phone numbers) and availability will also be collected.

Those expressing a procedure preference at baseline will be asked to nominate one or more reasons from a list of eight, developed as part of the pilot trial.

1. General anaesthetic (GA): want to be asleep (PS).
2. Fear of GA or desire to be awake and in control (PM).
3. Fetus: do not want to see fetus (PS).
4. Pain: perceived medical as more painful (PS).
5. Visits to hospital: wanted minimum (PS).
6. Duration of procedure: less time in hospital (PS).
7. Previous experience (i.e. had prior TOP): PM or PS.
8. Other (< 5% of responses).

All participants will be invited to return for an outpatient (hospital or community clinic) assessment 2 weeks after the procedure. Outcome data will be collected at 2 weeks (by interview and questionnaire) and at 3 months (by questionnaire) after the procedure. For women who do not attend their visit for 2-week follow-up, collection of outcome data will be attempted where previously agreed via telephone interview, mobile text message and postal or web-based questionnaire. All visits and telephone interviews will be conducted by a research nurse.

Acceptability

This will be determined at 2 weeks and 3 months after the procedure by responses to the closed question 'If you ever have another termination of pregnancy, would you opt for the same method?' This simple question has been used in previous preference trials of TOP[14,15] and can, if necessary, be easily determined by phone or text message.

Strength of preference

To measure women's strength of preference for medical or surgical termination we will measure willingness to pay. This technique is being increasingly used in health technology assessment[32] and has been used previously for assessing strength of preference for abortion method.[23,33] Interviews will be conducted, using the payment card method,[34] in all women in the preference arm prior to the procedure where they will be asked to state their maximum 'willingness to pay' amount for the termination method they have chosen. Interviews will also be conducted on all women in both the randomised and preference arms at 2 weeks after the procedure when they will be asked to state their maximum 'willingness to pay' amount to receive their preferred option at a future date. The validity of women's responses will be tested by examining the correlation between stated 'willingness to pay' and level of income.

Satisfaction with care

The methodological pitfalls of measuring satisfaction with care have been reviewed recently.[35] Women will be asked to rate the quality of care during the termination and the counselling and support afterwards using a 5-point Likert scale (from excellent to poor) at 2 weeks and 3 months after the procedure. Measures in which patients are asked to rate the quality of aspects of their care show greater response variability than measures which seek direct ratings of satisfaction[36] and are better predictors of whether patients will return to the same doctor in the future.[36] For analysis we will distinguish those who rate their care as excellent from the remainder as this provides better discrimination.[37] A similar assessment has been used in our pilot trial. Ratings of care will be supplemented by information on satisfaction with care from the qualitative study.

Experience of care

To provide information about the reasons underlying acceptability judgements, we will use a semantic differential rating technique administered at 2 weeks and 3 months post procedure. This instrument uses a pair of opposite adjectives (for example, 'painless–painful') as end points on a graphic Likert scale. Women will be asked to indicate their experience by placing a mark on

the scale. Twelve bipolar adjectives will be used, scored along an evaluation dimension representing a positive or negative attitude ranging from 3 to –3. Rating scores are quick and easy to complete and have been used previously to measure attitude towards termination of pregnancy.[14,38]

We plan to undertake a further analysis to explore the relationships between willingness to pay, satisfaction and acceptability measures.

Distress, anxiety and depression
Distress will be measured using the IES at 2 weeks and 3 months after the procedure. This 15-item scale measures subjective distress to a specific event (in this case termination of pregnancy)[39] and is the most likely to pick up a difference in actual experience of having one procedure rather than another. Two subscales measure intrusion and avoidance and both are likely to arise differently from the procedures under comparison. Anxiety and depression will be measured using the HADS at 2 weeks and 3 months after the procedure. This is a widely used 14-item self-report scale designed for medical patients.[40] Depression is the main problem service providers have been concerned about.[21] Both the IES and HADS have been used in women after termination of pregnancy[21–23] and in our pilot study.

Quality of Life (EQ-5D)
This is a six-itemed validated questionnaire developed by a European committee to provide a preference-based measure of quality of life, needed for the economic evaluation.[41]

Emergency admission
Efficacy will be determined by comparing the rates of emergency admission (on the day of the procedure or after discharge) at 2 weeks and 3 months after the procedure. All women will be questioned about adverse events at the 2-week and 3-month follow-up to ensure that data are also captured for admissions or visits to another hospital or their GP. The rationale for choosing this outcome is that it is likely to include all women with significant procedure-related morbidity due to (1) incomplete abortion, missed abortion or ongoing pregnancy (all of which require surgical evacuation) and (2) pelvic infection without retained products of conception. Further there is evidence to suggest that women experiencing a failed termination (requiring surgical evacuation) or excessive pain and/or bleeding (resulting in admission) are more likely to classify the experience as unsatisfactory[42] and to opt not to have the same procedure again in the future.[20,42]

Frequency and extent of symptoms
The incidence of nausea, vomiting, diarrhoea, dizziness and abdominal pain on the day of the procedure will be recorded as well as an assessment of the severity of pain (using a 10-cm visual analogue scale) and analgesic use. Symptoms after discharge will be ascertained at the 2-week follow-up visit by the research nurse. Specifically the duration and severity of vaginal bleeding and pain as well as the length of time taken off work and to return to normal activity will be recorded.[15]

Concomitant medications will be recorded at baseline and at the time of the termination procedure by abstraction from the medical notes. Women will be asked about concomitant medications at 2-week follow-up.

Substudy
Semi-structured interviews: 32 participants will be invited to take part in one semi-structured interview with a trained interviewer. The highly selected nature of the sample, and the topic sensitivity, mean that decision-making and experiences of termination will be their indirect rather than direct focus. Interviews will be of up to 90 minutes duration and will be divided into two discrete sections.

In part 1 women will be asked about general issues connected with their experience of entering and participating in the trial, and their understanding of its design and methods. This part of the interview will indirectly elicit accounts of their experience of referral pathways into the service and trial, specific accounts of their experiences of termination, and its outcome.

