Abortion care guideline

Supplementary material 2: Evidence-to-Decision frameworks for the clinical service recommendations

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Contents

Note: Details of all PICO (population, intervention, comparator, outcome) questions are provided in Annex 9 in the main guideline document: *Abortion care guideline* (2021).[1]

[1] The main guideline is available at: **https://apps.who.int/iris/handle/10665/349316**.

Acronyms and abbreviations

CI:	confidence interval
ER	emergency room
ERRG	Evidence and Recommendations Review Group
EtD	Evidence-to-Decision
GRADE	Grading of Recommendations Assessment, Development and Evaluation
hCG	human chorionic gonadotropin
IV	intravenous
LMP	last menstrual period
MD	mean difference
NRS	non-randomized study
NSAIDs	non-steroidal anti-inflammatory drugs
OR	odds ratio
PCA	patient-controlled analgesia
PCB	paracervical block
PCEA	patient-controlled epidural analgesia
Rh	Rhesus (blood group)
RR	risk ratio
SoF	Summary of Findings

GRADE Working Group grades of certainty of evidence

(use as a reference for the SoF tables)

- **High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect
- **Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
- **Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
- **Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. EtD framework for Rh isoimmunization

Recommendation 8: For both medical and surgical abortion at < 12 weeks: **Recommend against** anti-D immunoglobulin administration.

PICO 1: PICO question: For an unsensitized Rh-negative individual seeking abortion at < 12 weeks of gestation, is no administration of anti-D a safe and effective alternative to routine anti-D administration? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global
Perspective: Population
Literature review: A systematic review assessed the effect of routine anti-D administration among unsensitized Rh-negative individuals who have an abortion. Of the 2649 studies, 79 were accessed for full-text review. There are few studies examining Rh isoimmunization in unsensitized Rh-negative individuals seeking abortion under 12 weeks. Currently, two studies have been included.
Study settings: Israel, United States of America (USA).

ASSESSMENT OF RESEARCH EVIDENCE

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

The overall judgements on the above questions are presented below to be considered by the Evidence and Recommendations Review Group (ERRG) in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Desirable effects:

Fewer women in the intervention group (anti-D administration) had antibody formation after the initial pregnancy compared with the women in the comparison group (no anti-D).

Certainty of evidence:

Very low.

Undesirable effects:

None

Summary of judgements:

Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	**X** May favour the intervention	Favours the intervention

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

Important uncertainty or variability	Possibly important uncertainty or variability	x Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

Unable to determine	Varies	Large costs	x Moderate costs	Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

		x				
Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

			x			
Unable to determine	Varies	Reduced	Probably reduced	Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

					x
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	x Probably Yes	Yes

ERRG members noted that the costs and shortage of supplies limit the feasibility of routine administration.

Justification for the recommendation

- In the 2016 *WHO recommendations on antenatal care for a positive pregnancy experience*, an existing recommendation states: "Antenatal prophylaxis with anti-D immunoglobulin in non-sensitized Rh-negative pregnant women at 28 and 34 weeks of gestation to prevent RhD alloimmunization is recommended only in the context of rigorous research."
- A study by Wiebe et al. (2019) compared Rh alloimmunization rates in two countries (Canada and the Netherlands) with completely different policies regarding abortion-related use of anti-D immunoglobulin to ultimately determine any benefits of its use. The findings suggested that:
  - the Dutch policy of not treating Rh-negative women having spontaneous abortions under 10 weeks of gestation, or induced abortions under 7 weeks, can be safely adopted by other countries;
  - the presence of fetal blood in Rh-negative women at early gestational ages does not necessarily correlate with development of Rh alloimmunization.
- In an experimental study conducted in 1956 (Stern et al.), Rh-negative incarcerated men were injected with Rh-positive blood and the minimum dose of 7.5 ml did not produce a titre above 16 in any of the 39 men. Application of these numbers (minimum dose of 7.5 ml to produce a titre) to the scenario in which the volume of blood in the fetus at 12 weeks is 4.2 ml, and where only half of that volume is present in the placenta, indicates that theoretically there should be zero chance of antibody formation.

References

Stern K, Davidsohn I, Masaitis L. Experimental studies on Rh immunization. Am J Clin Pathol. 1956;26:833–43.

Wiebe E, Campbell M, Aiken A, Albert A. Can we safely stop testing for Rh status and immunizing Rh-negative women having early abortions? A comparison of Rh alloimmunization in Canada and the Netherlands. Contraception. 2019;1(100001).

WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: World Health Organization; 2016 (https://www.who.int/publications/i/item/9789241549912).

SUMMARY OF FINDINGS TABLE

Rh Immunization – Anti-D immunoglobulin versus placebo for unsensitized individuals seeking abortion < 12 weeks

Patient or population: Unsensitized individuals seeking abortion < 12 weeks
Intervention: Rh immunization with administration of anti-D immunoglobulin
Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	Risk with anti-D administration			
Isoimmunization in subsequent pregnancy	not pooled	not pooled	not pooled	(0 studies)	-
Antibody formation after initial pregnancy	44 per 1000	12 per 1000 (1 to 95)	**RR 0.27** (0.03 to 2.15)	316 (2 RCTs) [1,2]	⊕◯◯◯ VERY LOW [a,b,c]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **OR:** odds ratio; RCT: randomized controlled trial; **RR:** risk ratio

Notes

a. One study not randomized and many unclear domains
b. This outcome is a surrogate for clinical relevant outcome
c. Confidence interval overlaps no effect

References

1. Goldman JA, Eckerling B. RH immunization in spontaneous abortion. Acta Eur Fertil. 1972.
2. Gavin PS. Rhesus sensitization in abortion. Obstet Gynecol. 1972.

2. EtD framework for Pain management for surgical abortion < 14 weeks

Recommendation 11. For pain management for surgical abortion at any gestational age:

a. **Recommend** that pain management should be offered routinely (e.g. non-steroidal anti-inflammatory drugs [NSAIDS]) and that it should be provided to those who want it; and
b. **Recommend against** the routine use of general anaesthesia.

NEW RECOMMENDATIONS BELOW INDICATE PAIN MANAGEMENT THAT IS *ADDITIONAL* TO NSAIDS.

Recommendation 12. (NEW) For pain management for surgical abortion at < 14 weeks:

a. **Recommend** the use of a paracervical block; and
b. **Suggest** that the option of combination pain management using conscious sedation plus paracervical block should be offered, where conscious sedation is available.

PICO 2: For a pregnant person seeking surgical abortion at < 14 weeks of gestation, is pain control with any particular method (I) safer, more effective and/or more satisfactory/acceptable compared with pain control with a different method or no pain control (C)? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global
Perspective: Population
Literature review: An update of an existing Cochrane review served as the evidence base for assessing the pain management regimens for surgical abortions less than 14 weeks of gestation. Thirty studies reporting on pain management for surgical abortion were identified by the search strategy. Of these studies, nine are the focus of this EtD framework.

- Six studies compared the paracervical block with a placebo
- One study compared the paracervical block with general anaesthesia
- Two studies compared sedation with paracervical block versus paracervical block alone

Study settings: France, Islamic Republic of Iran, Norway, Turkey, USA

ASSESSMENT OF RESEARCH EVIDENCE

For the analysis, research evidence was assessed for the following criteria:

- desirable effects

- undesirable effects
- certainty of evidence
- values
- balance of effects

Sub-PICOs were combined to address the following comparisons:

1. Paracervical block (PCB) versus placebo
2. PCB versus general anaesthesia
3. Sedation + PCB versus PCB alone

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Sub-PICO 1 – PCB versus placebo

Desirable effects:

The mean pain score was lower in the intervention group (paracervical block) compared with the mean pain score in the comparison group (placebo). The certainty of evidence is moderate. (*This trend occurred in women with and without conscious sedation*).

Fewer women in the intervention group (paracervical block) experienced complications related to the pain control methods compared with women in the comparison group (placebo). The certainty of evidence is low.

Fewer women in the intervention group (paracervical block) required additional analgesic medication compared with women in the comparison group (placebo). The certainty of evidence is high.

More women in the intervention group (paracervical block) expressed satisfaction towards their pain control compared with women in the comparison group (placebo). The certainty of evidence is moderate.

Undesirable effects:

More women in the intervention group (paracervical block) required supplemental narcotics compared with women in the comparison group (placebo). The certainty of evidence is low.

Draft judgement: Favours the intervention (PCB)

Sub-PICO 2 – PCB versus general anaesthesia

Desirable effects:

None

Undesirable effects:

More women in the intervention group (PCB) experienced high pain within 24 hours of the procedure compared with women in the comparison group (general anaesthesia). The certainty of evidence is moderate.

Draft judgement: Favours the comparison (general anaesthesia)

Sub-PICO 3 – Sedation + PCB versus PCB alone (sedation: nitrous oxide or fentanyl and midazolam)

Desirable effects:

The mean pain score was lower in the intervention group (sedation+ PCB) compared with the mean pain score in the comparison group (PCB alone). The certainty of evidence is moderate.

Fewer women in the intervention group (sedation+ PCB) experienced side-effects of nausea and vomiting compared with women in the comparison group (PCB alone). The certainty of evidence is low.

More women in the intervention group (sedation+ PCB) expressed satisfaction towards their pain control compared with women in the comparison group (PCB alone). The certainty of evidence is high.

Undesirable effects:

More women in the intervention group (sedation+ PCB) experienced side-effect of paraesthesia compared with women in the comparison group (PCB alone). The certainty of evidence is low.

More women in the intervention group (sedation+ PCB) experienced some form of side-effects compared with women in the comparison group (PCB alone). The certainty of evidence is low.

Draft judgement: Favours the intervention (sedation + paracervical block)

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

			x
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

Unable to determine	Varies	Large costs	Moderate costs	x Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	x Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

Unable to determine	Varies	Reduced	Probably reduced	x Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

SUMMARY OF FINDINGS TABLES

SoF Table 1: Pain management for surgical abortion first trimester: *Paracervical block (PCB) vs placebo*

Patient or population: Surgical abortion first trimester

Intervention: PCB

Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with PCB**			
Worst pain within 24 hours – Without conscious sedation assessed in mm Scale: 0 to 100 mm	The mean worst pain within 24 hours – Without conscious sedation was **85**	MD **30.86 lower** (36.48 lower to 25.25 lower)	-	155 (3 RCTs) [1,2,3]	⨁⨁⨁◯ MODERATE [a]
Worst pain within 24 hours – With conscious sedation assessed in mm Scale: 0 to 100 mm	The mean worst pain within 24 hours – With conscious sedation was **65**	MD **8.77 lower** (13.6 lower to 3.94 lower)	-	376 (3 RCTs) [4,5,6]	⨁⨁⨁◯ MODERATE [b]
Anxiety scores	The mean anxiety scores was **0**	not pooled	-	(0 studies)	-
Side-effects (overall, individual)	not pooled	not pooled	not pooled	(0 studies)	-
Complications related to pain-control methods	67 per 1000	**13 per 1000** (1 to 267)	**RR 0.20** (0.01 to 4.00)	60 (1 RCT) [1]	⨁⨁◯◯ LOW [c]
Use of any supplemental narcotic	162 per 1000	**254 per 1000** (146 to 442)	**RR 1.57** (0.90 to 2.73)	210 (2 RCTs) [1,5]	⨁⨁◯◯ LOW [a,d]
Use of any additional analgesic medication	367 per 1000	**202 per 1000** (84 to 469)	**RR 0.55** (0.23 to 1.28)	60 (1 RCT) [1]	⨁⨁⨁⨁ HIGH [a]
Duration of recovery time	The mean duration of recovery time was **0**	not pooled	-	(0 studies)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	Risk with PCB			
Satisfaction	295 per 1000	355 per 1000 (195 to 650)	**RR 1.20** (0.66 to 2.20)	89 (1 RCT) [4]	⨁⨁⨁◯ MODERATE [d]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **RR:** risk ratio

Notes

a. Downgraded one level due to substantial heterogeneity
b. One study does not report on pain during suction; one study is not blinded and one study allocation concealment is insufficient
c. Downgraded two levels due to broad confidence intervals
d. Downgraded one level due to broad confidence intervals

References for SoF Table 1

1. Renner RM, Nichols MD, Jensen JT, Li H, Edelman AB. Paracervical block for pain control in first-trimester surgical abortion: a randomized controlled trial. Obstet Gynecol. 2012.
2. Glantz JC, Shomento S. Comparison of paracervical block techniques during first trimester pregnancy termination. Int J Gynaecol Obstet. 2001.
3. Aksoy H, Aksoy U, Ozyurt S, Ozoglu N, Acmaz G, Aydın T, İdem Karadağ Ö, Tayyar AT. Comparison of lidocaine spray and paracervical block application for pain relief during first-trimester surgical abortion: a randomised, double-blind, placebo-controlled trial. J Obstet Gynaecol. 2016.
4. Kan AS, Ng EH, Ho PC. The role and comparison of two techniques of paracervical block for pain relief during suction evacuation for first-trimester pregnancy termination. Contraception. 2004.
5. Amirian M, Rajai M, Alavi A, Zare S, Aliabadi E. Comparison of lidocaine 1% and normal saline in paracervical anesthesia for decreasing of pain in curettage. Pak J Biol Sci. 2009.
6. Conti JA, Lerma K, Shaw KA, Blumenthal PD. Self-administered lidocaine gel for pain control with first-trimester surgical abortion: a randomized controlled trial. Obstet Gynecol. 2016.

SoF Table 2: Pain management for surgical abortion first trimester: *Paracervical block (PCB) vs general anaesthesia*

Patient or population: Surgical abortion first trimester
Intervention: PCB
Comparison: General anaesthesia

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with general anaesthesia	Risk with PCB			
Worst pain within 24 hours	36 per 1000	**387 per 1000** (54 to 1000)	**RR 10.84** (1.50 to 78.11)	59 (1 RCT) [1]	⨁⨁⨁◯ MODERATE [a]
Anxiety scores	The mean anxiety scores was **0**	not pooled	-	(0 studies)	-
Side-effects (overall, individual)	not pooled	not pooled	not pooled	(0 studies)	-
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-
Duration of recovery time	The mean duration of recovery time was **0**	not pooled	-	(0 studies)	-
Satisfaction	The mean satisfaction was **0**	not pooled	-	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **OR:** Odds ratio

Notes
a. Downgraded one level for broad confidence intervals

Reference for SoF Table 2
1. Raeder JC. Propofol anaesthesia versus paracervical blockade with alfentanil and midazolam sedation for outpatient abortion. Acta Anaesthesiol Scand. 1992.

SoF Table 3: Pain management for surgical abortion first trimester: *Sedation + paracervical block (PCB) vs PCB*

Patient or population: Surgical abortion first trimester
Intervention: Sedation + PCB
Comparison: PCB

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with PCB	Risk with sedation + PCB			
Worst pain within 24 hours – Nitrous oxide	The mean worst pain within 24 hours – Nitrous Oxide was **0**	MD **3 lower** (16.22 lower to 10.22 higher)	-	72 (1 RCT) [1]	⨁⨁⨁◯ MODERATE [a]
Anxiety scores	The mean anxiety scores was **0**	not pooled	-	(0 studies)	-
Side-effects (overall, individual) – Nitrous oxide – Nausea	111 per 1000	**83 per 1000** (20 to 346)	**RR 0.75** (0.18 to 3.11)	72 (1 RCT) [1]	⨁⨁◯◯ LOW [b]
Side-effects (overall, individual) – Nitrous oxide – Vomiting	56 per 1000	**11 per 1000** (1 to 224)	**RR 0.20** (0.01 to 4.03)	72 (1 RCT) [1]	⨁⨁◯◯ LOW [b]
Side-effects (overall, individual) – Nitrous oxide – Paraesthesia	83 per 1000	**444 per 1000** (142 to 1000)	**RR 5.33** (1.70 to 16.73)	72 (1 RCT) [1]	⨁⨁◯◯ LOW [b]
Side-effects (overall, individual) – Nitrous oxide – Total	500 per 1000	**970 per 1000** (700 to 1000)	**RR 1.94** (1.40 to 2.71)	72 (1 RCT) [1]	⨁⨁◯◯ LOW [b]
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-
Duration of recovery time	The mean duration of recovery time was **0**	not pooled	-	(0 studies)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with PCB	Risk with sedation + PCB			
Satisfaction – fentanyl and midazolam	200 per 1000	500 per 1000 (270 to 930)	**RR 2.50** (1.35 to 4.65)	100 (1 RCT) [2]	⨁⨁⨁⨁ HIGH

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio; **OR:** Odds ratio

Notes
a. Downgraded one level due to broad confidence intervals
b. Downgraded two levels for very broad confidence intervals

References for SoF Table 3

1. Agostini A, Maruani J, Roblin P, Champion J, Cravello L, Gamerre M. A double-blind, randomized controlled trial of the use of a 50:50 mixture of nitrous oxide/oxygen in legal abortions. Contraception. 2012.
2. Wong CY, Ng EH, Ngai SW, Ho PC. A randomized, double blind, placebo-controlled study to investigate the use of conscious sedation in conjunction with paracervical block for reducing pain in termination of first trimester pregnancy by suction evacuation. Hum Reprod. 2002.

3. EtD framework for Pain management for surgical abortion ≥ 14 weeks

Recommendation 13. (NEW) For pain management for cervical priming with osmotic dilators prior to surgical abortion at ≥ 14 weeks: **Suggest** the use of a paracervical block.

Recommendation 14. (NEW) For pain management for surgical abortion at ≥ 14 weeks:

a. **Recommend** the use of a paracervical block; and
b. **Suggest** that the option of combination pain management using conscious sedation plus paracervical block should be offered, where conscious sedation is available.

PICO 3: For a pregnant person seeking surgical abortion at ≥ 14 weeks of gestation (including cervical priming prior to the procedure), is pain control with any particular method (I) safer, more effective and/or more satisfactory/acceptable compared with pain control with a different method or no pain control (C)? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global

Perspective: Population

Literature review: A systematic review assessed the pain management regimens for surgical abortions greater than 14 weeks gestation. Three studies reporting on pain management for D&Es were identified by the search strategy. All three studies focused on pain management during the cervical ripening prior to the surgical procedure. Cervical priming was performed with laminaria. No studies were identified that focused on pain management for the D&E procedure.

Study settings: USA

ASSESSMENT OF RESEARCH EVIDENCE

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

Sub-PICOs were combined to address the following comparisons:

1. Pain regimens with laminaria insertion
2. Pain regimens for the surgical procedure (D&E)

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Sub-PICO 1 – Pain management during cervical priming

a) Paracervical block (PCB) versus placebo

Desirable effects:

The mean pain score was lower in the intervention group (paracervical block) compared with the mean pain score in the comparison group (placebo). The certainty of evidence is high.

More women in the intervention group (paracervical block) expressed satisfaction towards their pain control compared with women in the comparison group (placebo). The certainty of evidence is moderate.

Undesirable effects:

None

Draft judgement: Favours the intervention (PCB)

b) PCB + intrauterine lidocaine versus PCB + placebo

Desirable effects:

Fewer women in the intervention group experienced side-effects (PCB+ intrauterine lidocaine) compared with the women in the comparison group (PCB alone). The certainty of evidence is moderate.

Undesirable effects:

The mean pain score was higher in the intervention group (PCB+ intrauterine lidocaine) compared with the mean pain score in the comparison group (PCB alone). The certainty of evidence is high.

Draft judgement: Favours the comparison (PCB alone)

c) PCB versus intravaginal gel

Desirable effects:

None

Undesirable effects:

The mean pain score was higher in the intervention group (PCB) compared with the mean pain score in the comparison group (intravaginal gel). The certainty of evidence is low.

Draft judgement: Favours the comparison (intravaginal gel)

Sub-PICO 2 – Pain management during D&E

There were no studies that met the inclusion criteria, therefore draft judgements could not be made.

Additional research evidence

A recent systematic review was published and will provide additional evidence to our discussions. The systematic review focused on pain management for medical and surgical termination of pregnancy between 13 and 24 weeks of gestation. In this review, four surgical abortion studies were included. Results from this review reflected that general anaesthesia and deep IV sedation alleviated pain while nitrous oxide was ineffective. There were no studies that assessed moderate IV sedation, IV/IM opioid, paracervical block without sedation, NSAID or nonpharmacological treatment.[2]

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

			x
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

[2] Jackson E, Kapp N. Pain management for medical and surgical termination of pregnancy between 13 and 24 weeks of gestation: a systematic review. BJOG. 2020;127(11):1348-1357. doi:10.1111/1471-0528.16212.

Unable to determine	Varies	Large costs	Moderate costs	x Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

Unable to determine	Varies	Favours the comparison	Probably favours the comparison	x Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

Unable to determine	Varies	Reduced	Probably reduced	x Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

	Varies	No	Probably No	Probably Yes	x Yes

Unable to determine					

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

SUMMARY OF FINDINGS TABLE

SoF Table 1: Pain management for surgical abortion second trimester: *Pain during osmotic dilator placement vs placebo*

Patient or population: Surgical abortion second trimester
Intervention: Pain management during osmotic dilator placement
Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with pain during osmotic dilator placement**			
Worst pain within 24 hours – Intrauterine lidocaine assessed in mm Scale: 0 to 100	The mean worst pain within 24 hours – Intrauterine lidocaine was **0**	MD **1 higher** (10.06 lower to 12.06 higher)	-	70 (1 RCT) [1]	⊕⊕⊕⊕ HIGH
Worst pain within 24 hours – Paracervical block vs placebo assessed in mm Scale: 0 to 100	The mean worst pain within 24 hours – Paracervical block vs placebo was **0**	MD **41 lower** (56.95 lower to 25.05 lower)	-	41 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Worst pain within 24 hours – Paracervical block vs intravaginally lidocaine assessed in mm Scale: 0 to 100	The mean worst pain within 24 hours – Paracervical block vs intravaginally lidocaine was **0**	MD **12 higher** (7.35 lower to 31.35 higher)	-	69 (1 RCT) [3]	⊕⊕◯◯ LOW [a,b]
Anxiety scores	The mean anxiety scores was **0**	not pooled	-	(0 studies)	-
Side-effects (overall, individual) – Total	235 per 1000	**167 per 1000** (64 to 431)	**RR 0.71** (0.27 to 1.83)	70 (1 RCT) [1]	⊕⊕⊕◯ MODERATE [b]
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with pain during osmotic dilator placement**			
Duration of recovery time	The mean duration of recovery time was **0**	not pooled	-	(0 studies)	-
Satisfaction	The mean satisfaction was **88** mm	MD **4 mm higher** (12.23 lower to 20.23 higher)	-	41 (1 RCT) [2]	⊕⊕⊕◯ MODERATE [b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio; **OR:** Odds ratio

Notes

a. Downgraded one level due to lack of blinding
b. Downgraded one level due to broad confidence intervals

References

1. Mercier RJ, Liberty A. Intrauterine lidocaine for pain control during laminaria insertion: a randomized controlled trial. Contraception. 2014.
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4. EtD framework for Pain management for medical abortion < 14 weeks

Recommendation 15. For medical abortion at any gestational age: **Recommend** that pain management should be offered routinely (e.g. non-steroidal anti-inflammatory drugs [NSAIDs]) and that it should be provided for the individual to use if and when wanted.

PICO 4: For a pregnant person seeking medical abortion at < 14 weeks of gestation, is pain control with any particular pharmacological method (i: given prophylactically or after onset of pain) or non-pharmacological method (ii) safer, more effective and/or more satisfactory/acceptable compared with any other such method or no treatment/placebo? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global

Perspective: Population

Literature review: A Cochrane systematic review serves as the evidence base for this key question. Five studies reporting on pain management for medical abortion < 14 weeks were identified by the search strategy. Of these studies, three were assessed by the following comparisons:

- ibuprofen versus placebo
- prophylactic versus therapeutic NSAIDs
- ibuprofen versus paracetamol

Study settings: Israel, United Kingdom of Great Britain and Northern Ireland, USA

ASSESSMENT OF RESEARCH EVIDENCE

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

Sub–PICOs were combined to answer the following questions

1. Comparison of Ibuprofen versus placebo
2. Comparison of prophylactic versus therapeutic NSAIDs
3. Comparison of Ibuprofen versus paracetamol

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations. A detailed EtD framework has been developed for the above question. The findings from the EtD frameworks are summarized here to help the ERRG review information and make a recommendation. The Summary of Findings table is provided in the appendix at the end of the document.

Sub-PICO 1 – NSAIDS versus placebo

Desirable effects:

The mean pain score in the intervention group (NSAID) was lower compared with the mean pain score in the comparison group (placebo). The certainty of evidence is high.

