National Institute for Health and Care Excellence

Draft for consultation

Termination of Pregnancy

[K] Medical versus surgical termination of pregnancy between 13+0 and 24+0 weeks' gestation

NICE guideline <TBC>

Evidence reviews

April 2019

Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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ISBN:

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Medical versus surgical termination of pregnancy between 13^{+0} and 24^{+0} weeks' gestation

Review question

What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

Introduction

The aim of this review is to determine the safety and efficacy of surgical compared with medical termination between 13^{+0} and 24^{+0} weeks' gestation.

PICO table

See Table 1 for a summary of the population, intervention, comparison and outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women who are having a termination of pregnancy between 13^{+0} and 24^{+0} weeks' gestation
Intervention	Surgical termination of pregnancy using either dilatation and evacuation, or vacuum aspiration
Comparison	Medical termination of pregnancy using mifepristone and misoprostol
Outcome	**Critical outcomes:** • Incomplete abortion with the need for surgical intervention • Haemorrhage requiring transfusion or ≥ 500ml of blood loss • Patient acceptability **Important outcomes:** • Abortion completed by • intended method • Uterine injury (including rupture) • Cervical injury requiring repair • Infection reported within 1 month of termination

For further details see the full review protocol in appendix A.

Clinical evidence

Included studies

Only studies conducted from 1985 onwards were considered for this review question, as mifepristone was made available in the UK in 1991 and evidence to support the use of mifepristone in practice is unlikely to be more than 5 years before its licensing

in 1991. The surgical techniques used pre-1990 were also different to those used currently, however for consistency, an overall date limit of 1985 was decided, and any eligible studies on surgical termination of pregnancy published between 1985-1990 were downgraded for indirectness for this reason instead.

For this review, both RCTs and non-randomised comparative studies with N ≥ 100 in each arm were eligible. We found none of the latter that met the inclusion criteria, but 2 RCTs both comparing medical to surgical termination of pregnancy between 13^{+0} and 24^{+0} weeks' gestation were included in this evidence review (Grimes 2004; Kelly 2010).

The included studies are summarised in Table 2.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

A summary of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study and setting	Population	Intervention/ comparison	Outcomes
Grimes 2004 RCT USA	n=18 English-speaking women aged ≥18 years with gestational age of 13.9 to 19.9 weeks, including women who had experienced a fetal death or had a fetus with congenital anomalies or chromosomal defect.	**Medical termination of pregnancy:** Oral mifepristone 200mg + vaginal misoprostol **Surgical termination of pregnancy:** Dilatation & evacuation performed under light general anaesthesia	• Incomplete abortion with the need for surgical intervention • Patient acceptability / satisfaction • Abortion completed by intended method *Only indirectly reported:* • *Haemorrhage requiring transfusion or ≥ 500ml of blood loss* • *Uterine injury (including rupture)* • *Cervical injury requiring repair* • *Infection reported within 1 month of termination*
Kelly 2010 RCT United Kingdom	n=122 Pregnant women requesting and accepted for TOP under clause C of the human	**Medical termination of pregnancy:** Oral mifepristone 200mg + vaginal misoprostol	• Incomplete abortion with the need for surgical intervention • Haemorrhage requiring transfusion

Study and setting	Population	Intervention/ comparison	Outcomes
	Fertilisation and Embryology Act (1990) amendment of the Abortion Act (1967), gestational age 13^{+0} to 19^{+6} weeks at the time of ToP; women aged < 16 years also eligible if deemed Fraser competent and had a parent/guardian present and consenting; previous caesarean section was not an exclusion criterion.	**Surgical termination of pregnancy:** Vacuum aspiration performed under general anaesthesia	or ≥ 500ml of blood loss • Patient acceptability / satisfaction. • Abortion completed by intended method • Uterine injury (including rupture) • Cervical injury requiring repair *Only indirectly reported:* • Infection reported within 1 month of termination

RCT: randomised controlled trial; ToP: termination of pregnancy

See the full evidence tables in appendix D and the forest plots in appendix E.

Quality assessment of clinical studies included in the evidence review

See the clinical evidence profiles in appendix F.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see supplementary material 2 for details).

Economic model

See economic analysis in appendix J

Evidence statements

Critical outcomes

Incomplete abortion with the need for surgical intervention

RCT evidence showed a higher clinically important difference in the rate of incomplete abortions requiring surgical intervention in the medical termination group

compared with the surgical termination group (2 RCTs, n=140; RR= 4.58 [95% CI 1.07, 19.64]; moderate quality).

Haemorrhage requiring transfusion or > 500ml of blood loss (only indirectly reported by one of the studies)[1]

RCT evidence did not detect a clinically important difference in the rate of haemorrhage requiring transfusion or ≥ 500ml blood loss between the medical termination group and the surgical termination group (2 RCTs, n=140; RR= 0.21 [95% CI 0.02, 1.72]; low quality); however, there was uncertainty around the estimate.

Patient acceptability

RCT evidence showed either a lower clinically important difference or no clinically important difference in patient satisfaction/acceptability between the medical termination group and the surgical termination group, depending on how patient satisfaction/acceptability was measured:

- Patient acceptability/satisfaction (scale from 1 [very satisfied] to 5 [very dissatisfied]; at discharge): No clinically important difference (1 RCT, n=18; median [IQR] =1 [1, 1] in both treatment groups; low quality).

- Patient acceptability ("Would choose the same method again"; at 2 weeks): Clinically importantly lower in the medical termination group (1 RCT, n=56; RR=0.54 [95% CI 0.39, 0.76]; very low quality).

- Patient acceptability ("Experience of termination of pregnancy worse than expected"; at 2 weeks): Clinically importantly favours surgical termination of pregnancy (1 RCT, n=56; RR=28.74 [95% CI 1.81, 456.75]; very low quality).

- Patient satisfaction (rating of satisfied with information/counselling pre-termination of pregnancy; at 2 weeks): No clinically important difference (1 RCT, n=65; RR=1.02 [95% CI 0.95, 1.11]; very low quality).

- Patient satisfaction (rating of satisfied with care during termination of pregnancy; at 2 weeks): No clinically important difference (1 RCT, n=65; RR=1.02 [95% CI 0.95, 1.11]; very low quality).

- Patient satisfaction (rating of satisfied with counselling/support post-termination of pregnancy; at 2 weeks): No clinically important difference (1 RCT, n=64; RR=0.96 [95% CI 0.88, 1.05]; very low quality).

Important outcomes

Abortion completed by intended method

RCT evidence did not detect a clinically important difference in the rate of abortions completed by the intended method between the medical termination group and the surgical termination group (2 RCTs, n=128; RR= 0.88 [95% CI 0.79, 0.98]; moderate quality); however there was uncertainty around this estimate.

[1] Not directly reported, but the authors report that no serious adverse events occurred.

Uterine injury (including rupture; only indirectly reported by one of the studies)[2]

RCT evidence reported no events of uterine injury in either the medical termination group or the surgical termination group; therefore differences between the groups could not be estimated (2 RCTs, n=140; low quality).

Cervical injury requiring repair; only indirectly reported by one of the studies)[3]

RCT did not detect a clinically important difference in the rate of cervical injury requiring repair between the medical termination group and the surgical termination group (2 RCTs, n=140; RR= 0.34 [95% CI 0.01, 8.29]; low quality); however, there was uncertainty around this estimate.

Infection reported within 1 month of termination; only indirectly reported by the 2 studies)[4]

RCT evidence did not detect a clinically important difference in the rate of infection reported within 1 month of termination between the medical termination group and the surgical termination group (2 RCTs, n=140; RR= 7 [95% CI 0.41, 118.69]; low quality); however, there was uncertainty around this estimate.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Incomplete abortion with the need for (repeat) surgical intervention was included as a critical outcome due to the impact that needing a second procedure will have on both the woman and on available resources. Although haemorrhage requiring transfusion or ≥ 500ml blood loss is a relatively rare outcome, the committee agreed to include it as a critical outcome as it can be very serious when it occurs. The committee also agreed to prioritise patient satisfaction as a critical outcome for decision making as termination of pregnancy is an area where women are known to have strong preferences. The committee further agreed that although cervical trauma, uterine perforation and infection within 1 month of termination are rare in women undergoing termination of pregnancy, they should be included as important outcomes given the seriousness of such events and to allow for a balance of the benefits and harms of the different methods for termination of pregnancy to be assessed. Abortion completed by the intended method was included as an important outcome to capture the failure rate of each abortion method as this also has implications for resource use and is likely to influence patient preference due to the need for a second visit if the chosen method fails.

The quality of the evidence

The evidence in the pairwise comparisons was assessed using the GRADE methodology. The quality of the evidence across all outcomes ranged from very low

[2] Not directly reported, but the authors report that no serious adverse events occurred.
[3] Not directly reported, but the authors report that no serious adverse events occurred.
[4] Not directly reported, but in one of the studies the authors report that after medical and surgical abortion 3/9 and 0/9 women, respectively, had fever (>38 degrees Celsius), and in the other study infection was included in the definition of complications in the method section, so presumably this outcome was looked for but not found.

to moderate, and was only downgraded for 2 reasons: imprecision due to low event rates and missing data.

Benefits and harms

The evidence showed that it was unclear whether or not there was a clinically important difference in the rates of haemorrhage requiring transfusion or ≥ 500ml blood loss, abortions completed by the intended method, uterine injury, cervical injury requiring repair, and infection reported within 1 month of termination between medical and surgical termination of pregnancy. There was a higher clinically important difference in patient satisfaction/acceptability in the surgical than medical termination group, and the rate of incomplete abortions requiring surgical intervention in the medical termination group compared with the surgical termination group.