In part 2 the interviewer will describe and demonstrate outcomes of a conjoint analysis (refer to section 15) using structured questions and flashcards. Subjects will be invited to comment on the model derived from conjoint analysis from the perspective of a 'notional other',[31] and will also be asked about the 'fit' between the 'willingness to pay' model and their own experiences.

With the consent of the participant, each interview will be audio-recorded using an unobtrusive mini-disk recorder and conference microphone, and later transcribed. Where participants do not consent to recording, handwritten notes will be made.

14.2 Data handling

Study data collected will be entered directly, where possible, to avoid transcription errors, into a web-based PowerTrial data capture system by the research nurse, or participant for the web-based questionnaires. The remaining study data will be entered from paper source. Audit trail and full daily back-up will be provided.

Data will be collected to standards required by CFR Title 21, part 11, and EU Directive 2001/20/EC, and adhere to the Data Protection Act 1998.

The quality and retention of study data will be the responsibility of the Newcastle Clinical Trials Unit. All study data will be archived in line with current University policy (currently 12 years).

15 Statistical considerations

15.1 Statistical analysis

The analysis strategy will be similar to that used in a partially randomised preference trial of treatment for depression.[43] The trial will contain four intervention groups:

1. randomised to medical termination (RM)
2. randomised to surgical termination (RS)
3. preference for medical termination (PM)
4. preference for surgical termination (PS).

The analysis will be on an intention-to-treat basis (although it is anticipated that women will always get the randomised or preferred intervention). Those in either medical arm (RM or PM) who subsequently receive surgical intervention, due to incomplete or missed abortion, will be analysed as per the assigned medical arm.

Baseline variables: although randomisation should balance out baseline characteristics, it will be important to compare these in the four groups to see if those who are prepared to be randomised differ from those who have a preference. If so, there are problems in extrapolating any conclusions from the randomised arms to the general population.

Primary analysis

Main comparison of randomised arms

1. Comparison of proportions of women finding the procedure acceptable. We will also investigate the interaction between past history of TOP and intervention group on acceptability and gestational age (as a continuous variable) and intervention group on acceptability.
2. Comparison of mean values on psychological and rating scales.
3. Comparison of proportions of women rating care as 'excellent'.
4. Comparison of WTP between those women in the two randomised groups.

Secondary analysis

Secondary comparison of medical and surgical arms (preference and randomised subgroups combined)

1. Comparison of proportions of women finding the procedure acceptable and rating the quality of care as 'excellent': the comparison will adjust for key baseline variables using logistic regression. We will also investigate the interaction between past history of TOP and intervention group on acceptability, and gestational age (as a continuous variable) and intervention group on acceptability.
2. Comparison of mean values of psychological and rating scales: the comparison will adjust for key baseline variables using multiple regression.
3. Comparison of proportions of women with emergency admission and particular symptoms: the comparison will adjust for key baseline variables using logistic regression.
4. Comparison of WTP between those women in the combined groups.

Tertiary comparison of combined preference and randomised groups

The aim of this comparison is to determine if receiving a preferred intervention improves key outcomes. Comparisons will be of acceptability, psychological and rating scales with methods as for secondary comparisons.

Cost-effectiveness analysis

Cost data relating NHS resource use (in both primary and secondary care) will be collected following established methods[44] up to 3 months post termination for both surgical and medical interventions. This will include data relating to the initial procedure, hospital stay, follow-up care as inpatients, any additional interventions and outpatient appointments. Data relating to GP consultations specifically for follow-up care relating to the TOP will be collected using the postal questionnaire at 3 months and, if agreed previously, by telephone where this is not returned. Data relating to secondary and primary follow-up care and any interventions required will be used to compare the burden placed on the patient's own resources when using either medical or surgical termination. The cost-effectiveness analysis will be

expressed as the cost per successfully completed termination. Extensive one-way and multivariate sensitivity analysis will be undertaken in the analysis of the final results.[45]

Clinical effectiveness analysis
Previous studies have used a variety of measures of clinical effectiveness but emphasis has been placed on failed TOP (with an ongoing viable pregnancy), incomplete abortion and presumed pelvic infection. Based on our proposed sample size, the precision with which we could detect differences in each of these complications is limited. Hence we have opted to use a combined measure of effectiveness which captures unplanned time spent in hospital, a key outcome for women.

Our definition of 'emergency admission' includes:

1. unplanned overnight stay on the day of termination
2. emergency hospital assessment or admission after discharge.

All cases of incomplete abortion, missed abortion, ongoing pregnancy (all of which require surgical evacuation) and pelvic infection without retained products of conception will therefore be included in this outcome. A very small number of women may be admitted to other units but we would anticipate collecting clinical outcome data from their hospital discharge summary and/or via our follow-up.

Qualitative substudy
Conjoint analysis or discrete choice experiment
In order to identify the key factors that shape women's preferences for termination services we will conduct a discrete choice experiment (DCE). This technique measures the strength of individual's preferences for the various attributes of a clinical intervention[46] and has been successfully used in research relating to the provision of services for women.[47] Interviews will be conducted with a sample of 100 non-pregnant women recruited from local contraception/sexual health clinics. Women will first be asked if they are interested in participating in a research interview, before provision of an information sheet, an informed discussion and written consent. These interviews will begin prior to recruitment for the main study. Previous research suggests this sample size should be adequate to provide precise parameter estimates with the number of attributes and choices we will use.[48] This sampling frame has been chosen to reduce the data collection burden on the trial sample and to avoid interference with women in the trial forming and stating preferences.

Qualitative analysis
We will use a model of preference developed from the discrete choice experiment as the basis for a semi-structured interview with 32 women (8 from each of the four groups: preference surgical, preference medical, randomised surgical and randomised medical). A conventional model of qualitative analysis will be used.[49] The analytic product of this work will be (1) a comparative model of preferences and their normative constraints and (2) a model of contextual features that affect decision-making about termination of pregnancy.