Fewer women in the intervention group (NSAID) required additional analgesic compared with women in the comparison group (placebo). The certainty of evidence is high.

Fewer women in the intervention group (NSAID) experienced side-effects of headache and vomiting compared with women in the comparison group (placebo). The certainty of evidence is moderate for both outcomes.

More women in the intervention group (NSAID) had a successful abortion compared with women in the comparison group (placebo). The certainty of evidence is high.

Undesirable effects:

More women in the intervention group (NSAID) experienced side-effects of dizziness, bleeding, shivering and nausea compared with women in the comparison group (placebo). The certainty of evidence is moderate for all four outcomes.

Draft judgement: Favours the intervention (NSAID)

Sub-PICO 2 – Prophylactic versus therapeutic NSAIDs

Desirable effects:

The mean pain score in the intervention group (prophylactic NSAID) was lower compared with the mean pain score in the comparison group (therapeutic NSAIDs). The certainty of evidence is low.

Fewer women in the intervention group (prophylactic NSAID) experienced pain greater than 7 VAS compared with the women in the comparison group (therapeutic NSAIDs). The certainty of evidence is moderate.

More women in the intervention group (prophylactic NSAID) expressed satisfaction towards their pain control compared with women in the comparison group (therapeutic NSAIDs). The certainty of evidence is moderate.

Undesirable effects:

More women in the intervention group (prophylactic NSAID) used additional analgesic medication compared with women in the comparison group (therapeutic NSAIDs). The certainty of evidence is low.

Fewer women in the intervention group (prophylactic NSAID) had a successful abortion compared with the women in the comparison group (therapeutic NSAIDs). The certainty of evidence is moderate.

Draft judgement: Probably favours the intervention (prophylactic NSAIDs)

Sub-PICO 3 – Ibuprofen versus paracetamol

Desirable effect:

Fewer women in the intervention group (ibuprofen) required additional analgesic medication compared with women in the comparison group (paracetamol). The certainty of evidence is high.

More women in the intervention group (ibuprofen) had a successful abortion compared with women in the comparison group (paracetamol). The certainty of evidence is high.

Undesirable effect:

The mean pain score in the intervention group (ibuprofen) was higher compared with the mean pain score in the comparison group (paracetamol). The certainty of evidence is moderate.

Draft judgement: Favours neither the intervention (ibuprofen) or comparison (paracetamol)

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

			x
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

				x		
Unable to determine	Varies	Large costs	Moderate costs	Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

				x		
Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

				x		
Unable to determine	Varies	Reduced	Probably reduced	Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

SUMMARY OF FINDINGS TABLE

SoF Table: Pain management for medical abortion in the first trimester: Pain management vs placebo

Patient or population: Pain management for medical abortion in first trimester
Intervention: Pain management
Comparison: Placebo

	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with pain management**			
Worst pain within 24 hours – Prophylactic vs therapeutic	The mean worst pain within 24 hours – Prophylactic vs therapeutic was **7.3** cm	MD **0.2 cm lower** (1.73 lower to 1.33 higher)	-	128 (1 RCT) [1]	⊕⊕◯◯ LOW [a,b]
Worst pain within 24 hours – Ibuprofen vs paracetamol	The mean worst pain within 24 hours – Ibuprofen vs paracetamol was **2.7** cm	MD **2.13 cm higher** (1.59 higher to 2.67 higher)	-	108 (1 RCT) [2]	⊕⊕⊕◯ MODERATE [b]
Worst pain within 24 hours – NSAIDs vs placebo	The mean worst pain within 24 hours – NSAIDs vs placebo was **4.8** cm	MD **2.72 cm lower** (4.33 lower to 1.11 lower)	-	61 (1 RCT) [3]	⊕⊕⊕⊕ HIGH
Worst pain within 24 hours (pain above VAS 7) – Prophylactic vs therapeutic	530 per 1000	**525 per 1000** (408 to 668)	**RR 0.99** (0.77 to 1.26)	228 (1 RCT) [1]	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Headache	219 per 1000	**103 per 1000** (28 to 363)	**RR 0.47** (0.13 to 1.66)	61 (1 RCT) [3]	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Dizziness	250 per 1000	**275 per 1000** (120 to 640)	**RR 1.10** (0.48 to 2.56)	61 (1 RCT) [3]	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Vomiting	281 per 1000	**70 per 1000** (17 to 293)	**RR 0.25** (0.06 to 1.04)	61 (1 RCT) [3]	⊕⊕⊕◯ MODERATE [b]

Anticipated absolute effects* (95% CI)			Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with pain management**			
Side-effects (overall, individual) – Bleeding	719 per 1000	**726 per 1000** (532 to 992)	**RR 1.01** (0.74 to 1.38)	61 (1 RCT) [3]	⊕⊕⊕◯ MODERATE [b]
Side-effects (overall, individual) – Shivering	219 per 1000	**378 per 1000** (171 to 847)	**RR 1.73** (0.78 to 3.87)	61 (1 RCT) [3]	⊕⊕⊕◯ MODERATE [b]
Side-effects (overall, individual) – Nausea	594 per 1000	**689 per 1000** (475 to 1000)	**RR 1.16** (0.80 to 1.69)	61 (1 RCT) [3]	⊕⊕⊕◯ MODERATE [b]
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-
Use of any additional analgesic medication – Prophylactic vs therapeutic	427 per 1000	**513 per 1000** (389 to 679)	**RR 1.20** (0.91 to 1.59)	228 (1 RCT) [1]	⊕⊕◯◯ LOW [a,b]
Use of any additional analgesic medication – Ibuprofen vs paracetamol	265 per 1000	**69 per 1000** (24 to 194)	**RR 0.26** (0.09 to 0.73)	108 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Use of any additional analgesic medication – Ibuprofen vs placebo	781 per 1000	**383 per 1000** (227 to 625)	**RR 0.49** (0.29 to 0.80)	61 (1 RCT) [3]	⊕⊕⊕⊕ HIGH
Time to expulsion	The mean time to expulsion was **0**	not pooled	-	(0 studies)	-
Satisfaction – Prophylactic vs therapeutic	521 per 1000	**579 per 1000** (454 to 730)	**RR 1.11** (0.87 to 1.40)	228 (1 RCT) [1]	⊕⊕⊕◯ MODERATE [a]

Anticipated absolute effects* (95% CI)			Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with pain management**			
Successful completion without additional surgical intervention – Prophylactic vs therapeutic	974 per 1000	**965 per 1000** (916 to 1000)	**RR 0.99** (0.94 to 1.04)	228 (1 RCT) [1]	⊕⊕⊕◯ MODERATE [a]
Successful completion without additional surgical intervention – Ibuprofen vs paracetamol	837 per 1000	**912 per 1000** (795 to 1000)	**RR 1.09** (0.95 to 1.27)	108 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Successful completion without additional surgical intervention – Ibuprofen vs placebo	875 per 1000	**963 per 1000** (831 to 1000)	**RR 1.10** (0.95 to 1.20)	61 (1 RCT) [3]	⊕⊕⊕⊕ HIGH

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **OR:** odds ratio

Notes

a. Downgraded one level due to lack of blinding
b. Downgraded one level due to wide confidence intervals

References

1. Raymond E, Weaver M, Louie K, Dean G, Porsch L, Lichtenberg E et al. Prophylactic compared with therapeutic ibuprofen analgesia in first-trimester medical abortion. Obstet Gynecol. 2013;122(3):558–64. doi:10.1097/AOG.0b013e31829d5a33.
2. Livshits A, Machtinger R, David LB, Spira M, Moshe-Zahav A, Seidman DS. Ibuprofen and paracetamol for pain relief during medical abortion: a double-blind randomized controlled study. Fertil Steril. 2009;91(5):1877–80. doi:10.1016/j.fertnstert.2008.01.084.
3. Avraham S, Gat I, Duvdevani NR, Haas J, Frenkel Y, Seidman DS. Pre-emptive effect of ibuprofen versus placebo on pain relief and success rates of medical abortion: a double-blind, randomized, controlled study. Fertil Steril. 2012;97(3):612-5. doi:10.1016/j.fertnstert.2011.12.041.

5. EtD framework for Pain management for medical abortion ≥ 14 weeks

Recommendation 15. For medical abortion at any gestational age: **Recommend** that pain management should be offered routinely (e.g. non-steroidal anti-inflammatory drugs [NSAIDs]) and that it should be provided for the individual to use if and when wanted.

NEW RECOMMENDATION BELOW INDICATES PAIN MANAGEMENT THAT IS *ADDITIONAL* TO NSAIDS.

Recommendation 16. (NEW) For pain management for medical abortion at ≥ 12 weeks: **Suggest** consideration of other methods to control pain or discomfort due to increased need with increasing gestational age. Such methods include certain anti-emetics and epidural anaesthesia, where available.

PICO 5: For a pregnant person seeking medical abortion at ≥ 14 weeks of gestation, is pain control with any particular (i) pharmacological method (given prophylactically or after onset of pain) or (ii) non-pharmacological method safer, more effective and/or more satisfactory/acceptable compared with any other such methods or no treatment/placebo? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global

Perspective: Population

Literature review: A systematic review was undertaken to address this key question. Eleven studies reporting on pain management for medical abortion > 14 weeks were identified by the search strategy. Of these studies, the following comparisons were made:

- PCB versus oral pain medication
- NSAIDs versus non-NSAIDs/placebo
- antiemetics versus placebo
- anti-epileptics versus anxiolytics
- intermittent versus continuous epidural
- patient controlled epidural versus patient controlled IV fentanyl
- patient controlled fentanyl versus patient-controlled morphine
- patient controlled IV tramadol versus patient-controlled IV fentanyl

Study settings: Belgium, Canada, Germany, Israel, Italy, Sweden, Thailand, USA

ASSESSMENT OF RESEARCH EVIDENCE

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

Sub–PICOs were combined to address the following comparisons:

1. PCB versus oral pain medication
2. NSAIDs versus non-NSAIDs/placebo
3. Antiemetics versus placebo
4. Anti-epileptics versus anxiolytics
5. Intermittent versus continuous epidural
6. Patient-controlled epidural versus patient-controlled IV fentanyl
7. Patient-controlled fentanyl versus patient-controlled morphine
8. Patient-controlled IV tramadol versus patient-controlled IV fentanyl

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Sub-PICO 1 – PCB versus oral pain medication

Desirable effects:

Fewer women in the intervention group (paracervical block) experienced side-effects of nausea, shivering and pruritus compared with women in the comparison group (oral pain medication). The certainty of evidence is low for all three outcomes.

The mean use of supplemental narcotic was lower for the intervention group (paracervical block) compared with the comparison group (oral pain medication). The certainty of evidence is high.

Equal number of women in the intervention and comparison group experienced the side-effect of dizziness. The certainty of evidence is low.

Undesirable effects:

More women in the intervention group (paracervical block) experienced pain above VAS 7 compared with women in the comparison group (oral pain medication). The certainty of evidence is moderate.

Mean expulsion time was higher in the intervention group (paracervical block) compared with women in the comparison group (oral pain medication). The certainty of evidence is moderate.

Draft judgement: Favours the comparison (oral pain medication)

Sub-PICO 2 – NSAIDs versus non-NSAIDs/placebo

- **NSAIDs (diclofenac) versus non-NSAIDs (paracetamol + codeine)**

Desirable effects:

Fewer women in the intervention group (NSAID) experienced side-effect of vomiting compared with women in the comparison group (non-NSAID). The certainty of evidence is moderate.

Fewer women in the intervention group (NSAID) required supplemental narcotics compared with women in the comparison group (non-NSAID). The certainty of evidence is high.

Fewer women in the intervention group (NSAID) required additional analgesic medication compared with women in the comparison group (non-NSAID). The certainty of evidence is moderate.

More women in the intervention group (NSAID) had a successful abortion compared with the women in the comparison group (non-NSAID). The certainty of evidence is moderate.

Mean expulsion time was lower in the intervention group (NSAID) compared with women in the comparison group (non-NSAID). The certainty of evidence is moderate.

Undesirable effects:

None

Draft judgement: Favours the intervention (NSAID)

- **NSAIDs versus placebo**

Desirable effects:

The mean pain score in the intervention group (NSAID) was lower compared with the mean pain score in the comparison group (placebo). The certainty of evidence is high.

Fewer women in the intervention group (NSAID) experienced side-effects of vomiting, fever and chills compared with women in the comparison group (placebo). The certainty of evidence is moderate for all three outcomes.

More women in the intervention group (NSAID) had a successful abortion compared with the women in the comparison group (placebo). The certainty of evidence is high.

Equal number of women in the intervention and comparison group experienced the side-effect of diarrhoea. The certainty of evidence is low.

Equal number of women in the intervention and comparison group required supplemental narcotic. The certainty of evidence is moderate.

Undesirable effects:

More women in the intervention group (NSAID) experienced the side-effect of itching compared with women in the comparison group (placebo). The certainty of evidence is low.

Mean expulsion time was higher in the intervention group (NSAID) compared with women in the comparison group (placebo). The certainty of evidence is low.

Draft judgement: Favours the intervention (NSAID)

- **NSAID versus non-NSAID/placebo (aggregated)**

Desirable effect:

Fewer women in the intervention group (NSAID) experienced side-effect of vomiting, compared with women in the comparison group (non-NSAID/placebo). The certainty of evidence is moderate.

Fewer women in the intervention group (NSAID) required supplemental narcotics compared with women in the comparison group (non-NSAID/placebo). The certainty of evidence is high.

More women in the intervention group (NSAID) had a successful abortion compared with the women in the comparison group (non-NSAID/placebo). The certainty of evidence is high.

Mean expulsion time was lower in the intervention group (NSAID) compared with women in the comparison group (non-NSAID/placebo). The certainty of evidence is moderate.

Undesirable effect:

None

Overall draft judgement: Favours the intervention (NSAID)

Sub-PICO 3 – Antiemetics versus placebo

Desirable effects:

Fewer women in the intervention group (anti-emetic) used supplemental narcotics compared with women in the comparison group (placebo). The certainty of evidence is moderate.

Mean expulsion time was lower in the intervention group (anti-emetic) compared with women in the comparison group (placebo). The certainty of evidence is moderate.

Undesirable effects:

None

Draft judgement: Favours the intervention (anti-emetic)

Sub-PICO 4 – Anti-epileptics versus anxiolytics

Desirable effects:

The mean pain score in the intervention group (antiepileptics) was lower compared with the mean pain score in the comparison group (anxiolytics). The certainty of evidence is moderate.

Fewer women in the intervention group (antiepileptics) used additional analgesic medication compared with women in the comparison group (anxiolytics). The certainty of evidence is moderate.

Mean expulsion time was lower in the intervention group (antiepileptics) compared with women in the comparison group (anxiolytics). The certainty of evidence is moderate.

Equal number of women in the intervention and comparison group experienced the side-effect of blurry vision. The certainty of evidence is low.

Undesirable effects:

Fewer women in the intervention group (antiepileptics) had a successful abortion compared with the women in the comparison group (anxiolytics). The certainty of evidence is high.

Draft judgement: Favours the intervention (antiepileptic)

Sub-PICO 5 – Intermittent versus continuous epidural

Desirable effects:

Fewer women in the intervention group (intermittent epidural) experienced side-effects of nausea, vomiting, sedation, respiratory depression compared with women in the comparison group (continuous epidural). The certainty of evidence is high (nausea), low (vomiting, sedation, respiratory depression).

Fewer women in the intervention group (intermittent epidural) experienced shivering from the pain control method compared with women in the comparison group (continuous epidural). The certainty of evidence moderate.

Mean expulsion time was lower in the intervention group (intermittent epidural) compared with women in the comparison group (continuous epidural). The certainty of evidence is moderate.

More women in the intervention group (intermittent epidural) expressed satisfaction towards their pain control compared with women in the comparison group (continuous epidural). The certainty of evidence is high.

Equal number of women in the intervention and comparison group had successful abortion without additional surgical intervention. The certainty of evidence is high.

Equal number of women in the intervention and comparison group experienced complications related to the pain control methods (hypertension and shivering). The certainty of evidence is moderate.

Undesirable effects:

More women in the intervention group (intermittent epidural) experienced side-effects of pruritus compared with women in the comparison group (continuous epidural). The certainty of evidence is moderate.

More women in the intervention group (intermittent epidural) experienced hypertension from the pain control method compared with women in the comparison group (continuous epidural). The certainty of evidence low.

Draft judgement: Favours the intervention (intermittent epidural)

Sub-PICO 6 – Patient-controlled analgesic epidural (PCEA) versus patient-controlled analgesic (PCA) IV fentanyl

Desirable effects:

The mean pain score in the intervention group (PCEA) was lower compared with the mean pain score in the comparison group (PCA fentanyl). The certainty of evidence is moderate.

Fewer women in the intervention group (PCEA) experienced side-effects of vomiting and mild sedation compared with women in the comparison group (PCA fentanyl). The certainty of evidence is moderate for both outcomes.

Fewer women in the intervention group (PCEA) required a change in their pain regimen compared with women in the comparison group (PCA fentanyl). The certainty of evidence is low.

More women in the intervention group (PCEA) had a successful abortion compared with women in the comparison group (PCA fentanyl). The certainty of evidence is moderate.

Mean expulsion time was lower in the intervention group (PCEA) compared with women in the comparison group (PCA fentanyl). The certainty of evidence is moderate.

More women in the intervention group (PCEA) expressed satisfaction towards their pain control compared with women in the comparison group (PCA fentanyl). The certainty of evidence is moderate.

Equal number of women in the intervention and comparison group experienced intermittent bladder catheterization and hypotension. The certainty of evidence is low.

Undesirable effects:

More women in the intervention group (PCEA) experienced side-effects of nausea and pruritus compared with women in the comparison group (PCA fentanyl). The certainty of evidence is moderate for both outcomes.

More women in the intervention group (PCEA) experienced complications related to the pain control methods compared with women in the comparison group (PCA fentanyl). The certainty of evidence is moderate.

Draft judgement: Favours the intervention (PCEA)

Sub-PICO 7 – Patient-controlled fentanyl versus patient-controlled morphine

Desirable effects:

The mean pain score in the intervention group (PCA fentanyl – 50 µg/3 or 6 min) was lower compared with the mean pain score in the comparison group (PCA morphine). The certainty of evidence is moderate.

Fewer women in the intervention group (PCA fentanyl – 25 µg/3 mins, 50 µg/3 or 6 min) experienced side-effects of nausea, vomiting, sedation, pruritus and dizziness compared with women in the comparison group (PCA morphine). The certainty of evidence is moderate for both outcomes. The certainty of evidence ranged from moderate to high.

Equal number of women in the intervention (PCA fentanyl – 50 µg/3 mins) and comparison group (PCA morphine) experienced the side-effect of nausea and dizziness. The certainty of evidence is moderate to high.

Undesirable effects:

The mean pain score in the intervention group (PCA fentanyl – 25 µg/3 min) was higher compared with the mean pain score in the comparison group (PCA morphine). The certainty of evidence is high.

Draft judgement: Favours the intervention (PCA fentanyl-50 µg)

Sub-PICO 8 – Patient-controlled analgesic (PCA) IV tramadol versus patient-controlled analgesic (PCA) IV fentanyl

Desirable effects:

The mean pain score in the intervention group (PCA tramadol) was lower compared with the mean pain score in the comparison group (PCA fentanyl). The certainty of evidence is moderate.

Fewer women in the intervention group (PCA tramadol) experienced overall side-effects compared with women in the comparison group (PCA fentanyl). The certainty of evidence is moderate.

Mean expulsion time was lower in the intervention group (PCA tramadol) compared with women in the comparison group (PCA fentanyl). The certainty of evidence is low.

Ratings of satisfaction were similar in the intervention (PCA tramadol) and comparison group (PCA fentanyl). The certainty of evidence is high.

Undesirable effects:

More women in the intervention group (PCA tramadol) used additional analgesic medication compared with women in the comparison group (PCA fentanyl). The certainty of evidence is low.

Draft judgement: Favours neither the intervention nor the comparison

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	x No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

Unable to determine	Varies	Large costs	Moderate costs	x Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

Unable to determine	Varies	Favours the comparison	Probably favours the comparison	x Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

				x		
Unable to determine	Varies	Reduced	Probably reduced	Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

					x
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

					x
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

SUMMARY OF FINDINGS TABLES

SoF Table 1: Pain management for medical abortion in second trimester: *Paracervical block vs oral pain medicine*

Patient or population: Pain management for medical abortion in second trimester
Setting: Sweden
Intervention: Paracervical block (PCB)
Comparison: Oral pain medicine

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with oral pain medicine	Risk with PCB			
Worst pain within 24 hours (pain above VAS 7)	640 per 1000	**781 per 1000** (595 to 1000)	**RR 1.22** (0.93 to 1.59)	102 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Nausea	160 per 1000	**154 per 1000** (62 to 378)	**RR 0.96** (0.39 to 2.36)	102 (1 RCT)	⊕⊕◯◯ LOW [b]
Side-effects (overall, individual) – Shivering	40 per 1000	**38 per 1000** (6 to 263)	**RR 0.96** (0.14 to 6.57)	102 (1 RCT)	⊕⊕◯◯ LOW [b]
Side-effects (overall, individual) – Dizziness	60 per 1000	**60 per 1000** (13 to 284)	**RR 1.00** (0.21 to 4.73)	102 (1 RCT)	⊕⊕◯◯ LOW [b]
Side-effects (overall, individual) – Pruritis	20 per 1000	**7 per 1000** (0 to 160)	**RR 0.33** (0.01 to 8.00)	102 (1 RCT)	⊕⊕◯◯ LOW [b]
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **5** mg	MD **0 mg** (2.6 lower to 2.6 higher)	-	102 (1 RCT)	⊕⊕⊕⊕ HIGH
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with oral pain medicine	**Risk with PCB**			
Successful completion without additional surgical intervention	not pooled	not pooled	not pooled	(0 studies)	-
Time to expulsion	The mean time to expulsion was **398** min	MD **37 min higher** (2 lower to 76 higher)	-	102 (1 RCT)	⨁⨁⨁◯ MODERATE [a]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio; **OR:** odds ratio; **MD:** mean difference

Notes

a. Downgraded one level; broad confidence intervals
b. Downgraded two levels; very broad confidence intervals

References

Andersson IM Andersson IM, Benson L, Christensson K, Gemzell-Danielsson K. Paracervical block as pain treatment during second-trimester medical termination of pregnancy: an RCT with bupivacaine versus sodium chloride. Hum Reprod. 2016;31(1):67–74.