The committee were aware that the included studies both had difficulties recruiting women to participate because this is an area of very strong patient preferences in terms of which method of termination they want. The committee noted the evidence from Evidence Reports A and B which showed that women valued a choice of procedure at all gestations and therefore they agreed that the recommendation should be to offer a choice of surgical or medical termination to all women to allow for the woman's preferred option. A table highlighting the benefits and risks of medical and surgical termination of pregnancy has been added to the 'providing information' section of the short guideline to help women make a choice about what type of procedure is right for them. Figures from this evidence review have been included to outline the risk of complications or need for additional procedures to remove retained products of conception in the case of incomplete abortion. Cervical injury was not included in the complications for medical termination of pregnancy as the committee agreed that the risk would be extremely low as no instruments or dilators are inserted into the cervix. For gestational ages not covered by this review question, figures were taken from a Cochrane review comparing medical and surgical termination of pregnancy (Say 2002) and national abortion statistics (Department of Health 2018).

Despite the limited evidence, the committee decided to prioritise other areas addressed by the guideline for future research and therefore made no research recommendations regarding surgical or medical termination between 13^{+0} and 24^{+0} weeks' gestation.

Cost effectiveness and resource use

From Abortion Statistics in England and Wales dataset (Department of Health 2018) 19,103 terminations of pregnancy were performed in 2017 between 13^{+0} and 23^{+6} weeks' gestation. Given the potential for a significant resource impact made from recommendations in this area bespoke economic modelling was undertaken. The economic model compared a base case of surgical termination of pregnancy to that of medical termination. Based on NHS Reference Costs the cost of a surgical termination of pregnancy was greater than that of a medical termination of pregnancy by £579. However, the majority of these terminations of pregnancy are provided in the independent sector. Clinical Commissioning Groups in England negotiate their own contracts with the independent sector to provide termination of pregnancy services. These contracts and costs, especially on the individual level, are commercially sensitive and are not available from public sources. It is very probable that the cost of terminations of pregnancy in the independent sector is significantly below that of NHS settings as they can take advantage of having sufficient expertise and economies of scale in specially designed clinics and theatres. It is also intuitive that Clinical Commissioning Groups would not 'contract out' services at a higher price than it could provide them 'in house'. Consequently the committee were of the

opinion that both the actual cost of both medical and surgical terminations and the difference between the 2 is overestimated. It was accepted though that the cost of a surgical termination of pregnancy would be greater than that of medical termination.

When adverse event costs, which were higher for medical termination of pregnancy, were added on surgical termination remained the more costly option. Even when the overnight stays for the medical group, observed in Kelly 2010, were added surgical termination of pregnancy remained the more costly by £236 per procedure. Quality of life was not explicitly explored in the analysis given the difficulties in estimating these as documented across the guideline and no published quality of life studies identified for this patient group. There was very low quality evidence that women preferred a surgical termination of pregnancy but the committee thought this effect was most likely down to attrition bias. The committee also strongly emphasised that quality of life and preference was likely to vary by participant based on their own preferences, expectations and previous experience of termination of pregnancy services. The adverse event rate for events likely to have a prolonged impact on health and quality of life were minimal and that whilst quality of life could potentially be impacted upon through anxiety previous studies suggested this impact was short term.

The economic model considered surgical termination of pregnancy as current practise as over three quarters were performed via this method in 2017 for this patient group. Provision however varies widely across England with some areas only offering the option for only 1 of the methods. For example 99.4% of terminations of pregnancy provided in Hartlepool are medical. There may be greater implementation costs for providing either medical or surgical terminations in some areas than for others where a choice of methods are already provided. The economic model did not attempt to estimate these implementation costs given the large variation across the country. The best method for implementation will also differ between areas with some able to offer travel to different areas whilst others will need to recruit individuals with the relevant skills and provide appropriate accommodation to provide the service themselves. It was unclear if implementation costs would be higher for areas that needed to increase medical provision or those requiring an increase in surgical.

Given the difficulties highlighted above the committee felt it was appropriate to offer both medical and surgical terminations for this group and that this would be an efficient use of NHS resources.

The evidence considered for this review question covered the gestational age range between 13^{+0} and 24^{+0} weeks' gestation. However, recommendations were made for women between 13^{+0} and 23^{+6} weeks' gestation to be consistent with the requirements of the 1967 Abortion Act

References

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Appendices

Appendix A – Review protocols

Review protocol for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

Field (based on PRISMA-P	Content
Review question in SCOPE	What is the effectiveness, safety and acceptability of surgical compared to medical termination in the second trimester?
Review question in guideline	What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?
Type of review question	Intervention
Objective of the review	To determine the safety and efficacy of surgical compared with medical termination between 13^{+0} and 24^{+0} weeks' gestation
Eligibility criteria – population	Women who are having a termination of pregnancy between 13^{+0} and 24^{+0} weeks' gestation Exclusions: - Studies with >10% of an indirect population
Eligibility criteria – intervention(s)	Surgical termination of pregnancy using either dilatation and evacuation, or vacuum aspiration Exclusions: - Sharp curettage
Eligibility criteria – comparator(s)	Medical termination of pregnancy using mifepristone and misoprostol
Outcomes and prioritisation	**Critical outcomes:** • Incomplete abortion with the need for surgical intervention • Haemorrhage requiring transfusion or > 500ml of blood loss • Patient acceptability **Important outcomes:** • Abortion completed by intended method • Uterine injury (including rupture) • Cervical injury requiring repair • Infection reported within 1 month of termination
Eligibility criteria – study design	- Systematic reviews of RCTs - RCTs - Non-randomised comparative studies with N ≥ 100 in each arm
Other inclusion exclusion criteria	Inclusion: - English-language
Proposed sensitivity/sub-group analysis, or meta-regression	Stratified analyses based on the following sub-groups of women, where possible:

Field (based on PRISMA-P	Content
	Medical conditions: - Complex pre-existing medical conditions - No complex pre-existing medical conditions - Fetal anomaly versus no fetal anomaly
Selection process – duplicate screening/selection/analysis	Dual weeding will not be performed for this question Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Quality control will be performed by the senior systematic reviewer. Dual data extraction will not be performed for this question.
Data management (software)	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). 'GRADEpro' will be used to assess the quality of evidence for each outcome. NGA STAR software will be used for study sifting, data extraction, recording quality assessment using checklists and generating bibliographies/citations,
Information sources – databases and dates	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase Limits (e.g. date, study design): Apply standard animal/non-English language exclusion Dates: from 1985 Studies conducted from 1985 onwards will be considered for this review question, as mifepristone was made available in the UK in 1991 and evidence to support the use of mifepristone in practice is unlikely to be more than 5 years before its licensing in 1991.
Identify if an update	Not an update
Author contacts	For details please see the guideline in development web site.
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	Standard study checklists will be used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist: • RoBIS for systematic reviews • Cochrane risk of bias tool for RCTs

Field (based on PRISMA-P	Content
	• Newcastle-Ottawa scale for non-randomised comparative studies The risk of bias across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for analysis – combining studies and exploring (in)consistency	Synthesis of data: Pairwise meta-analysis will be conducted where appropriate for all other outcomes. When meta-analysing continuous data, change scores will be pooled in preference to final scores. For details regarding inconsistency, please see the methods chapter Minimally important differences: For 'haemorrhage requiring transfusion or > 500ml of blood loss', statistical significance will be used. For the remaining outcomes, default values will be used: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual. If sufficient relevant RCT evidence is available, publication bias will be explored using RevMan software to examine funnel plots.
Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – Current management	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by The National Guideline Alliance and chaired by Profession Iain Cameron in line with section 3 of Developing NICE guidelines: the manual. Staff from The National Guideline Alliance will undertake systematic literature searches, appraise the evidence, conduct meta-analysis and cost-effectiveness analysis where appropriate, and draft the guideline in collaboration with the committee. For details please see the methods chapter.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds The National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England
PROSPERO registration number	Not registered

GRADE: Grading of Recommendations Assessment, Development and Evaluation; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; NGA: National Guideline Alliance; RCT: randomised controlled trial

Appendix B – Literature search strategies

Literature search strategy for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

The search for this topic was last run on 8th March 2018. It was decided not to undertake a re-run for this topic in November 2018 as the results of the economic model and corresponding sensitivity analysis suggest very strongly that the conclusions are unlikely to change as a result of any update search. Moreover, the Guideline Committee were not aware of any new relevant studies.

