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Society of Family Planning Clinical Recommendation: Medication abortion between 14 0/7 and 27 6/7 weeks of gestation★,☆,☆☆ Jointly developed with the Society for Maternal-Fetal Medicine

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ABSTRACT

The objective of this Clinical Recommendation is to review relevant literature and provide evidence-based recommendations for medication abortion between 14 0/7 and 27 6/7 weeks of gestation, with a focus on mifepristone-misoprostol and misoprostol-only regimens. We systematically reviewed PubMed articles published between 2008 and 2022 and reviewed reference lists of included articles to identify additional publications. See Search Strategy for more details. Several randomized trials of medication abortion between 14 0/7 and 27 6/7 weeks of gestation demonstrate that mifepristone 200 mg orally before misoprostol increases effectiveness (complete abortion at 24 or 48 hours) compared to misoprostol only. Studies continue to evaluate different doses, routes, and dosing intervals for misoprostol. If mifepristone is unavailable, several misoprostol regimens with individual doses of at least 200 mcg or more are effective. Adjunctive osmotic dilators are of limited benefit. It is important to individualize care, with consideration to reducing misoprostol dose in low-resource settings or at 24 0/7 weeks of gestation or later (or equivalent uterine size). Misoprostol in the setting of two or more previous cesarean sections is associated with increased risk of uterine rupture compared to one or none, but risk remains low. Most contraceptives can be started during or immediately following abortion. Appropriately trained and credentialed advanced practice clinicians can provide medication abortion between 14 0/7 and 27 6/7 weeks of gestation with appropriate backup within the confines of local regulations and licensure.

1. Introduction and background

Medication abortion affects expulsion of the fetus and placenta from the uterus without instrumentation. In settings without experienced dilation and evacuation clinicians, medication abortion is the primary method of later abortion care [1–3]. Ideally, individuals undergoing abortion care should have a treatment choice—either medication or procedural abortion—using a shared decision-making model with their care providers. Though important for all patients, those experiencing pregnancy complications have emphasized the importance of being able to choose their method of pregnancy termination [4]. Treatment choice is often limited to procedural abortion, in part due to the segregation of US abortion care to outpatient ambulatory clinics. Abortion method is

★ This document uses the term medication abortion to refer to any abortion with medications (including mifepristone and misoprostol, misoprostol only, or other abortifacientor medication) used with the intention of ending and expelling a pregnancy regardless of the setting, context, or pregnancy duration. Historically, a variety of terms have been used to refer to medication abortion: medical abortion, RU486, abortion pill(s), abortion with pills, pharmaceutical abortion, medicinal abortion, no test abortion, no touch abortion, history-based screening, self-managed abortion, advance provision, medically induced, medical/medication induction, and induction termination.

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often further constrained by access to insurance, system barriers, socioeconomic status, educational attainment, and age, among other factors.

This Clinical Recommendation reviews relevant literature and provides evidence-based recommendations for medication abortion between 14 0/7 and 27 6/7 weeks of gestation, with focus on mifepristone-misoprostol and misoprostol-only regimens. Similar techniques may be used beyond 27 6/7 weeks of gestation but will not be explicitly addressed in this guideline.

Comparing or combining data from studies investigating medication abortion is challenging due to inconsistent reporting in studies and confounding factors:

- *Gestational duration*—reports may include various gestational duration ranges or base regimens on uterine size (where ultrasound is not readily available).
- *Additional interventions*—osmotic dilator use or routine dilation and aspiration after fetal expulsion may complicate data interpretation.
- *Fetal demise status*—some studies include patients both with and without spontaneous fetal demise. Fetal demise has been associated with shorter abortion times in some studies.
- *Procedure length*—no standardized definition or terminology for medication abortion length exists. This guideline uses "abortion time," defined as the interval from the start of uterotonic medication, usually prostaglandin (i.e., not mifepristone), until expulsion of all pregnancy tissue.
- *Successful abortion*—no universally accepted definition of successful abortion exists. Some studies define success as complete abortion without the need for procedural intervention. Other studies define success as fetal and placental expulsion within a prespecified time frame, usually 24 or 48 hours. For the purpose of this guideline, a successful abortion is defined as expulsion of the entire pregnancy by the medical method intended without additional intervention.
- *Failed medication abortion*—no accepted definition of failure exists. Many studies arbitrarily set a specific time frame, usually 24 or 48 hours or if a procedural intervention is necessary to remove the fetus, placenta, or both. Time frames do not correspond to increased risk of complications, nor do they indicate that success will not eventually occur. For the purpose of this guideline, a failed abortion is the counterpart to our defined successful abortion.

1.1. Medication abortion agents

Medication abortion regimens cause uterine contractions sufficient to expel the fetus and placenta. The prostaglandin E1 (PGE1) analogs misoprostol and gemeprost, either alone or in combination with other agents, have supplanted most other methods because of high effectiveness and ease of use. Relevant pharmacologic agents include:

- *Mifepristone:* an antiprogestin taken orally before prostaglandin analog administration. It competitively binds progesterone receptors, causing endometrial decidual degradation, cervical softening and dilation, and an increase in myometrial sensitivity to prostaglandin effects [5].
- *Misoprostol:* a PGE1 analog that is stable at room temperature and inexpensive. Although misoprostol is U.S. Food and Drug Administration labeled for oral ingestion, it is effective for abortion when administered vaginally, sublingually, and buccally [6]. PGE1 analogs bind to smooth muscle cells in the uterus, causing contractions. Cervical dilation is produced via collagen degradation in the stromal connective tissue and reduced cervical tone in response to contractions [7].
- *Gemeprost*: a PGE1 analog that is chemically similar to misoprostol. It is formulated as a vaginal suppository that requires refrigeration. Gemeprost is not available in the United States.
- *Oxytocin:* used in doses higher than for obstetric term induction of labor, presumably because of the relative paucity of oxytocin receptor expression earlier in gestation. Oxytocin increases contraction frequency, baseline tone (transiently), and contraction amplitude (strength) [8].