SoF Table 2: Pain management for medical abortion in second trimester: *NSAIDs vs non-NSAIDS or placebo*

Patient or population: Pain management for medical abortion in second trimester
Setting: Sweden and Thailand
Intervention: NSAIDs
Comparison: Non-NSAIDS or placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with non-NSAIDS or placebo	Risk with NSAIDs			
Worst pain within 24 hours – Celecoxib vs placebo	The mean worst pain within 24 hours – Celecoxib vs placebo was **7.3** cm on VAS	MD **2.7 cm on VAS lower** (4.02 lower to 1.38 lower)	-	56 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – vomiting	364 per 1000	**251 per 1000** (149 to 425)	**RR 0.69** (0.41 to 1.17)	130 (2 RCTs)	⊕⊕⊕◯ MODERATE [a]
Side-effects – vomiting – Diclofenac vs paracetamol and codeine	421 per 1000	**278 per 1000** (147 to 531)	**RR 0.66** (0.35 to 1.26)	74 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – vomiting – Celecoxib vs placebo	286 per 1000	**214 per 1000** (86 to 537)	**RR 0.75** (0.30 to 1.88)	56 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – fever – Celecoxib vs placebo	536 per 1000	**498 per 1000** (300 to 830)	**RR 0.93** (0.56 to 1.55)	56 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Chills – Celecoxib vs placebo	607 per 1000	**534 per 1000** (340 to 844)	**RR 0.88** (0.56 to 1.39)	56 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Itching – Celecoxib vs placebo	36 per 1000	**71 per 1000** (7 to 744)	**RR 2.00** (0.19 to 20.82)	56 (1 RCT)	⊕⊕◯◯ LOW [b]
Side-effects – Diarrhoea – Celecoxib vs placebo	71 per 1000	**71 per 1000** (11 to 472)	**RR 1.00** (0.15 to 6.61)	56 (1 RCT)	⊕⊕◯◯ LOW [b]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with non-NSAIDS or placebo	Risk with NSAIDs			
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	652 per 1000	**645 per 1000** (508 to 814)	**RR 0.99** (0.78 to 1.25)	130 (2 RCTs)	⊕⊕⊕⊕ HIGH
Use of any supplemental narcotic – Diclofenac vs paracetamol and codeine	816 per 1000	**808 per 1000** (644 to 1000)	**RR 0.99** (0.79 to 1.23)	74 (1 RCT)	⊕⊕⊕⊕ HIGH
Use of any supplemental narcotic – Celecoxib vs placebo	429 per 1000	**429 per 1000** (236 to 784)	**RR 1.00** (0.55 to 1.83)	56 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Use of any additional analgesic medication – Diclofenac vs paracetamol and codeine	421 per 1000	**248 per 1000** (126 to 493)	**RR 0.59** (0.30 to 1.17)	74 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Successful completion without additional surgical intervention	652 per 1000	**697 per 1000** (567 to 853)	**RR 1.07** (0.87 to 1.31)	130 (2 RCTs)	⊕⊕⊕⊕ HIGH
Successful completion without additional surgical intervention – Diclofenac vs paracetamol and codeine	447 per 1000	**474 per 1000** (286 to 774)	**RR 1.06** (0.64 to 1.73)	74 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Successful completion without additional surgical intervention – Celecoxib vs placebo	929 per 1000	**1000 per 1000** (882 to 1000)	**RR 1.08** (0.95 to 1.21)	56 (1 RCT)	⊕⊕⊕⊕ HIGH
Time to expulsion	The mean time to expulsion ranged from **6.5 to 15.2** hours	MD **0.99 hours lower** (2.39 lower to 0.41 higher)	-	130 (2 RCTs)	⊕⊕⊕◯ MODERATE [a]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with non-NSAIDS or placebo	Risk with NSAIDs			
Time to expulsion – Diclofenac vs paracetamol and codeine	The mean time to expulsion – Diclofenac vs paracetamol and codeine was **6.5** hours	MD **1.1 hours lower** (2.51 lower to 0.31 higher)	-	74 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Time to expulsion – Celecoxib vs placebo	The mean time to expulsion – Celecoxib vs placebo was **15.2** hours	MD **4.2 hours higher** (5.66 lower to 14.06 higher)	-	56 (1 RCT)	⨁⨁◯◯ LOW [b]

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **OR:** odds ratio

Notes

a. Downgraded one level; wide confidence intervals

b. Downgraded two levels; very wide confidence intervals

References

Fiala C, Swahn ML, Stephansson O, Gemzell-Danielsson K. The effect of non-steroidal anti-inflammatory drugs on medical abortion with mifepristone and misoprostol at 13–22 weeks gestation. Hum Reprod. 2005;20(11):3072–7. doi:10.1093/humrep/dei216.

Tinatara H, Voradithi P, Choobun T. Effectiveness of celecoxib for pain relief and antipyresis in second trimester medical abortions with misoprostol: a randomized controlled trial. Arch Gynecol Obstet. 2018;297:709–15. doi:10.1007/s00404-018-4653-4.

SoF Table 3: Pain management for medical abortion in second trimester: *Antiemetics vs placebo*

Patient or population: Pain management for medical abortion in second trimester

Setting: USA

Intervention: Antiemetics

Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	Risk with antiemetics			
Worst pain within 24 hours	The mean worst pain within 24 hours was **0**	not pooled	-	(0 studies)	-
Side-effects (overall, individual)	not pooled	not pooled	not pooled	(0 studies)	-
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic ranged from **28 mg to 52** mg	MD **20.14 mg lower** (28.84 lower to 11.44 lower)	-	47 (2 RCTs)	⨁⨁⨁◯ MODERATE [a]
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-
Successful completion without additional surgical intervention	not pooled	not pooled	not pooled	(0 studies)	-
Time to expulsion	The mean time to expulsion was **0** hours	MD **4.29 hours lower** (7.18 lower to 1.41 lower)	-	47 (2 RCTs)	⨁⨁⨁◯ MODERATE [a]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Note

a. Downgraded one level; allocation and blinding uncertain

References for SoF Table 3

Rosenblatt WH, Cioffi AM, Sinatra R, Saberski LR, Silverman DG. Metoclopramide: an analgesic adjunct to patient-controlled analgesia. Anesth Analg. 1991;73(5):553–5. doi:10.1213/00000539-199111000-00007.

Rosenblatt WH, Cioffi AM, Sinatra R, Silverman DG. Metoclopramide-enhanced analgesia for prostaglandin-induced termination of pregnancy. Anesth Analg. 1992;75(5):760–3. doi:10.1213/00000539-199211000-00019.

SoF Table 4: Pain management for medical abortion in second trimester: *Antiepileptics vs anxiolytics*

Patient or population: Pain management for medical abortion in second trimester
Setting: Belgium
Intervention: Antiepileptics
Comparison: Anxiolytics

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with anxiolytics	Risk with antiepileptics			
Worst pain within 24 hours	The mean worst pain within 24 hours was **73** mm on VAS	MD **9.5 mm on VAS lower** (16.94 lower to 2.06 lower)	-	48 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Side-effects – Blurry vision	0 per 1000	**0 per 1000** (0 to 0)	**RR 3.00** (0.13 to 70.16)	48 (1 RCT)	⨁⨁◯◯ LOW [b]
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-
Use of any additional analgesic medication	958 per 1000	**748 per 1000** (585 to 958)	**RR 0.78** (0.61 to 1.00)	48 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Successful completion without additional surgical intervention	875 per 1000	**831 per 1000** (656 to 1000)	**RR 0.95** (0.75 to 1.20)	48 (1 RCT)	⨁⨁⨁⨁ HIGH
Time to expulsion	The mean time to expulsion was **942** min	MD **113 min lower** (334.1 lower to 108.1 higher)	-	48 (1 RCT)	⨁⨁⨁◯ MODERATE [a]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **OR:** odds ratio

Notes
a. Downgraded one level; confidence interval crosses clinical irrelevant effect
b. Downgraded two levels; very wide confidence intervals

References for SoF Table 4

Lavand'homme P.M. Roelants F. Evaluation of pregabalin as an adjuvant to patient-controlled epidural analgesia during late termination of pregnancy. Anesthesiology. 2011;113:1186–91.

SoF Table 5: Pain management for medical abortion in second trimester: *Intermittent compared with continuous epidural*

Patient or population: Pain management for medical abortion in second trimester
Setting: Italy
Intervention: Intermittent
Comparison: Continuous epidural

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with continuous epidural	**Risk with Intermittent**			
Worst pain within 24 hours	The mean worst pain within 24 hours was **0**	not pooled	-	(0 studies)	-
Side-effects (overall, individual) – Nausea	346 per 1000	**135 per 1000** (62 to 294)	**RR 0.39** (0.18 to 0.85)	104 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects (overall, individual) – Vomiting	58 per 1000	**19 per 1000** (2 to 179)	**RR 0.33** (0.04 to 3.10)	104 (1 RCT)	⊕⊕◯◯ LOW [a]
Side-effects (overall, individual) – Pruritis	269 per 1000	**326 per 1000** (180 to 592)	**RR 1.21** (0.67 to 2.20)	104 (1 RCT)	⊕⊕⊕◯ MODERATE [b]
Side-effects (overall, individual) – Sedation	58 per 1000	**8 per 1000** (1 to 156)	**RR 0.14** (0.01 to 2.70)	104 (1 RCT)	⊕⊕◯◯ LOW [a]
Side-effects (overall, individual) – Respiratory depression	38 per 1000	**8 per 1000** (0 to 157)	**RR 0.20** (0.01 to 4.07)	104 (1 RCT)	⊕⊕◯◯ LOW [a]
Complications related to pain-control methods	125 per 1000	**125 per 1000** (61 to 253)	**RR 1.00** (0.49 to 2.02)	208 (1 RCT)	⊕⊕⊕◯ MODERATE [b]
Complications related to pain-control methods – Hypertension	38 per 1000	**77 per 1000** (15 to 402)	**RR 2.00** (0.38 to 10.45)	104 (1 RCT)	⊕⊕◯◯ LOW [a]
Complications related to pain-control methods – Shivering	212 per 1000	**173 per 1000** (78 to 383)	**RR 0.82** (0.37 to 1.81)	104 (1 RCT)	⊕⊕⊕◯ MODERATE [b]
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with continuous epidural	**Risk with Intermittent**			
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-
Successful completion without additional surgical intervention	981 per 1000	**981 per 1000** (932 to 1000)	**RR 1.00** (0.95 to 1.06)	104 (1 RCT)	⊕⊕⊕⊕ HIGH
Time to expulsion	The mean time to expulsion was **20** hours	MD **1.4 hours lower** (4.4 lower to 1.6 higher)	-	104 (1 RCT)	⊕⊕⊕◯ MODERATE [b]
Patient satisfaction assessed in VAS out of 100 mm	The mean patient satisfaction was **73** mm	MD **10.8 mm higher** (4.06 higher to 17.54 higher)	-	104 (1 RCT)	⊕⊕⊕⊕ HIGH

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Notes
a. Downgraded two levels; very wide confidence intervals
b. Downgraded one level; broad confidence intervals

References for SoF Table 5

Leone Roberti Maggiore U, Silanos R, Carlevaro S, Gratarola A, Venturini PL, Ferrero S, Pelosi P. Programmed intermittent epidural bolus versus continuous epidural infusion for pain relief during termination of pregnancy: a prospective, double-blind, randomized trial. Int J Obstet Anesth. 2016;25:37–44. doi:10.1016/j.ijoa.2015.08.014.

SoF Table 6: Pain management for medical abortion in second trimester: *Patient-controlled epidural vs patient-controlled IV fentanyl*

Patient or population: Pain management for medical abortion in second trimester
Setting: Canada
Intervention: Patient-controlled epidural
Comparison: Patient-controlled IV fentanyl

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with patient controlled IV fentanyl	**Risk with Patient controlled epidural**			
Worst pain within 24 hours assessed as maximum pain out of 10	The mean worst pain within 24 hours was **0** VAS in cm	MD **1.7 VAS in cm lower** (3.44 lower to 0.04 higher)	-	37 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Nausea	450 per 1000	**473 per 1000** (234 to 945)	**RR 1.05** (0.52 to 2.10)	37 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Vomiting	350 per 1000	**294 per 1000** (115 to 760)	**RR 0.84** (0.33 to 2.17)	37 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Pruritus	350 per 1000	**413 per 1000** (182 to 938)	**RR 1.18** (0.52 to 2.68)	37 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual) – Mild sedation	200 per 1000	**58 per 1000** (8 to 478)	**RR 0.29** (0.04 to 2.39)	37 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Complications related to pain-control methods	50 per 1000	**69 per 1000** (23 to 209)	**RR 1.38** (0.45 to 4.18)	148 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Complications related to pain-control methods – Intermittent bladder catherization	0 per 1000	**0 per 1000** (0 to 0)	**RR 8.17** (0.45 to 147.76)	37 (1 RCT)	⊕⊕◯◯ LOW [b]
Complications related to pain-control methods – Hypotension	0 per 1000	**0 per 1000** (0 to 0)	**RR 5.83** (0.30 to 113.75)	37 (1 RCT)	⊕⊕◯◯ LOW [b]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with patient controlled IV fentanyl	**Risk with Patient controlled epidural**			
Complications related to pain-control methods – Respiratory depression	0 per 1000	**0 per 1000** (0 to 0)	not estimable	37 (1 RCT)	-
Complications related to pain-control methods – Changed to epidural	200 per 1000	**26 per 1000** (2 to 450)	**RR 0.13** (0.01 to 2.25)	37 (1 RCT)	⨁⨁◯◯ LOW [b]
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-
Successful completion without additional surgical intervention	700 per 1000	**826 per 1000** (574 to 1000)	**RR 1.18** (0.82 to 1.69)	37 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Time to expulsion assessed in hours	The mean time to expulsion was **19** hours	MD **3 hours lower** (8 lower to 2 higher)	-	37 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Satisfaction assessed with a scale up to 10	The mean satisfaction was **7.8**	MD **0.6 higher** (0.43 lower to 1.63 higher)	-	37 (1 RCT)	⨁⨁⨁◯ MODERATE [a]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Notes

a. Downgraded one level; wide confidence intervals
b. Downgraded two levels; very wide confidence intervals

Reference

Smith RL, Siddiqui N, Henderson T, Teresi J, Downey K, Carvalho JC. Analgesia for medically induced second trimester termination of pregnancy: a randomized trial. J Obstet Gynaecol Can. 2016;38:147–53.

SoF Table 7: Pain management for medical abortion in second trimester: Patient-controlled fentanyl vs patient-controlled morphine

Patient or population: Pain management for medical abortion in second trimester
Setting: Canada
Intervention: Patient-controlled fentanyl
Comparison: Patient-controlled morphine

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with patient-controlled morphine	Risk with patient-controlled fentanyl			
Worst pain within 24 hours – 50 µg fentanyl/6 min lockout	The mean worst pain within 24 hours – 50 µg fentanyl/6 min lockout was **31** mm on VAS	MD **4 mm on VAS lower** (17.22 lower to 9.22 higher)	-	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Worst pain within 24 hours – 25 µg fentanyl/3 min lockout	The mean worst pain within 24 hours – 25 µg fentanyl/3 min lockout was **31** mm on VAS	MD **19.6 mm on VAS higher** (3.01 higher to 36.19 higher)	-	40 (1 RCT)	⊕⊕⊕⊕ HIGH
Worst pain within 24 hours – 50 µg fentanyl/3 min lockout	The mean worst pain within 24 hours – 50 µg fentanyl/3 min lockout was **31** mm on VAS	MD **4.9 mm on VAS lower** (17.63 lower to 7.83 higher)	-	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Nausea – 50 µg fentanyl/6 min lockout	750 per 1000	**353 per 1000** (180 to 668)	**RR 0.47** (0.24 to 0.89)	40 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – Nausea – 25 µg fentanyl/3 min lockout	750 per 1000	**653 per 1000** (435 to 975)	**RR 0.87** (0.58 to 1.30)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Nausea – 50 µg fentanyl/3 min lockout	750 per 1000	**750 per 1000** (525 to 1000)	**RR 1.00** (0.70 to 1.43)	40 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – Vomiting – 50 µg fentanyl/6 min lockout	550 per 1000	**50 per 1000** (6 to 352)	**RR 0.09** (0.01 to 0.64)	40 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – Vomiting – 25 µg fentanyl/3 min lockout	550 per 1000	**501 per 1000** (275 to 902)	**RR 0.91** (0.50 to 1.64)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with patient-controlled morphine	Risk with patient-controlled fentanyl			
Side-effects – Vomiting – 50 µg fentanyl/3 min lockout	550 per 1000	**402 per 1000** (204 to 781)	**RR 0.73** (0.37 to 1.42)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Sedation – 50 µg fentanyl/6 min lockout	400 per 1000	**152 per 1000** (48 to 484)	**RR 0.38** (0.12 to 1.21)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Sedation – 25 µg fentanyl/3 min lockout	400 per 1000	**152 per 1000** (48 to 484)	**RR 0.38** (0.12 to 1.21)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Sedation – 50 µg fentanyl/3 min lockout	400 per 1000	**100 per 1000** (24 to 412)	**RR 0.25** (0.06 to 1.03)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Pruritus – 50 µg fentanyl/6 min lockout	550 per 1000	**50 per 1000** (6 to 352)	**RR 0.09** (0.01 to 0.64)	40 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – Pruritus – 25 µg fentanyl/3 min lockout	550 per 1000	**149 per 1000** (50 to 457)	**RR 0.27** (0.09 to 0.83)	40 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – Pruritus – 50 µg fentanyl/3 min lockout	550 per 1000	**198 per 1000** (77 to 523)	**RR 0.36** (0.14 to 0.95)	40 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – Dizziness – 50 µg fentanyl/6 min lockout	250 per 1000	**23 per 1000** (3 to 385)	**RR 0.09** (0.01 to 1.54)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Dizziness – 25 µg fentanyl/3 min lockout	250 per 1000	**150 per 1000** (43 to 545)	**RR 0.60** (0.17 to 2.18)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Dizziness – 50 µg fentanyl/3 min lockout	250 per 1000	**250 per 1000** (85 to 733)	**RR 1.00** (0.34 to 2.93)	40 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with patient-controlled morphine	**Risk with patient-controlled fentanyl**			
Use of any additional analgesic medication	not pooled	not pooled	not pooled	(0 studies)	-
Successful completion without additional surgical intervention	not pooled	not pooled	not pooled	(0 studies)	-
Time to expulsion	The mean time to expulsion was **0**	not pooled	-	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **OR:** odds ratio

Note
a. Downgraded one level; broad confidence intervals

References for SoF Table 7

Castro C, Tharmaratnam U, Brockhurst N, Tureanu L, Tam K, Windrim R. Patient-controlled analgesia with fentanyl provides effective analgesia for second trimester labour: a randomized controlled study. Can J Anaesth. 2003;50(10):1039–46. doi:10.1007/BF03018370.

SoF Table 8: Pain management for medical abortion in second trimester: Patient-controlled IV tramadol vs patient-controlled IV fentanyl

Patient or population: Pain management for medical abortion in second trimester
Setting: Israel
Intervention: Patient-controlled IV tramadol
Comparison: Patient-controlled IV fentanyl

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with patient-controlled IV fentanyl	**Risk with patient-controlled IV tramadol**			
Worst pain within 24 hours	The mean worst pain within 24 hours was **54** mm on VAS	MD **7.6 mm on VAS lower** (29.81 lower to 14.61 higher)	-	29 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects (overall, individual)	385 per 1000	**188 per 1000** (54 to 642)	**RR 0.49** (0.14 to 1.67)	29 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Complications related to pain-control methods	not pooled	not pooled	not pooled	(0 studies)	-
Use of any supplemental narcotic	The mean use of any supplemental narcotic was **0**	not pooled	-	(0 studies)	-
Use of any additional analgesic medication	77 per 1000	**250 per 1000** (32 to 1000)	**RR 3.25** (0.41 to 25.64)	29 (1 RCT)	⊕⊕◯◯ LOW [b]
Successful completion without additional surgical intervention	not pooled	not pooled	not pooled	(0 studies)	-
Time to expulsion	The mean time to expulsion was **1233** min	MD **211 min lower** (858.58 lower to 436.58 higher)	-	29 (1 RCT)	⊕⊕◯◯ LOW [b]
Patient satisfaction assessed with a scale from 1 to 10	The mean patient satisfaction was **8**	MD **0** (1.72 lower to 1.72 higher)	-	29 (1 RCT)	⊕⊕⊕⊕ HIGH

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **OR:** odds ratio

Notes

a. Downgraded one level; wide confidence intervals
b. Downgraded two levels; very wide confidence intervals

References

Orbach-Zinger S, Paul-Keslin L, Nichinson E, Chinchuck A, Nitke S, Eidelman LA. Tramadol-metoclopramide or remifentanil for patient-controlled analgesia during second trimester abortion: a double-blinded, randomized controlled trial. J Clin Anesthesia. 2012;24(1):28–32.

6. EtD framework for Cervical priming prior to surgical abortion < 12 weeks

Recommendation 17: Prior to surgical abortion at < 12 weeks:

a. If cervical priming is used: **Suggest** the following medication regimens:

- ❑ **Mifepristone** 200 mg **orally** 24–48 hours prior to the procedure
- ❑ **Misoprostol** 400 µg **sublingually** 1–2 hours prior to the procedure
- ❑ **Misoprostol** 400 µg **vaginally or buccally** 2–3 hours prior to the procedure

b. **Recommend against** the use of osmotic dilators for cervical priming.

PICO 6a: For a pregnant person seeking surgical abortion at < 12 weeks of gestation, is cervical priming effective, safe and acceptable? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global

Perspective: Population perspective

Literature review: An update of an existing Cochrane review serves as the evidence base for this question. The update identified 8 new studies which makes a total of 61 included studies that assesses cervical preparation methods for first trimester surgical abortion. From this review, approximately half of the included studies were evaluated to contribute towards the development of this evidence to decision framework. The review includes the following cervical priming methods:

- Medication with mifepristone and/or misoprostol
- Mechanical methods with osmotic dilators and synthetic dilators

ASSESSMENT OF RESEARCH EVIDENCE

Analyses were performed across seven sub-PICOs. For each of the sub PICOs, research evidence was assessed for the following criteria

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

Sub-PICOs were combined with a view to ensure that the ERRG can review the material in a systematic manner to make recommendations for cervical priming for surgical abortion less than 12–14 weeks.

1. Misoprostol versus placebo
    a. Sub-analysis of misoprostol route
    b. Sub-analysis of interval timing between misoprostol and procedure
    c. Sub-analysis of misoprostol dosage
2. Misoprostol versus mifepristone
3. Misoprostol versus combination mifepristone + misoprostol
4. Mifepristone versus placebo
5. Mifepristone versus combination mifepristone + misoprostol
6. Dilators versus placebo
7. Misoprostol versus dilators.

The overall draft judgements on the above questions are presented below to be considered by the ERRG towards the recommendations.

Sub-PICO 1 – Misoprostol versus placebo

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (misoprostol) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (placebo). The certainty of evidence is low.

Fewer women in the intervention group (misoprostol) required further dilation compared with the women in the comparison group (placebo). The certainty of evidence is low.

Time to complete the procedure with the intervention (misoprostol) was less than the time to complete the procedure with the comparison (placebo). The certainty of evidence is very low.

Fewer women in the intervention group (misoprostol) experienced the complication of a cervical injury compared with the women in the comparison group (placebo). The certainty of evidence is low.

Fewer women in the intervention group (misoprostol) experienced the need for a re-aspiration/incomplete abortion compared with the women in the comparison group (placebo). The certainty of evidence is high.

Fewer women in the intervention group (misoprostol) experienced the side-effects of nausea compared with the women in the comparison group (placebo). The certainty of evidence is low.

Undesirable effects:

More women in the intervention group (misoprostol) experienced vomiting, diarrhoea, cramping compared with women in the comparison group (placebo). The certainty of evidence is low-moderate.

More women in the intervention group (misoprostol) experienced a complication of uterine perforation compared with women in the comparison group (placebo). The certainty of evidence is low.

Balance of effects:

				X
Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

a) Sub-analysis of misoprostol route

i. Vaginal versus oral

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (vaginal misoprostol) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (oral misoprostol). The certainty of evidence is moderate.
Fewer women in the intervention group (vaginal misoprostol) required further dilation compared with the women in the comparison group (oral misoprostol). The certainty of evidence is very low.
Time to complete the procedure with the intervention (vaginal misoprostol) was lesser than the time to complete the procedure with the comparison (oral misoprostol). The certainty of evidence is low.
Fewer women in the intervention group (vaginal misoprostol) experienced the side-effects of nausea compared with the women in the comparison group (oral misoprostol). The certainty of evidence is low.

Undesirable effects:

More women in the intervention group (vaginal misoprostol) experienced the side-effect of abdominal pain/cramping compared with the women in the comparison group (oral misoprostol). The certainty of evidence is very low.

Draft judgement: Favours the intervention (vaginal misoprostol)

ii. Vaginal versus sublingual

Desirable effects:

Fewer women in the intervention group (vaginal misoprostol) experienced the side-effect of nausea compared with the women in the comparison group (sublingual misoprostol). The certainty of evidence is low.

Fewer women in the intervention group (vaginal misoprostol) experienced the side-effect of abdominal pain/cramping compared with the women in the comparison group (sublingual misoprostol). The certainty of evidence is moderate.

More women in the intervention group (vaginal misoprostol) expressed satisfaction compared with the women in the comparison group (sublingual misoprostol). The certainty of evidence is very low.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (vaginal misoprostol) was lower compared with the pre-procedure cervical dilation of the women in the comparison group (sublingual misoprostol). The certainty of evidence is very low.

More women in the intervention group (vaginal misoprostol) required further dilation compared with the women in the comparison group (sublingual misoprostol). The certainty of evidence is low.

Time to complete the procedure with the intervention (vaginal misoprostol) was greater than the time to complete the procedure with the comparison (sublingual misoprostol). The certainty of evidence is moderate.

Draft judgement: Favours the comparison (sublingual misoprostol)

iii. Sublingual versus oral

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (sublingual misoprostol) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (oral misoprostol). The certainty of evidence is moderate.

Fewer women in the intervention group (sublingual misoprostol) required further dilation compared with the women in the comparison group (oral misoprostol). The certainty of evidence is low.

Undesirable effects:

None

Draft judgement: Favours the intervention (sublingual misoprostol)

Overall draft judgement: sublingual > vaginal > oral routes

b) Sub-analysis of interval timing

i. 3 hours (400 µg vaginal) versus 2 hours (600 µg vaginal)

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (3-hour interval) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (2-hour interval). The certainty of evidence is high.