Database: Medline & Embase (Multifile)

Last searched on **Embase Classic+Embase** 1947 to 2018 March 07, **Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)** 1946 to Present

Date of last search: 8th March 2018

#	Searches
1	exp abortion/ use emczd
2	exp pregnancy termination/ use emczd
3	exp Abortion, Induced/ use ppez
4	Abortion Applicants/ use ppez
5	exp Abortion, Spontaneous/ use ppez
6	exp Abortion, Criminal/ use ppez
7	Aborted fetus/ use ppez
8	fetus death/ use emczd
9	abortion.mp.
10	(abort$ or postabort$ or preabort$).tw.
11	((f?etal$ or f?etus$ or gestat$ or midtrimester$ or pregnan$ or prenatal$ or pre natal$ or trimester$) and terminat$).tw.
12	((f?etal$ or f?etus$) adj loss$).tw.
13	((gestat$ or midtrimester$ or pregnan$ or prenatal$ or pre natal$ or trimester$) adj3 loss$).tw.
14	(((elective$ or threaten$ or voluntar$) adj3 interrupt$) and pregnan$).tw.
15	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16	exp Curettage/ use ppez
17	"dilation and evacuation"/ use emczd
18	"dilatation and curettage"/ use emczd
19	vacuum aspiration/ use emczd
20	((dilat$ or vacuum$ or suction$ or surgical) adj5 (evac$ or extract$ or curet$ or aspirat$)).tw.
21	curettage$.tw.
22	16 or 17 or 18 or 19 or 20 or 21
23	Mifepristone/ use ppez

#	Searches
24	mifepristone/ use emczd
25	(mifepriston$ or mifeprex$ or mifegyn$ or ru-486$ or ru486$ or ru-38486$ or ru38486$).mp.
26	Misoprostol/ use ppez
27	misoprostol/ use emczd
28	(misoprostol$ or cytotec$ or arthrotec$ or oxaprost$ or cyprostol$ or mibetec$ or prostokos$ or misotrol$).mp.
29	(medica$ adj5 evac$).tw.
30	23 or 24 or 25 or 26 or 27 or 28 or 29
31	15 and 22 and 30
32	(surg$ adj6 (abortion$ or termination$)).tw.
33	(medica$ adj6 (abortion$ or termination$)).tw.
34	32 and 33
35	31 or 34
36	limit 35 to english language
37	remove duplicates from 36 [general exclusions filter applied]

Database: Cochrane Library via Wiley Online

Date of last search: 8th March 2018

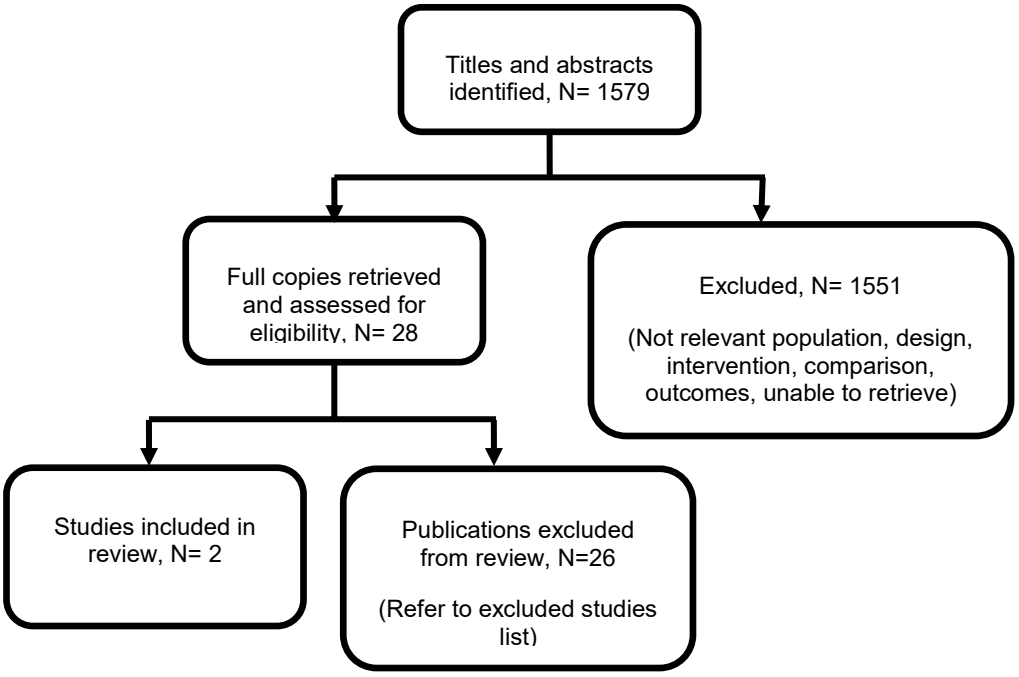
#	Searches
#1	MeSH descriptor: [Abortion, Induced] explode all trees
#2	MeSH descriptor: [Abortion Applicants] explode all trees
#3	MeSH descriptor: [Abortion, Spontaneous] explode all trees
#4	MeSH descriptor: [Abortion, Criminal] explode all trees
#5	MeSH descriptor: [Aborted Fetus] explode all trees
#6	"abortion":ti,ab,kw (Word variations have been searched)
#7	(abort* or postabort* or preabort*):ti,ab,kw (Word variations have been searched)
#8	((fetal* or fetus* or foetal* or foetus* or gestat* or midtrimester* or pregnan* or prenatal* or pre natal* or trimester*) and terminat*):ti,ab,kw (Word variations have been searched)
#9	((fetal* or fetus* or foetal* or foetus*) next loss*):ti,ab,kw (Word variations have been searched)
#10	((gestat* or midtrimester* or pregnan* or prenatal* or pre natal* or trimester*) near/3 loss*):ti,ab,kw (Word variations have been searched)
#11	(((elective* or threaten* or voluntar*) near/3 interrupt*) and pregnan*):ti,ab,kw (Word variations have been searched)
#12	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13	MeSH descriptor: [Curettage] explode all trees
#14	((dilat* or vacuum* or suction* or surgical) near/5 (evac* or extract* or curet* or aspirat*)):ti,ab,kw (Word variations have been searched)
#15	curettage:ti,ab,kw (Word variations have been searched)
#16	#13 or #14 or #15
#17	MeSH descriptor: [Abortifacient Agents] explode all trees
#18	abortifacient*:ti,ab,kw (Word variations have been searched)
#19	MeSH descriptor: [Mifepristone] explode all trees

#	Searches
#20	(mifepriston* or mifeprex* or mifegyn* or ru-486* or ru486* or ru-38486* or ru38486*):ti,ab,kw (Word variations have been searched)
#21	MeSH descriptor: [Misoprostol] explode all trees
#22	(misoprostol* or cytotec* or arthrotec* or oxaprost* or cyprostol* or mibetec* or prostokos* or misotrol*):ti,ab,kw (Word variations have been searched)
#23	(medica* near/5 evac*):ti,ab,kw (Word variations have been searched)
#24	#17 or #18 or #19 or #20 or #21 or #22 or #23
#25	(surg* near/6 (abortion* or termination*)):ti,ab,kw (Word variations have been searched)
#26	(medica* near/6 (abortion* or termination*)):ti,ab,kw (Word variations have been searched)
#27	#25 and #26
#28	#12 and #16 and #24
#29	#27 or #28

Appendix C – Clinical evidence study selection

Clinical evidence study selection for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation

Figure 1: Study selection flow chart



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation

Study details	Participants	Interventions	Outcomes and Results	Comments
Full citation Grimes,D.A., Smith,M.S., Witham,A.D., Mifepristone and misoprostol versus dilation and evacuation for midtrimester abortion: a pilot randomised controlled trial, BJOG: An International Journal of Obstetrics and Gynaecology, 111, 148-153, 2004 **Ref Id** 117411 **Country/ies where the study was carried out**	**Sample size** n = 18 randomised (47 women eligible, but 29 declined participation as they had a clear preference for termination method. These 29 women differed [unclear of this is statistically significantly] from those who were randomised on the following characteristics: They were older, more likely to be white, fewer previous pregnancies, and lower gestational age; only 1 of 11 women with confirmed fetal abnormalities consented to participate, and an additional 3 women with fetal death did not consent to participate) **Characteristics** mToP: n = 9; Median age (IQR) = 25 (22-27) years; race white/black: n = 1/8; median (IQR) gravidity: 3 (3-4); median	**mToP:** Day 1: Oral mifepristone 200mg. Day 3 vaginal misoprostol 800micrograms (mcg) (4 tablets); then misoprostol 400mcg orally every 3 hours (max 4 doses) until termination of pregnancy occurred. Women also received prophylactic prochlorperazine and diphenoxylate (against vomiting and diarrhoea), a continuous infusion of morphine using a patient-controlled system, and prophylactic oral oxycycline. Placental removal was undertaken if the placenta failed to pass spontaneously within 2 hours of the fetus. **sToP:** Day 1: Multiple laminaria were placed in the cervix under paracervical anaesthesia with 20cc of 0.25% bupivacaine. Day 2 to 3 (Day 2 until July 2002, Day 3 thereafter): D & E performed	**Outcomes: Incomplete abortion with the need for surgical intervention** mToP: 4/9 sToP: 1/9 **Outcome: Haemorrhage requiring transfusion or > 500ml of blood loss** Not directly reported, but the authors report that no serious adverse events occurred. **Outcome: Patient acceptability (Scale from 1 [very satisfied] to 5 [very dissatisfied]); at discharge median (IQR)** mToP (n = 9): 1 (1-1) sToP (n = 9): 1 (1-1). Please note, this outcome appears to be a mix of	**Limitations** **Quality of study:** Risk of bias assessed using Cochrane risk of bias tool Random sequence generation: Low risk; computer-generated list; the person responsible for generating the randomisation list did not take part in enrolment Allocation concealment: Low risk; sequentially numbered opaque sealed envelopes; the person responsible for sealing the envelopes did not take part in enrolment Blinding of participants and personnel: Unblinded; low risk as all reported outcomes are either objective outcomes or only possible by women knowing what they went through (patient satisfaction/acceptability). Blinding of outcome assessment: Unblinded; low risk as all