2. Clinical questions

2.1. What is the effectiveness of medication regimens for medication abortion between 14 0/7 and 27 6/7 weeks of gestation?

2.1.1. Mifepristone and misoprostol: combined regimens for medication abortion

2.1.1.1. Effectiveness. Mifepristone followed by a PGE1 analog is the most effective regimen for medication abortion between 14 0/7 and 27 6/7 weeks of gestation [9–13]. A systematic review and meta-analysis found that the combination regimen compared to misoprostol only resulted in lower ongoing pregnancy rates at 24 hours (4% vs 32%) and 48 hours (2% vs 10%). Combination regimens also have a shorter mean time to complete expulsion, with mean abortion times ranging from 5.8 hours to 8 hours [14]. Table 1 summarizes several studies' key outcomes for mifepristone/misoprostol compared to misoprostol-only regimens.

2.1.1.2. Mifepristone and misoprostol: recommended doses, routes, and dosing intervals

2.1.1.2.1. Mifepristone dose. Mifepristone 200 mg is as effective as 600 mg when used in a combination with misoprostol [14]. In a randomized controlled trial (RCT) of mifepristone 600 mg compared with 200 mg, each followed 36 to 48 hours later by vaginal misoprostol, the two regimens had the same mean abortion times: 6.9 h [14].[1] Table 2 summarizes selected studies comparing the dose and frequency of combination mifepristone-misoprostol regimens.

2.1.1.2.2. Timing between mifepristone and first misoprostol dose. Traditionally, regimens used a 36 to 48 hours interval between mifepristone and the first PGE1 dose. Three RCTs of medication abortion ranging from 13 to 16–13–24 weeks of gestation compared mifepristone dosed 1 or 2 days prior to misoprostol [30,23,28]. A 2020 meta-analysis of these RCTs found no significant difference in the induction-to-abortion time between 1- or 2-day mifepristone-misoprostol intervals (odds ratio 1.44, 95% confidence interval [CI] −0.26 to 1.70) or the successful abortion rate (odds ratio 0.76, 95% CI 0.32–1.80) [26]. A 1-day interval between mifepristone and misoprostol may increase the time to fetal expulsion slightly compared to a 2-day interval, but the time to successful abortion is still reduced compared to PGE1 analog alone.

Shorter intervals have been explored. An RCT found that simultaneous mifepristone and buccal misoprostol resulted in lower expulsion rates within 24 hours of taking misoprostol (85.0% vs 94.4%, risk ratio (RR 1.11), longer median misoprostol treatment times (13 vs 7.7 hours; $p < 0.001$), and more misoprostol doses (5 vs 3; $p < 0.001$) compared to waiting 24 hours after mifepristone for misoprostol administration. However, by 48 hours after the first misoprostol dose, both regimens were effective (95.7% [simultaneous]−96.8% [24-hour interval]-RR 1.01) [31].

2.1.1.2.3. Misoprostol regimens (dose, route, timing) after administration of mifepristone. Misoprostol regimens after mifepristone vary considerably. A commonly studied regimen is

[1] Misoprostol is the most commonly studied PGE1 analog for medication abortion, but gemeprost following mifepristone 200 or 600 mg has also proven effective with an average time to fetal expulsion of 7.5 hours [23].

mifepristone 200 mg followed 36 to 48 hours later by misoprostol 800 mcg vaginally, then an additional 400 mcg vaginally every 3 hours [24,32,33].

Recent evidence has suggested that loading doses (> 200 mcg) do not hasten abortion times or improve outcomes. Several studies cited in Table 1 demonstrate the effectiveness of mifepristone 200 mg followed by misoprostol 200 mcg every 3 to 4 hours, with or without a 400 mcg loading dose (Table 1).

Lower doses of misoprostol may also be effective, particularly for greater than 24 weeks of gestation. Some experts note that lower doses may decrease the risk of uterine rupture in a scarred uterus.

Previous World Health Organization recommendations advised re-evaluation of the patient after five doses of misoprostol. If a patient is otherwise doing well, then continue the regimen until complete expulsion, which usually occurs by 48 hours. Studies using an "unlimited dosing" protocol for misoprostol (400 mcg sublingually or buccally every 3 hours, 24–48 hours after mifepristone) for abortions 13 to 22 weeks report high effectiveness, tolerability, and safety. Patients are unlikely to need more than six doses of misoprostol [34,35]. Because most patients will experience complete abortion < 48 hours after the first misoprostol dose, clinical decision-making can be individualized in instances where continued misoprostol dosing is needed past 48 hours. There is no clear safety rationale for a "break" or to stop after five consecutive doses of misoprostol.

2.1.1.2.4. Misoprostol route of administration. Vaginal administration is associated with shorter abortion times compared to oral administration [32,36–39]. Side effect incidence is lower for vaginal use, except for transient fever [39]. Data are more limited for the buccal route. A small study (n = 114) demonstrated little difference in median abortion times comparing buccal and vaginal use (15 vs 12 hours; p = 0.44) [40].