Fewer women in the intervention group (3-hour interval) required further dilation compared with the women in the comparison group (2-hour interval). The certainty of evidence is high.

Fewer women in the intervention group (3-hour interval) experienced pain with cervical priming compared with the women in the comparison group (2-hour interval). The certainty of evidence is high.

Undesirable effects:

None

Draft judgement: May favour the intervention (3-hour interval)

ii. **3 hours versus 1 hour**

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (3-hour, vaginal) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (1-hour, vaginal). The certainty of evidence is moderate.

Fewer women in the intervention group (3-hour interval, sublingual and vaginal) experienced side-effect of nausea compared with the women in the comparison group (1-hour interval, sublingual and vaginal). The certainty of evidence is low.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (3-hour, sublingual) was lower compared with the pre-procedure cervical dilation of the women in the comparison group (1-hour, sublingual). The certainty of evidence is moderate.

More women in the intervention group (3-hour interval, sublingual and vaginal) experienced pain with cervical priming compared with the women in the comparison group (1-hour interval, sublingual and vaginal). The certainty of evidence is low-moderate.

Time to complete the procedure with the intervention (3-hour interval, sublingual and vaginal) was greater than the time to complete the procedure with the comparison (1-hour interval, sublingual and vaginal). The certainty of evidence is moderate.

Draft judgement: May favour the intervention (3-hour interval, vaginal)

c) Sub-analysis of misoprostol dosage (400 µg vs 200 µg)

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (400 µg oral, vaginal, sublingual) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (200 µg, oral, vaginal, sublingual). The certainty of evidence is high (oral), moderate (sublingual) and low (vaginal).

Fewer women in the intervention group (400 µg vaginal, sublingual) required further dilation compared with the women in the comparison group (200 µg vaginal, sublingual). The certainty of evidence is moderate (sublingual) and high (vaginal).

Time to complete the procedure with the intervention (400 µg vaginal, sublingual) was lesser than the time to complete the procedure with the comparison (200 µg vaginal, sublingual). The certainty of evidence is moderate (sublingual and vaginal).

Undesirable effects:

More women in the intervention group (400 µg vaginal, sublingual) experienced pain with cervical priming compared with the women in the comparison group (200 µg vaginal, sublingual). The certainty of evidence is low-high.

Draft judgement: Favours the intervention (400 µg vaginal, sublingual, oral)

Sub-PICO 2 – Misoprostol versus mifepristone

Desirable effects:

Time to complete the procedure with the intervention (misoprostol) was less than the time to complete the procedure with the comparison (mifepristone). The certainty of evidence is moderate.

Fewer women in the intervention group (misoprostol) experienced cramping and vomiting compared with the women in the comparison group (mifepristone). The certainty of evidence is very low for both outcomes.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (misoprostol) was less compared with the pre-procedure cervical dilation of the women in the comparison group (mifepristone). The certainty of evidence is moderate.

Pre-procedure cervical dilation of the women in the intervention group (misoprostol 800 µg and 400 µg) was less compared with the pre-procedure cervical dilation of the women in the comparison group (mifepristone 200 mg). The certainty of evidence is moderate.

Pre-procedure cervical dilation of the women in the intervention group (misoprostol 600 µg) was less compared with the pre-procedure cervical dilation of the women in the comparison group (mifepristone 400 mg). The certainty of evidence is high.

More women in the intervention group (misoprostol) experienced nausea compared with the women in the comparison group (mifepristone). The certainty of evidence is very low.

Balance of effects:

		X No difference between the intervention and the comparison		
Favours the comparison	May favour the comparison		May favour the intervention	Favours the intervention

Sub-PICO 3 – Misoprostol versus combination mifepristone + misoprostol

Desirable effects:

Fewer women in the intervention group (misoprostol)) experienced the side-effect of abdominal pain/cramping compared with women in the comparison group (mifepristone + misoprostol). The certainty of evidence is very low.

There was no difference in nausea between the two groups. The certainty of evidence is very low.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (misoprostol) was lower compared with the pre-procedure cervical dilation of the women in the comparison group (mifepristone + misoprostol). The certainty of evidence is moderate.

Time to complete the procedure with the intervention group (misoprostol) was greater than the time to complete the procedure with the comparison group (mifepristone + misoprostol). The certainty of evidence is moderate.

More women in the intervention group (misoprostol) experienced the side-effect of vomiting compared with women in the comparison group (mifepristone + misoprostol). The certainty of evidence is very low.

Balance of effects:

	X 	No difference between the intervention and the comparison		
Favours the comparison	May favour the comparison		May favour the intervention	Favours the intervention

Sub-PICO 4 – Mifepristone versus placebo

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (mifepristone) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (placebo). The certainty of evidence is high.

Fewer women in the intervention group (mifepristone) required further dilation compared with the women in the comparison group (placebo). The certainty of evidence is low.

Undesirable effects:

None

Balance of effects:

				X
Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Sub-PICO 5 – Mifepristone versus combination mifepristone + misoprostol

Desirable effects:

There was no difference in the occurrence of nausea as a side-effect between the two groups. The certainty of evidence is low.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (mifepristone) was lower compared with the pre-procedure cervical dilation of the women in the comparison group (mifepristone + misoprostol). The certainty of evidence is moderate.

Time to complete the procedure with the intervention (mifepristone) was higher than the time to complete the procedure with the comparison (mifepristone + misoprostol). The certainty of evidence is moderate.

More women in the intervention group (mifepristone) experienced the side-effects of vomiting and abdominal cramping compared with women in the comparison group (mifepristone + misoprostol). The certainty of evidence is very low for both outcomes.

Balance of effects:

	X			
Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Sub-PICO 6 – Dilators versus placebo

No meta-analysis or GRADE performed – Mean cervical dilation in the intervention (osmotic dilators) were higher compared with the mean dilation of the women in the comparison group (placebo).

Sub-PICO 7 – Misoprostol versus dilators

a) Misoprostol versus laminaria

Desirable effects:

Fewer women in the intervention group (misoprostol 400 µg) required further dilation compared with the women in the comparison group (laminaria). The certainty of evidence is moderate.

More women in the intervention group (misoprostol) expressed greater satisfaction towards their cervical ripening method compared with women in the comparison group (laminaria). The certainty of evidence is moderate.

Undesirable effects:

More women in the intervention group (misoprostol) required further dilation compared with the women in the comparison group (laminaria). The certainty of evidence is low.

More women in the intervention group (misoprostol 200 µg) required further dilation compared with the women in the comparison group (laminaria). The certainty of evidence is low.

Balance of effects: May favour the intervention (misoprostol)

b) Misoprostol versus Dilapan

Desirable effects:

Time to complete the procedure with the intervention (misoprostol) was lower than the time to complete the procedure with the comparison (Dilapan). The certainty of evidence is high.

Fewer women in the intervention group (misoprostol) required re-aspiration compared with the women in the comparison group (Dilapan). The certainty of evidence is low.

There was no difference in cervical laceration/injury between the two groups. The certainty of evidence is low.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (misoprostol) was lower compared with the pre-procedure cervical dilation of the women in the comparison group *(*Dilapan). The certainty of evidence is high.

More women in the intervention group (misoprostol) required further dilation compared with the women in the comparison group (Dilapan). The certainty of evidence is low.

Balance of effects: No difference between the intervention and comparison

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

Unable to determine	Varies	No	x Probably No	Probably Yes	Yes

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

Unable to determine	Varies	Large costs	Moderate costs	x Negligible costs or savings	Moderate savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favours the intervention or the comparison?

Judgement (draft)

Unable to determine	Varies	Favours the comparison	Probably favours the comparison	x Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

Unable to determine	Varies	Reduced	Probably reduced	x Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

Unable to determine	Varies	No	Probably No	**x** Probably Yes	Yes

Research evidence on satisfaction was considered as a secondary outcome and the evidence presented above.

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	X Yes

SUMMARY OF FINDINGS TABLES

Summary of Findings tables for Cervical preparation for surgical abortion less than 12–14 weeks

SoF Table 1: Cervical priming prior to first-trimester surgical abortion: Misoprostol versus placebo/control

Patient or population: First-trimester surgical abortion
Intervention: Misoprostol
Comparison: Placebo/control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo/control	**Risk with misoprostol**			
Cervical dilation at procedure start assessed in mm	The mean cervical dilation at procedure start ranged from **3.4 to 6.0** mm	MD **1.39 mm higher** (1.22 higher to 1.56 higher)	-	6249 (8 RCTs)	⨁⨁◯◯ LOW [a]
Cervical dilation at procedure start – Misoprostol 400 µg, vaginal	The mean cervical dilation at procedure start – Misoprostol 400 µg, vaginal ranged from **3.6 to 5.9** mm	MD **0.9 mm higher** (0.7 higher to 1.1 higher)	-	5731 (4 RCTs)	⨁⨁◯◯ LOW [a]
Cervical dilation at procedure start – Misoprostol 400 µg, sublingual	The mean cervical dilation at procedure start – Misoprostol 400 µg, sublingual ranged from **3.4 to 5.0** mm	MD **3.87 mm higher** (3.39 higher to 4.34 higher)	-	210 (2 RCTs)	⨁⨁⨁◯ MODERATE [b]
Cervical dilation at procedure start – Misoprostol 600 µg, oral	The mean cervical dilation at procedure start – Misoprostol 600 µg, oral was **4.5** mm	MD **1.4 mm higher** (0.51 higher to 2.29 higher)	-	30 (1 RCT)	⨁⨁⨁⨁ HIGH
Cervical dilation at procedure start – Misoprostol 600 µg, vaginal	The mean cervical dilation at procedure start – Misoprostol 600 µg, vaginal was **6.0** mm	MD **1.6 mm higher** (1.14 higher to 2.06 higher)	-	278 (1 RCT)	⨁⨁⨁◯ MODERATE [c]
Side-effects – Nausea	54 per 1000	**34 per 1000** (26 to 44)	**OR 0.62** (0.47 to 0.81)	5660 (6 RCTs)	⨁⨁◯◯ LOW [a]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo/control	**Risk with misoprostol**			
Side-effects – Nausea – Misoprostol 400 µg, vaginal	47 per 1000	**16 per 1000** (11 to 23)	**OR 0.32** (0.22 to 0.47)	5172 (3 RCTs)	⊕⊕◯◯ LOW [a]
Side-effects – Nausea – Misoprostol 400 µg, sublingual	29 per 1000	**237 per 1000** (90 to 493)	**OR 10.58** (3.38 to 33.12)	210 (2 RCTs)	⊕⊕⊕◯ MODERATE [b]
Side-effects – Nausea – Misoprostol 600 µg, vaginal	182 per 1000	**177 per 1000** (105 to 286)	**OR 0.97** (0.53 to 1.80)	278 (1 RCT)	⊕⊕◯◯ LOW [c,d]
Procedure length (minutes)	The mean procedure length (minutes) ranged from **3.4 to 9.0** min	MD **1.23 min fewer** (1.53 fewer to 0.93 fewer)	-	971 (5 RCTs)	⊕◯◯◯ VERY LOW [a,b]
Procedure length (minutes) – Misoprostol 400 µg, vaginal	The mean procedure length (minutes) – Misoprostol 400 µg, vaginal ranged from **3.4 to 4.9** min	MD **0.31 min fewer** (0.66 fewer to 0.04 more)	-	761 (3 RCTs)	⊕⊕⊕◯ MODERATE [e]
Procedure length (minutes) – Misoprostol, 400 µg, sublingual	The mean procedure length (minutes) - Misoprostol, 400 µg, sublingual ranged from **8.5 to 9.0** min	MD **3.65 min fewer** (4.22 fewer to 3.09 fewer)	-	210 (2 RCTs)	⊕⊕⊕◯ MODERATE [b]
Need for additional mechanical dilation	773 per 1000	**577 per 1000** (551 to 605)	**OR 0.40** (0.36 to 0.45)	5720 (3 RCTs)	⊕⊕◯◯ LOW [a]
Need for additional mechanical dilation – Misoprostol 400 µg, vaginal	769 per 1000	**589 per 1000** (558 to 615)	**OR 0.43** (0.38 to 0.48)	5570 (2 RCTs)	⊕⊕⊕◯ MODERATE [e]
Need for additional mechanical dilation – Misoprostol 400 µg, sublingual	933 per 1000	**123 per 1000** (0 to 359)	**OR 0.01** (0.00 to 0.04)	150 (1 RCT)	⊕⊕⊕◯ MODERATE [b]
Cervical laceration/injury	1 per 1000	**0 per 1000** (0 to 3)	**OR 0.20** (0.01 to 4.17)	4970 (1 RCT)	⊕⊕◯◯ LOW [f]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo/control	Risk with misoprostol			
Need for re-aspiration/incomplete abortion	20 per 1000	**7 per 1000** (4 to 12)	**OR 0.33** (0.20 to 0.56)	5598 (3 RCTs)	⊕⊕⊕⊕ HIGH
Need for re-aspiration/incomplete abortion – Misoprostol 400 µg, vaginal	20 per 1000	**7 per 1000** (4 to 12)	**OR 0.34** (0.20 to 0.58)	5448 (2 RCTs)	⊕⊕⊕⊕ HIGH
Need for re-aspiration/incomplete abortion – Misoprostol 400 µg, sublingual	27 per 1000	**5 per 1000** (0 to 101)	**OR 0.19** (0.01 to 4.12)	150 (1 RCT)	⊕◯◯◯ VERY LOW [b,f]
Uterine perforation	1 per 1000	**2 per 1000** (0 to 7)	**OR 1.25** (0.33 to 4.67)	5559 (2 RCTs)	⊕⊕◯◯ LOW [f]
Uterine perforation – Misoprostol 400 µg, vaginal	1 per 1000	**2 per 1000** (0 to 7)	**OR 1.25** (0.33 to 4.67)	5559 (2 RCTs)	⊕⊕◯◯ LOW [f]
Uterine perforation – Misoprostol 400 µg, sublingual	not pooled	not pooled	not pooled	(0 studies)	-
Side-effects – Diarrhoea	5 per 1000	**18 per 1000** (10 to 32)	**OR 4.02** (2.21 to 7.33)	5710 (3 RCTs)	⊕⊕⊕◯ MODERATE [e]
Side-effects – Diarrhoea – Misoprostol 400 µg, vaginal	5 per 1000	**19 per 1000** (10 to 33)	**OR 4.02** (2.21 to 7.33)	5560 (2 RCTs)	⊕⊕⊕◯ MODERATE [e]
Side-effects – Diarrhoea – Misoprostol 400 µg, sublingual	0 per 1000	**0 per 1000** (0 to 0)	not estimable	150 (1 RCT)	-
Side-effects – Vomiting	6 per 1000	**8 per 1000** (4 to 16)	**OR 1.32** (0.69 to 2.53)	4971 (1 RCT)	⊕⊕◯◯ LOW [f]
Infection	9 per 1000	**12 per 1000** (7 to 20)	**OR 1.32** (0.79 to 2.21)	5447 (2 RCTs)	⊕⊕⊕◯ MODERATE [d]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo/control	**Risk with misoprostol**			
Side-effects – Abdominal pain/cramping	194 per 1000	**502 per 1000** (471 to 532)	**OR 4.19** (3.71 to 4.74)	5710 (3 RCTs)	⊕⊕⊕◯ MODERATE [e]
Side-effects – Abdominal pain/cramping – Misoprostol 400 µg, vaginal	197 per 1000	**509 per 1000** (478 to 540)	**OR 4.24** (3.74 to 4.79)	5560 (2 RCTs)	⊕⊕⊕◯ MODERATE [d]
Side-effects – Abdominal pain/cramping – Misoprostol 400 µg, sublingual	80 per 1000	**147 per 1000** (57 to 330)	**OR 1.98** (0.69 to 5.66)	150 (1 RCT)	⊕◯◯◯ VERY LOW [b,f]
Estimated blood loss (ml)	The mean estimated blood loss (ml) ranged from **15 to 38** ml	MD **3.07 ml fewer** (4.87 fewer to 1.28 fewer)	-	750 (2 RCTs)	⊕◯◯◯ VERY LOW [a,b]
Estimated blood loss (ml) – Misoprostol 400 µg, vaginal	The mean estimated blood loss (ml) – Misoprostol 400 µg, vaginal was **15** ml	MD **0.79 ml fewer** (2.83 fewer to 1.25 more)	-	600 (1 RCT)	⊕⊕⊕⊕ HIGH
Estimated blood loss (ml) – Misoprostol 400 µg, sublingual	The mean estimated blood loss (ml) – Misoprostol 400 µg, sublingual was **38** ml	MD **11 ml fewer** (14.8 fewer to 7.2 fewer)	-	150 (1 RCT)	⊕⊕⊕◯ MODERATE [b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Notes

a. Downgraded two levels due to I^2 above 90%
b. Downgraded one level due to lack of blinding
c. Downgraded one level due to inadequate allocation concealment
d. Downgraded one level; wide confidence intervals
e. Downgraded one level due to I^2 above 50%
f. Downgraded two levels due to very wide confidence intervals

References

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 2: Cervical priming prior to first trimester surgical abortion: Route of misoprostol administration versus placebo

Patient or population: First trimester surgical abortion
Intervention: Route of misoprostol administration
Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with route of misoprostol administration**			
Cervical dilation at procedure start – 400 µg vaginal vs oral	The mean cervical dilation at procedure start – 400 µg vaginal versus oral ranged from **6 to 7** mm	MD **0.5 mm higher** (0.13 higher to 0.87 higher)	-	277 (3 RCTs)	⨁⨁⨁◯ MODERATE [a]
Cervical dilation at procedure start – 400 µg vaginal vs sublingual	The mean cervical dilation at procedure start – 400 µg vaginal versus sublingual ranged from **7 to 9** mm	MD **0.15 mm lower** (0.24 lower to 0.07 lower)	-	1782 (4 RCTs)	⨁◯◯◯ VERY LOW [a,b]
Cervical dilation at procedure start – 400 µg sublingual vs oral	The mean cervical dilation at procedure start – 400 µg sublingual versus oral was **7** mm	MD **0.5 mm higher** (0.55 lower to 1.55 higher)	-	32 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Need for additional mechanical dilation – 400 µg vaginal vs oral	100 per 1000	**50 per 1000** (9 to 234)	**OR 0.47** (0.08 to 2.75)	80 (1 RCT)	⨁◯◯◯ VERY LOW [a,c]
Need for additional mechanical dilation – 400 µg vaginal vs sublingual	539 per 1000	**623 per 1000** (574 to 669)	**OR 1.41** (1.15 to 1.73)	1524 (2 RCTs)	⨁⨁◯◯ LOW [a,d]
Side-effects: nausea – 400 µg vaginal vs oral	313 per 1000	**211 per 1000** (106 to 384)	**OR 0.59** (0.26 to 1.37)	157 (2 RCTs)	⨁⨁◯◯ LOW [a,e]
Side-effects: nausea – 400 µg vaginal vs sublingual	163 per 1000	**64 per 1000** (48 to 87)	**OR 0.35** (0.26 to 0.49)	1856 (5 RCTs)	⨁⨁◯◯ LOW [a,d]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with route of misoprostol administration**			
Procedure length (minutes) – 400 µg vaginal vs oral	The mean procedure length (minutes) – 400 µg vaginal versus oral ranged from **4 to 6** min	MD **0.23 min lower** (0.61 lower to 0.15 higher)	-	157 (2 RCTs)	⨁⨁◯◯ LOW [a,d]
Procedure length (minutes) – 400 µg vaginal vs sublingual	The mean procedure length (minutes) – 400 µg vaginal versus sublingual ranged from **3 to 8** mm	MD **0.35 mm higher** (0.1 higher to 0.6 higher)	-	1702 (3 RCTs)	⨁⨁⨁◯ MODERATE [a]
Patient dissatisfaction	108 per 1000	**12 per 1000** (1 to 193)	**OR 0.10** (0.01 to 1.97)	73 (1 RCT)	⨁◯◯◯ VERY LOW [a,c]
Need for re-aspiration/incomplete abortion	0 per 1000	**0 per 1000** (0 to 0)	not estimable	120 (1 RCT)	-
Uterine perforation	not pooled	not pooled	not pooled	298 (3 RCTs)	-
Uterine perforation – 400 µg vaginal vs oral	0 per 1000	**0 per 1000** (0 to 0)	not estimable	120 (1 RCT)	-
Uterine perforation – 400 µg vaginal vs sublingual	not pooled	not pooled	not pooled	178 (2 studies)	-
Side-effects: abdominal pain/cramping – 400 µg vaginal vs oral	59 per 1000	**174 per 1000** (53 to 441)	**OR 3.37** (0.90 to 12.64)	120 (1 RCT)	⨁◯◯◯ VERY LOW [e,f]
Side-effects: abdominal pain/cramping – 400 µg vaginal vs sublingual	670 per 1000	**346 per 1000** (222 to 494)	**OR 0.26** (0.14 to 0.48)	178 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Estimated blood loss (ml)	The mean estimated blood loss (ml) ranged from **44 to 45** ml	MD **1.22 ml lower** (7.08 lower to 4.64 higher)	-	178 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Cervical laceration/injury	0 per 1000	**0 per 1000** (0 to 0)	not estimable	178 (1 RCT)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with route of misoprostol administration**			
Unplanned expulsion prior to procedure	0 per 1000	**0 per 1000** (0 to 0)	not estimable	178 (1 RCT)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Notes

a. Downgraded one level due to risk of bias
b. Downgraded two levels due to I2 above 90%
c. Downgraded two levels due to very wide confidence intervals
d. Downgraded one level due to I2 above 50%
e. Downgraded one level due to wide confidence intervals
f. Downgraded two levels due to risk of bias

References

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 3: Cervical priming prior to first trimester surgical abortion: Interval between misoprostol application and procedure vs placebo

Patient or population: First trimester surgical abortion

Intervention: Interval between misoprostol application and procedure

Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with interval between misoprostol application and procedure**			
Cervical dilation at procedure start – 3 hours vs 2 hours	The mean cervical dilation at procedure start – 3 hours vs 2 hours was **7** mm	MD **1.5 mm higher** (1.42 higher to 1.58 higher)	-	60 (1 RCT)	⨁⨁⨁⨁ HIGH
Cervical dilation at procedure start – 3 hours vs 1 hour, sublingual	The mean cervical dilation at procedure start – 3 hours versus 1 hour, sublingual was **8 mm**	MD **0.3 lower** (0.96 lower to 0.36 higher)	-	91 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Cervical dilation at procedure start – 3 hours vs 1 hour, vaginal	The mean cervical dilation at procedure start – 3 hours versus 1 hour, vaginal was **7** mm	MD **0.7 mm higher** (0.07 higher to 1.33 higher)	-	87 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Need for additional mechanical dilation	833 per 1000	**48 per 1000** (0 to 286)	**OR 0.01** (0.00 to 0.08)	60 (1 RCT)	⨁⨁⨁⨁ HIGH
Pain with cervical priming	441 per 1000	**482 per 1000** (359 to 608)	**OR 1.18** (0.71 to 1.97)	238 (2 RCTs)	⨁◯◯◯ VERY LOW [b,c]
Pain with cervical priming – 3 hours vs 2 hours	533 per 1000	**103 per 1000** (22 to 308)	**OR 0.10** (0.02 to 0.39)	60 (1 RCT)	⨁⨁⨁⨁ HIGH
Pain with cervical priming – 3 hours vs 1 hour, sublingual	667 per 1000	**673 per 1000** (462 to 832)	**OR 1.03** (0.43 to 2.48)	91 (1 RCT)	⨁⨁◯◯ LOW [a,c]
Pain with cervical priming – 3 hours vs 1 hour, vaginal	140 per 1000	**545 per 1000** (297 to 774)	**OR 7.40** (2.60 to 21.08)	87 (1 RCT)	⨁⨁⨁◯ MODERATE [a]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with interval between misoprostol application and procedure**			
Procedure length (minutes)	The mean procedure length (minutes) ranged from **6 to 7** min	MD **0.81 min higher** (0.03 higher to 1.58 higher)	-	178 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Procedure length (minutes) – 3 hours vs 1 hour, sublingual	The mean procedure length (minutes) – 3 hours vs 1 hour, sublingual was **6** min	MD **1.3 min higher** (0.04 higher to 2.56 higher)	-	91 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Procedure length (minutes) – 3 hours vs 1 hour, vaginal	The mean procedure length (minutes) – 3 hours vs 1 hour, vaginal was **7** min	MD **0.5 min higher** (0.49 lower to 1.49 higher)	-	87 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Estimated blood loss (ml)	0 per 1000	**0 per 1000** (0 to 0)	not estimable	178 (1 study)	-
Estimated blood loss (ml) – 3 hours vs 1 hour, sublingual	0 per 1000	**0 per 1000** (0 to 0)	not estimable	91 (1 study)	-
Estimated blood loss (ml) – 3 hours vs 1 hour, vaginal	0 per 1000	**0 per 1000** (0 to 0)	not estimable	87 (1 study)	-
Cervical laceration/injury	0 per 1000	**0 per 1000** (0 to 0)	not estimable	178 (1 study)	-
Cervical laceration/injury – 3 hours vs 1 hour, sublingual	0 per 1000	**0 per 1000** (0 to 0)	not estimable	91 (1 study)	-
Cervical laceration/injury – 3 hours vs 1 hour, vaginal	0 per 1000	**0 per 1000** (0 to 0)	not estimable	87 (1 study)	-
Uterine perforation	1.047 per 1000	**0 per 1000** (0 to 0)	not estimable	133 (1 study)	-