Study details	Participants	Interventions	Outcomes and Results	Comments
USA **Study type** Randomised controlled trial **Aim of the study** "To test the feasibility of mounting a randomised controlled trial comparing mifepristone–misoprostol versus dilation and evacuation (D&E) for midtrimester abortion." (p. 148) **Study dates** January 2002-January 2003 **Source of funding** Not information reported	(IQR) parity: 2 (1-2); median (IQR) prior ToP: 1 (0-1); median (IQR) gestational age in completed weeks: 18 (17-18). sToP: n = 9; Median age (IQR) = 26 (24-28) years; race white/black: n = 2/7; median (IQR) gravidity: 3 (3-5); median (IQR) parity: 2 (1-2); median (IQR) prior ToP: 1 (0-2); median (IQR) gestational age in completed weeks: 18 (16-19). One woman went into labour after placement of laminaria and aborted (uneventfully) without receiving D & E; this woman is analysed in this group. **Inclusion criteria** Age ≥ 18 years; English speaking; gestational age of 13.9 to 19.9 weeks (i.e., fetal biparietal diameter of 26 to 46 mm on ultrasound; also including women who had experienced a fetal death or had a fetus with congenital anomalies or chromosomal defect.	under light general anaesthesia without intubation was used for each D & E. Women also received prophylactic oral doxycycline.	acceptability and satisfaction **Outcome:** **Abortion completed by intended method** mToP: 5/9 sToP: 8/9 **Outcome: Uterine injury (including rupture)** Not directly reported, but the authors report that no serious adverse events occurred. **Outcome: Cervical injury requiring repair** Not directly reported, but the authors report that no serious adverse events occurred. **Outcome: Infection reported within 1 month of termination** Not directly reported, but the authors report that in mToP 3/9 and in sToP 0/9 had fever (>38° C).	reported outcomes are either objective outcomes or only possible by women knowing what they went through (patient satisfaction/acceptability). Attrition: Low risk; ITT analyses done for all outcomes. Selective reporting: Low risk Other bias: None reported **Other information** Study stopped early due to slow recruitment; had planned to recruit 60 women. "Patients receiving care in our abortion clinic are predominantly women of limited financial means, those with medical or social problems, and those with abnormal fetuses." (p. 149)

Study details	Participants	Interventions	Outcomes and Results	Comments
	Exclusion criteria Prior caesarean delivery, prior myomectomy; medical conditions listed in package labelling as contraindications to use of mifepristone or misoprostol (e.g., chronic renal failure, asthma); transportation difficulties relating to the ToP visits; women unwilling to return or to be contacted by telephone or letter two weeks later in follow up.			
Full citation Kelly, T., Suddes, J., Howel, D., Hewison, J., Robson, S., Comparing medical versus surgical termination of pregnancy at 13-20 weeks of gestation: A randomised controlled trial, BJOG: An International Journal of	**Sample size** n = 122 (out of 229 eligible; n = 107 refused participation) **Characteristics** mToP: n = 60; Mean age (SD) = 23.9 (6.3) years; mean gestation (SD) = 14.7 (1.6) weeks; primapara: n = 24; previous TOP: n = 14; previous CS [caesarean?]: N = 3. n = 8 did not receive mToP as they continued with their pregnancy.	**mToP:** Day 1: Oral mifepristone 200mg orally. 36 to 48 hours later at 0800 hours: Vaginal misoprostol 800mcg, followed by vaginal or oral 400mcg misoprostol (depending on level of vaginal bleeding) every 3 hours (max 4 doses). If by 2400 hours the termination of pregnancy had not occurred, 200mg oral mifepristone administered, followed by 1mg vaginal gemeprost 3-hourly from 0800 hours (max 5 doses). MToP was considered to have failed if still no termination by the following	**Outcome: Incomplete abortion with the need for surgical intervention** mToP: 5/60 sToP: 1/62 **Outcome: Haemorrhage requiring transfusion or ≥ 500ml of blood loss** mToP: 1/60 sToP: 5/62 **Outcome: Patient acceptability**	**Limitations** **Quality of study:** Risk of bias assessed using Cochrane risk of bias tool Random sequence generation: Low risk; computer-generated list; the person responsible for generating the randomisation list did not take part in enrolment Allocation concealment: Low risk; sequentially numbered opaque sealed envelopes; the person responsible for sealing

Study details	Participants	Interventions	Outcomes and Results	Comments
Obstetrics and Gynaecology, 117, 1512-1520, 2010 **Ref Id** 801908 **Country/ies where the study was carried out** United Kingdom **Study type** Randomised controlled trial **Aim of the study** "To compare the psychological impact, acceptability and clinical effectiveness of medical versus surgical termination of pregnancy (TOP) at 13–20 weeks of	sToP: n = 62; Mean age (SD) = 23.5 (5.8) years; mean gestation (SD) = 15.1 (1.9) weeks; primapara: n = 29; previous TOP: n = 21; previous CS [caesarean?]: N = 1. n = 4 did not receive sToP as they continued with their pregnancy. **Inclusion criteria** Pregnant women requesting and accepted for TOP under clause C of the human Fertilisation and Embryology Act (1990) amendment of the Abortion Act (1967), gestational age 13^{+0} to 19^{+6} weeks at the time of ToP; women aged < 16 years also eligible if deemed Fraser competent and had a parent/guardian present and consenting; previous caesarean section was not an exclusion criterion. **Exclusion criteria** Fetal congenital abnormality; medical disease precluding MTOP; unable to speak	morning at 0800 hours. sToP was then undertaken. If the placenta was not passed within 4 hours of expulsion of the fetus despite a further dose of prostaglandin (in cases without significant bleeding), it was evacuated surgically. The women also received periabortion antibiotic prophylaxis with doxycycline 100mg orally twice daily, starting on the day prior to termination of pregnancy. **sToP:** Day 1: Priming with Gemeprost 1mg vaginally 3 and 6 hours prior to sToP (nulliparous women and multiparous women ≥ 17 weeks of gestation) or with Gemeprost 1mg vaginally 3 hours prior to sToP (multiparous women between 13^{+0} and 16^{+6} weeks' gestation). Vacuum aspiration performed under general anaesthesia with progressive dilation to 13mm in women with 13^{+0} to 13^{+6} weeks' gestational age using Hegar graded cervical dilators and vacuum aspiration performed using a 12-mm aspiration curette; or	"Would choose the same method again" at 2 weeks mToP: 16/30 sToP: 26/26 [It should possibly be 36/36 as n = 36 analysed in this group. However, Table 2 lists n = 26] "Experience of ToP worse than expected" at 2 weeks mToP: 16/30 sToP: 0/26 [It should possibly be 0/36 as n = 36 analysed in this group. However, Table 2 lists N = 26] Satisfied/not satisfied with information/counselling pre-ToP at 2 weeks mToP: satisfied/no satisfied 29/0 sToP: satisfied/no satisfied 35/1 Satisfied/not satisfied with care during ToP at 2 weeks mToP: satisfied/no satisfied 29/0 sToP: satisfied/no satisfied 35/1	the envelopes did not take part in enrolment Blinding of participants and personnel: Unblinded; low risk as all reported outcomes are either objective outcomes or only possible by woman knowing what they went through (patient satisfaction/acceptability). Blinding of outcome assessment: Unblinded; low risk as all reported outcomes are either objective outcomes or only possible by woman knowing what they went through (patient satisfaction/acceptability). Attrition: Low risk for all outcomes (ITT analyses done for majority of outcomes) apart from patient satisfaction/acceptability which is at high risk due to ≥ 50% missing data in each group. Selective reporting: Low risk Other bias: None reported **Other information** Trial registration number: ISRCTN17262711

Study details	Participants	Interventions	Outcomes and Results	Comments
gestation." (p. 1512) **Study dates** May 2000 to February 2004 **Source of funding** University of Newcastle upon Tyne	English (<5% of women presenting for TOP)	dilation up to 15mm in women with 14^{+0} to 14^{+6} weeks' gestational age and vacuum aspiration performed using a 14-mm aspiration curette, with any residual products removed with sponge forceps under ultrasound guidance; or progressive dilation using Hegar graded cervical dilators up to a diameter in mm corresponding to the gestational age in week in women with ≥15^{+0} weeks' gestational age, with the products of conception removed by Sopher's forceps under ultrasound guidance. Routine perioperative uterotonic agents not used; and intravenous oxytocin (5 units) administered in 2 women with persistent post-evacuation bleeding. The women also received periabortion antibiotic prophylaxis with doxycycline 100mg orally twice daily, starting on the day prior to ToP, and metronidazole 1g rectally at the time of ToP.	<u>Satisfied/not satisfied with counselling/support post-ToP at 2 weeks</u> mToP: satisfied/no satisfied 28/1 sToP: satisfied/no satisfied 35/0 **Outcome: Abortion completed by intended method** mToP: 47/52 sToP: 57/58 **Outcome: Uterine injury (including rupture)** mToP: 0/60 sToP: 0/62 **Outcome: Cervical injury requiring repair** mToP: 0/60 sToP: 1/62 **Outcome: Infection reported within 1 month of termination:** Not directly reported, but infection included in the definition of complications in the methods section, so	

Study details	Participants	Interventions	Outcomes and Results	Comments
			presumably it was looked for, just not observed.	