Sublingual administration appears similar in effectiveness to vaginal administration but with a greater side effect incidence [41–43]. Table 3 summarizes select studies comparing misoprostol administration routes in combined regimens.

Evidence regarding patient acceptability is mixed, with one study reporting preference for buccal or sublingual over vaginal and another study finding no difference in acceptability between these routes [37,40]. The most common reasons cited for not liking vaginal administration were pain and inconvenience with insertion [37].

Studies use a range of doses (100–800 mcg per dose), intake routes, and dosing schedules, and many regimens incorporate a higher initial 'loading' dose [48–50]. Several nonoral misoprostol regimens demonstrate effectiveness when used after mifepristone. Insufficient data exist to strongly recommend one regimen over others, but the data seem to support a minimum effective PGE1 dose of 400 mcg for any administration route for a combined regimen.

2.1.1.2.5. Misoprostol-only regimen. If using a misoprostol-only regimen, higher doses (400 and 600 mcg) are more effective [51]. Misoprostol doses of 400 and 600 mcg with either a 4- or 6-hour dosing interval have a similar time to abortion (11–12 hours) [52]. One study (N = 150, 18–30 weeks of gestation) found similar mean abortion times and success rates at 24 and 48 hours when starting with a loading dose (misoprostol 600 mcg vaginally followed by misoprostol 200 mcg vaginally every 6 hours) compared to misoprostol 400 mcg vaginally every 6 hours. Both regimens were more effective than misoprostol 200 mcg every 6 hours [51]. Side effects were more common in the loading dose group, leading authors to conclude that 400 mcg was the preferred dose. Misoprostol-only regimens' effectiveness is included in Table 1.

When a misoprostol 400 mcg dose with dosing 3-hour intervals is compared to the same dose every 6 or 8 hours at 14 0/7 to 22 6/7 weeks of gestation, abortion times are shorter and effectiveness higher (78%–98%) with a 3-hour dosing schedule [53,54].

2.1.2. Effect of gestational duration on success of regimens

Mifepristone in addition to misoprostol results in faster time to complete abortion in all gestational duration ranges [15,16]. Allanson et al. found that mifepristone's effect on time to abortion was similar for pregnancies < 20 weeks of gestation vs 20 weeks of gestation or more [55]. The misoprostol dosing regimen in this study was 600 mcg vaginally, then 400 mcg sublingually every 3 hours. The combined regimen added mifepristone 200 mg 24 hours before the first misoprostol dose.

2.1.3. Medication abortion beyond 24 weeks' gestation

Medication abortion beyond 24 weeks of gestation accounts for a small percentage of abortions, and studies include limited data past 22 to 24 weeks of gestation. Three relevant studies included in this document used misoprostol 200 mcg buccally or vaginally every 3 hours (Table 1) [55,22,20]. Two reported no serious adverse events [20,22]. The third, Allanson et al., reported several adverse events, but the majority were retained placenta (the weeks of gestation of these cases were not noted). Most adverse events occurred in the misoprostol-only group [55].

2.1.4. Alternate agents

Overall, misoprostol appears to be more effective than carboprost (PGF 2α), dinoprostone (PGE2), high-dose oxytocin, and ethacridine lactate when adequate doses are used [21]. Both PGE2 and PGF 2α analogs are expensive and require refrigeration, in contrast to misoprostol, which is inexpensive and stable at room temperature.

Oxytocin is less effective than misoprostol for medication abortion likely due to the paucity of oxytocin receptors at < 20 weeks of gestation. Oxytocin is associated with longer medication to complete abortion intervals compared to mifepristone and PGE1 regimens (11.3 ± 7.4 hours vs 7.0 ± 4.9 hours; p < 0.001) and higher risk of side effects such as hemorrhage [56–58].

Nonetheless, high-dose oxytocin is an option when misoprostol is not available or when there is a desire to avoid prostaglandins [59,60]. Oxytocin requires intravenous access and a potentially more complicated regimen. Several regimens using only oxytocin for medication abortion have been described; one begins with oxytocin 100 units infused over 3 hours followed by 1 hour without oxytocin to allow diuresis for water intoxication prevention, then increased 50 units per 3 hours until fetal expulsion is achieved, to a maximum of 300 units over 3 hours [61].

2.2. What is the safety of medication abortion at 14 0/7 to 27 6/7 weeks of gestation?

2.2.1. Safety

Retained placenta is the most common complication that can occur with medication abortion between 14 0/7 and 27 6/7 weeks of gestation (12%–33%) and can be treated safely with aspiration without subsequent hemorrhage or need for transfusion [62,63]. Studies are too small to determine if this occurs more at certain gestational durations. An RCT found that placental retention rates were reduced to 10% with routine administration of oxytocin 10 units after fetal delivery compared with misoprostol 600 mcg orally or expectant management (29% and 31%, respectively) [64]. After medication abortion with regimens that include misoprostol, it is safe to wait at least 4 hours after fetal expulsion for placental delivery. Using this approach, a retrospective study of second-trimester misoprostol abortion (18–23 weeks of gestation, misoprostol dosed every 6 hours) reported an operative intervention rate of 6% for retained placenta [65]. The majority of these procedures were performed to expedite hospital discharge rather than because of bleeding; waiting and medically managing with ongoing misoprostol dosing for more than 4 hours was not associated with increased morbidity (in contrast to term pregnancy where a delay in