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with interval between misoprostol application and procedure**			
Uterine perforation – 3 hours vs 1 hour, sublingual	∞ per 1000	**NaN per 1000** (NaN to NaN)	not estimable	46 (1 study)	-
Uterine perforation – 3 hours vs 1 hour, vaginal	0 per 1000	**0 per 1000** (0 to 0)	not estimable	87 (1 study)	-
Side-effects – Nausea	216 per 1000	**144 per 1000** (72 to 268)	**OR 0.61** (0.28 to 1.33)	178 (2 RCTs)	⨁⨁◯◯ LOW [a,c]
Side-effects – Nausea – 3 hours vs 1 hour, sublingual	244 per 1000	**195 per 1000** (83 to 398)	**OR 0.75** (0.28 to 2.04)	91 (1 RCT)	⨁⨁◯◯ LOW [a,c]
Side-effects – Nausea – 3 hours vs 1 hour, vaginal	186 per 1000	**91 per 1000** (27 to 265)	**OR 0.44** (0.12 to 1.58)	87 (2 RCTs)	⨁⨁◯◯ LOW [a,c]
Unplanned expulsion prior to procedure	not pooled	not pooled	not pooled	178 (2 studies)	-
Unplanned expulsion prior to procedure – 3 hours vs 1 hour, sublingual	0 per 1000	**0 per 1000** (0 to 0)	not estimable	91 (1 study)	-
Unplanned expulsion prior to procedure – 3 hours vs 1 hour, vaginal	not pooled	not pooled	not pooled	87 (2 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Notes

a. Downgraded one level due to lack of blinding
b. Downgraded two levels due to I^2 above 90%
c. Downgraded one level due to wide confidence intervals

Reference

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 4: Cervical priming prior to first-trimester surgical abortion: Misoprostol dose: 400 µg vs 200 µg

Patient or population: First-trimester surgical abortion
Intervention: 400 µg misoprostol
Comparison: 200 µg misoprostol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with 200 µg misoprostol	**Risk with 400 µg misoprostol**			
Cervical dilation at procedure start – Oral misoprostol	The mean cervical dilation at procedure start – Oral misoprostol ranged from **5 to 7** mm	MD **0.53 mm higher** (0.3 higher to 0.77 higher)	-	632 (2 RCTs)	⨁⨁⨁⨁ HIGH
Cervical dilation at procedure start – Vaginal misoprostol	The mean cervical dilation at procedure start – Vaginal misoprostol ranged from **6 to 7** mm	MD **0.92 mm higher** (0.53 higher to 1.31 higher)	-	137 (2 RCTs)	⨁⨁◯◯ LOW [a]
Cervical dilation at procedure start – Sublingual misoprostol	The mean cervical dilation at procedure start – Sublingual misoprostol was **6** mm	MD **2.2 mm higher** (1.61 higher to 2.79 higher)	-	120 (1 RCT)	⨁⨁⨁◯ MODERATE [b]
Need for additional mechanical dilation	700 per 1000	**85 per 1000** (45 to 189)	**OR 0.04** (0.02 to 0.10)	180 (2 RCTs)	⨁⨁◯◯ LOW [b,c]
Need for additional mechanical dilation – Vaginal misoprostol	767 per 1000	**32 per 1000** (0 to 228)	**OR 0.01** (0.00 to 0.09)	60 (1 RCT)	⨁⨁⨁⨁ HIGH
Need for additional mechanical dilation – Sublingual misoprostol	667 per 1000	**123 per 1000** (57 to 254)	**OR 0.07** (0.03 to 0.17)	120 (1 RCT)	⨁⨁⨁◯ MODERATE [b]
Pain with cervical priming	333 per 1000	**556 per 1000** (396 to 704)	**OR 2.50** (1.31 to 4.75)	180 (2 RCTs)	⨁⨁◯◯ LOW [b,c]
Pain with cervical priming – Vaginal misoprostol	67 per 1000	**367 per 1000** (103 to 744)	**OR 8.11** (1.61 to 40.77)	60 (1 RCT)	⨁⨁⨁⨁ HIGH
Pain with cervical priming – Sublingual misoprostol	467 per 1000	**617 per 1000** (438 to 769)	**OR 1.84** (0.89 to 3.80)	120 (1 RCT)	⨁⨁◯◯ LOW [b,d]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with 200 µg misoprostol	**Risk with 400 µg misoprostol**			
Procedure length (minutes)	The mean procedure length (minutes) was **5** min	MD **1.22 min lower** (1.72 lower to 0.71 lower)	-	197 (2 RCTs)	⨁⨁◯◯ LOW [b,c]
Procedure length (minutes) – Vaginal misoprostol	The mean procedure length (minutes) – Vaginal misoprostol was **5** min	MD **0.3 min lower** (1.34 lower to 0.74 higher)	-	77 (1 RCT)	⨁⨁⨁◯ MODERATE [d]
Procedure length (minutes) – Sublingual misoprostol	The mean procedure length (minutes) – Sublingual misoprostol was **5** min	MD **1.5 min lower** (2.08 lower to 0.92 lower)	-	120 (1 RCT)	⨁⨁⨁◯ MODERATE [b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Notes

a. Downgraded two levels due to I^2 above 90%
b. Downgraded one level due to lack of blinding
c. Downgraded one level due to I^2 above 50%
d. Downgraded one level due to wide confidence intervals

Reference

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 5: Cervical priming prior to first-trimester surgical abortion: Misoprostol vs mifepristone

Patient or population: First-trimester surgical abortion
Intervention: Misoprostol
Comparison: Mifepristone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with mifepristone	**Risk with misoprostol**			
Cervical dilation at procedure start	The mean cervical dilation at procedure start ranged from **7 to 8** mm	MD **0.55 mm lower** (0.93 lower to 0.17 lower)	-	197 (3 RCTs)	⊕⊕⊕◯ MODERATE [a]
Cervical dilation at procedure start – 800 µg misoprostol vs 200 mg mifepristone	The mean cervical dilation at procedure start – 800 µg misoprostol vs 200 mg mifepristone was **8** mm	MD **0.7 mm lower** (1.3 lower to 0.1 lower)	-	60 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Cervical dilation at procedure start – 600 µg misoprostol vs 400 mg mifepristone (divided doses)	The mean cervical dilation at procedure start – 600 µg misoprostol vs 400 mg mifepristone (divided doses) was **7** mm	MD **1 mm lower** (1.89 lower to 0.11 lower)	-	30 (1 RCT)	⊕⊕⊕⊕ HIGH
Cervical dilation at procedure start – 400 µg misoprostol vs 200 mg mifepristone	The mean cervical dilation at procedure start – 400 µg misoprostol vs 200 mg mifepristone was **8** mm	MD **0.2 mm lower** (0.79 lower to 0.39 higher)	-	107 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects: nausea and vomiting	89 per 1000	**68 per 1000** (16 to 245)	**OR 0.75** (0.17 to 3.33)	90 (2 RCTs)	⊕◯◯◯ VERY LOW [a,b]
Side-effects: nausea and vomiting – 800 µg misoprostol vs 200 µg mifepristone	67 per 1000	**13 per 1000** (1 to 225)	**OR 0.19** (0.01 to 4.06)	60 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with mifepristone	**Risk with misoprostol**			
Side-effects: nausea and vomiting – 600 µg misoprostol vs 400 mg mifepristone (divided doses)	133 per 1000	**200 per 1000** (34 to 638)	**OR 1.63** (0.23 to 11.46)	30 (1 RCT)	⨁⨁◯◯ LOW [b]
Procedure length (minutes)	The mean procedure length (minutes) was **7** min	MD **0 min** (1.58 lower to 1.58 higher)	-	107 (1 RCT)	⨁⨁⨁◯ MODERATE [a]
Estimated blood loss (ml)	The mean estimated blood loss (ml) was **276** ml	MD **53 ml higher** (6 higher to 100 higher)	-	107 (1 RCT)	⨁⨁◯◯ LOW [a,c]
Cervical laceration/injury	0 per 1000	**0 per 1000** (0 to 0)	not estimable	107 (1 study)	-
Uterine perforation	0 per 1000	**0 per 1000** (0 to 0)	not estimable	107 (1 study)	-
Side-effects – Nausea	36 per 1000	**78 per 1000** (15 to 327)	**OR 2.30** (0.40 to 13.12)	107 (1 RCT)	⨁◯◯◯ VERY LOW [a,b]
Side-effects – Diarrhoea	0 per 1000	**0 per 1000** (0 to 0)	not estimable	107 (1 study)	-
Side-effects – Vomiting	54 per 1000	**19 per 1000** (2 to 166)	**OR 0.35** (0.04 to 3.51)	107 (1 RCT)	⨁◯◯◯ VERY LOW [a,b]
Unplanned expulsion prior to procedure	0 per 1000	**0 per 1000** (0 to 0)	not estimable	107 (1 study)	-
Side-effects – Abdominal pain/cramping	107 per 1000	**79 per 1000** (22 to 243)	**OR 0.71** (0.19 to 2.67)	107 (1 RCT)	⨁◯◯◯ VERY LOW [a,b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Notes

a. Downgraded one level due to risk of bias

b. Downgraded two levels due to very wide confidence intervals

c. Downgraded one level due to wide confidence intervals

References

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 6: Cervical priming prior to first-trimester surgical abortion: Misoprostol vs mifepristone + misoprostol

Patient or population: First-trimester surgical abortion
Intervention: Misoprostol
Comparison: Mifepristone + misoprostol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with mifepristone + misoprostol	Risk with misoprostol			
Cervical dilation at procedure start	The median cervical dilation at procedure start was **9** mm	MD **1.3 mm fewer** (2.01 fewer to 0.59 fewer)	-	106 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Procedure length (minutes)	The mean procedure length (minutes) was **5** min	MD **2 min higher** (0.53 higher to 3.47 higher)	-	106 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Estimated blood loss (ml)	The mean estimated blood loss (ml) was **222** ml	MD **107 ml higher** (67.76 higher to 146.24 higher)	-	106 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Cervical laceration/injury	0 per 1000	**0 per 1000** (0 to 0)	not estimable	106 (1 RCT)	-
Uterine perforation	0 per 1000	**0 per 1000** (0 to 0)	not estimable	106 (1 RCT)	-
Side-effects – Nausea	0 per 1000	**0 per 1000** (0 to 0)	**OR 10.52** (0.55 to 200.38)	106 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]
Side-effects – Diarrhoea	0 per 1000	**0 per 1000** (0 to 0)	not estimable	106 (1 RCT)	-
Side-effects – Vomiting	18 per 1000	**20 per 1000** (1 to 247)	**OR 1.08** (0.07 to 17.73)	106 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]
Unplanned expulsion prior to procedure	0 per 1000	**0 per 1000** (0 to 0)	not estimable	106 (1 RCT)	-
Side-effects – Abdominal pain/cramping	91 per 1000	**78 per 1000** (22 to 251)	**OR 0.85** (0.22 to 3.36)	106 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Notes

a. Downgraded one level due to risk of bias
b. Downgraded two levels due to very wide confidence intervals

References

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 7: Cervical priming prior to first trimester surgical abortion: Dose of mifepristone vs placebo
Patient or population: First trimester surgical abortion
Intervention: Dose of mifepristone
Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with dose of mifepristone**			
Need for additional mechanical dilation	958 per 1000	**945 per 1000** (734 to 991)	**OR 0.74** (0.12 to 4.62)	102 (1 RCT)	⨁⨁◯◯ LOW [a]
Cervical dilation at procedure start	The mean cervical dilation at procedure start was **7** mm	MD **0 mm** (0.74 lower to 0.74 higher)	-	102 (1 RCT)	⨁⨁⨁⨁ HIGH

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **OR:** odds ratio; **MD:** mean difference

Note:
a. Downgraded two levels due to very wide confidence intervals

References
Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 8: Cervical priming prior to first trimester surgical abortion: Mifepristone vs mifepristone + misoprostol

Patient or population: first trimester surgical abortion
Intervention: Mifepristone
Comparison: mifepristone + misoprostol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with mifepristone + misoprostol	**Risk with Mifepristone**			
Cervical dilation at procedure start	The mean cervical dilation at procedure start was **9** mm	MD **1.1 mm lower** (1.82 lower to 0.38 lower)	-	111 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Procedure length (minutes)	The mean procedure length (minutes) was **5** min	MD **2 min higher** (1.05 higher to 2.95 higher)	-	111 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Estimated blood loss (ml)	The mean estimated blood loss (ml) was **222** ml	MD **54 ml higher** (18.77 higher to 89.23 higher)	-	111 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Cervical laceration/injury	0 per 1000	**0 per 1000** (0 to 0)	not estimable	111 (1 study)	-
Uterine perforation	0 per 1000	**0 per 1000** (0 to 0)	not estimable	111 (1 study)	-
Side-effects – Nausea	0 per 1000	**0 per 1000** (0 to 0)	**OR 5.09** (0.24 to 108.52)	111 (1 RCT)	⊕⊕◯◯ LOW [a,b]
Side-effects – Diarrhoea	0 per 1000	**0 per 1000** (0 to 0)	not estimable	111 (1 study)	-
Side-effects – Vomiting	18 per 1000	**54 per 1000** (6 to 360)	**OR 3.06** (0.31 to 30.33)	111 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]
Unplanned expulsion prior to procedure	0 per 1000	**0 per 1000** (0 to 0)	not estimable	111 (1 study)	-
Side-effects – Abdominal pain/cramping	91 per 1000	**107 per 1000** (33 to 295)	**OR 1.20** (0.34 to 4.19)	111 (1 RCT)	⊕◯◯◯ VERY LOW [a,b]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Notes

a. Downgraded one level due to risk of bias
b. Downgraded two levels due to very wide confidence intervals

References

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 9: Cervical priming prior to first trimester surgical abortion: Osmotic dilators vs placebo
Patient or population: First trimester surgical abortion
Intervention: Osmotic dilators
Comparison: Placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with placebo	**Risk with osmotic dilators**			
Cervical dilation at procedure start	The mean cervical dilation at procedure start was **0**	MD **0** (0 to 0)	-	40 (1 study)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference

References

Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 10: Cervical priming prior to first trimester surgical abortion: Misoprostol vs laminaria

Patient or population: First trimester surgical abortion
Intervention: Misoprostol
Comparison: Laminaria

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with laminaria	**Risk with misoprostol**			
Need for additional mechanical dilation	617 per 1000	**626 per 1000** (436 to 785)	**OR 1.04** (0.48 to 2.26)	131 (2 RCTs)	⊕⊕◯◯ LOW [a,b]
Need for additional mechanical dilation – 200 µg misoprostol	667 per 1000	**702 per 1000** (462 to 867)	**OR 1.18** (0.43 to 3.25)	70 (1 RCT)	⊕⊕◯◯ LOW [a,b]
Need for additional mechanical dilation – 400 µg misoprostol	500 per 1000	**468 per 1000** (213 to 744)	**OR 0.88** (0.27 to 2.90)	61 (1 RCT)	⊕⊕⊕◯ MODERATE [b]
Procedure length (minutes)	The mean procedure length (minutes) was **4** min	MD **0.1 min lower** (1.09 lower to 0.89 higher)	-	70 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Patient dissatisfaction	576 per 1000	**296 per 1000** (140 to 533)	**OR 0.31** (0.12 to 0.84)	70 (1 RCT)	⊕⊕⊕◯ MODERATE [a]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **OR:** odds ratio; **MD:** mean difference

Notes
a. Downgraded one level due to risk of bias
b. Downgraded one level due to wide confidence intervals

References
Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

SoF Table 11: Cervical priming prior to first trimester surgical abortion: Misoprostol vs Dilapan

Patient or population: First trimester surgical abortion
Intervention: Misoprostol
Comparison: Dilapan

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with Dilapan	**Risk with misoprostol**			
Cervical dilation at procedure start	The mean cervical dilation at procedure start was **11** mm	MD **0.6 mm lower** (1.21 lower to 0.01 higher)	-	122 (1 RCT)	⨁⨁⨁⨁ HIGH
Need for additional mechanical dilation	950 per 1000	**952 per 1000** (792 to 990)	**OR 1.04** (0.20 to 5.34)	122 (1 RCT)	⨁⨁◯◯ LOW [a]
Procedure length (minutes)	The mean procedure length (minutes) was **3** min	MD **0.02 min lower** (0.46 lower to 0.42 higher)	-	122 (1 RCT)	⨁⨁⨁⨁ HIGH
Cervical laceration/injury	0 per 1000	**0 per 1000** (0 to 0)	**OR 2.95** (0.12 to 73.88)	122 (1 RCT)	⨁⨁◯◯ LOW [a]
Need for re-aspiration/incomplete abortion	33 per 1000	**32 per 1000** (4 to 196)	**OR 0.97** (0.13 to 7.09)	122 (1 RCT)	⨁⨁◯◯ LOW [a]

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Note
a. Downgraded two levels due to very wide confidence intervals

References
Kapp N, Nguyen A, Atrio J, Lohr P. Cervical preparation for Cervical preparation for surgical abortion less than 14 weeks. Cochrane Database Syst Rev. (unpublished).

7. EtD framework for Cervical priming prior to surgical abortion ≥ 12 weeks

Recommendation 18 (NEW): Prior to surgical abortion (MVA or D&E) at later gestational ages:

a. For surgical abortion at ≥ 12 weeks: **Suggest** cervical priming prior to the procedure.

b. For surgical abortion between 12 and 19 weeks: **Suggest** cervical priming with medication alone (a combination of mifepristone plus misoprostol is preferred) or with an osmotic dilator plus medication (mifepristone, misoprostol, or a combination of both).

c. For surgical abortion between 12 and 19 weeks, when using an osmotic dilator for cervical priming: **Suggest** that the period between osmotic dilator placement and the procedure should not extend beyond two days.

d. For surgical abortion at ≥ 19 weeks: **Recommend** cervical priming with an osmotic dilator plus medication (mifepristone, misoprostol, or a combination of both).

PICO 6b: For a pregnant person seeking surgical abortion at ≥ 12 weeks of gestation, is cervical priming with mifepristone plus misoprostol or with mifepristone alone a safe, effective and satisfactory/acceptable alternative to cervical preparation with misoprostol alone?

PICO 7: For a pregnant person seeking surgical abortion at ≥ 12 weeks of gestation, is cervical priming with medical methods (mifepristone, misoprostol, or both) a safe, effective and satisfactory/acceptable alternative to mechanical methods (laminaria, Foley bulb, Dilapan)?

PICO 8: For a pregnant person seeking surgical abortion at ≥ 12 weeks of gestation, is cervical priming with medication(s) plus laminaria a safe, effective and satisfactory/acceptable alternative to cervical preparation with laminaria alone?

PICO 9: For a pregnant person seeking surgical abortion (D&E) at ≥ 12 weeks of gestation, is cervical priming with one mechanical method a safe, effective and satisfactory/acceptable alternative to cervical priming with a different mechanical method? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global
Perspective: Population perspective

Literature review: A Cochrane review served as the evidence base for this question. The review evaluates cervical preparation methods for second-trimester surgical abortion. From this review, 16 studies were included towards the development of this evidence to decision framework. The review included the following cervical priming methods:

- Medication with mifepristone and/or misoprostol
- Mechanical methods with osmotic dilators and synthetic dilators

- One versus two-day procedures with laminaria.

Study settings: Israel, South Africa, Spain, United Kingdom, USA

ASSESSMENT OF RESEARCH EVIDENCE

Analyses were performed across four sub-PICOs. For each of the sub PICOs, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects.

Sub-PICOs were combined with a view to ensure that the ERRG can review the material in a systematic manner to make recommendations for cervical priming for surgical abortion beyond 12–14 weeks.

1. Mifepristone + misoprostol or mifepristone alone versus misoprostol alone
2. Medical methods versus mechanical methods
3. Medical methods with laminaria versus laminaria alone
4. Two different mechanical methods.

The overall draft judgements on the above questions are presented below to be considered by the ERRG towards the recommendations.

Sub-PICO 1 – Mifepristone + misoprostol versus misoprostol alone

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (mifepristone and misoprostol) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (misoprostol alone). The certainty of evidence is very low.

Pre-procedure cervical dilation of the women in the intervention group (mifepristone and sublingual misoprostol) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (sublingual misoprostol). The certainty of evidence is moderate.

Pre-procedure cervical dilation of the women in the intervention group (mifepristone and vaginal misoprostol) was less compared with the pre-procedure cervical dilation of the women in the comparison group (vaginal misoprostol). The certainty of evidence is low.

Fewer women in the intervention group (mifepristone and misoprostol) required further dilation compared with the women in the comparison group (misoprostol alone). The certainty of evidence is moderate.

Time to complete the procedure with the intervention (mifepristone + misoprostol) was less than the time to complete the procedure with the comparison (misoprostol alone). The certainty of evidence is moderate.

Time to complete the procedure with the intervention (mifepristone + sublingual misoprostol) was less than the time to complete the procedure with the comparison (sublingual misoprostol). The certainty of evidence is moderate.

Time to complete the procedure with the intervention (mifepristone + vaginal misoprostol) was less than the time to complete the procedure with the comparison (vaginal misoprostol). The certainty of evidence is low.

Providers expressed greater satisfaction with the use of mifepristone + misoprostol compared with the use of misoprostol alone for cervical priming prior to surgical abortion. The certainty of evidence is moderate.

Fewer women in the intervention group (mifepristone + misoprostol) experienced the complication of a cervical tear compared with the women in the comparison group (misoprostol alone). The certainty of evidence is very low.

Undesirable effects:

Women in the intervention group (mifepristone + misoprostol) had lower rates of satisfaction compared with the women in the comparison group (misoprostol alone). The certainty of evidence is low.

More women in the intervention group (mifepristone + misoprostol) experienced nausea, vomiting or diarrhoea compared with women in the comparison group (misoprostol alone). The certainty of evidence is low to moderate.

More women in the intervention group (mifepristone + misoprostol) experienced a complication of pre-procedure expulsion compared with women in the comparison group (misoprostol alone). The certainty of evidence is moderate.

Balance of effects:

			X	
Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Sub-PICO 2 – Medical methods versus mechanical methods

Desirable effects:

Time to complete the procedure with the intervention (medication) was less than the time to complete the procedure with the comparison (mechanical methods). The certainty of evidence is very low.

Time to complete the procedure with the intervention (misoprostol alone) was less than the time to complete the procedure with the comparison (mechanical methods). The certainty of evidence is low.

Fewer women in the intervention group (medication) experienced nausea compared with the women in the comparison group (mechanical method). The certainty of evidence is moderate.

Fewer women in the intervention group (medication) experienced bleeding compared with the women in the comparison group (mechanical method). The certainty of evidence is low.

Fewer women in the intervention group (medication) experienced the complication of needing an additional intervention compared with the women in the comparison group (mechanical methods). The certainty of evidence is low.

There were no differences between the two groups in the complication of a uterine perforation. The certainty of evidence is low.

Fewer women in the intervention group (medication) experienced post procedure pain compared with the women in the comparison group (mechanical method). The certainty of evidence is very low.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (medication) was less compared with the pre-procedure cervical dilation of the women in the comparison group (mechanical method). The certainty of evidence is low.

Pre-procedure cervical dilation of the women in the intervention group (mifepristone alone) was less compared with the pre-procedure cervical dilation of the women in the comparison group (mechanical method). The certainty of evidence is moderate.

Pre-procedure cervical dilation of the women in the intervention group (misoprostol alone) was less compared with the pre-procedure cervical dilation of the women in the comparison group (mechanical method). The certainty of evidence is low.