D&E: dilatation and evacuation; IQR: interquartile range; ITT: intention to treat; mcg: micrograms; mToP: medical termination of pregnancy; sToP: surgical termination of pregnancy; ToP: termination of pregnancy

Appendix E – Forest plots

Forest plots for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

Figure 1. Incomplete abortion with the need for surgical intervention

Study or Subgroup	Medical ToP Events	Medical ToP Total	Surgical ToP Events	Surgical ToP Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Grimes 2004	4	9	1	9	50.4%	4.00 [0.55, 29.17]
Kelly 2010	5	60	1	62	49.6%	5.17 [0.62, 42.94]
Total (95% CI)		**69**		**71**	**100.0%**	**4.58 [1.07, 19.64]**
Total events	9		2			

Heterogeneity: Chi² = 0.03, df = 1 (P = 0.86); I² = 0%
Test for overall effect: Z = 2.05 (P = 0.04)

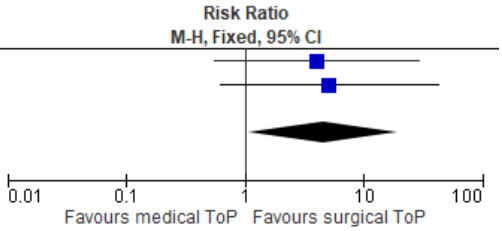
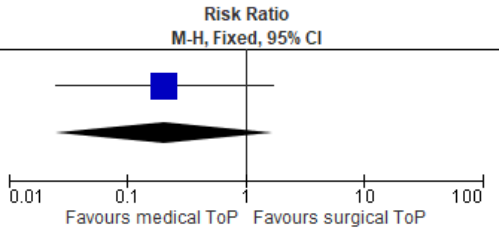


Figure 2. Haemorrhage requiring transfusion or ≥ 500ml blood loss

Study or Subgroup	Medical ToP Events	Medical ToP Total	Surgical ToP Events	Surgical ToP Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Grimes 2004 (1)	0	9	0	9		Not estimable
Kelly 2010	1	60	5	62	100.0%	0.21 [0.02, 1.72]
Total (95% CI)		**69**		**71**	**100.0%**	**0.21 [0.02, 1.72]**
Total events	1		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.14)



Footnotes
(1) Not directly reported, but the authors report that no serious adverse events occurred.

Figure 3. Abortion completed by intended method

Study or Subgroup	Medical ToP Events	Medical ToP Total	Surgical ToP Events	Surgical ToP Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Grimes 2004	5	9	8	9	12.9%	0.63 [0.33, 1.17]
Kelly 2010	47	52	57	58	87.1%	0.92 [0.84, 1.01]
Total (95% CI)		**61**		**67**	**100.0%**	**0.88 [0.79, 0.98]**
Total events	52		65			

Heterogeneity: Chi² = 1.91, df = 1 (P = 0.17); I² = 48%
Test for overall effect: Z = 2.27 (P = 0.02)

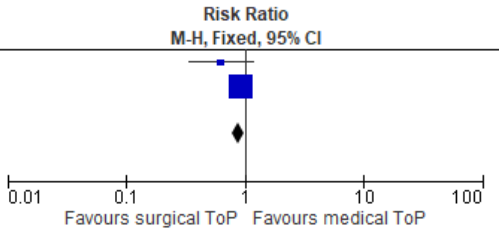
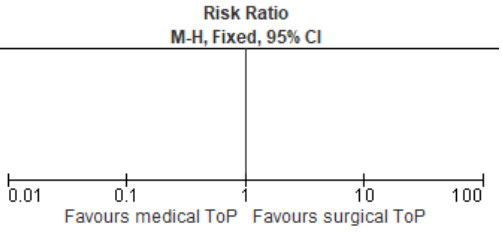


Figure 4. Uterine injury (including rupture)

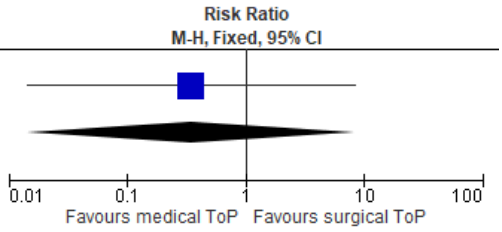
Study or Subgroup	Medical ToP Events	Medical ToP Total	Surgical ToP Events	Surgical ToP Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Grimes 2004 (1)	0	9	0	9		Not estimable
Kelly 2010	0	60	0	62		Not estimable
Total (95% CI)		**69**		**71**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



Footnotes
(1) Not directly reported, but the authors report that no serious adverse events occurred.

Figure 5. Cervical injury requiring repair

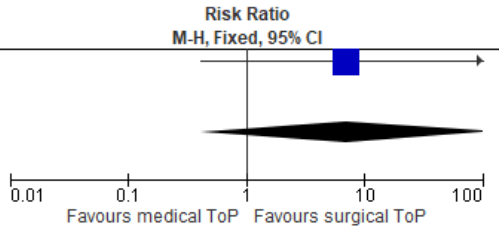
Study or Subgroup	Medical ToP Events	Medical ToP Total	Surgical ToP Events	Surgical ToP Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Grimes 2004 (1)	0	9	0	9		Not estimable
Kelly 2010	0	60	1	62	100.0%	0.34 [0.01, 8.29]
Total (95% CI)		**69**		**71**	**100.0%**	**0.34 [0.01, 8.29]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						



Footnotes
(1) Not directly reported, but the authors report that no serious adverse events occurred.

Figure 6. Infection reported within 1 month of termination

Study or Subgroup	Medical ToP Events	Medical ToP Total	Surgical ToP Events	Surgical ToP Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Grimes 2004 (1)	3	9	0	9	100.0%	7.00 [0.41, 118.69]
Kelly 2010 (2)	0	60	0	62		Not estimable
Total (95% CI)		**69**		**71**	**100.0%**	**7.00 [0.41, 118.69]**
Total events	3		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.35 (P = 0.18)						



Footnotes
(1) Not directly reported, but the authors report that in mToP 3/9 and in sToP 0/9 had fever (>38° C).
(2) Not directly reported, but infection included in the definition of complications in the methods section, so presumably it was looked for, just not...

Appendix F – GRADE tables

GRADE tables for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

Table 3: Clinical evidence profile: Surgical versus medical ToP between 13^{+0} and 24^{+0} weeks' gestation

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Medical top	Surgical top	Relative (95% CI)	Absolute	Quality	Importance
Incomplete abortion with the need for surgical intervention												
2 (Grimes 2004; Kelly 2010)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[1]	None	9/69 (13%)	2/71 (2.8%)	RR 4.58 (1.07 to 19.64)	101 more per 1000 (from 2 more to 525 more)	MODERATE	CRITICAL
Haemorrhage requiring transfusion or ≥ 500ml of blood loss												
2 (Grimes 2004; Kelly 2010)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[2]	None	1/69 (1.4%)	5/71 (7%)	RR 0.21 (0.02 to 1.72)	56 fewer per 1000 (from 69 fewer to 51 more)	LOW	CRITICAL
Patient acceptability/satisfaction - Patient acceptability (Scale from 1 [very satisfied] to 5 [very dissatisfied]); at discharge												
1 (Grimes 2004)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[3]	None	Median (IQR) 1 (1-1) (N = 9)	Median (IQR) 1 (1-1) (N = 9)	Not estimable	Not estimable	LOW	CRITICAL
Patient acceptability/satisfaction - Patient acceptability ("Would choose the same method again"); at 2 weeks												
1 (Kelly 2010)	Randomised trials	Very serious[4]	No serious inconsistency	No serious indirectness	Very serious[5]	None	16/30 (53.3%)	26/26 (100%)[6]	RR 0.54 (0.39 to 0.76)	460 fewer per 1000 (from 240 fewer to 610 fewer)	VERY LOW	CRITICAL
Patient acceptability/satisfaction - Patient acceptability ("Experience of top worse than expected"); at 2 weeks												

1 (Kelly 2010)	Randomised trials	Very serious[4]	No serious inconsistency	No serious indirectness	Very serious[5]	None	16/30 (53.3%)	0/26 (0%)[7]	RR 28.74 (1.81 to 456.75)	Not estimable	VERY LOW	CRITICAL
Patient acceptability/satisfaction - Patient satisfaction (rating of satisfied with information/counselling pre-top); at 2 weeks												
1 (Kelly 2010)	Randomised trials	Very serious[4]	No serious inconsistency	No serious indirectness	Very serious[5]	None	29/29 (100%)	35/36 (97.2%)	RR 1.02 (0.95 to 1.11)	19 more per 1000 (from 49 fewer to 107 more)	VERY LOW	CRITICAL
Patient acceptability/satisfaction - Patient satisfaction (rating of satisfied with care during top); at 2 weeks												
1 (Kelly 2010)	Randomised trials	Very serious[4]	No serious inconsistency	No serious indirectness	Very serious[5]	None	29/29 (100%)	35/36 (97.2%)	RR 1.02 (0.95 to 1.11)	19 more per 1000 (from 49 fewer to 107 more)	VERY LOW	CRITICAL
Patient acceptability/satisfaction - Patient satisfaction (rating of satisfied with counselling/support post-top); at 2 weeks												
1 (Kelly 2010)	Randomised trials	Very serious[4]	No serious inconsistency	No serious indirectness	Very serious[5]	None	28/29 (96.6%)	35/35 (100%)	RR 0.96 (0.88 to 1.05)	40 fewer per 1000 (from 120 fewer to 50 more)	VERY LOW	CRITICAL
Abortion completed by intended method												
2 (Grimes 2004; Kelly 2010)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[1]	None	52/61 (85.2%)	65/67 (97%)	RR 0.88 (0.79 to 0.98)	116 fewer per 1000 (from 19 fewer to 204 fewer)	MODERATE	IMPORTANT
Uterine injury (including rupture)												
2 (Grimes 2004; Kelly 2010)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[8]	None	0/69 (0%)	0/71 (0%)	Not estimable	Not estimable	LOW	IMPORTANT
Cervical injury requiring repair												
2 (Grimes 2004; Kelly 2010)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[9]	None	0/69 (0%)	1/71 (1.4%)	RR 0.34 (0.01 to 8.29)	9 fewer per 1000 (from 14 fewer to 103 more)	LOW	IMPORTANT
Infection reported within 1 month of termination												
2 (Grimes 2004; Kelly 2010)	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[10]	None	3/69 (4.3%)	0/71 (0%)	RR 7 (0.41 to 118.69)	Not estimable	LOW	IMPORTANT

MID: minimally important difference; ToP: termination of pregnancy; RR: relative risk
[1] 95% confidence interval crossed 1 MID
[2] The MID for this outcome is statistical significance, and the imprecision ratings were undertaken on that basis by using the optimum information size so that if the total event rate ≥300, then the quality was not downgraded, if the event rate = 150-299, then the quality was downgraded by 1 level and if the event rate <150, then the quality was downgraded by 2 levels
[3] No MID available for this outcome as it is only reported as medians and ranges. Imprecision ratings were undertaken by using the optimum information size so that if the total n ≥400, then the quality was not downgraded, if the total n = 200-399, then the quality was downgraded by 1 level and if the total n <200, then the quality was downgraded by 2 levels
[4] ≥ 50% missing data in each group
[5] Small sample size (N < 66)
[6] 26/26 should possibly be 36/36 as N = 36 analysed in this group. However, Table 2 lists N = 26.
[7] 0/26 should possibly be 0/36 as N = 36 analysed in this group. However, Table 2 lists N = 26.
[8] Low event rate (no events were observed in a total of 140 patients).
[9] Low event rate (one event was observed in a total of 140 patients).
[10] 95% confidence interval crosses 2 MIDs

Appendix G – Economic evidence study selection

Economic evidence for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

No economic evidence was identified which was applicable to this review question.