Table 1
Selected comparisons of the efficacy of combination mifepristone-misoprostol to misoprostol alone[a]

Author, year, country[b]	Participants (*n*)	Gestational duration (wk)	Intervention 1	Ongoing pregnancy at 24 h from first miso dose (%)	Ongoing pregnancy at 48 h from first miso dose (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Intervention 2	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Serious adverse events[c]
Akkenapally et al. [15], 2016, India	200	14–20	200 mg mifepristone oral 24 h → 600 mcg misoprostol vaginal loading dose → 400 mcg misoprostol sublingual every 3 h up to five doses	4	NA	99	6.19 (2.70)	Incidence of side effects reported as "similar in both groups": nausea (7), vomiting (8), diarrhea (2), fever (7), shivering (5)	600 mcg misoprostol vaginal loading dose → 400 mcg misoprostol sublingual every 3 h up to five doses	11	NA	97	10.67 (3.96)	Incidence of side effects reported as "similar in both groups": nausea (7), vomiting (8), diarrhea (2), fever (7), shivering (5)	Not reported
Dabash et al. [16], 2015, Tunisia	120	14–21	200 mg mifepristone oral 24 h → 400 mcg misoprostol buccal every 3 h up to five doses	11.7	8.3	95	10.4 (6.6)	Nausea (46.7), vomiting (43.3), diarrhea (41.7), chills (38.3), headache (23.3)	Placebo 24 h → 400 mcg misoprostol buccal every 3 h up to five doses	51.7	28.3	78.3	20.6 (9.7)	Nausea (60.0), vomiting (48.3), diarrhea (55.0), chills (36.7), headache (20.0)	Not reported
Kapp et al. [17], 2007, The United States	64	18–23	200 mg mifepristone oral 24 h → 400 mcg misoprostol buccal loading dose → 200 mcg misoprostol buccal every 6 h	3	NA	96.9	10 (95% CI 8–12)	Nausea (56.0), vomiting (42.0)	Placebo 24 h → 400 mcg misoprostol buccal loading dose → 200 mcg misoprostol buccal every 6 h	28	NA	95.7	18 (95% CI 15–22)	Nausea (49.9), vomiting (40.0%)	One patient in the mifepristone arm required blood transfusion after heavy bleeding due to retained placenta, and one patient in the placebo arm required D&E for heavy bleeding
Kulkarni [18], 2014, India	60	13–20	200 mg mifepristone oral 48 h → 400 mcg misoprostol vaginal loading dose → 200 mcg misoprostol vaginal every 6 h	0	0	Not reported	8.25 (SD not reported)	Chills (10.0), fever (23.3)	Placebo 48 h → 400 mcg misoprostol vaginal loading dose → 200 mcg misoprostol vaginal every 6 h	53.5	10	Not reported	24 (SD not reported)	Chills (56.6), fever (63.3)	None reported
Mukhopadhyay et al. [19], 2012, India	122	12–20	200 mg mifepristone oral 48 h → 400 mcg misoprostol vaginal loading dose → 200 mcg misoprostol vaginal every 4 h up to five doses	Not reported	0	90	6.62 (2.34)	Vomiting (6.7), diarrhea (0), fever (3.3)	Placebo 48 h → 400 mcg misoprostol vaginal loading dose → 200 mcg misoprostol vaginal every 4 h up to five doses	Not reported	3.23	85.49	12.19 (3.96)	Vomiting (3.2), diarrhea (3.2), fever (9.7)	None reported

(*continued on next page*)

Table 1 (*continued*)

Author, year, country[b]	Participants (*n*)	Gestational duration (wk)	Intervention 1	Ongoing pregnancy at 24 h from first miso dose (%)	Ongoing pregnancy at 48 h from first miso dose (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Intervention 2	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Serious adverse events[c]
Nagaria and Sirmor [20], 2011, India	200	12–28	200 mg mifepristone oral 12 h → 600 mcg misoprostol vaginal loading dose → 300 mcg misoprostol vaginal every 3 h up to doses	0	0	95	6.72 (2.26)	Nausea/ vomiting (10), fever (18), diarrhea (2)	600 mcg misoprostol vaginal loading dose → 300 mcg misoprostol vaginal every 3 h up to five doses	Not reported (15 h cutoff)	Not reported (15 h cutoff)	90	12.93 (3.4)	Nausea/ vomiting (14), fever (23), diarrhea (2)	None reported
Ngoc et al. [17], 2011, Vietnam	260	14–21	200 mg mifepristone oral 24 h → 400 mcg misoprostol buccal every 3 h up to doses	Not reported (15 h cutoff)	Not reported (15 h cutoff)	96.7	8.1 (2.8)	Nausea (44.2), vomiting (31.8), chills (16.3), diarrhea (41.9), headache (14.0)	Placebo 24 h → 400 mcg misoprostol buccal every 3 h up to five doses	Not reported (15 h cutoff)	not reported (15 h cutoff)	98	10.6 (2.5)	Nausea (38.0), vomiting (24.8), chills (15.5), diarrhea (48.1), headache (10.9)	None reported
Bracken et al. [21], 2020, Vietnam, Mexico	176	14–28	200 mg mifepristone oral 24 h → 200 mcg misoprostol buccal every 3 h for up to 16 doses	Not reported	82.2	Not reported	7 (± 5)	Nausea (15.6), vomiting (3.3), chills (15.6), diarrhea (4.4), headache (8.9)	Placebo 24 h → 200 mcg misoprostol buccal every 3 h for up to 16 doses	Not reported	81.4	Not reported	12 (± 13)	Nausea (18.6), vomiting (7.0), chills (5.8),diarrhea (8.1), headache (7.0)	None reported
Allanson et al. [22], 2021, Australia	66	14–28	200 mg mifepristone oral 24 h → 400 mcg misoprostol vaginally every 6 h if ≤24 wk gestation, 200 mcg misoprostol vaginally every 4 h if >24)	0	0	Not reported	6.8 (IQR 5.3–10.6)	Not reported	Placebo 24 h → 400 mcg misoprostol vaginally every 6 h if ≤24 wk gestation, 200 mcg misoprostol vaginally every 4 h if >24)	11.7	Not reported	Not reported	10.5 (IQR 8.0–15.0)	Not reported	Mifepristone arm: 1 blood transfusion; Readmission: 2 in mifepristone arm (retained products of conception and endometritis), 3 in placebo arm (retained products of conception).