Interview transcripts will form the formal data for analysis. Following the conventional model of constant comparative analysis of transcribed data set,[49] transcripts will be interpreted iteratively, developing themes (or categories) within respondents' discourse. To facilitate qualitative analysis, and to provide an audit trail for governance purposes, we will use QSR software to manage data transcripts, coding and memoing. Initial thematic analysis will be conducted by the qualitative researcher. Transcripts will be searched for common themes and deviant cases (in relation to part 1 of the interview). Themes will be indexed (as 'codes') and searches for discrete instances of codeable items of speech will be undertaken in both cumulative comparisons (i.e. between interviews in the same arm of the trial) and condition comparisons (i.e. across interviews gathered from different arms of the trial). This will provide a robust account of the common themes relating to women's responses of joining and participating in the trial, and these themes (and deviant cases) will be recorded in a simple frame.[50] Because part 2 of each interview will involve some structured questions (and flashcards showing simple histograms of quantitative data), direct thematic comparisons will be made across a range of responses, and some simple quantification of results will also be possible. Once initial analysis has been undertaken by the qualitative researcher, qualitative inter-rater checking will be undertaken on a sample of cumulative and condition comparisons. This will add value to analysis[51] and will enable secure claims about the quality of data to be made.

15.2 Sample size calculation

The power of the study is based on the main comparison of acceptability between women randomised to medical or surgical TOP. Assuming the acceptability of medical termination to be 75%, we would need responses from 335 women in each randomised arm to detect a difference in acceptability of 10% (i.e. from 75% to 85%) with a significance level of 5% and power of 90%. We believe this difference in the level of acceptability is important for both consumers and providers; a similar difference was employed by Ashok *et al*.[15] in their large randomised comparison of abortion methods.

Based on the power calculation we need primary outcome data on 670 women randomised to medical or surgical TOP at < 14 weeks' gestation. In order to achieve this number we calculated:

1. 1116 women need to be randomised (assuming 40% of women randomised fail to attend for follow-up and primary outcome data are therefore not available)
2. 2232 women need to be recruited (assuming 50% of women agreeing to participate in the study have a preference for medical or surgical TOP and are therefore not suitable for randomisation)
3. 3188 women need to be approached (assuming 30% of women accepted for TOP will decline involvement in the study).

Justification for assumptions

All three assumptions were based on our experience from an earlier pilot trial conducted at the RVI involving women requesting TOP at 9–13 weeks' gestation. For reasons detailed in Kumar *et al*.[25] we believe our assumption of 60% follow-up is conservative. Further, previous trials conducted in the UK have reported that 54%[14] and 82%[15] of recruited women undergoing TOP at < 9 weeks and 9–13 weeks respectively were prepared to have their method of TOP determined by randomisation. Thus our estimate of 50% may also be conservative. The proportions of women accepted for TOP who agreed to join these two randomised preference trials were not reported. Data from non-randomised studies conducted in the UK suggest 87–93% of similar women are prepared to participate in studies involving follow-up (including psychological questionnaires) after TOP, suggesting our assumption of 70% (based on the pilot study) is realistic.

16 Compliance and withdrawal

In order to increase the proportion of participants returning for follow-up after 2 weeks, an option to attend a community clinic has been incorporated in the design, thus allowing ease of access and evening appointments.

A range of contact processes are also included to maximise capture of primary and secondary data where participants fail to attend the 2-week follow-up visit. These include telephone contact (up to two attempts) for all participants to capture the primary variable, and postal questionnaires or a web-based questionnaire option. For agreeable participants text messaging will be used for a visit reminder at week 2 and collection of the primary variable (up to two attempts).

Following reasonable attempts to capture data and non-response, participants will be considered lost to follow-up. Participants who withdraw their consent following the procedure will not be replaced.

17 Data monitoring

17.1 Discontinuation rules

The trial may be prematurely discontinued on the basis of new safety information, or for other reasons given by the Trial Steering Committee (see below), regulatory authority or ethics committee concerned.

17.2 Monitoring, quality control and assurance

The trial will be managed through the Clinical Trials Unit (CTU), University of Newcastle in accordance with the EU Trials Directive, the Research Governance Framework for Health and Social Care and MRC Guidelines for Good Clinical Practice in Clinical Trials. Professor S. Robson will have overall responsibility for the day-to-day conduct of the trial supported by the nurse coordinator, CTU Trial Manager and Trial Management group (TMG). The TMG will include the principal investigators, co-applicants and nurse representation.

The Trial Steering Committee (TSC) will be chaired by Professor Alan Templeton, University of Aberdeen, to include two other independent members and two lay members. It is proposed the TSC will meet twice during the first year of the trial and then annually. Their role is to monitor and supervise the trial, to ensure it is conducted to

high standards in accordance with the protocol, the principles of GCP, and with regard to patient safety.

The Trial Manager will ensure that the study is conducted in accordance with GCP through a combination of central monitoring and site monitoring visits.

Central monitoring
- All documentation essential for study initiation will be reviewed prior to site authorisation.

Site monitoring
- Consent forms will be reviewed as part of the study file and the presence of a copy in medical records confirmed.
- Consent forms will be compared against the study participant identification list.
- Inclusion/exclusion criteria will be reviewed for 20% of participants.
- Serious adverse events will be verified against medical records.
- The presence of essential documents in the study file will be checked.
- Management of the IMP will be reviewed periodically.

All monitoring findings will be reported and followed up with the appropriate persons in a timely manner. A final site visit will be performed at the end of the study:

- to complete final monitoring requirements, as above
- to review archiving of study site documentation.

18 Pharmacovigilance

18.1 Definitions

An 'adverse event' (AE) is any untoward medical occurrence which does not necessarily have a causal relationship with the treatment.

A 'serious adverse event' (SAE) is any untoward medical occurrence or effect that at any dose:

- results in death
- is life-threatening
- requires hospitalisation or prolongation of existing inpatients' hospitalisation
- results in persistent or significant disability or incapacity.

'Life-threatening' in the definition of a serious adverse event or serious adverse reaction refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

Medical judgement should be exercised in deciding whether an adverse event or reaction is serious in other situations. Important adverse events or reactions that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

An 'adverse reaction' is an untoward or unintended response to an investigational medicinal product (IMP) related to any dose administered.