Appendix H – Economic evidence tables

Economic evidence tables for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

No economic evidence was identified which was applicable to this review question.

Appendix I –Economic evidence profiles

Economic evidence profiles for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

No economic evidence was identified which was applicable to this review question

Appendix J –Economic analysis

Economic analysis for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

The cost effectiveness of medical versus surgical termination of pregnancy between 13^{+0} and 23^{+6} weeks' gestation

Introduction

Medical termination of pregnancy has become an alternative to more traditional surgical termination of pregnancy in developed countries for women in their second trimester of pregnancy. In 2017, for England and Wales, 1 in 5 terminations between 13^{+0} and 23^{+6} weeks' gestation were medical terminations (Department of Health 2018). The optimal method is still debated with the proportion of terminations performed using medical methods varying widely amongst different developed nations. Terminations performed between 13^{+0} and 23^{+6} weeks gestational age account for a disproportionate amount of morbidity compared to earlier terminations, which may differ in frequency between surgical and medical terminations.

This economic evaluation considers the effectiveness and costs of both medical and surgical terminations. It also considers the effect on quality of life needed for either approach to be considered cost effective.

Methods

Population

The population considered by this economic model are individuals over the age of 18, between 13^{+0} and 23^{+6} weeks' gestation, undergoing a termination of pregnancy at NHS or other licensed clinic. There were no exclusions based on reason for termination with elective terminations and terminations due to fetal death, congenital anomalies or chromosomal anomalies all considered by economic model.

Intervention and comparator

Both medical and surgical terminations are used widely within NHS and licensed clinics. In 2017, 4,161 (21.8%) medical terminations and 14,942 (78.2%) surgical terminations were performed between 13^{+0} and 24^{+0} weeks' gestation (Department of Health 2018). For the purposes of this economic evaluation, surgical termination was considered the comparator as it is more widely used and, therefore, the most representative of current clinical practice.

There are 2 predominant methods for surgical termination of pregnancy,-'vacuum aspiration' and 'dilatation and evacuation' (D&E). Vacuum aspiration is a method of induced termination which removes the contents of the uterus using a pump through a dilated cervix. D&E involves the dilation of the cervix followed by the surgical evacuation of the contents of the uterus. Both methods are used in England for terminations between 13^{+0} and 24^{+0} weeks' gestation. However, vacuum aspiration is more common in individuals between 13^{+0} and 14^{+6} weeks' gestation (58% of all terminations, 70% of surgical terminations) and D&E is used

almost exclusively used for surgical terminations between 15^{+0} and 19^{+6} gestation (75% of all termination, 96% of surgical interventions; Department of Health, 2018). After 20^{+0} weeks' gestation, another surgical method, feticide with a surgical evacuation, is also often used. This accounts for 14% of all terminations in this gestational age range.

This economic evaluation considers both vacuum aspiration and D&E and assumes a proportion identical to that reported by the Department of Health (2018). Feticide with surgical evacuation was not considered by the economic model as it accounted for less than 3% of all terminations performed after 13^{+0} weeks' gestation and no evidence for this method of termination was identified during the accompanying clinical evidence review.

The intervention considered by the economic model is medical termination of pregnancy. Over 99% of medical terminations performed between 13^{+0} and 19^{+6} weeks' gestation used an antiprogesterone. Half of medical terminations performed after 20^{+0} weeks' gestation used feticide followed by an antiprogesterone. As with feticide and surgical evacuation, this method accounts for less than 3% of all terminations after 13^{+0} weeks' gestation and again no evidence was identified for this method in the accompanying clinical evidence review. Therefore, this method was not considered in the economic model.

It was assumed that all medical terminations in the economic model were carried out using mifepristone and misoprostol to match the comparator for the clinical evidence review. Only a small number of terminations (<1%) use an alternative medical agent. The model assumed that medical termination of pregnancy consisted of oral mifepristone 200mg and vaginal misoprostol, as this was the only regimen identified during the clinical evidence review and is the predominant method for medical termination of pregnancy in England.

Model Parameters

Clinical Inputs

All clinical inputs for the economic model were taken solely from the accompanying clinical evidence review. In summary, 2 randomised controlled trials (RCTs) were identified which compared oral mifepristone 200mg and vaginal misoprostol to D&E under general anaesthetic (Grimes 2004, Kelly 2010). Both studies had similar gestational ages (13.9 to 19.9 weeks versus 13^{+0} to 19^{+6} weeks) and reported all clinical outcomes used to inform the economic model. These outcomes were combined using meta-analysis (see Supplementary Material 1 for methods) and the combined results were used to inform the model in the base-case.

The outcomes which were used to inform the economic model were: the number of incomplete abortions, percentage of haemorrhages, percentage of uterine injuries, percentage of cervical injuries and percentage of infections. Definitions for these outcomes, as used in this economic model, are presented in Table 4.

Table 4: Definitions of clinical outcomes used to inform the economic model

Outcome	Definition
Incomplete abortion	Any termination for which an individual requires further surgical intervention to complete the termination or evacuate retained products

Outcome	Definition
Haemorrhage	Any haemorrhage which requires either a transfusion or results in greater than 500ml of blood loss.
Uterine injury	Any perforation to the uterus requiring medical intervention
Cervical injury	Any injury to the cervix requiring medical intervention
Infection	Pelvic infection defined as pain or bleeding with a temperature greater than 37.5oc

The larger study (Kelly 2010) [n=122 versus n=18] was performed in a UK setting at 1 tertiary teaching hospital. In the UK approximately 3 out of 4 terminations between 13^{+0} and 19^{+6} weeks' gestation are performed in settings outside of the NHS, predominately in independent sector clinics (Department of Health 2018). The committee agreed that the predominant RCT may underestimate the effectiveness of independent clinics due to their ability to specialise, and their higher caseload leading to more experienced staff. However, as the smaller study was from the USA, a secondary analysis was performed only using outcomes from the UK study.

The outcomes reported in the clinical evidence reviews sufficiently covered the time horizon of the model and all clinical outcomes that the committee considered useful in making recommendations. Therefore, no extrapolation was performed to try and estimate clinical outcomes beyond those reported in the clinical evidence reviews. In the base-case, clinical outcomes from the economic model will, therefore, be identical to those reported in the clinical evidence review. Uterine injury was not observed in either of the 2 included RCTs. It was the committee's opinion that this was a rare event and it was not considered by the economic model.

All events were estimated in the model as a function of the relative risk (medical versus surgical) and the baseline observed percentages from the accompanying clinical evidence review. This was true for all clinical outcomes of the model apart from infection, where no events were observed in the surgical arms of either RCT. This outcome was estimated as the reported baseline from the clinical evidence review for the medical group and assumed to be zero for the surgical group in all analyses.

A full discussion of the clinical evidence, including quality assessment of the clinical outcomes is available in the accompanying clinical evidence section. The parameters used in the economic model are summarised in Table 5.

Table 5: Clinical outcomes from the clinical evidence reviews used to inform the economic model.

Parameter	Value
Incomplete abortion requiring Surgical Intervention	
Relative risk	4.58
Baseline (surgical)	2.8%
Haemorrhage requiring transfusion or ≥ 500ml blood loss	
Relative risk	0.21
Baseline (surgical)	7.0%

Parameter	Value
Uterine injury including rupture	
Relative risk	No events
Baseline (surgical)	No events
Cervical injury requiring repair	
Relative risk	0.34
Baseline (surgical)	1.4%
Infection	
Relative risk (surgical versus medical)	N/A
Baseline (medical)	4.3%

Costs

Costs of termination of pregnancy

Costs for termination of pregnancy in the base case were taken from NHS reference costs 2016-2017 in line with the NICE Guidelines Manual 2016. No reference cost description was identified which exactly matched the gestational age considered by this economic evaluation. Therefore, reference costs for 14 to 20 weeks' gestation were used to inform the model. This range represents over 80% of terminations of pregnancy performed in England and Wales between 13^{+0} and 23^{+6} weeks gestational age (Department of Health 2018). This gestational age range is also descriptive of all the participants in the 2 RCTs used to inform the economic model. Whilst NHS Reference Costs do report costs for terminations after 20 weeks' gestation, they do not disaggregate between medical and surgical terminations. It is therefore not useful to include this cost in this analysis. Given the more complex nature of termination of pregnancy after 20 weeks' gestation, the NHS reference cost is higher in the majority of settings than that estimated for this economic model.