CI, confidence interval; IQR, interquartile range; NA, not available. SD, standard deviation.

[a] Adapted from Whitehouse et al. [12] with update to include studies past May 2017 and additional information.

[b] All studies are RCTs unless otherwise noted.

[c] Serious adverse events include hospitalization postabortion, infection, blood transfusion, need for postevacuation surgery, or death.

placental delivery is associated with increased risk for complications).

Events such as blood transfusion, readmission, and infection are uncommon (Tables 1–3). Existing studies demonstrate a 2% to 20% hemorrhage incidence related to medication abortion, but blood transfusion is rare [63,66].

2.2.2. Side effects

The medications used in medication abortion are well tolerated, but medication abortion, like any process involving contractions, can be painful. Tables 1–3 list side effects.

2.2.2.1. Mifepristone. Side effects associated with mifepristone include vaginal bleeding, uterine cramping, and headaches [67]. The addition of mifepristone to a prostaglandin appears to lower nausea and vomiting rates compared to prostaglandin alone, possibly because the abortion time is shorter and fewer prostaglandin doses are needed [68].

2.2.2.2. Misoprostol/ PGE1. Misoprostol is associated with several side effects, including nausea/vomiting, diarrhea, and transient chills and fever. Administration route, dose, and cumulative misoprostol dose influence side effect frequency [69]. Transient pyrexia occurs in 5% to 10% of patients. Fever may be difficult to differentiate from infection but resolves within several hours of stopping misoprostol. Health care clinicians should maintain a high index of suspicion for infection and treat appropriately, given the morbidity associated with untreated infection. Evaluation could include clinical and laboratory evaluation and/or judicious antibiotic use, though practices may vary by setting. A fever persisting for several hours after misoprostol administration should raise concern for possible infection. Vaginal misoprostol administration may result in higher transient fever rates compared to sublingual administration [41,42]. Studies on misoprostol use for first trimester abortion have shown dramatically lower rates of nausea, vomiting, diarrhea, and chills in those who receive vaginal vs oral misoprostol [70,71].

2.3. What are the contraindications to medication abortion from 14 0/7 to 27 6/7 weeks of gestation?

Very few absolute contraindications exist to medication abortion from 14 0/7 to 27 6/7 weeks of gestation. Allergies are rare. Mifepristone retains some contraindications to use in its package insert (e.g., current long-term systemic corticosteroid therapy, inherited porphyria). Patients with these comorbidities may still undergo medication abortion with mifepristone and misoprostol, but they may need more monitoring or management of their condition. Alternatively, misoprostol only or high-dose oxytocin can be used in the rare circumstances where mifepristone or mifepristone and misoprostol are contraindicated. Most patients' co-existing conditions can be safely monitored and managed during a medication abortion, which typically occurs in a medical facility. Care should be individualized to the patient's context and comorbidities.

Clinicians should use particular caution in individuals with suspected placenta accreta spectrum, a prior uterine scar (see below), or placenta previa. Patients with risk factors for placenta accreta spectrum (e.g., placenta previa in the setting of previous cesarean deliveries, particularly multiple cesarean deliveries, in vitro fertilization pregnancies, advanced maternal age) should be screened with ultrasound [72,73]. If concerns exist regarding abnormal placentation, the patient should be referred to a tertiary care center where adjacent emergency services, such as blood bank, surgical services, or interventional radiology, are immediately available. Management strategies are not standardized and depend on imaging findings, reproductive desires, and available interventions [74,75]. A trial of medication abortion may be reasonable depending on the situation and patient preference, but if high certainty of abnormal placentation exists, gravid hysterectomy is the least morbid option [74,75].

Case reports exist demonstrating successful medication abortions in patients with placenta previa, but care teams must prepare for and patients made aware of increased hemorrhage risk, transfusion, and emergency surgical interventions [76,77]. This risk likely increases with weeks of gestation and placental volume, but the body of evidence is too small to discern a gestational duration cutoff. If bleeding occurs, clinicians may be able to remove the placenta via electric or manual vacuum aspiration and then continue with the medication abortion, thereby removing the source of bleeding and avoiding a laparotomy. Conversion to dilation and evacuation is also an option, if technically feasible.