More women in the intervention group (medication with misoprostol) required further dilation compared with the women in the comparison group (mechanical method). The certainty of evidence is low.

Ease of procedure was noted as less with the intervention group (medication) compared with the comparison group (mechanical method). The certainty of evidence is moderate.

Time to complete the procedure with the intervention (medication with mifepristone) was more than the time to complete the procedure with the comparison (mechanical methods). The certainty of evidence is low

Women in the intervention group (medication) had lower rates of satisfaction compared with the women in the comparison group (mechanical methods). The certainty of evidence is moderate.

Providers expressed lower rates of satisfaction towards the intervention (medication) compared with the comparison (mechanical methods). The certainty of evidence is high.

More women in the intervention group (medication) experienced the side-effects of vomiting or diarrhoea compared with women in the comparison group (mechanical methods). The certainty of evidence is low.

More women in the intervention group (medication) experienced the complication of pre-procedure expulsion compared with women in the comparison group (mechanical methods). The certainty of evidence is low.

More women in the intervention group (medication) had a higher pain score compared with women in the comparison group (mechanical methods). The certainty of evidence is low.

Balance of effects:

X Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Sub-PICO 3 – Medical methods + laminaria versus laminaria alone

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (medication + laminaria) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (laminaria alone). The certainty of evidence is high.

Pre-procedure cervical dilation of the women in the intervention group (mifepristone + laminaria) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (laminaria alone). The certainty of evidence is high.

Pre-procedure cervical dilation of the women in the intervention group (misoprostol + laminaria) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (laminaria alone). The certainty of evidence is high.

Fewer women in the intervention group (medical + laminaria) required further dilation compared with the women in the comparison group (laminaria alone). The certainty of evidence is high.

Fewer women in the intervention group (mifepristone + laminaria) required further dilation compared with the women in the comparison group (laminaria alone). The certainty of evidence is high.

Fewer women in the intervention group (misoprostol + laminaria) required further dilation compared with the women in the comparison group (laminaria alone). The certainty of evidence is high.

Ease of procedure was noted more with the intervention group (medication + laminaria) compared with the comparison group (laminaria alone). The certainty of evidence is high.

Time to complete the procedure with the intervention group (medication + laminaria) was less than the time to complete the procedure with the comparison group (laminaria alone). The certainty of evidence is low.

Time to complete the procedure with the intervention group (mifepristone + laminaria) was less than the time to complete the procedure with the comparison group (laminaria alone). The certainty of evidence is high.

Time to complete the procedure with the intervention group (misoprostol + laminaria) was less than the time to complete the procedure with the comparison group (laminaria alone). The certainty of evidence is low.

Providers expressed higher rates of satisfaction towards the intervention (medication + laminaria) compared with the comparison (laminaria alone). The certainty of evidence is moderate.

Fewer women in the intervention group (medication + laminaria) experienced the side-effect of nausea compared with women in the comparison group (laminaria alone). The certainty of evidence is high.

Fewer women in the intervention group (medication + laminaria) experienced the side-effect of diarrhoea compared with women in the comparison group (laminaria alone). The certainty of evidence is low.

Fewer women in the intervention group (medication + laminaria) experienced the side-effect of bleeding compared with women in the comparison group (laminaria alone). The certainty of evidence is moderate.

Fewer women in the intervention group (medication + laminaria) experienced the complication of needing additional interventions compared with women in the comparison group (laminaria alone). The certainty of evidence is low.

There was no difference in uterine perforation rates between the two groups. The certainty of evidence is low.

Undesirable effects:

Women in the intervention group (medication + laminaria) had lower rates of satisfaction compared with the women in the comparison group (laminaria alone). The certainty of evidence is moderate.

More women in the intervention group (medication + laminaria) experienced the complication of pre-procedure expulsion compared with women in the comparison group (laminaria alone). The certainty of evidence is moderate.

More women in the intervention group (medication + laminaria) experienced post procedure pain compared with the women in the comparison group (laminaria alone). The certainty of evidence is high.

More women in the intervention group (medication) had a higher pain score compared with women in the comparison group (mechanical methods). The certainty of evidence is moderate.

Balance of effects:

			X	
Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Sub-PICO 4 – Comparison between two different mechanical methods

a) 2 days of mechanical method versus 1 day of mechanical method

Desirable effects:

Pre-procedure cervical dilation of the women in the intervention group (2 days of mechanical method) was greater compared with the pre-procedure cervical dilation of the women in the comparison group (1 day of mechanical method). The certainty of evidence is moderate.
Time to complete the procedure with the intervention group (2 days of mechanical method) was less than the time to complete the procedure with the comparison group (1 day of mechanical method). The certainty of evidence is low.

Undesirable effects:

More women in the intervention group (2 days of mechanical method) experienced post procedure pain compared with the women in the comparison group (1 day of mechanical method). The certainty of evidence is low.

Balance of effects:

			X	

Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

b) Synthetic dilator versus laminaria

Desirable effects:

Women in the intervention group (synthetic dilator) had higher rates of satisfaction compared with the women in the comparison group (laminaria). The certainty of evidence is moderate.

Fewer women in the intervention group (synthetic dilator) experienced the side-effect of nausea compared with women in the comparison group (laminaria). The certainty of evidence is high.

Fewer women in the intervention group (synthetic dilator) experienced the side-effect of vomiting compared with women in the comparison group (laminaria). The certainty of evidence is high.

There was no difference in the occurrence of diarrhoea as a side-effect between the two groups. The certainty of evidence is low.

Fewer women in the intervention group (synthetic dilator) experienced post procedure pain compared with the women in the comparison group (laminaria). The certainty of evidence is high.

Undesirable effects:

Pre-procedure cervical dilation of the women in the intervention group (synthetic dilator) was lesser compared with the pre-procedure cervical dilation of the women in the comparison group *(*laminaria). The certainty of evidence is high.

More women in the intervention group (synthetic dilator) required further dilation compared with the women in the comparison group (laminaria). The certainty of evidence is high.

Time to complete the procedure with the intervention group (synthetic dilator) was less than the time to complete the procedure with the comparison group (laminaria). The certainty of evidence is moderate.

Balance of effects:

Favours the comparison	**X** May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

			x		
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

			x		
Unable to determine	Varies	Large costs	Moderate costs	Negligible costs or savings	Moderate savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

x						
Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

			x			
Unable to determine	Varies	Reduced	Probably reduced	Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

				x	
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

Research evidence on satisfaction was considered as a secondary outcome and the evidence presented above.

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

					x
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

SUMMARY OF FINDINGS TABLES

SoF Table 1: Cervical priming prior to surgical abortion > 12–14 weeks: Mifepristone + misoprostol vs misoprostol alone

Patient or population: Cervical preparation
Intervention: Mifepristone + misoprostol
Comparison: Misoprostol alone

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with misoprostol	**Risk with mifepristone + misoprostol**		
Pre-procedure cervical dilation	The mean pre-procedure cervical dilation was **9.3** mm	MD **3.65 mm higher** (3.29 higher to 4.01 higher)	973 (2 RCTs)	⊕◯◯◯ VERY LOW [a,b]
Pre-procedure cervical dilation – Sublingual misoprostol	The mean pre-procedure cervical dilation – Sublingual misoprostol was **8.9** mm	MD **3.7 mm higher** (3.21 higher to 4.19 higher)	438 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Pre-procedure cervical dilation – Vaginal misoprostol	The mean pre-procedure cervical dilation – Vaginal misoprostol was **9.5** mm	MD **3.59 mm higher** (3.04 higher to 4.14 higher)	535 (2 RCTs)	⊕⊕◯◯ LOW [a,b]
Need for further dilation	537 per 1000	**306 per 1000** (258 to 360)	877 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Ease of procedure	The mean ease of procedure was **0**	not pooled	(0 studies)	-
Time to complete procedure	The mean time to complete procedure was **13.0** min	MD **0.95 min lower** (1.61 lower to 0.3 lower)	973 (2 RCTs)	⊕⊕⊕◯ MODERATE [a]
Time to complete procedure – Sublingual misoprostol	The mean time to complete procedure – Sublingual misoprostol was **13.0** min	MD **1.1 min lower** (2 lower to 0.2 lower)	438 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Time to complete procedure – Vaginal misoprostol	The mean time to complete procedure – Vaginal misoprostol was **13.0** min	MD **0.79 min lower** (1.74 lower to 0.17 higher)	535 (2 RCTs)	⊕⊕◯◯ LOW [a,c]
Satisfaction (client and provider)/acceptability	781 per 1000	**789 per 1000** (742 to 836)	899 (2 RCTs)	⊕⊕◯◯ LOW [a,d]

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with misoprostol	Risk with mifepristone + misoprostol		
Satisfaction/acceptability – Client	834 per 1000	**826 per 1000** (776 to 876)	803 (2 RCTs)	⊕⊕◯◯ LOW [a,d]
Satisfaction/acceptability – Provider	333 per 1000	**437 per 1000** (263 to 730)	96 (1 RCT)	⊕⊕⊕◯ MODERATE [c]
Side-effects – Nausea	49 per 1000	**90 per 1000** (55 to 150)	891 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Vomiting	38 per 1000	**68 per 1000** (38 to 122)	891 (1 RCT)	⊕⊕◯◯ LOW [a,c]
Side-effects – Diarrhoea	11 per 1000	**36 per 1000** (13 to 98)	891 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Complications – Cervical tear	7 per 1000	**2 per 1000** (0 to 23)	847 (1 RCT)	⊕◯◯◯ VERY LOW [a,c]
Complications – Pre-procedure expulsion	6 per 1000	**33 per 1000** (10 to 102)	943 (2 RCTs)	⊕⊕⊕◯ MODERATE [a]
Pre- and post-procedure pain	The mean pre and post procedure pain was **0**	not pooled	(0 studies)	-
Cost (comparative cost and cost to the patient)	The mean cost (comparative cost and cost to the patient) was **0**	not pooled	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Notes

a. The main study, Carbonell 2007, was not blinded
b. Heterogeneity is more than 90%; if the small study by Casey 2016 is excluded it drops down to 55%
c. Broad confidence intervals
d. Heterogeneity is more than 80%

References

1. Casey FE, Ye PP, Perritt JD, Moreno-Ruiz NL, Reeves MF. A randomized controlled trial evaluating same-day mifepristone and misoprostol compared with misoprostol alone for cervical preparation prior to second-trimester surgical abortion. Contraception. 2016.

2. Carbonell JL, Gallego FG, Llorente MP, Bermudez SB, Sala ES, González LV, Texido CS. Vaginal vs sublingual misoprostol with mifepristone for cervical priming in second-trimester abortion by dilation and evacuation: a randomized clinical trial. Contraception. 2007.

SoF Table 2: Cervical priming prior to surgical abortion > 12–14 weeks: Medical vs mechanical

Patient or population: Cervical preparation
Intervention: Medical
Comparison: Mechanical

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with mechanical	Risk with medical		
Pre-procedure cervical dilation	-	SMD **0.82 lower** (1.08 lower to 0.57 lower)	266 (4 RCTs)	⊕⊕◯◯ LOW [a,b]
Pre-procedure cervical dilation – Mifepristone alone	-	SMD **0.98 lower** (1.58 lower to 0.39 lower)	49 (1 RCT)	⊕⊕⊕◯ MODERATE [c]
Pre-procedure cervical dilation – Misoprostol + mifepristone	not pooled	not pooled	(0 studies)	-
Pre-procedure cervical dilation – Misoprostol alone	-	SMD **0.79 lower** (1.07 lower to 0.5 lower)	217 (3 RCTs)	⊕⊕◯◯ LOW [a,b]
Need for further dilation	178 per 1000	**454 per 1000** (313 to 657)	323 (3 RCTs)	⊕⊕◯◯ LOW [a,b]
Need for further dilation – Mifepristone alone	not pooled	not pooled	(0 studies)	-
Need for further dilation – Misoprostol + mifepristone	not pooled	not pooled	(0 studies)	-
Need for further dilation – Misoprostol alone	178 per 1000	**454 per 1000** (313 to 657)	323 (3 RCTs)	⊕⊕◯◯ LOW [a,b]
Ease of procedure	745 per 1000	**537 per 1000** (425 to 678)	132 (3 RCTs)	⊕⊕⊕◯ MODERATE [c]
Time to complete procedure	The mean time to complete procedure was **8.7** min	MD **0.14 min lower** (0.82 lower to 0.54 higher)	372 (4 RCTs)	⊕◯◯◯ VERY LOW [a,b,d]
Time to complete procedure – Mifepristone alone	The mean time to complete procedure – Mifepristone alone was **8.0** min	MD **1.9 min higher** (0.16 lower to 3.96 higher)	49 (1 RCT)	⊕⊕◯◯ LOW [c,d]

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with mechanical	Risk with medical		
Time to complete procedure – Misoprostol + mifepristone	The mean time to complete procedure – Misoprostol + mifepristone was **0**	not pooled	(0 studies)	-
Time to complete procedure – Misoprostol alone	The mean time to complete procedure – Misoprostol alone was **9.0** min	MD **0.39 min lower** (1.1 lower to 0.33 higher)	323 (3 RCTs)	⊕⊕◯◯ LOW [a,b]
Satisfaction (client and provider)/acceptability	983 per 1000	**767 per 1000** (688 to 846)	239 (2 RCTs)	⊕◯◯◯ VERY LOW [b,c]
Satisfaction/acceptability – Client	1000 per 1000	**970 per 1000** (930 to 1000)	156 (1 RCT)	⊕⊕⊕◯ MODERATE [c]
Satisfaction/acceptability – Provider	952 per 1000	**362 per 1000** (248 to 552)	83 (1 RCT)	⊕⊕⊕⊕ HIGH
Side-effects – Nausea	314 per 1000	**295 per 1000** (226 to 386)	373 (4 RCTs)	⊕⊕⊕◯ MODERATE [a]
Side-effects – Vomiting	80 per 1000	**136 per 1000** (77 to 242)	373 (4 RCTs)	⊕⊕◯◯ LOW [a,d]
Side-effects – Diarrhoea	59 per 1000	**108 per 1000** (55 to 213)	373 (4 RCTs)	⊕⊕◯◯ LOW [c,d]
Side-effects (nausea, vomiting, bleeding) – Bleeding	111 per 1000	**33 per 1000** (14 to 81)	340 (4 RCTs)	⊕⊕◯◯ LOW [a,e]
Complications – Cervical tear	not pooled	not pooled	(0 studies)	-
Complications – Pre-procedure expulsion	7 per 1000	**12 per 1000** (3 to 58)	290 (3 RCTs)	⊕⊕◯◯ LOW [a,d]
Complications – Need for additional interventions	24 per 1000	**8 per 1000** (0 to 194)	82 (1 RCT)	⊕⊕◯◯ LOW [d]
Complications – Uterine perforation	0 per 1000	**0 per 1000** (0 to 0)	239 (2 RCTs)	⊕⊕◯◯ LOW [d]

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with mechanical	Risk with medical		
Pre- and post-procedure pain – Binary	172 per 1000	**156 per 1000** (89 to 275)	256 (3 RCTs)	⊕◯◯◯ VERY LOW [a,b,d]
Pre- and post-procedure pain – Continuous	The mean pre and post procedure pain – continuous was **3**	MD **2.5 higher** (0.24 lower to 5.24 higher)	84 (1 RCT)	⊕⊕◯◯ LOW [c,d]
Cost (comparative cost and cost to the patient)	The mean cost (comparative cost and cost to the patient) was **0**	not pooled	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **SMD:** standardized mean difference; **RR:** risk ratio; **MD:** mean difference

Notes

a. More studies with high risk of bias in blinding combined with very high heterogeneity
b. I^2 more than 75%
c. Study not blinded
d. Broad confidence intervals
e. I^2 more than 60%

References

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SoF Table 3: Cervical priming prior to surgical abortion > 12–14 weeks: Medical + laminaria vs laminaria

Patient or population: Cervical preparation

Intervention: Medical + laminaria

Comparison: Laminaria

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with laminaria	**Risk with medical + laminaria**		
Pre-procedure cervical dilation	-	SMD **0.34 higher** (0.2 higher to 0.49 higher)	743 (4 RCTs)	⊕⊕⊕⊕ HIGH
Pre-procedure cervical dilation – Mifepristone alone	-	SMD **0.41 higher** (0.13 higher to 0.69 higher)	197 (1 RCT)	⊕⊕⊕⊕ HIGH
Pre-procedure cervical dilation – Misoprostol + mifepristone	not pooled	not pooled	(0 studies)	-
Pre-procedure cervical dilation – Misoprostol alone	-	SMD **0.32 higher** (0.15 higher to 0.48 higher)	546 (4 RCTs)	⊕⊕⊕⊕ HIGH
Need for further dilation	507 per 1000	**410 per 1000** (365 to 466)	743 (5 RCTs)	⊕⊕◯◯ LOW [a,b]
Need for further dilation – Mifepristone alone	263 per 1000	**92 per 1000** (45 to 186)	197 (1 RCT)	⊕⊕⊕⊕ HIGH
Need for further dilation – Misoprostol + mifepristone	not pooled	not pooled	(0 studies)	-
Need for further dilation – Misoprostol alone	594 per 1000	**523 per 1000** (469 to 594)	546 (4 RCTs)	⊕⊕◯◯ LOW [c,d]
Ease of procedure	735 per 1000	**808 per 1000** (720 to 904)	320 (2 RCTs)	⊕⊕⊕⊕ HIGH
Time to complete procedure	The mean time to complete procedure was **10.1** min	MD **1.72 min lower** (2 lower to 1.44 lower)	743 (4 RCTs)	⊕⊕◯◯ LOW [a]
Time to complete procedure – Mifepristone alone	The mean time to complete procedure – Mifepristone alone was **11.6** min	MD **1.45 min lower** (1.88 lower to 1.02 lower)	197 (1 RCT)	⊕⊕⊕⊕ HIGH

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with laminaria	**Risk with medical + laminaria**		
Time to complete procedure – Misoprostol + mifepristone	The mean time to complete procedure – Misoprostol + mifepristone was **0**	not pooled	(0 studies)	-
Time to complete procedure – Misoprostol alone	The mean time to complete procedure – Misoprostol alone was **9.9** min	MD **1.91 min lower** (2.27 lower to 1.54 lower)	546 (4 RCTs)	⊕⊕◯◯ LOW [a]
Satisfaction (client and provider)/acceptability	724 per 1000	**818 per 1000** (738 to 905)	452 (2 RCTs)	⊕⊕⊕◯ MODERATE [d]
Satisfaction/acceptability – Client	933 per 1000	**719 per 1000** (504 to 1000)	29 (1 RCT)	⊕⊕⊕◯ MODERATE [d]
Satisfaction/acceptability – Provider	709 per 1000	**822 per 1000** (737 to 915)	423 (2 RCTs)	⊕⊕⊕◯ MODERATE [d]
Side-effects – Nausea	469 per 1000	**314 per 1000** (225 to 436)	224 (2 RCTs)	⊕⊕⊕⊕ HIGH
Side-effects – Vomiting	not pooled	not pooled	(0 studies)	-
Side-effects – Diarrhoea	159 per 1000	**91 per 1000** (45 to 186)	224 (2 RCTs)	⊕⊕◯◯ LOW [d]
Side-effects – Bleeding	108 per 1000	**95 per 1000** (62 to 148)	589 (2 RCTs)	⊕⊕⊕◯ MODERATE [d]
Complications – Cervical tear	26 per 1000	**8 per 1000** (2 to 28)	619 (3 RCTs)	⊕⊕⊕◯ MODERATE [d]
Complications – Pre-procedure expulsion	20 per 1000	**46 per 1000** (19 to 111)	589 (2 RCTs)	⊕⊕⊕◯ MODERATE [d]
Complications – Need for additional interventions	30 per 1000	**14 per 1000** (4 to 44)	589 (2 RCTs)	⊕⊕◯◯ LOW [d]
Complications – Uterine perforation	10 per 1000	**10 per 1000** (1 to 162)	195 (1 RCT)	⊕⊕◯◯ LOW [d]
Pre- and post-procedure pain – Binary	516 per 1000	**825 per 1000** (634 to 1000)	126 (1 RCT)	⊕⊕⊕⊕ HIGH
Pre- and post-procedure pain – Continuous	The mean pre and post procedure pain – continuous was **24.3** mm	MD **19.6 mm higher** (0.74 higher to 38.46 higher)	29 (1 RCT)	⊕⊕⊕◯ MODERATE [d]

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with laminaria	**Risk with medical + laminaria**		
Cost (comparative cost and cost to the patient)	The mean cost (comparative cost and cost to the patient) was **0**	not pooled	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardized mean difference

Notes

a. I^2 more than 75%
b. Funnel plot skewed combined with massive heterogeneity
c. I^2 more than 60%
d. Broad confidence intervals

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SoF Table 4: Cervical priming prior to surgical abortion > 12–14 weeks: One mechanical compared with another mechanical method

Patient or population: Cervical priming
Intervention: One mechanical method
Comparison: Another mechanical method

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with another mechanical method	**Risk with one mechanical method**		
Pre-procedure cervical dilation – Binary	464 per 1000	**478 per 1000** (362 to 631)	219 (1 RCT)	⊕⊕⊕◯ MODERATE [a]
Pre-procedure cervical dilation – 2 days vs 1 day	The mean pre-procedure cervical dilation – Two days versus one day was **18.2** mm	MD **4.2 mm higher** (2.81 higher to 5.59 higher)	60 (1 RCT) [b]	⊕⊕⊕◯ MODERATE [a]
Pre-procedure cervical dilation – Synthetic dilator vs laminaria	The mean pre-procedure cervical dilation – Synthetic dilator vs laminaria was **59.7** mm	MD **11.7 mm lower** (16.74 lower to 6.66 lower)	69 (1 RCT) [c]	⊕⊕⊕⊕ HIGH
Need for further dilation – Synthetic dilator vs laminaria	229 per 1000	**647 per 1000** (336 to 1000)	69 (1 RCT)	⊕⊕⊕⊕ HIGH
Ease of procedure	not pooled	not pooled	(0 studies)	-
Time to complete procedure – 2 days vs 1 day	The mean time to complete procedure – 2 days vs 1 day was **6.6** min	MD **0.3 min lower** (1.93 lower to 1.33 higher)	60 (1 RCT)	⊕⊕◯◯ LOW [a,d]
Time to complete procedure – Synthetic dilator vs laminaria	The mean time to complete procedure – Synthetic dilator vs laminaria was **5.9** min	MD **2.2 min higher** (0.12 higher to 4.28 higher)	69 (1 RCT)	⊕⊕⊕◯ MODERATE [d]
Satisfaction (client and provider)/acceptability – Client	686 per 1000	**768 per 1000** (569 to 1000)	69 (1 RCT)	⊕⊕⊕◯ MODERATE [d]
Satisfaction (client and provider)/acceptability – Provider	not pooled	not pooled	(0 studies)	-
Side-effects – Nausea	343 per 1000	**58 per 1000** (14 to 243)	69 (1 RCT) [e]	⊕⊕⊕⊕ HIGH
Side-effects – Vomiting	371 per 1000	**89 per 1000** (26 to 282)	69 (1 RCT) [e]	⊕⊕⊕⊕ HIGH

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with another mechanical method	Risk with one mechanical method		
Side-effects – Diarrhoea	29 per 1000	**29 per 1000** (2 to 451)	69 (1 RCT) [e]	⊕⊕◯◯ LOW [d]
Side-effects – Bleeding	not pooled	not pooled	288 (2 RCTs) [f]	⊕⊕◯◯ LOW [f]
Complications – Cervical tear	not pooled	not pooled	288 (2 RCTs) [f]	⊕◯◯◯ VERY LOW [a,f]
Complications – Pre-procedure expulsion	not pooled	not pooled	(0 studies)	-
Complications – Need for additional interventions	not pooled	not pooled	129 (2 RCTs)	⊕◯◯◯ VERY LOW [a,f]
Complications – Uterine perforation	not pooled	not pooled	(0 studies)	-
Pre- and post-procedure pain – Binary – 2 day vs 1 day	219 per 1000	**287 per 1000** (118 to 687)	60 (1 RCT)	⊕⊕◯◯ LOW [a,d]
Pre and post procedure pain – Binary – Synthetic dilator vs laminaria	657 per 1000	**59 per 1000** (13 to 230)	69 (1 RCT)	⊕⊕⊕⊕ HIGH
Pre- and post-procedure pain – Continuous	The mean pre and post procedure pain – continuous was **0**	not pooled	(0 studies)	-
Cost (comparative cost and cost to the patient)	The mean cost (comparative cost and cost to the patient) was **0**	not pooled	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio; **MD:** mean difference; **OR:** odds ratio

Notes

a. Lack of blinding
b. Measured as mm in diameter
c. Measured as mm in circumference
d. Broad confidence intervals
e. Synthetic dilator vs laminaria
f. Not pooled as they were investigating two different approaches

References

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8. EtD framework for New medical methods for abortion

Medical management of induced abortion at gestational ages < 12 weeks:

Recommendation 27c. (NEW) Suggest the use of a combination regimen of letrozole plus misoprostol (letrozole 10 mg orally each day for 3 days followed by misoprostol 800 µg sublingually on the fourth day) as a safe and effective option.