Three types of termination of pregnancy are described in the NHS reference costs:

- Medical termination of pregnancy
- D&E
- Vacuum aspiration with cannula

As discussed above, D&E and vacuum aspiration with cannula are 2 different methods of surgical termination. However, the economic model considers both of these together and referred to them as surgical termination of pregnancy.

As the patient group for the economic model does not exclude any reasons for termination, all 4 NHS settings are considered where all 3 types of termination are reported in the reference costs. These settings are elective inpatient, non-elective short stay, non-elective long stay and day case. Outpatient setting was excluded as a reference cost was only reported for medical termination for gestational age 14 to 20 weeks and only 26 procedures were reported across the UK. The NHS Reference Cost description, setting, full consultant episodes (FCEs; total number of procedures) and reported NHS Reference Cost are reported Table 6.

Table 6: NHS Reference Costs 2016/2017 for termination of pregnancy

Setting	Currency code and description	Number of FCEs	National average unit cost
Elective Inpatient	MA18D Medical Termination of Pregnancy, 14 to 20 weeks' gestation	571	£839
Elective Inpatient	MA17D Dilatation and Evacuation, 14 to 20 weeks' gestation	90	£2,005
Elective Inpatient	MA19B Vacuum Aspiration with Cannula, 14 to 20 weeks' gestation	178	£1,763
Non elective Long Stay	MA18D Medical Termination of Pregnancy, 14 to 20 weeks' gestation	409	£2,564
Non elective Long Stay	MA17D Dilatation and Evacuation, 14 to 20 weeks' gestation	266	£3,300
Non elective Long Stay	MA19B Vacuum Aspiration with Cannula, 14 to 20 weeks' gestation	281	£2,940
Non elective Short Stay	MA18D Medical Termination of Pregnancy, 14 to 20 weeks' gestation	1,237	£1,022
Non elective Short Stay	MA17D Dilatation and Evacuation, 14 to 20 weeks' gestation	290	£1,595
Non elective Short Stay	MA19B Vacuum Aspiration with Cannula, 14 to 20 weeks' gestation	413	£1,499
Day Case	MA18D Medical Termination of Pregnancy, 14 to 20 weeks' gestation	834	£441
Day Case	MA17D Dilatation and Evacuation, 14 to 20 weeks' gestation	448	£736
Day Case	MA19B Vacuum Aspiration with Cannula, 14 to 20 weeks' gestation	862	£904
Mean Cost Medical Terminations	Number of FCEs * National average unit cost		£1,036
Mean Cost Surgical Termination	Number of FCEs * National average unit cost*weighted proportion MA17D (66%) & MA19B (34%)		£1,614

FCE: Full Consultant Episode

An estimated cost for medical and surgical termination in the model was estimated by taking a mean cost of all NHS reference costs weighted by the number of FCEs. Surgical termination of pregnancy was further weighted by the proportion of vacuum aspirations (34%) and D&Es (66%) between 13^{+0} and 23^{+6} weeks' gestation reported by the Department of Health (2018). The mean cost of surgical termination is greater than medical termination for all settings.

The accuracy of NHS Reference Costs in estimating the true costs of a termination may be reduced for the interventions considered by this economic model as only a minority of NHS funded terminations are performed in NHS settings with the majority being performed in the independent sector which do not feed into the cost estimates. Clinical Commissioning Groups in England negotiate their own contracts with the independent and charity sector to provide termination of pregnancy services. These contracts and costs, especially on the individual level, are commercially sensitive and are not publically available. It is almost

certain that the cost of terminations in the independent sector is significantly below that of NHS settings as they can take advantage of expertise and economies of scale in specially designed clinics and theatres. It is also intuitive that Clinical Commissioning Groups would not 'contract out' services at a higher price than they couple provide themselves. It is almost certain that these cost savings would be realised for both medical and surgical terminations of pregnancy.

Cost of adverse events

The cost of an incomplete abortion requiring surgical intervention for retained products was costed as equivalent to the mean cost of a surgical termination of pregnancy. The surgical procedure to remove retained products is in the vast majority of cases likely to be less intensive than that of a surgical termination of pregnancy and, therefore, this assumption likely over estimates the true cost of an incomplete abortion.

The cost of a haemorrhage was taken from the health economic model for the NICE (2015) blood transfusion guideline (NG24) and inflated to 2016/17 price using the hospital & community health services (HCHS) index (Curtis 2017); this results in an estimated cost of £178.54 per adverse event. It was assumed that any haemorrhage would only require 1 transfusion and consequently future transfusions were not considered by the model. Infection and surgical injury were not costed in the economic model. It was assumed that these would be treated and diagnosed as part of follow-up after the termination, would not incur any additional time for health care professionals and require limited additional resources. The upper cost for these adverse events is likely to be similar to 1 course of antibiotics.

Cost of additional unplanned overnight stay

The accompanying clinical evidence review did not look for length of stay as an outcome and it was not considered by the committee to be an outcome that would differ between the 2 types of termination of pregnancy considered. The Kelly 2010 RCT identified that 16 out of 60 individuals (27%) in the medical termination group had an unplanned overnight stay in hospital. A sensitivity analysis was performed assuming that the same proportion of the medical termination cohort of the model had an unplanned overnight stay. It was assumed that all individuals would then be discharged after 1 night and no additional hospital stay, as a result of the termination of pregnancy, would occur. The committee speculated that individuals in this RCT were admitted to care late in the day and that numbers much lower than this would be observed in practice.

The cost of 1 additional unplanned night was taken from NHS Reference Costs 2016/2017 and costed as 1 non-elective additional bed day for 'Medical Termination of Pregnancy, 14 to 20 weeks' gestation (MA18D)' which equalled £749.68.

Quality of life and patient satisfaction

No studies were identified which measured or estimated quality of life for any intervention in individuals undergoing a termination between 13^{+0} and 23^{6} weeks' gestation. One quality of life study was identified which compared women undergoing a medical (n=42) or surgical (n=55) termination up to 9^{+0} weeks' gestation (Westhoff 2003). This study was a prospective cohort study of women undergoing termination at a private practice in the United States. Quality of life was collected through structured interviews using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C30) at baseline, at the routine 1 week follow-up and 1 month post procedure during a telephone

interview. Despite being a quality of life instrument intended for use in individuals with cancer, it included components important for individuals undergoing a termination, including specific questions around physical, emotional and social wellbeing, as well as global function scores.

At baseline women undergoing a surgical termination had worse scores in emotional cognitive and social wellbeing as well as greater problems with fatigue and insomnia when compared to women undergoing a medical termination. For all other dimensions of the EORTC QLQ C30, including global health score, there was no statistically significant difference between the 2 groups. Differences between the 2 groups had all but disappeared at 1 month suggesting there is no difference in quality of life between the 2 interventions.

It is difficult to draw values from this study for use in our economic model given that the adverse events for individuals undergoing these procedures between 13^{+0} and 23^{+6} weeks' gestation will be significantly more frequent and severe than for women receiving earlier terminations. Social and emotional wellbeing may also differ between the UK and the USA, given differences in social and cultural views of termination of pregnancy.

The findings of Westhoff 2003 are somewhat supported by the findings around patient preference from the accompanying clinical evidence review where there was no difference between medical and surgical termination groups for most of the dimensions although "Would choose the same method again" at 2 weeks favoured surgical termination, with all 26 individuals in the arm responding in the positive compared to just over half (16 out of 30) for the medical termination of pregnancy arm (RR=0.54 [95% CI 0.39-0.76]). The quality of the estimates around patient satisfaction were rated as low or very Low using GRADE given the risk of bias (>50% of data is missing) and imprecision due to small sample sizes.

The committee discussed using this quality of life evidence to estimate QALYs for the 2 groups in this economic analysis. However, given the issues discussed above, it was decided that it would be difficult to have any confidence in these estimates. It was, therefore, decided that where a difference in cost was identified between the 2 interventions that the number of additional QALYs required to make the more costly intervention cost effective at a threshold of £20,000 per additional QALY would be calculated.

Discounting

All clinical outcomes included in the economic model occurred within 1 year and it was therefore not appropriate to perform any discounting in the economic model.

Results

In the base-case analysis, medical terminations led to a reduction in overall costs of £436. This cost saving is £100 greater than the inputted difference in unit cost between a surgical and medical termination suggesting some greater costs for medical termination from treating adverse events. For surgical termination to be cost effective in the base-case, at a £20,000 per QALY threshold, it would need to result in a 0.02 QALY increase in quality of life, equivalent to 8 days in perfect health. When the Kelly 2010 UK results were used to populate the model, medical termination remained cost saving, although the cost of treating adverse events was remained higher than for surgical termination. However, this remained small compared to the difference in cost between the 2 different types of termination.

When overnight hospital stays were included in the economic model the cost savings from medical terminations remained although they were halved. At a threshold of £20,000 per QALY, surgical termination would be cost effective in these circumstances if it led to relative increase of just over 0.01 QALYs.