2.4. Does adjunctive use of osmotic dilators, mechanical dilators, or amniotomy affect outcomes?

2.4.1. Osmotic dilators

Historic medication abortion studies using natural prostaglandins found that placing osmotic dilators 4 to 24 hours before misoprostol administration decreased abortion time [78–83]. This adjunctive benefit does not occur when modern prostaglandin analogs are used. Two randomized studies examined the use of cervical preparation with laminaria at the time of misoprostol induction [48,84]. Both studies demonstrated that laminaria placement increased the time to abortion; this difference was statistically significant in one of the trials [48,84]. Patients who received laminaria had increased analgesic needs during the abortion [84]. Few studies examine the use of osmotic dilators prior to abortion with misoprostol only. One study examined overnight laminaria with subsequent misoprostol vs misoprostol-only and reported longer time to abortion (6 hours more) and lower completion rates by 24 hours (61% vs 91%) with the addition of dilators [85]. Dilators have also been studied in addition to mifepristone and misoprostol, and time to abortion was significantly longer for those with dilators (18 vs 10 hours) [86]. In contrast, one study of second-trimester fetal demise (publication did not specify weeks of gestation) showed that synthetic osmotic dilators in conjunction with mifepristone and misoprostol may reduce time to complete abortion [87].

Compared with misoprostol only, laminaria in conjunction with high-dose oxytocin also results in lower success rates (defined as complete abortion at 48 hours after the first intervention) and longer mean abortion duration (22 vs 14 hours) [88,89].

2.4.2. Mechanical dilation: intrauterine (transcervical) Foley catheter

Intrauterine Foley catheter as an adjuvant to misoprostol may lower time to successful abortion compared to misoprostol alone (7.5 vs 11.8 hours) [90]. An RCT comparing intrauterine Foley balloon with double balloon catheters as an adjunct to oxytocin found that Foley resulted in a significantly shorter time from placement to abortion (21 vs 39 hours) [91].

2.4.3. Amniotomy

There are no current data on the effect of amniotomy in medication abortion. Some studies performed amniotomy as part of their protocol but without comparison groups. There is insufficient evidence to recommend for or against amniotomy use with medication abortion.

2.5. Can medication abortion with mifepristone-misoprostol be provided in the setting of prior cesarean delivery?

A meta-analysis reported a 0.47% uterine rupture risk following the misoprostol administration (doses varied widely among studies) for second-trimester medication abortion (gestational duration not

Table 2
Selected comparisons of dosing of combination mifepristone-misoprostol[a]

Author, year, country[b]	Participants (*N*)	Gestational duration (wk)	Intervention 1	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Intervention 2	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Serious adverse events[c]
Abbas et al. [24], 2016, Vietnam	509	12–22	200 mg mifepristone oral + 400 mcg misoprostol buccal (given simultaneously) → 400 mcg misoprostol buccal every 3 h	15	4.3	99.993	13 (4.9–47.8)	Nausea (26.0), vomiting (24.8), diarrhea (53.9), chills (21.3)	200 mg mifepristone oral 24 h → 400 mcg misoprostol buccal every 3 h	5.6	3.2	99.997	7.7 (2.1–40.3)	Nausea (27.1), vomiting (22.7), diarrhea (33.1), chills (16.3)	Two patients in the 24-h interval arm were diagnosed with infection and received antibiotics; one patient in the simultaneous arm received a blood transfusion
Chai et al. [25], 2009, Hong Kong, China	141	12–20	200 mg mifepristone oral + 600 mcg misoprostol vaginal loading dose (given simultaneously) → 400 mcg misoprostol vaginal every 3 h up to four doses	8.5	1.4	93	10 (3.5–126)	Nausea (53.5), diarrhea (25.4), chills (59.2), headache (9.9), fever (73.2), dizziness (22.5), fatigue (26.8), breast tenderness (9.9)	200 mg mifepristone oral 36–38 h → 600 mcg misoprostol vaginal loading dose → 400 mcg misoprostol vaginal every 3 h up to four doses	0	0	98.6	4.9 (1.8–13.8)	Nausea (52.9), diarrhea (14.3), chills (40.0), headache (8.6), fever (34.3), dizziness (22.9), fatigue (20.0), breast tenderness (2.9)	One patient from the immediate dosing group required antibiotics for presumed pelvic infection
Chaudhuri et al. [26], 2014, India	95	13–20	200 mg mifepristone oral 24 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol vaginal every 3 h for a maximum of four doses	6.4	Not reported	93.6	8.6 (4.1)	Nausea/vomiting (4.2), chills (8.5), fever (2.1)	200 mg mifepristone oral 48 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol vaginal every 3 h for a maximum of four doses	4.2	Not reported	0	8.7 (3.9)	Nausea/vomiting (0), chills (12.5), fever (2.1)	One patient from the 24 h group required a blood transfusion (initial Hgb 8.5 g/dL)
Chen et al. [27], 2013,[d] China	1112	8–16	(1st group) 200 mg mifepristone oral 24 h → 600 mcg misoprostol vaginal loading dose → 600 mcg misoprostol vaginal every 3 h up to four doses	Not reported	Not reported	74.5	5.0	Nausea (35.9), vomiting (12.6), diarrhea (1.9), chills (8.5), fever (14.8), headache (2.6), fatigue (10.3)	(2nd group) 200 mg mifepristone oral 24 h → 600 mcg misoprostol vaginal loading dose → 600 mcg misoprostol oral every 3 h up to four doses	not reported	Not reported	70.3	5.1	Nausea (35.6), vomiting (14.6), diarrhea (1.1), chills (9.1), fever (9.9), headache (1.5), fatigue (15.4)	None reported