A 'suspected unexpected serious adverse reaction' (SUSAR) is a severe adverse reaction, the nature of which is not consistent with the applicable product information.

18.2 Expected adverse reactions

18.2.1 Expected side effects of the termination procedure

Some degree of abdominal pain and vaginal bleeding is expected during and after a medical or surgical termination of pregnancy. Major complications are uterine perforation, pelvic sepsis and haemorrhage (requiring blood transfusion).

18.2.2 Expected adverse reactions to misoprostol

Misoprostol may cause diarrhoea, abdominal pain, nausea, vomiting, headache, dizziness and, more rarely, chills and fever. Uterine bleeding, sometimes heavy and prolonged, may occur. Very frequent uterine contractions are observed in the hours following prostaglandin intake.

18.2.3 Expected adverse reactions to mifepristone

Refer to Appendix A, Summary of Product Characteristics.

18.3 Protocol specifications

For the purposes of this protocol all non-serious adverse drug reactions and serious adverse events will be recorded.

The incidence of nausea, vomiting, diarrhoea, dizziness, abdominal pain and bleeding will be recorded following explicit questioning; all other adverse drug reactions will be recorded as AEs.

The following are expected serious adverse events which are being explicitly recorded during the study: emergency admissions for incomplete abortion, missed abortion, or ongoing pregnancy (all of which require surgical evacuation) and pelvic infection without retained products of conception. These events will not be considered SAEs for reporting purposes, as described below.

18.4 Reporting serious adverse events

All SAEs, as specified by the protocol above, shall be reported to the Newcastle CTU *immediately* by fax or email.

The initial report must contain the following minimum information:

1. study identifier
2. subject's unique study number
3. age
4. event description
5. start date of event
6. reason for seriousness, i.e. death, life-threatening, hospitalisation, disability/ incapacity or other
7. date of termination procedure
8. causality to procedure (medical or surgical) or mifepristone or misoprostol
9. reporter's name and date.

The follow-up report must contain all of the above, plus:

1. gender
2. stop date of event
3. mifepristone and misoprostol (dose, route, duration dates)
4. concomitant medication (name, dose, route, duration dates, indication)
5. outcome, including diagnosis
6. reporter's name and date.

The CTU must report all SAEs which are also unexpected adverse drug reactions to the regulatory authority and ethics committee concerned within 15 days (7 days if life-threatening or resulting in death). Therefore it is very important that the initial report is faxed or emailed to the CTU within 24 hours of discovery.

19 Ethical considerations

Prior to commencement of the trial, a Clinical Trial Authorisation will be obtained from the MHRA and favourable opinions will be sought from the Research Ethics Committee and Trust R&D.

Information sheets will be provided to all eligible subjects and written informed consent obtained prior to any study procedures.

Non-English-speaking subjects will be included where possible: as part of the NHS service interpreters are provided at the initial consultation; and translation of the information sheet will be provided in six additional languages (choice of languages based on demand for translation services at the RVI).

20 Finance and insurance

The NHS Trust has liability for clinical negligence that harms individuals toward whom they have a duty of care. NHS Indemnity covers NHS staff and medical academic staff with honorary contracts conducting the trial.

The NIHR Health Technology Assessment programme is funding this study. The Newcastle Primary Care Trust are providing additional funds to support the community clinics used for follow-up visits.

21 Study reporting

Results of the study will be reported to the HTA, and be available on their web site. Participants may have access to the results on request.

All data collected during the study, and any intellectual property arising from the use of those data, shall be owned by the University of Newcastle.

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23 Appendices

Appendix A: Mifepristone, summary of product characteristics

Exelgyn Laboratoires

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France

Telephone:	**+44 (0)1491 642 137**
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Document last updated on the *e*MC: **Tue 04 December 2001**

Mifegyne

1. NAME OF THE MEDICINAL PRODUCT

Mifegyne

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains: Active Ingredient – Mifepristone 200mg

3. PHARMACEUTICAL FORM

Light yellow, cylindrical, bi-convex tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

(1) Medical termination of intra uterine pregnancy of up to 63 days gestation.
(2) Softening and dilatation of the cervix uteri prior to mechanical cervical dilatation for pregnancy termination.
(3) For use in combination with gemeprost for termination of pregnancy between 13 and 24 weeks gestation.
(4) Labour induction in fetal death in utero
For termination of pregnancy mifepristone may only be administered **in accordance with the Abortion Act 1967 as amended by The Human**

Fertilisation and Embryology Act 1990.

As a consequence, when used for termination of pregnancy, mifepristone and any treatment necessary to effect complete termination of the pregnancy can only be prescribed by a medical doctor and administered in a NHS or non NHS hospital or centre (having approval to undertake termination of pregnancy). The product will be administered under the supervision of a medical practitioner.

4.2 Posology and method of administration

(1) Therapeutic termination of pregnancy of up to 63 days gestation.

600mg of mifepristone (3x200mg tablets) by mouth in a single dose. The dosage is independent of body weight.

Unless abortion has already been completed, gemeprost 1.0mg p.v should be given 36 – 48 hour later in the treatment centre.

(2) Softening and dilatation of the cervix

600mg mifepristone by mouth 36-48 hours prior to the planned operative procedure.

(3) For use in combination with gemeprost for termination of pregnancy between 13 – 24 weeks gestation

600mg mifepristone (3x200mg tablets) is taken by mouth 36-48 prior to scheduled prostaglandin termination of pregnancy

The patient must return to the treatment centre 36-48 hours later, the recommended procedure for therapeutic termination of pregnancy with gemeprost **must** then be followed. ***See gemeprost SPC***

(4) Labour induction for fetal death in utero

600 mg of mifepristone (200mg x 3 tablets) in a single oral daily dose for two consecutive days.

Labour should be induced by the usual methods if it has not started within 72 hours following the first administration of mifepristone.

If the patient vomits shortly after administration of the mifepristone she should inform the doctor.