Table 7: Results of base-case economic model

	Incomplete abortion	Haemorrhage	Uterine injury	Cervical injury	Infection	Cost	Difference cost
Base Case							
Surgical	2.8%	7.0%	No Events	1.4%	No Events	£1,672.11	
Medical	12.3%	1.5%	No Events	0.5%	4.3%	£1,236.45	-£435.66
Kelly 2010 values							
Surgical	1.6%	8.1%	No Events	1.6%	No Events	£1,654.47	
Medical	8.3%	1.7%	No Events	0.0%	No Events	£1,173.21	-£481.26
Additional overnight stays included							
Surgical	2.8%	7.0%	No Events	1.4%	No Events	£1,672.11	
Medical	12.3%	1.5%	No Events	0.5%	4.3%	£1,436.36	-£235.74

Discussion

Surgical termination is the predominant method in this patient group in England, accounting for 4 in 5 terminations. Based on UK cost data and clinical data predominately drawn from a UK RCT, medical termination was estimated to be cost saving compared to surgical termination even under the unfavourable assumptions around costly overnight stays in hospital. The model did not attempt to estimate cost effectiveness given the difficulties with quality of life estimates in this area. Therefore, strong recommendations for either method would be difficult to make. However, it was the committee's belief that offering a choice of method would lead to an increase in women opting for medical termination and ultimately reduce overall costs. The procedures and the profile of adverse events differs widely between the 2 methods and quality of life will vary between different women. Allowing women to make an informed choice and opt for their preferred method should not lead to any reduction in quality of life and in all likelihood would increase it. It is, therefore, likely that offering a choice of termination method would be cost saving compared to current practise and would improve both quality of life and women's experience of termination services.

Appendix K – Excluded studies

Excluded studies for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

Clinical studies

Study	Reason for Exclusion
Ashok, P. W., Hamoda, H., Flett, G. M. M., Kidd, A., Fitzmaurice, A., Templeton, A., Patient preference in a randomized study comparing medical and surgical abortion at 10-13 weeks gestation, Contraception, 71, 143-148, 2005	Population not in PICO (gestational age 10-13 weeks)
Ashok, P. W., Kidd, A., Flett, G. M. M., Fitzmaurice, A., Graham, W., Templeton, A., A randomized comparison of medical abortion and surgical vacuum aspiration at 10-13 weeks gestation, Human Reproduction, 17, 92-98, 2002	Population not in PICO (gestational age 10-13 weeks)
Autry, A. M., Hayes, E. C., Jacobson, G. F., Kirby, R. S., A comparison of medical induction and dilation and evacuation for second-trimester abortion, American Journal of Obstetrics and Gynecology, 187, 393-397, 2002	Interventions/comparisons not in PICO (medical termination of pregnancy not undertaken with mifepristone and misoprostol)
Baldwin, M., Basnett, I., Dangol, D. S., Karki, C., Castleman, L., Edelman, A. B., Introduction of second trimester medical and surgical abortion in Nepal, International Journal of Gynaecology and Obstetrics, 3), S290, 2012	Not RCT. Published as abstract only, not enough information available to ascertain relevance.
Cowett, A. A., Golub, R. M., Grobman, W. A., Cost-effectiveness of dilation and evacuation versus the induction of labor for second-trimester pregnancy termination, American Journal of Obstetrics & Gynecology, 194, 768-73, 2006	Not a systematic review and no original data.
Debby, A, Golan, A, Sagiv, R, Sadan, O, Glezerman, M, Midtrimester abortion in patients with a previous uterine scar, European journal of obstetrics, gynecology, and reproductive biology, 109, 177-180, 2003	Not RCT; non-comparative study
Di Carlo, C., Savoia, F., Ferrara, C., Sglavo, G., Tommaselli, G. A., Giampaolino, P., Cagnacci, A., Nappi, C., "In patient" medical abortion versus surgical abortion: patient's satisfaction, Gynecological Endocrinology, 32, 650-654, 2016	Population not in PICO (gestational age < 7 weeks)
Grossman,D., Blanchard,K., Blumenthal,P., Complications after Second Trimester Surgical and Medical Abortion, Reproductive Health Matters, 16, 173-182, 2008	Systematic review; checked for relevant studies, which are included separately in the current review
Lohr, Patricia A, Hayes, Jennifer L, Gemzell-Danielsson, Kristina, Surgical versus medical methods for second trimester induced abortion, Cochrane Database of Systematic Reviews, 2008	Systematic review; checked for relevant studies, which are included separately in the current review
Lowenstein, L., Deutcsh, M., Gruberg, R., Solt, I., Yagil, Y., Nevo, O., Bloch, M., Psychological distress symptoms in women undergoing medical vs. surgical termination of pregnancy, General Hospital Psychiatry, 28, 43-47, 2006	Population not in PICO (gestational age < 64 days)

Study	Reason for Exclusion
Lyus, R., Comparing medical versus surgical termination of pregnancy at 13-20 weeks of gestation: A randomised controlled trial, BJOG: An International Journal of Obstetrics and Gynaecology, 118, 1148-1149, 2011	Letter to the editor about Kelly et al., 2010 (and no other relevant data)
Medarametla, V., A comparative study of vaginal misoprostol versus trans-cervical foley catheter insertion along with vaginal misoprostol in termination of mid-trimester pregnancies, European Journal of Contraception and Reproductive Health Care, 21, 57-58, 2016	Does not appear to be an RCT. Published as abstract only, not enough information available to ascertain relevance, although comparison is probably not in PICO
Moreau, C., Trussell, J., Desfreres, J., Bajos, N., Medical vs. surgical abortion: The importance of women's choice, Contraception, 84, 224-229, 2011	Population not in PICO (gestational age < 8 weeks)
Moreau, C., Trussell, J., Desfreres, J., Bajos, N., Medical versus surgical abortion: The importance of women's choice, Contraception, 82 (2), 205, 2010	Not an RCT. Published as an abstract only; not enough information to ascertain relevance, but population probably not in PICO as appears to be a report of the same data as reported by Moreau 2011
Rademakers, J., Koster, E., Jansen-Van Hees, A. C. V., Willems, F., Medical abortion as an alternative to vacuum aspiration: First experiences with the 'abortion pill' in The Netherlands, European Journal of Contraception and Reproductive Health Care, 6, 185-191, 2001	Population not in PICO (gestational age < 50 days)
Robson, S. C., Kelly, T., Howel, D., Deverill, M., Hewison, J., Lie, M. L. S., Stamp, E., Armstrong, N., May, C. R., Randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation (TOPS), Health Technology Assessment, 13, 1-124, 2009	Includes population up to gestational age of 14 weeks; no subgroup analyses for subsection of population in PICO (i.e., gestational age 13-14 weeks)
Rodriguez, M. I., Mendoza, W. S., Guerra-Palacio, C., Guzman, N. A., Tolosa, J. E., Medical abortion and manual vacuum aspiration for legal abortion protect women's health and reduce costs to the health system: Findings from Colombia, Reproductive Health Matters, Part S1. 22, 125-133, 2015	Population not in PICO (first trimester only); also appears that medical terminations of pregnancy were with misoprostol only and not in combination with mifepristone
Say, Lale, Brahmi, Dalia, Kulier, Regina, Campana, Aldo, Gülmezoglu, A Metin, Medical versus surgical methods for first trimester termination of pregnancy, Cochrane Database of Systematic Reviews, 2002	Systematic review; included studies checked for relevance
Slade, P., Heke, S., Fletcher, J., Stewart, P., Termination of pregnancy: Patients' perceptions of care, Journal of Family Planning and Reproductive Health, 27, 72-77, 2001	Not RCT; population not in PICO (first trimester termination of pregnancy)
Sonalkar, S., Ogden, S. N., Tran, L. K., Chen, A. Y., Comparison of complications associated with induction by misoprostol versus dilation and evacuation for second-trimester abortion, International Journal of Gynecology and Obstetrics, 138, 272-275, 2017	Comparison not in PICO (medical termination of pregnancy performed with misoprostol alone, and no mifepristone)
Vijayasree, M., A comparative study of vaginal misoprostol versus trans - Cervical foley catheter insertion along with	Does not appear to be an RCT. Published as abstract only, not enough information available to

Study	Reason for Exclusion
vaginal misoprostol in termination of mid-trimester pregnancies, Journal of Obstetrics and Gynaecology Research, 43, 23, 2017	ascertain relevance, although comparison is probably not in PICO
Virgo, K. S., Carr, T. R., Hile, A., Virgo, J. M., Sullivan, G. M., Kaikati, J. G., Medical versus surgical abortion: A survey of knowledge and attitudes among abortion clinic patients, Women's Health Issues, 9, 143-154, 1999	Analyses/outcomes not in PICO (survey completed while waiting for the appointment for termination of pregnancy)
Wadhera, S., Millar, W. J., Second trimester abortions: trends and medical complications, Health reports / Statistics Canada, Canadian Centre for Health Information = Rapports sur la sante / Statistique Canada, Centre canadien d'information sur la sante, 6, 441-454, 1994	Not RCT. Unclear if any mTOP performed with mifepristone and misoprostol; comparisons not in PICO.
Xia, W., She, S., Lam, T. H., Medical versus surgical abortion methods for pregnancy in China: A cost-minimization analysis, Gynecologic and Obstetric Investigation, 72, 257-263, 2011	Population not in PICO (gestational age up to 49 days)
Yilmaz, N., Kanat-Pektas, M., Kilic, S., Gulerman, C., Medical or surgical abortion and psychiatric outcomes, Journal of Maternal-Fetal and Neonatal Medicine, 23, 541-544, 2010	Population not in PICO (gestational age up to 12 weeks)
Zou, Y, Liang, Y, Wu, Sc, Li, Yp, Yan, L, Mei, L, Zhang, Jq, Tong, L, Study on meta analysis regarding the acceptability of medical abortion compared with surgical abortion (Provisional abstract), Chinese Journal of Epidemiology, 27, 68-71, 2006	Full text not in English

mToP: medical termination of pregnancy; PICO: population, intervention, comparison and outcomes; RCT: randomised controlled trial

Economic studies

No economic evidence was identified for this review. See supplementary material 2 for further information.

Appendix L – Research recommendations

Research recommendations for review question: What is the effectiveness, safety and acceptability of surgical compared to medical termination between 13^{+0} and 24^{+0} weeks' gestation?

No research recommendations were made for this review question.