PICO 10: For a pregnant person seeking medical abortion, is medical abortion with letrozole plus misoprostol a safe, effective and satisfactory/acceptable alternative to medical abortion with misoprostol alone?

PICO 11: For a pregnant person seeking medical abortion, is medical abortion with letrozole plus misoprostol a safe, effective and satisfactory alternative to medical abortion with mifepristone plus misoprostol?

PICO 12: For a pregnant person seeking medical abortion, is medical abortion with mifepristone plus letrozole a safe, effective and satisfactory alternative to medical abortion with misoprostol alone? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global

Perspective: Population

Literature review: A systematic review assessed the efficacy, safety, and acceptability of alternative methods of medication abortion to the routine mifepristone and misoprostol. Seven studies reporting on induced abortion were identified by the search strategy. All seven of the studies reported on the combination of letrozole and misoprostol compared versus misoprostol alone for medical abortion. No studies were identified that compared the combination of letrozole and misoprostol to mifepristone and misoprostol.

Study settings: China, Egypt, Islamic Republic of Iran

ASSESSMENT OF RESEARCH EVIDENCE

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence

- values
- balance of effects

Sub–PICOs were combined to address the following comparisons:

1. Letrozole + misoprostol versus misoprostol alone
2. Letrozole + misoprostol versus mifepristone + misoprostol
3. Letrozole + mifepristone versus misoprostol alone

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Sub-PICO 1 – Letrozole + misoprostol versus misoprostol alone for medical abortion

Desirable effects:

Fewer women in the intervention group (letrozole + misoprostol) had an ongoing pregnancy compared with the women in the comparison group (misoprostol alone). The certainty of evidence is low.

More women in the intervention group (letrozole + misoprostol) had a successful abortion (uterine emptying without surgical intervention) compared with the women in the comparison group (misoprostol alone). The certainty of evidence is very low.

Expulsion time from initiation of treatment was lower in the intervention group (letrozole + misoprostol) compared with the expulsion time in the comparison group (misoprostol alone).

Fewer women in the intervention group (letrozole + misoprostol) experienced the side-effect of lower abdominal pain compared with the women in the comparison group (misoprostol alone). The certainty of evidence is moderate.

Fewer women in the intervention group (letrozole + misoprostol) experienced the side-effect of nausea compared with the women in the comparison group (misoprostol alone). The certainty of evidence is moderate.

Fewer women in the intervention group (letrozole + misoprostol) experienced the side-effect of vomiting compared with the women in the comparison group (misoprostol alone). The certainty of evidence is low.

Fewer women in the intervention group (letrozole + misoprostol) experienced the side-effect of diarrhoea compared with the women in the comparison group (misoprostol alone). The certainty of evidence is low.

Undesirable effects:

More women in the intervention group (letrozole + misoprostol) experienced the side-effect of fever and chills/rigors compared with the women in the comparison group (misoprostol alone). The certainty of evidence is high.

Summary of judgements:

				X
Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

		x	
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

			x			
Unable to determine	Varies	Large costs	Moderate costs	Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	x Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

Unable to determine	Varies	Reduced	Probably reduced	x Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

	x				
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

The ERRG discussed the 3 days of letrozole may reduce acceptability of this regimen.

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	x Probably Yes	Yes

Sub-PICO 2 – Comparison of letrozole + misoprostol versus mifepristone + misoprostol for medical abortion

Sub-PICO 3 – Comparison of letrozole + mifepristone versus misoprostol alone for medical abortion

There were no studies identified that made the above comparisons.

SUMMARY OF FINDINGS TABLE

SoF Table Sub-PICO1: Letrozole + misoprostol vs misoprostol for medical abortion

Patient or population: Medical abortion
Setting: Egypt, Hong Kong SAR (China) and Islamic Republic of Iran
Intervention: Letrozole + misoprostol
Comparison: Misoprostol

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with misoprostol	**Risk with letrozole + misoprostol**		
Ongoing pregnancy	106 per 1000	**73 per 1000** (33 to 165)	246 (2 RCTs)	⊕⊕◯◯ LOW [a]
Completed without surgical intervention	617 per 1000	**1000 per 1000** (642 to 1000)	673 (6 RCTs)	⊕◯◯◯ VERY LOW [b,c,d,e]
Serious adverse events and complications	not pooled	not pooled	214 (2 RCTs)	-
Expulsion time from initiation of treatment	The mean expulsion time from initiation of treatment was **10.7 mins**	MD **2.42 lower** (3.62 lower to 1.21 lower)	427 (4 RCTs)	⊕⊕◯◯ LOW [f,g]
Side-effects – Lower abdominal pain	388 per 1000	**361 per 1000** (303 to 435)	474 (4 RCTs)	⊕⊕⊕◯ MODERATE [b]
Side-effects – Nausea	327 per 1000	**232 per 1000** (173 to 317)	428 (3 RCTs)	⊕⊕⊕◯ MODERATE [h]
Side-effects – Vomiting	37 per 1000	**28 per 1000** (6 to 122)	214 (2 RCTs)	⊕⊕◯◯ LOW [b,h]
Side-effects – Diarrhoea	190 per 1000	**139 per 1000** (93 to 207)	474 (4 RCTs)	⊕⊕◯◯ LOW [b,h]
Side-effects – Fever	425 per 1000	**434 per 1000** (370 to 510)	428 (3 RCTs)	⊕⊕⊕⊕ HIGH
Side-effects – Chills/rigors	402 per 1000	**406 per 1000** (334 to 494)	428 (3 RCTs)	⊕⊕⊕⊕ HIGH
Side-effects – Total	525 per 1000	**498 per 1000** (351 to 708)	121 (1 RCT)	⊕⊕⊕⊕ HIGH

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with misoprostol	**Risk with letrozole + misoprostol**		
Satisfaction	The mean satisfaction was **0**	not pooled	(0 studies)	-
Cost	The mean cost was **0**	not pooled	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio; **MD:** mean difference

Notes

a. Downgraded two levels; very broad confidence intervals
b. Downgraded one level; several studies has unclear allocation and are generally not reported well
c. Downgraded two levels due to substantial heterogeneity
d. Downgraded one level; effectiveness of the control group ranges from 13% to 97% which indicates heterogeneity but also that some of the setups might not be generalizable
e. Downgraded one level; funnel plot asymmetrical
f. Downgraded one level; two studies with unclear allocation and one not blinded and one with uncertain blinding
g. Downgraded one level; moderate heterogeneity and average expulsion ranges from 9 to 24 hours on average in the control group
h. Downgraded one level; broad confidence intervals

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9. EtD framework for Medical management of missed abortion < 14 weeks

Recommendation 31 (NEW): For missed abortion at < 14 weeks, for individuals preferring medical management: **Recommend** the use of combination mifepristone plus misoprostol over misoprostol alone.

- ❑ Recommended regimen: 200 mg mifepristone administered orally, followed by 800 µg misoprostol administered by any route (buccal, sublingual, vaginal).
- ❑ Alternate regimen: 800 µg misoprostol administered by any route (buccal, sublingual, vaginal).

PICO 13: For a pregnant person with missed abortion at < 14 weeks of gestation, is medical management with mifepristone plus misoprostol a safe, effective and satisfactory/acceptable alternative to medical management with misoprostol alone?

PICO 14: For a pregnant person with missed abortion at < 14 weeks of gestation, is medical management (all regimens) a safe, effective and satisfactory/acceptable alternative to expectant management?

PICO 15: For a pregnant person with missed abortion at < 14 weeks of gestation, is surgical management a safe, effective and satisfactory/acceptable alternative to medical or expectant management? (Full details available in Annex 9 in the guideline)

BACKGROUND

Setting: Global

Perspective: Population

Literature review: A systematic review was undertaken to address this key question. Twenty studies reporting on management for missed abortion were identified by the search strategy. Of these studies, 19 were assessed by the following comparisons:

- Mifepristone + misoprostol versus misoprostol alone
- Medical versus expectant management
- Surgical versus medical/expectant management

Study settings: China, Hong Kong SAR (China), India, Israel, Malaysia, Sweden, Thailand, United Kingdom, USA, Yemen

ASSESSMENT OF RESEARCH EVIDENCE

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

Sub-PICOs were combined to answer the following questions

1. Combination mifepristone + misoprostol versus misoprostol
2. Medical versus expectant management
3. Surgical versus medical/expectant management

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Sub-PICO 1 – Combination mifepristone + misoprostol versus misoprostol

Desirable effects:

Fewer women in the intervention group (mifepristone + misoprostol) had failed expulsion compared with women in the comparison group (misoprostol). The certainty of evidence is low.

More women in the intervention group (mifepristone + misoprostol) had a completed abortion without surgical intervention compared with women in the comparison group (misoprostol). The certainty of evidence is moderate.

Fewer women in the intervention group (mifepristone + misoprostol) had complications resulting in uterine aspiration compared with women in the comparison group (misoprostol). The certainty of evidence is high.

Fewer women in the intervention group (mifepristone + misoprostol) experienced the side-effects of chills, diarrhoea and severe cramping compared with women in the comparison group (misoprostol). The certainty of evidence is high (chills, diarrhoea) and moderate (severe cramping).

More women in the intervention group (mifepristone + misoprostol) expressed satisfaction compared with women in the comparison group (misoprostol). The certainty of evidence is high.

Undesirable effects:

More women in the intervention group (mifepristone + misoprostol) had bleeding requiring transfusion compared with women in the comparison group (misoprostol). The certainty of evidence is low.

More women in the intervention group (mifepristone + misoprostol) experienced a serious adverse event of infection compared with women in the comparison group (misoprostol). The certainty of evidence is low.

More women in the intervention group (mifepristone + misoprostol) experienced side-effects of fatigue, headache, dizziness, nausea, vomiting and fever compared with women in the comparison group (misoprostol). The certainty of evidence is moderate to high.

Draft judgement: Favours the intervention (mifepristone + misoprostol)

Sub-PICO 2 – Medical versus expectant management

Desirable effects:

Fewer women in the intervention group (medical) had failed expulsion (at all follow-up points) compared with women in the comparison group (expectant). The certainty of evidence is high.

More women in the intervention group (medical) had a completed abortion without surgical intervention at 2 days, 7 days, 14 and 31 days follow up compared with women in the comparison group (expectant). The certainty of evidence is moderate to high.

Fewer women in the intervention group (medical) had complications resulting in uterine aspiration compared with women in the comparison group (expectant). The certainty of evidence is moderate.

Fewer women in the intervention group (medical) had complications resulting in hospitalization compared with women in the comparison group (expectant). The certainty of evidence is very low.

Fewer women in the intervention group (medical) experienced the side-effects of bleeding leading to an emergency room (ER) encounter, headache, dyspepsia, vomiting, and lower duration of bleeding compared with women in the comparison group (expectant). The certainty of evidence is high (headache), moderate (vomiting, duration of bleeding) and low (ER encounter, dyspepsia).

More women in the intervention group (medical) expressed satisfaction towards their method compared with women in the comparison group (expectant). The certainty of evidence is moderate.

The complication of blood transfusion was comparable between the intervention and comparison groups. The certainty of evidence is very low.

The occurrence of fever as a side-effect were comparable between the intervention and comparison groups. The certainty of evidence is low

Undesirable effects:

More women in the intervention group (medical) experienced the side-effects of vaginal bleeding, spotting, menstrual cramping, abdominal cramping, nausea and diarrhoea compared with women in the comparison group (expectant). The certainty of evidence is moderate (vaginal bleeding, nausea) and low (spotting, menstrual cramping, abdominal cramping, diarrhoea).

Draft judgement: Favours the intervention (medical management)

Sub-PICO 3 – Surgical versus medical management

Desirable effect:

Fewer women in the intervention group (surgical) had failed expulsion compared with women in the comparison group (medical). The certainty of evidence is moderate.

More women in the intervention group (surgical) had a completed abortion without additional surgical intervention compared with women in the comparison group (medical/expectant). The certainty of evidence is very low.

Fewer women in the intervention group (surgical) had complications resulting in surgical evacuation compared with women in the comparison group (medical/expectant). The certainty of evidence is high.

Fewer women in the intervention group (surgical) had complications requiring transfusion or admissions compared with women in the comparison group (medical/expectant). The certainty of evidence is very low (transfusions) and moderate (admissions).

Fewer women in the intervention group (surgical) experienced the side-effects of nausea, diarrhoea, pain or bleeding compared with women in the comparison group (medical/expectant). The certainty of evidence is moderate (nausea, diarrhoea), low (pain) and very low (bleeding).

More women in the intervention group (surgical) expressed satisfaction towards their method compared with women in the comparison group (medical/expectant). The certainty of evidence is moderate.

The complication of uterine perforation was comparable between the intervention and comparison groups. The certainty of evidence is very low.

Undesirable effect:

More women in the intervention group (surgical) had failed expulsion compared with women in the comparison group (expectant). The certainty of evidence is low.

Draft judgement: Favours the intervention (surgical)

Additional considerations

Cost of treatment was noted in one study. The mean cost differences in pounds sterling were: £1610.30 for surgical, £1192.50 for expectant and £1453.80 for medical management.

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

Important uncertainty or variability	Possibly important uncertainty or variability	x Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

Unable to determine	Varies	Large costs	Moderate costs	x Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	x Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

Unable to determine	Varies	Reduced	Probably reduced	x Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

Unable to determine	Varies	No	Probably No	**x** Probably Yes	Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

SUMMARY OF FINDINGS TABLES

SoF Table 1: Missed abortion – Mifepristone + misoprostol vs misoprostol

Patient or population: Missed abortion
Intervention: Mifepristone + misoprostol
Comparison: Misoprostol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with misoprostol	Risk with mifepristone + misoprostol			
Failed expulsion/ongoing retained products	193 per 1000	**104 per 1000** (41 to 261)	**RR 0.54** (0.21 to 1.35)	115 (1 RCT) [1]	⊕⊕◯◯ LOW [a,b]
Completed without surgical intervention	689 per 1000	**786 per 1000** (703 to 882)	**RR 1.14** (1.02 to 1.28)	412 (2 RCTs) [1,2]	⊕⊕⊕◯ MODERATE [c]
Safety[3] – Uterine aspiration	228 per 1000	**87 per 1000** (48 to 160)	**RR 0.38** (0.21 to 0.70)	297 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Safety – Bleeding resulting in transfusion	7 per 1000	**20 per 1000** (2 to 193)	**RR 3.02** (0.32 to 28.70)	297 (1 RCT) [2]	⊕⊕◯◯ LOW [d]
Safety – Infection	13 per 1000	**14 per 1000** (2 to 95)	**RR 1.01** (0.14 to 7.05)	297 (1 RCT) [2]	⊕⊕◯◯ LOW [d]
Expulsion time from initiation of treatment	The mean expulsion time from initiation of treatment was **0**	not pooled	-	(0 studies)	-
Side-effects – Fatigue	772 per 1000	**795 per 1000** (710 to 895)	**RR 1.03** (0.92 to 1.16)	297 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Side-effects – Headache	483 per 1000	**594 per 1000** (478 to 734)	**RR 1.23** (0.99 to 1.52)	297 (1 RCT)	⊕⊕⊕◯ MODERATE [2,b]

[3] Here and below, "safety" is defined as: serious adverse events and complications.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with misoprostol	Risk with mifepristone + misoprostol			
Side-effects – Dizziness	456 per 1000	**525 per 1000** (420 to 666)	**RR 1.15** (0.92 to 1.46)	297 (1 RCT)	⊕⊕⊕◯ MODERATE [2,b]
Side-effects – Chills	470 per 1000	**460 per 1000** (362 to 587)	**RR 0.98** (0.77 to 1.25)	297 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Side-effects – Nausea	376 per 1000	**380 per 1000** (282 to 507)	**RR 1.01** (0.75 to 1.35)	297 (1 RCT)	⊕⊕⊕⊕ HIGH [2]
Side-effects – Diarrhoea	295 per 1000	**278 per 1000** (192 to 396)	**RR 0.94** (0.65 to 1.34)	297 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Side-effects – Vomiting	154 per 1000	**270 per 1000** (171 to 428)	**RR 1.75** (1.11 to 2.77)	297 (1 RCT)	⊕⊕⊕◯ MODERATE [2,b]
Side-effects – Severe cramping	141 per 1000	**135 per 1000** (76 to 238)	**RR 0.96** (0.54 to 1.69)	297 (1 RCT) [2]	⊕⊕⊕◯ MODERATE [b]
Side-effects – Fever	60 per 1000	**68 per 1000** (28 to 161)	**RR 1.12** (0.47 to 2.67)	297 (1 RCT) [2]	⊕⊕◯◯ LOW [d]
Satisfaction/acceptability	872 per 1000	**890 per 1000** (820 to 968)	**RR 1.02** (0.94 to 1.11)	297 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Cost of treatment	The mean cost of treatment was **0**	not pooled	-	(0 studies)	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio; **MD:** mean difference

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SoF Table 2: Missed abortion – Medical vs expectant management

Patient or population: Missed abortion
Intervention: Medical management
Comparison: Expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with expectant management	**Risk with medical management**			
Failed expulsion/ongoing retained products	293 per 1000	**76 per 1000** (41 to 138)	**RR 0.26** (0.14 to 0.47)	272 (2 RCTs) [1,2]	⊕⊕⊕⊕ HIGH
Failed expulsion/ongoing retained products – 7 days follow-up	711 per 1000	**135 per 1000** (64 to 291)	**RR 0.19** (0.09 to 0.41)	83 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Failed expulsion/ongoing retained products – 31 days follow-up	126 per 1000	**53 per 1000** (19 to 145)	**RR 0.42** (0.15 to 1.15)	189 (1 RCT) [1]	⊕⊕◯◯ LOW [a,b]
Completed without surgical intervention	403 per 1000	**830 per 1000** (689 to 992)	**RR 2.06** (1.71 to 2.46)	406 (5 RCTs) [1,2,3,4,5]	⊕⊕⊕◯ MODERATE [c]
Completed without surgical intervention – 2 days follow-up	159 per 1000	**697 per 1000** (342 to 1000)	**RR 4.38** (2.15 to 8.94)	90 (2 RCTs) [3,5]	⊕⊕⊕⊕ HIGH
Completed without surgical intervention – 7 days follow-up	289 per 1000	**866 per 1000** (521 to 1000)	**RR 2.99** (1.80 to 4.99)	83 (1 RCT) [2]	⊕⊕⊕⊕ HIGH
Completed without surgical intervention – 14 days follow-up	316 per 1000	**799 per 1000** (401 to 1000)	**RR 2.53** (1.27 to 5.05)	44 (1 RCT) [4]	⊕⊕⊕⊕ HIGH
Completed without surgical intervention – 31 days follow-up	579 per 1000	**863 per 1000** (712 to 1000)	**RR 1.49** (1.23 to 1.80)	189 (1 RCT) [1]	⊕⊕⊕◯ MODERATE [a]
Safety[4] – Dilatation and curettage	326 per 1000	**108 per 1000** (55 to 206)	**RR 0.33** (0.17 to 0.63)	189 (1 RCT) [1]	⊕⊕⊕◯ MODERATE [a]

[4] Here and below, "safety" is defined as: serious adverse events and complications.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with expectant management	**Risk with medical management**			
Safety – Received blood transfusion	11 per 1000	**11 per 1000** (1 to 168)	**RR 1.01** (0.06 to 15.92)	189 (1 RCT) [1]	⨁◯◯◯ VERY LOW [a,d]
Safety – Hospitalized	42 per 1000	**32 per 1000** (7 to 139)	**RR 0.76** (0.17 to 3.30)	189 (1 RCT) [1]	⨁◯◯◯ VERY LOW [a,d]
Expulsion time from initiation of treatment	The mean expulsion time from initiation of treatment was **0**	not pooled	-	(0 studies)	-
Side-effects – Emergency room encounter	176 per 1000	**23 per 1000** (2 to 409)	**RR 0.13** (0.01 to 2.32)	36 (1 RCT) [3]	⨁⨁◯◯ LOW [d]
Side-effects – Vaginal bleeding	235 per 1000	**791 per 1000** (325 to 1000)	**RR 3.36** (1.38 to 8.15)	36 (1 RCT) [3]	⨁⨁⨁◯ MODERATE [b]
Side-effects – Vaginal spotting	118 per 1000	**368 per 1000** (88 to 1000)	**RR 3.13** (0.75 to 13.07)	36 (1 RCT) [3]	⨁⨁◯◯ LOW [d]
Side-effects – Menstrual cramping	479 per 1000	**685 per 1000** (556 to 848)	**RR 1.43** (1.16 to 1.77)	258 (3 RCTs) [1,3,5]	⨁⨁◯◯ LOW [a,c]
Side-effects – Abdominal cramping	59 per 1000	**158 per 1000** (18 to 1000)	**RR 2.68** (0.31 to 23.43)	36 (1 RCT) [3]	⨁⨁◯◯ LOW [d]
Side-effects – Headache	564 per 1000	**530 per 1000** (423 to 671)	**RR 0.94** (0.75 to 1.19)	204 (2 RCTs) [1,3]	⨁⨁⨁⨁ HIGH
Side-effects – Dyspepsia	118 per 1000	**105 per 1000** (16 to 668)	**RR 0.89** (0.14 to 5.68)	36 (1 RCT) [3]	⨁⨁◯◯ LOW [d]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with expectant management	**Risk with medical management**			
Side-effects – Nausea	405 per 1000	**445 per 1000** (348 to 567)	**RR 1.10** (0.86 to 1.40)	258 (3 RCTs) [1,3,5]	⊕⊕⊕◯ MODERATE [a]
Side-effects – Vomiting	117 per 1000	**73 per 1000** (30 to 172)	**RR 0.62** (0.26 to 1.47)	204 (2 RCTs) [1,3]	⊕⊕⊕◯ MODERATE [b]
Side-effects – Constipation	118 per 1000	**53 per 1000** (5 to 529)	**RR 0.45** (0.04 to 4.50)	36 (1 RCT) [3]	⊕⊕◯◯ LOW [d]
Side-effects – Diarrhoea	149 per 1000	**204 per 1000** (122 to 339)	**RR 1.37** (0.82 to 2.28)	258 (3 RCTs) [1,3,5]	⊕⊕◯◯ LOW [a,b]
Side-effects – Fever	0 per 1000	**0 per 1000** (0 to 0)	**RR 9.00** (0.51 to 159.43)	54 (1 RCT) [5]	⊕⊕◯◯ LOW [d]
Side-effects – Duration of bleeding	The mean side-effects: Duration of bleeding was **0**	MD **2.3 lower** (4.58 lower to 0.02 lower)	-	168 (1 RCT) [1]	⊕⊕⊕◯ MODERATE [a]
Satisfaction/acceptability	706 per 1000	**734 per 1000** (487 to 1000)	**RR 1.04** (0.69 to 1.57)	36 (1 RCT) [3]	⊕⊕⊕◯ MODERATE [b]
Cost of treatment	The mean cost of treatment was **0**	MD **0** (0 to 0)	-	(1 observational study) [6]	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio; **MD:** mean difference

Notes

a. Downgraded one level due to risk of bias
b. Downgraded one level due to wide confidence intervals
c. Downgraded one level due to I^2 above 50%
d. Downgraded two levels due to very wide confidence intervals

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SoF Table 3: Missed abortion – Surgical versus medical/expectant management