4.3 Contraindications

Suspected ectopic pregnancy

Pregnancy not confirmed by ultrasound scan or biological tests

Chronic adrenal failure

Severe Asthma not controlled by therapy

Known allergy to mifepristone or any component of the product

Inherited porphyria

If gemeprost is used, any contraindication to gemeprost (see gemeprost product information).

4.4 Special warnings and special precautions for use

WARNINGS

In the absence of specific studies, mifepristone is not recommended in patients with: Renal failure, hepatic failure or malnutrition.

Patients with prosthetic heart valves or who have had one previous episode of infective endocarditis should receive chemoprophylaxis according to the current UK recommendations.

1) Medical termination of pregnancy of up to 63 days gestation

The method requires active involvement of the woman who should be informed of the requirements of the methods:

- the necessity to combine treatment with prostaglandin to be administered at a second visit.
- The need for a follow up visit within 10 to 14 days after intake of mifepristone to check that abortion is complete.
- The possibility of failure of the method which may require termination by another method.

In the case of a pregnancy occurring with an intra-uterine device in situ, this device must be removed before administration of mifepristone.

The expulsion may take place before prostaglandin administration (in about 3% of cases). This does not preclude the follow up visit to check that the abortion is complete.

-Risks related to the method

- Failures

The non-negligible risk of failure, makes the follow up visit mandatory to check that abortion is complete.

- Bleeding

The patient must be informed of the occurrence of prolonged vaginal bleeding (up to 12 days after intake of mifepristone) which may be heavy. Bleeding occurs in almost all cases and it not in any way proof of complete expulsion.

The patient should receive precise instructions on whom she should contact and where to go in the event of any problems, particularly in the case of very heavy vaginal bleeding**.**

A follow-up visit must take place within a period of 10 to 14 days after

administration of mifepristone to verify by the appropriate means (clinical examination, ultrasound scan, and Beta-HCG measurement) that expulsion has been completed and that vaginal bleeding has stopped or substantially reduced. In case of persistent bleeding beyond the control visit, its disappearance should be checked within a few days.

If continuing pregnancy is suspected, a further ultrasound scan may be required to evaluate its viability.

Persistence of vaginal bleeding at this point could signify incomplete abortion, or an unnoticed extra-uterine pregnancy, and appropriate treatment should be considered.

In the event of continuing pregnancy diagnosed after the control visit, termination by another method will be proposed to the woman.

Since heavy bleeding requiring hemostatic curettage occurs in 0 to 1.4% of the cases during the medical method of pregnancy termination, special care should be given to patients with hemostatic disorders with hypocoagulability, or with anemia. The decision to use the medical or the surgical method should be decided with specialised consultants according to the type of hemostatic disorder and the level of anaemia.

2) Softening and dilatation of the cervix uteri prior to surgical pregnancy termination

For the full efficacy of therapy, the use of Mifepristone must be followed 36 to 48 hours later and not beyond, by surgical termination.

-Risks related to the method

- Bleeding

The woman will be informed of the risk of vaginal bleeding which may be heavy, following intake of mifepristone. She should be informed of the risk of abortion prior to surgery (although minimal): she will be informed on where to go in order to check for the completeness of expulsion, or in any case of emergency.

Other risks

They are those of the surgical procedure.

3) For use with gemeprost for termination of pregnancy between 13 – 24 weeks.

For the full efficacy of therapy, Mifepristone must be followed, 36 to 48 hours later by initiation of gemeprost.

-Risks related to the method

- Bleeding

The woman will be informed of the risk of vaginal bleeding following intake of mifepristone. She should be informed of the risk of abortion prior to administration of gemeprost (although minimal): she will be informed on where to go in case of

emergency.

Other risks

They are those of gemeprost administration.

A follow-up visit is recommended at an appropriate interval after delivery of the fetus to verify that vaginal bleeding has stopped or has substantially reduced. Persistence of vaginal bleeding could signify incomplete abortion and appropriate investigation/treatment should be considered.

4) In all instances

The use of mifepristone requires rhesus determination and hence the prevention of rhesus allo-immunisation as well as other general measures taken usually during any termination of pregnancy.

During clinical trials, pregnancies occurred between embryo expulsion and the resumption of menses.

To avoid potential exposure of a subsequent pregnancy to mifepristone, it is recommended that conception be avoided during the next menstrual cycle. Reliable contraceptive precautions should therefore commence as early as possible after mifepristone administration.

PRECAUTIONS

1) In all instances

In case of suspected acute adrenal failure, dexamethasone administration is recommended. 1 mg of dexamethasone antagonises a dose of 400 mg of mifepristone.

Due to the antiglucocorticoid activity of mifepristone, the efficacy of long-term corticosteroid therapy, including inhaled corticosteroids in asthmatic patients, may be decreased during the 3 to 4 days following intake of mifepristone. Therapy should be adjusted.

A decrease of the efficacy of the method can theoretically occur due to the antiprostaglandin properties of non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin (acetyl salicylic acid). Use non-NSAI analgesics.

2) Medical termination of intra-uterine pregnancy with mifepristone and gemeprost

Rare serious cardiovascular accidents have been reported following the intra muscular administration of the prostaglandin analogue sulprostone (withdrawn in 1992). No such cases have been reported since analogues of PGE_1 (gemeprost or misoprostol) have been used. For these reasons and as a special precautionary measure, the medical method is not recommended for use in women over 35 years of age and who smoke more than 10 cigarettes a day.

<u>Method of prostaglandin administration</u>

During administration and for a minimum of three hours following administration and in accordance with clinical judgement, the patients should be monitored in the

treatment centre, which must be equipped with the appropriate equipment.

3) For the sequential use of mifepristone - prostaglandin, whatever the indication

The precautions related to the prostaglandin used should be followed where relevant.

The treatment procedure should be fully explained and completely understood by the patient. There is a Patient Information Leaflet available for each of the indications in the tablet carton. Prior to administration of mifepristone the appropriate leaflet should be given to the patient to read.

4.5 Interaction with other medicinal products and other forms of Interaction

In view of the single dose administration, no specific interactions have been studied. However, there could be interactions with drugs which modulate or inhibit prostaglandin synthesis and metabolism. See PRECAUTIONS above.