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Table 2 (*continued*)

Author, year, country[b]	Participants (*N*)	Gestational duration (wk)	Intervention 1	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Intervention 2	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Mean (SD) or median time to pregnancy expulsion (h)	Side effects (%)	Serious adverse events[c]
			(3rd group) 200 mg mifepristone oral 24 h → 600 mcg misoprostol oral loading dose → 600 mcg misoprostol oral every 3 h up to four doses	Not reported	Not reported	69.5	4.8	Nausea (47.5), vomiting (8.2), diarrhea (1.4), chills (9.6), fever (8.5), headache (1.8), fatigue (12.8)	(4th group) 100 mg mifepristone oral 24 and 48 h → 600 mcg misoprostol vaginal loading dose → 600 mcg misoprostol oral every 12 h up to three doses	Not reported	Not reported	45.1	4.5	Nausea (25.0), vomiting (8.3), diarrhea (1.5), chills (7.6), fever (10.1), headache (1.1), fatigue (8.3)	None reported
Hou et al. [28], 2010, China	100	13–16	200 mg mifepristone oral 24 h → 600 mcg misoprostol vaginal loading dose → 400 mcg misoprostol orally every 6 h up to two doses	54	Not reported	22[e]	7 (3.0)	Nausea/vomiting (28.0), diarrhea (18.0), chills (14.0), fever (24.0)	200 mg mifepristone oral 48 h → 600 mcg misoprostol vaginal loading dose → 400 mcg misoprostol orally every 6 h up to two doses	42	Not reported	6	6.8 (4.3)	Nausea/vomiting (30.0), diarrhea (8.0), chills (14.0), fever (24.0), fatigue (2.0), numbness (2.0)	None reported
Mentula et al. [16], 2011, Finland	227	13–24	200 mg mifepristone oral 24 h → 400 mcg misoprostol vaginal every 3 h up to five doses	95	Not reported	75	8.5 (IQR 6.3–12.3)	Not reported	200 mg mifepristone oral 48 h → 400 mcg misoprostol vaginal every 3 h up to five doses	94	Not reported	63	7.2 (IQR 5.8–9.2)	Not reported	Two patients in the 24 h group had perforations during dilation and curettage requiring laparoscopic repair; three patients in the 24 h group received blood transfusions as well as one in the 48 h group; infections were reported in 11.3% of the 24 h group and 8.9% of the 48 h group
Webster et al. [29], 1996, the United Kingdom	70	13–20	600 mg mifepristone oral 36–48 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol orally every 3 h up to four doses	Not reported	Not reported	86.7	6.9	Nausea/vomiting (34.3), diarrhea (25.7)	200 mg mifepristone oral 36–48 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol orally every 3 h up to four doses	Not reported	Not reported	91.4	6.86	Nausea/vomiting (25.7), diarrhea (25.7)	One patient from each group required a blood transfusion

[a] Adapted from Whitehouse et al. [12] with update to include studies past May 2017 and additional information.
[b] All studies are RCTs unless otherwise noted.
[c] Serious adverse events include hospitalization postabortion, infection, blood transfusion, need for postevacuation surgery, or death.
[d] Data for first and second trimester cases presented jointly as disaggregated data were not available.
[e] Routine curettage performed on patients.

Table 3
Selected comparisons of route of administration of combination mifepristone-misoprostol[a]

Author, year, country[b]	Participants (*n*)	Gestational duration (wk)	Intervention 1	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Time to pregnancy expulsion (h)	Side effects (%)	Intervention 2	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Time to pregnancy expulsion (h)	Side effects (%)	Serious adverse events[c]
Chen et al. [27], 2013, China	556	8–16	200 mg mifepristone oral 24 h → 600 mcg misoprostol vaginal every 3 h up to four doses	Not reported	Not reported	74.5	5.0	Nausea (35.9), vomiting (12.6), diarrhea (1.9), chills (8.5), fever (14.8), headache (2.6), fatigue (10.3)	200 mg mifepristone oral 24 h → 600 mcg misoprostol oral every 3 h up to four doses	Not reported	Not reported	69.5	4.8	Nausea (47.5), vomiting (8.2), diarrhea (1.4), chills (9.6), fever (8.5), headache (1.8), fatigue (12.8)	None reported
Dickinson et al. [44], 2014 Australia	302	14–22	200 mg mifepristone oral 24–48 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol vaginal every 4 h up to five doses	3.9	Not reported	Not reported	7.4	Not reported	200 mg mifepristone oral 24–48 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol sublingual every 4 h up to five doses	4	Not reported	Not reported	7.8	Not reported	Five patients received blood transfusions - two in the oral group, one in the vaginal group (case complicated by uterine rupture) and two in the sublingual group
			(3rd group) 200 mg mifepristone oral 24–48 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol oral every 4 h up to five doses	11	Not reported	Not reported	9.5	Not reported							
El-Refaey and Templeton [30], 1995, the United Kingdom	69	13–20	600 mg mifepristone oral 36–48 h → 600 mcg misoprostol vaginal loading dose → 400 mcg misoprostol vaginal every 3 h	3	Not reported	Not reported	6.0	Vomiting (57%), diarrhea (29)	600 mg mifepristone oral 36–48 h → 600 mcg misoprostol vaginal loading dose → 400 mcg misoprostol oral every 3 h	3	Not reported	Not reported	6.7	Vomiting (61%), diarrhea (35)	There was one patient in the vaginal group and five in the oral group with "retained placenta." It is unclear if they all received curettage. There is mention of another patient who received curettage 2 wk after abortion for heavy bleeding