Patient or population: Missed abortion

Intervention: Surgical management

Comparison: Medical/expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with medical/expectant management	**Risk with surgical management**			
Failed expulsion/ongoing retained products – Medical	167 per 1000	**22 per 1000** (10 to 47)	**RR 0.13** (0.06 to 0.28)	695 (4 RCTs) [1,2,3,4]	⊕⊕⊕◯ MODERATE [a]
Failed expulsion/ongoing retained products – Expectant	13 per 1000	**26 per 1000** (7 to 102)	**RR 1.97** (0.50 to 7.79)	461 (1 RCT) [4]	⊕⊕◯◯ LOW [a,b]
Completed without surgical intervention – Medical	670 per 1000	**979 per 1000** (932 to 1000)	**RR 1.46** (1.39 to 1.54)	1487 (8 RCTs) [1,2,4,5,6,7,8,9]	⊕◯◯◯ VERY LOW [a,c]
Completed without surgical intervention – Expectant	580 per 1000	**852 per 1000** (789 to 928)	**RR 1.47** (1.36 to 1.60)	833 (4 RCTs) [4,8,10,11]	⊕◯◯◯ VERY LOW [a,c]
Safety[5] – Surgical evacuation	425 per 1000	**21 per 1000** (9 to 43)	**RR 0.05** (0.02 to 0.10)	972 (2 RCTs) [4,5]	⊕⊕⊕⊕ HIGH
Safety – Uterine perforation	0 per 1000	**0 per 1000** (0 to 0)	**RR 3.00** (0.13 to 70.30)	50 (1 RCT) [5]	⊕◯◯◯ VERY LOW [a,d]
Safety – Transfusion	17 per 1000	**3 per 1000** (1 to 19)	**RR 0.20** (0.04 to 1.14)	1029 (2 RCTs) [2,4]	⊕◯◯◯ VERY LOW [a,d]
Safety – Admissions	124 per 1000	**49 per 1000** (17 to 134)	**RR 0.40** (0.14 to 1.08)	199 (1 RCT) [11]	⊕⊕⊕◯ MODERATE [a,b]
Expulsion time from initiation of treatment	The mean expulsion time from initiation of treatment was **0**	not pooled	-	(0 studies)	-

[5] Here and below, defined as: serious adverse events and complications.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with medical/expectant management	**Risk with surgical management**			
Side-effects – Nausea	480 per 1000	**19 per 1000** (0 to 307)	**RR 0.04** (0.00 to 0.64)	50 (1 RCT) [5]	⨁⨁⨁◯ MODERATE [a]
Side-effects – Diarrhoea	480 per 1000	**19 per 1000** (0 to 307)	**RR 0.04** (0.00 to 0.64)	50 (1 RCT) [5]	⨁⨁⨁◯ MODERATE [a]
Side-effects – Pain	622 per 1000	**510 per 1000** (330 to 778)	**RR 0.82** (0.53 to 1.25)	75 (1 RCT) [1]	⨁⨁◯◯ LOW [a]
Side-effects – Infection	35 per 1000	**39 per 1000** (20 to 74)	**RR 1.13** (0.59 to 2.15)	1029 (2 RCTs) [2,4]	⨁◯◯◯ VERY LOW [a,d]
Side-effects – Bleeding	77 per 1000	**55 per 1000** (13 to 232)	**RR 0.71** (0.17 to 3.02)	107 (1 RCT) [2]	⨁◯◯◯ VERY LOW [a,d]
Satisfaction/acceptability	619 per 1000	**854 per 1000** (718 to 1000)	**RR 1.38** (1.16 to 1.63)	182 (2 RCTs) [1,2]	⨁⨁⨁◯ MODERATE [a]
Cost of treatment	The mean cost of treatment was **0**	not pooled	-	(0 studies) [12,13]	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio; **MD:** mean difference

Notes

a. Downgraded one level due to risk of bias
b. Downgraded one level due to wide confidence intervals
c. Downgraded two levels due to I^2 above 90
d. Downgraded two levels due to very wide confidence intervals

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10. EtD framework for: Self-management of medical abortion

Recommendation 50: For medical abortion at < 12 weeks (using the combination of mifepristone plus misoprostol or using misoprostol alone): **Recommend** the option of self-management of the medical abortion process in whole or any of the three component parts of the process:

- self-assessment of eligibility (determining pregnancy duration; ruling out contraindications)
- self-administration of abortion medicines outside of a health-care facility and without the direct supervision of a trained health worker, and management of the abortion process
- self-assessment of the success of the abortion.

PICO 16: For a pregnant person seeking medical abortion, is self-management of the process of medical abortion (assessing eligibility, administration of mifepristone and/or misoprostol, self-assessing outcome/success), without direct supervision of a trained health worker, a safe, effective and satisfactory/acceptable alternative to medical abortion managed by a trained health worker?

PICO 16a: For a pregnant person seeking medical abortion, is self-assessment of eligibility[6] for medical abortion a safe, effective and satisfactory/acceptable alternative to eligibility assessment by a physician or other trained health-care provider?

PICO 16b: For a person seeking medical abortion, is self-administration of medications for medical abortion, when provided with instructions for their use from a reliable source, a safe, effective and satisfactory/acceptable alternative to administration of medications by a trained health worker?

PICO 16c: For an individual who has undergone medical abortion, is self-assessment of the outcome/success of medical abortion a safe, effective and satisfactory/acceptable alternative to assessment of the outcome/success by a trained health worker?

BACKGROUND – Assessment of eligibility

Setting: Global

Perspective: Population

Literature review: A systematic review on PICO 1.1 and 1.3 serves as the evidence base for this key question. There were four studies that addressed assessment of eligibility. All four studies had the intervention of gestational age determination by last menstrual period (LMP) (self-assessment). Comparators included provider assessment (history and physical exam), ultrasound assessment.

[6] Eligibility criteria defined as: < 12 weeks; no contraindications; no signs or symptoms of ectopic pregnancy.

Study settings: South Africa, United Kingdom, USA

ASSESSMENT OF RESEARCH EVIDENCE – Assessment of eligibility

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

There was no research evidence that allowed for pooled analysis or application of GRADE. We did not populate a SoF table.

Additional considerations

A systematic review that included studies that compared gestational age dating by LMP versus ultrasound (Schonberg et al.) had the following conclusions:

Our results support that LMP can be used to assess gestational age prior to medication abortion at ≤ 63 days. Further research looking at patient outcomes and identifying women eligible for medication abortion by LMP but ineligible by ultrasound is needed to confirm the safety and effectiveness of providing medication abortion using LMP alone to determine gestational age.

Summary of judgements:

		X No difference between the intervention and the comparison		
Favours the comparison	May favour the comparison		May favour the intervention	Favours the intervention

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability
		x	

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

Unable to determine	Varies	Large costs	Moderate costs	Negligible costs or savings	Moderate savings	Large savings
				x		

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention
					x	

Equity:

What would be the impact on health equity?

Judgement (draft)

Unable to determine	Varies	Reduced	Probably reduced	Probably no impact	**x** Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

BACKGROUND – Self-administration

Setting: Global
Perspective: Population
Literature review: A Cochrane systematic review serves as the evidence base for this key question. Eighteen studies (2 RCTs and 16 non-randomized studies [NRS]) were identified and included in the review. All 18 studies focused on women undergoing early medical abortion (≤ 9 weeks gestation). The medication regimen was predominantly the combination of mifepristone and misoprostol.

Study settings: Albania, Bangladesh, China, France, India, Nigeria, Tunisia, Turkey, Viet Nam

ASSESSMENT OF RESEARCH EVIDENCE – Self-administration

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Desirable effects:

(adherence) Fewer women in the intervention group (self-administration) did not complete the protocol compared with women in the comparison group (provider administration). The certainty of evidence is very low.

(adherence) Fewer women in the intervention group (self-administration) did not take the misoprostol on time compared with women in the comparison group (provider administration). The certainty of evidence is low.

(adherence) Fewer women in the intervention group (self-administration) did not return to confirm the abortion status compared with women in the comparison group (provider administration). The certainty of evidence is very low.

Fewer women in the intervention group (self-administration) had unscheduled clinic visits compared with women in the comparison group (provider administration). The certainty of evidence is low.

Fewer women in the intervention group (self-administration) experienced nausea compared with women in the comparison group (provider administration). The certainty of evidence is very low.

Fewer women in the intervention group (self-administration) experienced pain/cramps and diarrhoea compared with women in the comparison group (provider administration). The certainty of evidence is low.

More women in the intervention group (self-administration) expressed satisfaction/high satisfaction compared with women in the comparison group (provider administration). The certainty of evidence is very low.

More women in the intervention group (self-administration) would choose medical abortion again compared with women in the comparison group (provider administration). The certainty of evidence is very low.

More women in the intervention group (self-administration) would recommend this method to a friend compared with women in the comparison group (provider administration). The certainty of evidence is very low.

(adherence) There was no difference in the perfect use between the two groups. The certainty of evidence is low.

There was no difference in the risk of haemorrhage between the two groups. The certainty of evidence is very low.

There was no difference in the hospitalization rate between the two groups. The certainty of evidence is very low.

Undesirable effects:

Fewer women (slightly) in the intervention group (self-administration) experienced successful medical abortion compared with women in the comparison group (provider administration). The certainty of evidence is moderate.

More women (slightly) in the intervention group (self-administration) experienced ongoing pregnancy compared with women in the comparison group (provider administration). The certainty of evidence is very low.

More women in the intervention group (self-administration) experienced any complication requiring surgical intervention compared with women in the comparison group (provider administration). The certainty of evidence is very low.

More women in the intervention group (self-administration) experienced incomplete abortion compared with women in the comparison group (provider administration). The certainty of evidence is low.

More women in the intervention group (self-administration) experienced heavy bleeding, vomiting and fever/chills compared with women in the comparison group (provider administration). The certainty of evidence is low.

More women in the intervention group (self-administration) called the clinic or help line compared with women in the comparison group (provider administration). The certainty of evidence is very low.

Draft judgement:

		X No difference between the intervention and the comparison		
Favours the comparison	May favour the comparison		May favour the intervention	Favours the intervention

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

		x	
Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

				x		
Unable to determine	Varies	Large costs	Moderate costs	Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

					x	
Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

Unable to determine	Varies	Reduced	Probably reduced	Probably no impact	**x** Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

SUMMARY OF FINDINGS TABLE – Self-administration

SoF Table 1: Self-management of medical abortion – Self-administered versus provider-administered

Patient or population: Self-management of medical abortion < 12 weeks

Intervention: Self-administered

Comparison: Provider-administered

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with provider-administered	**Risk with self-administered**			
Success of medical abortion – RCTs	963 per 1000	**954 per 1000** (934 to 973)	**RR 0.99** (0.97 to 1.01)	919 (2 RCTs)	⊕⊕⊕◯ MODERATE [a]
Success of medical abortion – NRS	940 per 1000	**931 per 1000** (912 to 950)	**RR 0.99** (0.97 to 1.01)	10124 (16 observational studies)	⊕⊕◯◯ LOW
Ongoing pregnancy	8 per 1000	**10 per 1000** (5 to 20)	**RR 1.28** (0.65 to 2.49)	6691 (11 observational studies)	⊕◯◯◯ VERY LOW [b]
Any complication requiring surgical intervention	26 per 1000	**56 per 1000** (21 to 150)	**RR 2.14** (0.80 to 5.71)	2452 (3 observational studies)	⊕◯◯◯ VERY LOW [b]
Haemorrhage	4 per 1000	**4 per 1000** (1 to 30)	**RR 1.14** (0.16 to 8.03)	1005 (2 observational studies)	⊕◯◯◯ VERY LOW [b]
Infection	12 per 1000	**3 per 1000** (0 to 58)	**RR 0.23** (0.01 to 4.68)	305 (1 observational study)	⊕◯◯◯ VERY LOW [b]
Requiring hospitalization	0 per 1000	**0 per 1000** (0 to 0)	**RR 1.58** (0.08 to 29.81)	2147 (2 observational studies)	⊕◯◯◯ VERY LOW [b]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with provider-administered	**Risk with self-administered**			
Incomplete	33 per 1000	**37 per 1000** (27 to 51)	**RR 1.12** (0.81 to 1.55)	7645 (12 observational studies)	⨁⨁◯◯ LOW
Nausea	335 per 1000	**285 per 1000** (238 to 342)	**RR 0.85** (0.71 to 1.02)	3874 (7 observational studies)	⨁◯◯◯ VERY LOW [c]
Heavy bleeding	209 per 1000	**218 per 1000** (191 to 251)	**RR 1.04** (0.91 to 1.20)	3272 (5 observational studies)	⨁⨁◯◯ LOW
Vomiting	123 per 1000	**135 per 1000** (110 to 165)	**RR 1.09** (0.89 to 1.34)	3568 (6 observational studies)	⨁⨁◯◯ LOW
Pain/cramps	315 per 1000	**302 per 1000** (271 to 340)	**RR 0.96** (0.86 to 1.08)	1640 (4 observational studies)	⨁⨁◯◯ LOW
Fever/chills	160 per 1000	**173 per 1000** (142 to 209)	**RR 1.08** (0.89 to 1.31)	2643 (4 observational studies)	⨁⨁◯◯ LOW
Diarrhoea	90 per 1000	**86 per 1000** (65 to 116)	**RR 0.96** (0.72 to 1.29)	3286 (4 observational studies)	⨁⨁◯◯ LOW
Satisfied or highly satisfied	909 per 1000	**919 per 1000** (882 to 955)	**RR 1.01** (0.97 to 1.05)	7582 (13 observational studies)	⨁◯◯◯ VERY LOW [b]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with provider-administered	**Risk with self-administered**			
Would choose medical abortion again	536 per 1000	**558 per 1000** (515 to 611)	**RR 1.04** (0.96 to 1.14)	3515 (6 observational studies)	⨁◯◯◯ VERY LOW [b]
Would recommend to a friend	527 per 1000	**595 per 1000** (511 to 690)	**RR 1.13** (0.97 to 1.31)	3513 (6 observational studies)	⨁◯◯◯ VERY LOW [c]
Perfect use	980 per 1000	**980 per 1000** (960 to 1000)	**RR 1.00** (0.98 to 1.02)	2988 (3 observational studies)	⨁⨁◯◯ LOW
Did not complete protocol	20 per 1000	**12 per 1000** (2 to 65)	**RR 0.61** (0.11 to 3.28)	2164 (4 observational studies)	⨁◯◯◯ VERY LOW [b]
Misoprostol not taken on time	19 per 1000	**8 per 1000** (3 to 20)	**RR 0.43** (0.18 to 1.05)	2608 (4 observational studies)	⨁⨁◯◯ LOW
Did not return to confirm abortion status	30 per 1000	**13 per 1000** (1 to 110)	**RR 0.42** (0.05 to 3.69)	2988 (3 observational studies)	⨁◯◯◯ VERY LOW [b]
Called clinic/hotline	117 per 1000	**158 per 1000** (76 to 329)	**RR 1.35** (0.65 to 2.81)	5277 (6 observational studies)	⨁◯◯◯ VERY LOW [c]
Unscheduled clinic visits	83 per 1000	**81 per 1000** (55 to 118)	**RR 0.98** (0.67 to 1.43)	5774 (6 observational studies)	⨁⨁◯◯ LOW

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; NRS: non-randomized study; RCT: randomized controlled trial; **RR:** risk ratio

Notes

a. Downgraded one level due to lack of blinding
b. Downgraded one level due to broad confidence intervals
c. Downgraded one level due to heterogeneity

References:
Gambir K, Kim C, Necastro KA, Ganatra B, Ngo TD. Self-administered versus provider-administered medical abortion. Cochrane Database of Systematic Reviews 2020, Issue 3. Art. No.: CD013181.

BACKGROUND – Outcome assessment

Setting: Global

Perspective: Population

Literature review: A systematic review serves as the evidence base for this key question. There were 10 studies that met the inclusion criteria.

Study settings: Austria, Finland, India, Mexico, Nepal, Norway, South Africa, Sweden, Uzbekistan, Viet Nam

ASSESSMENT OF RESEARCH EVIDENCE – Outcome assessment

For the analysis, research evidence was assessed for the following criteria:

- desirable effects
- undesirable effects
- certainty of evidence
- values
- balance of effects

The overall judgements on the above questions are presented below to be considered by the ERRG in conjunction with information on values, resources, equity, acceptability or feasibility to arrive at recommendations.

Desirable effects:

More women in the intervention group (self-assessment) completed the abortion without surgical intervention compared with women in the comparison group (provider assessment). The certainty of evidence is high.

More women in the intervention group (self-assessment) expressed satisfaction compared with women in the comparison group (provider assessment). The certainty of evidence is low.

Fewer women in the intervention group (self-assessment) experienced serious adverse events such as a blood transfusion or hospitalization compared with women in the comparison group (provider assessment). The certainty of evidence is low.

Fewer women in the intervention group (self-assessment) experienced fever or an infection compared with women in the comparison group (provider assessment). The certainty of evidence is moderate.

There was no difference in the proportion of pregnant persons assessed to have successful abortion between the two groups. The certainty of evidence is high.

Undesirable effects:

More women in the intervention group (self-assessment) experienced ongoing pregnancy compared with women in the comparison group (provider assessment). The certainty of evidence is moderate.

More women in the intervention group (self-assessment) experienced bleeding and pain compared with women in the comparison group (provider assessment). The certainty of evidence is moderate.

Summary of judgements:

			X	
Favours the comparison	May favour the comparison	No difference between the intervention and the comparison	May favour the intervention	Favours the intervention

Additional considerations

The outcome of "accuracy of assessments" was approached differently amongst the included studies. Therefore, we have provided a narrative summary of the findings:

> Several studies compared two different assessments in the same group, similar a setup used in a diagnostic study. In a South African study (Constant et al., 2015) a questionnaire had a sensitivity of between 30 and 50% for detecting incomplete abortion. In another South African study (Constant et al., 2017) a combination of checklist and low sensitivity pregnancy tests provided a sensitivity of between 60 and 70% for diagnosing incomplete abortion by self-assessment. In a Nepalese study (Anderson et al., 2018) a questionnaire identified 44% (sensitivity) of the women requiring additional care. A Mexican study (Anger et al., 2019) compared home hCG with clinical evaluation but found only 1 ongoing pregnancy where no meaningful sensitivity could be calculated. A Vietnamese study (Blum et al., 2016) found sensitivity of 100% of home hCG tests and a decent specificity at 1 week after abortion.

References

Andersen K, Fjerstad M, Basnett I, Neupane S, Acre V, Sharma S, Jackson E. Determination of medical abortion success by women and community health volunteers in Nepal using a symptom checklist. BMC Preg Childbirth. 2018;18:161. doi:10.1186/s12884-018-1804-3.

Anger H, Dabash R, Pena M, Coutino D, Bousieguez M, Sanhueza P, Winikoff B. Use of an at-home multilevel pregnancy test and an automated call-in system to follow-up the outcome of medical abortion. Int J Gynaecol Obstet. 2019;144(1):97–102. doi:10.1002/ijgo.12679.

Blum J, Sheldon WR, Ngoc NT, Winikoff B, Nga NT, Martin R, Van Thanh L, Blumenthal PD. Randomized trial assessing home use of two pregnancy tests for determining early medical abortion outcomes at 3, 7 and 14 days after mifepristone. Contraception. 2016;94(2):115–21. doi:10.1016/j.contraception.2016.04.001.

Constant D, de Tolly K, Harries J, Myer L. Assessment of completion of early medical abortion using a text questionnaire on mobile phones compared with a self-administered paper questionnaire among women attending four clinics, Cape Town, South Africa. Reprod Health Matters. 2015;22(Sup44):83–93. doi:10.1016/S0968-8080(14)43791-1.

Constant D, Harries J, Daskilewicz K, Myer L, Gemzell-Danielsson K. Is self-assessment of medical abortion using a low-sensitivity pregnancy test combined with a checklist and phone text messages feasible in South African primary healthcare settings? A randomized trial. PLoS ONE. 2017;12(6):e0179600. doi:10.1371/journal.pone.0179600.

Additional criteria

Values:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

Judgement (draft)

Important uncertainty or variability	Possibly important uncertainty or variability	x Probably no important uncertainty or variability	No important uncertainty or variability

Resources required:

How large are the resource requirements (costs)?

Judgement (draft)

Unable to determine	Varies	Large costs	Moderate costs	x Negligible costs or savings	Moderate savings	Large savings

Cost-effectiveness:

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

Judgement (draft)

				x		
Unable to determine	Varies	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention

Equity:

What would be the impact on health equity?

Judgement (draft)

					x	
Unable to determine	Varies	Reduced	Probably reduced	Probably no impact	Probably increased	Increased

Acceptability:

Is the intervention acceptable to key stakeholders?

Judgement (draft)

					x
Unable to determine	Varies	No	Probably No	Probably Yes	Yes

Feasibility:

Is the intervention feasible to implement?

Judgement (draft)

Unable to determine	Varies	No	Probably No	Probably Yes	x Yes

SUMMARY OF FINDINGS TABLE – Outcome assessment

SoF Table: Self-management of medical abortion – Self-assessment versus provider assessment for outcome of abortion

Patient or population: Self-management of medical abortion < 12 weeks – outcome of abortion
Intervention: Self-assessment of outcome of abortion
Comparison: Provider assessment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with provider-assessment	**Risk with self-assessment**			
Proportion of pregnant persons assessed to have successful abortion	940 per 1000	**940 per 1000** (922 to 969)	**RR 1.00** (0.98 to 1.03)	1632 (2 RCTs) [1,2]	⊕⊕⊕⊕ HIGH
Proportion of pregnant persons assessed to have successful abortion – NRS	954 per 1000	**916 per 1000** (859 to 983)	**RR 0.96** (0.90 to 1.03)	237 (1 observational study) [3]	⊕⊕◯◯ LOW
Accuracy of these assessments when measured against an independent verifier and/or diagnostic standard – not reported				-	-
Ongoing pregnancy rate	4 per 1000	**11 per 1000** (3 to 37)	**RR 3.01** (0.90 to 10.02)	1632 (2 RCTs) [1,2]	⊕⊕⊕◯ MODERATE [a]
Completed without surgical intervention	954 per 1000	**963 per 1000** (944 to 982)	**RR 1.01** (0.99 to 1.03)	1632 (2 RCTs) [1,2]	⊕⊕⊕⊕ HIGH
Safety[7] – Blood transfusion	3 per 1000	**1 per 1000** (0 to 22)	**RR 0.31** (0.01 to 7.53)	700 (1 RCT) [2]	⊕⊕◯◯ LOW [b]
Safety – Hospitalization	3 per 1000	**1 per 1000** (0 to 22)	**RR 0.31** (0.01 to 7.53)	700 (1 RCT) [2]	⊕⊕◯◯ LOW [b]
Safety – Surgery beyond evacuation – not measured	-	-	-	-	-

[7] Here and below, "safety" defined as: serious adverse events.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with provider-assessment	**Risk with self-assessment**			
Safety – Death – not reported	-	-	-	-	-
Expulsion time from initiation of treatment – not reported	-	-	-	-	-
Side-effects – Infection including fever	39 per 1000	**25 per 1000** (14 to 42)	**RR 0.63** (0.36 to 1.08)	1632 (2 RCTs) [1,2]	⨁⨁⨁◯ MODERATE [a]
Side-effects – Bleeding	25 per 1000	**66 per 1000** (31 to 139)	**RR 2.66** (1.25 to 5.64)	731 (1 RCT) [2]	⨁⨁⨁◯ MODERATE [a]
Side-effects – Pain	33 per 1000	**52 per 1000** (26 to 106)	**RR 1.58** (0.78 to 3.21)	731 (1 RCT) [2]	⨁⨁⨁◯ MODERATE [a]
Physical and emotional experience (side-effects, positive and negative emotions, internalized stigma), knowing when to seek medical care (unscheduled visits; phone calls to the clinics, emergency visits) – not reported	-	-	-	-	-
Satisfaction/acceptability including reports of overall satisfaction with self-management	757 per 1000	**893 per 1000** (538 to 1000)	**RR 1.18** (0.71 to 1.96)	1276 (2 RCTs) [1,2]	⨁⨁◯◯ LOW [c]
Cost (comparative and cost to the patient) – not reported	-	-	-	-	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RR:** risk ratio

Notes

a. Downgraded one level due to broad confidence intervals

b. Downgraded two levels due to very broad confidence intervals

c. Downgraded two levels due to heterogeneity and therefore broad confidence intervals. It is likely that lack of blinding can influence this outcome. Iyengar et al. shows no difference whereas Oppegaard et al. indicates that self-management is favourable. In the paper Oppegaard (Nordic countries) reports on how many would prefer self-management whereas Iyengar et al. (India) reports on satisfaction with follow-up methods.

References

1. Oppegaard KS, Qvigstad E, Fiala C, Heikinheimo O, Benson L, Gemzell-Danielsson K. Clinical follow-up compared with self-assessment of outcome after medical abortion: a multicentre, non-inferiority, randomised, controlled trial. Lancet. 2015.
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3. Mählck T, Bäckström CG. Follow-up after early medical abortion: Comparing clinical assessment with self-assessment in a rural hospital in northern Norway. Eur J Obstet Gynecol Reprod Biol. 2017.