4.6 Pregnancy and lactation

In animals (see section 5.3 Pre-clinical safety data), the abortifacient effect of mifepristone precludes the proper assessment of any teratogenic effect of the molecule.

Mifepristone is a lipophilic compound and may theoretically be excreted in the mother's breast milk. However, no data is available. Consequently, mifepristone use should be avoided during breast-feeding.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Most frequently reported undesirable effects (mifepristone)

• Urogenital

- Bleeding

Heavy bleeding occurs in about 5% of the cases and may require hemostatic curettage in up to 0.7% of cases.

- Very common uterine contractions or cramping (10 to 45%) in the hours following prostaglandin intake.

- During induction of second trimester termination of uterine rupture has been uncommonly reported after prostaglandin intake. The reports occurred particularly in multiparous women or in women with a caesarean section scar.

• Gastrointestinal

- Cramping, light or moderate.

- Nausea, vomiting.

Other undesirable effects (mifepristone)

• Hypersensitivity and skin

- Hypersensitivity: skin rashes uncommon (0.2%), single cases of urticaria.

- Single cases of erythroderma, erythema nodosum, epidermal necrolysis have also been reported.

• **Other systems**

- Rare cases of headaches, malaise, vagal symptoms (hot flushes, dizziness, chills have been reported) and fever.

Undesirable effects (gemeprost)

- nausea, vomiting or diarrhoea, and rarely hypotension (0.25%)

4.9 Overdose

Tolerance studies have shown that administration of doses of mifepristone of up to

requires treatment in a specialist environment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mifepristone is a synthetic steroid with an antiprogestational action as a result of competition with progesterone at the progesterone receptors.
At doses ranging from 3 to 10mg/kg orally, it inhibits the action of endogenous or exogenous progesterone in different animal species (rat, mouse, rabbit and monkey). This action is manifested in the form of pregnancy termination in rodents.
In women at doses of greater than or equal to 1mg/kg, mifepristone antagonises the endometrial and myometrial effects of progesterone. During pregnancy it sensitises the myometrium to the contraction inducing action of prostaglandins.
Mifepristone induces softening and dilatation of the cervix, softening and dilatation has been shown to be detectable from 24 hours after administration of mifepristone and increases to a maximum at approximately 36 – 48 hours after administration.
In the majority of cases, abortion will occur within 4 hours of administration of gemeprost.
During the termination of pregnancy between 13 and 20 weeks gestation, mifepristone administered at a 600-mg dose, 36 to 48 hours prior to the first administration of prostaglandins, reduces the induction-abortion interval, and also decreases the dose of gemeprost required for the expulsion.
Mifepristone binds to the glucocorticoid receptor*.* In animals at doses of 10 to 25 mg/kg it inhibits the action of dexamethasone. In man the antiglucocorticoid action is manifested at a dose equal to or greater than 4.5 mg/kg by a compensatory elevation of ACTH and cortisol.
Mifepristone has a weak anti-androgenic action which only appears in animals during prolonged administration of very high doses.

5.2 Pharmacokinetic properties

After oral administration of a single dose of 600 mg mifepristone is rapidly absorbed. The peak concentration of 1.98 mg/l is reached after 1.30 hours (means of 10 subjects).
There is a non-linear dose response. After a distribution phase, elimination is at first slow, the concentration decreasing by a half between about 12 and 72 hours, and then more rapid, giving an elimination half-life of 18 hours. With radio receptor

assay techniques, the terminal half-life is of up to 90 hours, including all metabolites of mifepristone able to bind to progesterone receptors.
After administration of low doses of mifepristone (20 mg orally or intravenously), the absolute bioavailability is 69%.
In plasma mifepristone is 98% bound to plasma proteins: albumin and principally alpha-1-acid glycoprotein (AAG), to which binding is saturable. Due to this specific binding, volume of distribution and plasma clearance of mifepristone are inversely proportional to the plasma concentration of AAG.
N-Demethylation and terminal hydroxylation of the 17-propynyl chain are primary metabolic pathways of hepatic oxidative metabolism.
Mifepristone is mainly excreted in faeces. After administration of a 600 mg labelled dose, 10% of the total radioactivity is eliminated in the urine and 90% in the faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous colloidal silica 3mg, Maize Starch 102mg, Povidone 12mg, Microcrystaline cellulose 30mg, Magnesium Stearate 3mg.

6.2 Incompatibilities

None known.

6.3 Shelf life

Tablets - 36 months.

6.4 Special precautions for storage

None.

6.5 Nature and contents of container

Blister pack (PVC and Aluminum foil and carton) containing 3 tablets.

6.6 Instructions for use and handling

The treatment procedure should be fully explained and completely understood by the patient.

Administrative Data

7. MARKETING AUTHORISATION HOLDER

Exelgyn S.A., 6 rue Christophe Colomb, 75008 Paris, France

8. MARKETING AUTHORISATION NUMBER(S)

Mifegyne Tablets 16152/0001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Renewal May 1999

10. DATE OF REVISION OF THE TEXT

August 2001

Appendix B: Willingness to pay
Methods and questions

Women will be asked to state their WTP for their preferred method of termination at the following points.

1. Pre TOP: for women expressing a preference and enrolled in the 'preference arm' we will ascertain the maximum amount WTP using the payment card method.
2. Post TOP: all women who underwent TOP will be asked which method they would choose if undergoing a future TOP and *if* they would be willing to pay an amount to receive that preferred option at a future date. If they answer yes to this, we will ascertain the maximum amount WTP using the payment card method.

Questioning strategy (outline)
1. Description of termination method.
2. Choice of termination method.
3. Willing to pay?
   i. If no: asked why not
   ii. If yes: payment card method used (see below).
4. Then asked to explain the amount indicated. NB There is a need to categorise protest zeros from non-demanders.

Payment card method
The concept of willingness to pay and the payment card method have been used previously in a study of women's preferences in the termination of pregnancy.[33]

In this study, once respondents have indicated if they have a preference for a particular method of termination and that they would be willing to pay to access that method, they will be handed a card containing a list of values from £0 to £1000 and £1000+.

> £0 £5 £10 £20 £30 £40 £50 £60 £70 £80 £90 £100 £110 £120 £140 £160 £180 £200 £225 £250 £275 £300 £350 £400 £450 £500 £600 £700 £800 £900 £1000 £1000+
>
> If £1000+, can you say what is the exact amount?

Respondents will be asked to put a cross by the amounts that they would definitely not pay and then to consider what would be the maximum amount they would be willing to pay by circling the relevant value. If respondents indicate '£1000+' they will asked to write in the amount. All respondents will be asked an open-ended question regarding why they chose the amount indicated.

Other data to be collected
Income, age, age at which left education, occupation, previous operation with a general anaesthetic (yes/no).

Appendix C: Satisfaction with care
The E5 satisfaction measure assesses satisfaction with:

1. procedure overall
2. technical quality (thoroughness, carefulness, competence)
3. interpersonal manner (courtesy, respect, sensitivity, friendliness) of the staff
4. length of wait from request to procedure
5. using a five-choice evaluation scale:

Excellent	Very good	Good	Fair	Poor

Appendix D: Experience of care

Semantic differential rating for acceptability of procedure

Painless						Painful
3	2	1	0	–1	–2	–3
Happy						Sad
3	2	1	0	–1	–2	–3
Good						Bad
3	2	1	0	–1	–2	–3
Pleasant						Unpleasant
3	2	1	0	–1	–2	–3
Positive						Negative
3	2	1	0	–1	–2	–3
Safe						Dangerous
3	2	1	0	–1	–2	–3
Attractive						Unattractive
3	2	1	0	–1	–2	–3
Mild						Harsh
3	2	1	0	–1	–2	–3
Agreeable						Disagreeable
3	2	1	0	–1	–2	–3
Active						Passive
3	2	1	0	–1	–2	–3
Easy						Hard
3	2	1	0	–1	–2	–3
Fast						Slow
3	2	1	0	–1	–2	–3

Appendix E: Impact of Event Scale

Below is a list of comments made by people after stressful life events. Using the following scale, please indicate (with a ✗) how frequently each of these comments were true for you *during the past seven days*.

	Not at all	Rarely	Sometimes	Often
I thought about it when I didn't mean to	.	.	.	.
I avoided letting myself get upset when I thought about it or was reminded of it	.	.	.	
I tried to remove it from memory	.	.	.	.
I had trouble falling asleep or staying asleep because of pictures or thoughts about it that came into my mind	.	.	.	.
I had waves of strong feelings about it	.	.	.	.
I had dreams about it	.	.	.	.
I stayed away from reminders of it	.	.	.	.
I felt as if it hadn't happened or wasn't real	.	.	.	.
I tried not to talk about it	.	.	.	.
Pictures about it popped into my mind	.	.	.	.
Other things kept making me think about it	.	.	.	.
I was aware that I still had a lot of feelings about it, but I didn't deal with them	.	.	.	.
I tried not to think about it	.	.	.	.
Any reminder brought back feelings about it	.	.	.	.
My feelings about it were kind of numb	.	.	.	.

Scoring: not at all, 0; rarely, 1; sometimes, 3; often, 5. Total = total the scores.

Appendix F: Hospital Anxiety and Depression Scale

The statements below are about how you are feeling in yourself.

Please read each statement and **circle the number** next to the answer which comes closest to how you have been feeling in the **past week**. (Please make sure you answer every statement).

a) I feel tense or 'wound up':
- Most of the time 1
- A lot of the time 2
- From time to time, occasionally 3
- Not at all 4

b) I still enjoy the things I used to enjoy:
- Definitely as much 1
- Not quite so much 2
- Only a little 3
- Hardly at all 4

c) I get a sort of frightened feeling as if something awful is going to happen:
- Very definitely and quite badly 1
- Yes, but not too badly 2
- A little, but it doesn't worry me 3
- Not at all 4

d) I can laugh and see the funny side of things:
- As much as I always could 1
- Not quite so much now 2
- Definitely not so much now 3
- Not at all 4

e) Worrying thoughts go through my mind:
- A great deal of the time 1
- A lot of the time 2
- From time to time, but not too often 3
- Only occasionally 4

f) I feel cheerful:
- Not at all 1
- Not often 2
- Sometimes 3

h) I feel as if I am slowed down:
- Nearly all the time 1
- Very often 2
- Sometimes 3
- Not at all 4

i) I get a sort of frightened feeling like butterflies in the stomach:
- Not at all 1
- Occasionally 2
- Quite often 3
- Very often 4

j) I have lost interest in my appearance:
- Definitely 1
- I don't take as much care as I should 2
- I take just as much care 3
- I take more care than I have previously 4

k) I feel restless, as if I have to be on the move
- Very much indeed 1
- Quite a lot 2
- Not very much 3
- Not at all 4

l) I look forward with enjoyment to things:
- As much as I ever did 1
- Rather less than I used to 2
- Hardly at all 3
- Not at all 4

m) I get sudden feelings of panic:
- Very often indeed 1
- Quite often 2
- Not very often 3
- Not at all 4

Most of the time ..... 4 **g) I can sit at ease and feel relaxed:** Definitely ..... 1 Usually ..... 2 Not often ..... 3 Not at all 4	**n) I can enjoy a good book or radio or TV programme:** Often ..... 1 Sometimes ..... 2 Not often ..... 3 Very seldom 4

Appendix G: Quality of Life Questionnaire (EQ-5D)

EQ-5D – This is Euro Qual – 5D for completion by the patient. This is a standard questionnaire which is used in large research studies in similar populations.

The next few questions are how you are **at present**. *For each of the five sets of statements below please **circle the number** that **best** describes your own health state **today.***

1. **Mobility**
   I have no problems in walking about 1
   I have some problems in walking about 2
   I am confined to bed 3

2. Self-Care
   I have no problems with self-care 1
   I have some problems washing or dressing myself 2
   I am unable to wash or dress myself 3

3. Usual Activities
   I have no problems with performing my usual activities
   (eg work, study, housework, family or leisure activities) 1
   I have some problems with performing my usual activities 2
   I am unable to perform my usual activities 3

4. **Pain/Discomfort**
   I have no pain or discomfort 1
   I have moderate pain or discomfort 2
   I have extreme pain or discomfort 3

5. **Anxiety/Depression**
   I am not anxious or depressed 1
   I am moderately anxious or depressed 2
   I am extremely anxious or depressed 3

EQ-5D cont.d

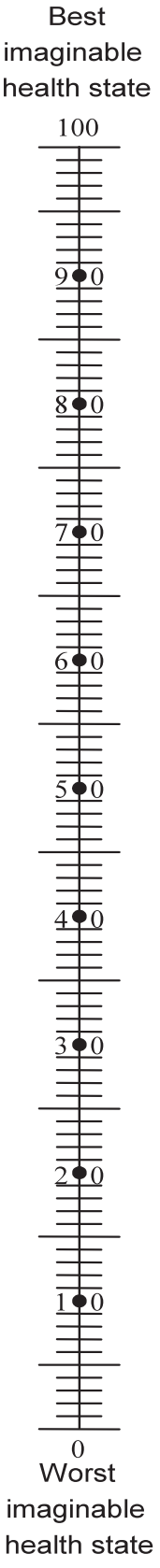
6. Now we would like you to tell us how good or bad is your own health today, in your opinion.

To help you say how good or bad your own health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0.

Please draw a line from the box below to whichever point on the scale indicates how good or bad you feel your health state is **today.**

Your own health

state today



Appendix 3

Individual-level unit costs and resource usage for each method of TOP

		MTOP (*n* = 960)		STOP (*n* = 811)	
Resource category	**Unit cost (£)**	**Number**	**Mean**	**Number**	**Mean**
Overnight stay	118.00	25	0.03	7	0.01
ERPC	483.79	25	0.03	10	0.01
Gemeprost	43.00	10	0.02	0	0.00
Misoprostol	0.17	642	0.93	11	0.02
Syntocinon	0.89	1	0.00	0	0.00
Metronidazole	2.40	5	0.01	2	0.00
Doxycycline	3.72	1	0.00	1	0.00
Cephalexin	2.83	5	0.01	1	0.00
Cocodamol	0.07	403	0.43	37	0.04
Codeine	0.08	19	0.03	92	0.18
Diclofenac	0.01	586	1.86	86	0.30
Morphine	5.00	0	0.00	3	0.00
Paracetamol	0.01	7	0.01	92	0.11
Pethidine	0.10	1	0.00	0	0.00
Trazodone	0.34	0	0.00	1	0.00
Cyclizine	0.07	6	0.01	8	0.01
Metoclopramide	0.06	0	0.00	1	0.00
Odansetron	3.14	2	0.00	3	0.00
Odansetron IV	5.39	0	0.00	2	0.00
Stemetil tab	0.07	1	0.00	0	0.00
Stemetil IM	0.54	139	0.15	8	0.01

ERPC, evacuation of retained products of conception.

Appendix 4

Individual-level unit costs and resource usage for each arm of the trial

TABLE 49 *Randomised arm*

		MTOP (*n* = 174)		STOP (*n* = 154)	
Resource category	**Unit cost (£)**	**Number**	**Mean**	**Number**	**Mean**
Overnight stay	118.00	4	0.03	0	0.00
ERPC	484.94	4	0.03	2	0.01
Gemeprost	43.00	2	0.02	0	0.00
Misoprostol	0.17	103	0.98	9	0.07
Syntocinon	0.89	0	0.00	0	0.00
Metronidazole	2.40	0	0.00	1	0.01
Doxycycline	3.72	0	0.00	0	0.00
Cephalexin	2.83	0	0.00	1	0.01
Cocodamol	0.07	71	0.46	10	0.06
Codeine	0.08	2	0.02	16	0.16
Diclofenac	0.01	95	1.85	25	0.42
Morphine	5.00	0	0.00	0	0.00
Paracetamol	0.01	0	0.00	16	0.09
Pethidine	0.10	0	0.00	0	0.00
Trazodone	0.34	0	0.00	0	0.00
Cyclizine	0.07	0	0.00	2	0.01
Metoclopramide	0.06	0	0.00	0	0.00
Odansetron	3.14	0	0.00	0	0.00
Odansetron IV	5.39	0	0.00	0	0.00
Stemetil tab	0.07	0	0.00	0	0.00
Stemetil IM	0.54	24	0.16	2	0.01

ERPC, evacuation of retained products of conception.

TABLE 50 *Preference arm*

		MTOP (*n* = 786)		STOP (*n* = 657)	
Resource category	**Unit cost (£)**	**Number**	**Mean**	**Number**	**Mean**
Overnight stay	118.00	21	0.03	7	0.01
ERPC	484.94	21	0.03	8	0.01
Gemeprost	43.00	8	0.03	0	0.00
Misoprostol	0.17	539	0.92	2	0.01
Syntocinon	0.89	1	0.00	0	0.00
Metronidazole	2.40	5	0.01	1	0.00
Doxycycline	3.72	1	0.00	1	0.00
Cephalexin	2.83	5	0.01	0	0.00
Cocodamol	0.07	332	0.42	27	0.04
Codeine	0.08	17	0.03	76	0.19
Diclofenac	0.01	491	1.87	61	0.26
Morphine	5.00	0	0.00	3	0.00
Paracetamol	0.01	7	0.01	76	0.12
Pethidine	0.10	1	0.00	0	0.00
Trazodone	0.34	0	0.00	1	0.00
Cyclizine	0.07	6	0.01	6	0.01
Metoclopramide	0.06	0	0.00	1	0.00
Odansetron	3.14	2	0.00	3	0.00
Odansetron IV	5.39	0	0.00	2	0.00
Stemetil tab	0.07	1	0.00	0	0.00
Stemetil IM	0.54	115	0.15	6	0.01

ERPC, evacuation of retained products of conception.

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We look forward to hearing from you.

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