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Table 3 (*continued*)

Author, year, country[b]	Participants (*n*)	Gestational duration (wk)	Intervention 1	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Time to pregnancy expulsion (h)	Side effects (%)	Intervention 2	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Time to pregnancy expulsion (h)	Side effects (%)	Serious adverse events[c]
Garg et al. [45], 2015, India	50	14–25	200 mg mifepristone oral 48 h → 400 mcg misoprostol buccal loading dose → 200 mcg misoprostol buccal every 6 h up to six doses	Not reported (36 h timepoint)	Not reported (36 h timepoint)	Not reported	14.6	Nausea (32), vomiting (32), diarrhea (4), chills (4), fever (4)	200 mg mifepristone oral 48 h → 200 mcg misoprostol vaginal every 6 h up to six doses	Not reported (36 h timepoint)	Not reported (36 h timepoint)	Not reported	11.85	Nausea (4), vomiting (312), diarrhea (0), chills (12), fever (0)	Ultrasound performed on all patients - one in buccal group and five in vaginal group determined to have retained products and underwent curettage
Hamoda et al. [46], 2005, the United Kingdom	76	13–20	200 mg mifepristone oral 36–48 h → 600 mcg misoprostol sublingual loading dose → 400 mcg misoprostol sublingual every 3 h up to five doses	3.1	0	91.7	5.3	Nausea (72.2),vomiting (69.4), diarrhea (52.8), chills (72.2), headache (19.4), dizziness (41.7), fatigue (63.9), hot flush (36.1)	200 mg mifepristone oral 36–48 h → 800 mcg misoprostol vaginal loading dose → 400 mcg misoprostol vaginal every 3 h up to five doses	0	0	97.5	5.4	Nausea (65.0), vomiting (62.5), diarrhea (52.5), chills (70.0), headache (35.0), dizziness (42.5), fatigue (87.5), hot flush (70.0)	One patient in the vaginal group received a blood transfusion. Two patients from the sublingual group and three from the vaginal group were treated for suspected pelvic infection and one was admitted to the hospital with fever.
Ho et al. [38], 1997, Hong Kong, China	98	14–20	200 mg mifepristone oral 36–48 h → 200 mcg misoprostol oral + placebo vaginal every 3 h up to five doses	31.6	Not reported	59.2	27.8	Nausea (30.6), vomiting (20.4), diarrhea (32.7), headache (22.4), dizziness (34.7), fatigue (38.8), breast tenderness (16.3)	200 mg mifepristone oral 36–48 h → 200 mcg misoprostol vaginal + placebo oral every 3 h up to five doses	11.2	Not reported	73.5	14.8	Nausea (40.8), vomiting (28.6), diarrhea (18.4), headache (14.3), dizziness (24.5), fatigue (16.3), breast tenderness (2.0)	None reported
Ngai et al. [47], 2000, Hong Kong, China	139	14–20	200 mg mifepristone oral 36–48 h → 400 mcg misoprostol oral + placebo vaginal every 3 h up to five doses	16	Not reported	100	20.8	Nausea (55.7),vomiting (44.3), diarrhea (40.0), headache (24.3), dizziness (30.0), breast tenderness (11.4)	200 mg mifepristone oral 36–48 h → 200 mcg misoprostol vaginal + placebo oral every 3 h up to five doses	18.6	Not reported	100	19.5	Nausea (47.8), vomiting (42.0), diarrhea (23.2), headache (18.8), dizziness (31.9), breast tenderness (13.0)	None reported

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Table 3 (*continued*)

Author, year, country[b]	Participants (*n*)	Gestational duration (wk)	Intervention 1	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Time to pregnancy expulsion (h)	Side effects (%)	Intervention 2	Ongoing pregnancy at 24 h (%)	Ongoing pregnancy at 48 h (%)	Abortion completion without procedural intervention (%)	Time to pregnancy expulsion (h)	Side effects (%)	Serious adverse events[c]
Tang et al. [48], 2005 Hong Kong, China	118	12–20	200 mg mifepristone oral 36–48 h → 400 mcg misoprostol oral + placebo sublingual every 3 h up to 5 doses	15	8.3	88.3	7.5	Nausea (43.3), diarrhea (21.7), chills (35.0), fever (0), headache (23.3), dizziness (36.7), fatigue (46.7), breast tenderness (15.0)	200 mg mifepristone oral 36–48 h → 400 mcg misoprostol sublingual + placebo oral every 3 h up to five doses	8.6	1.7	82.7	5.5	Nausea (37.9), diarrhea (13.8), chills (36.2), fever (20.7), headache (22.4), dizziness (29.3), fatigue (34.5), breast tenderness (10.3)	None reported

All studies are randomized controlled trials unless otherwise noted.

[a] Adapted from Whitehouse et al. [12] with update to include studies past May 2017 and additional information.

[b] All studies are RCTs unless otherwise noted.

[c] Serious adverse events include hospitalization postabortion, infection, blood transfusion, need for postevacuation surgery, or death.

specified) in patients who had one previous cesarean delivery; this was not statistically significant when compared with the background uterine rupture rate without a prior uterine scar (0.08%) [92]. The increased relative uterine rupture risk among those with history of one cesarean delivery was not statistically significant (RR, 2.36; 95% CI, 0.39–14.32). Though the rupture risk was 2.5% in patients with two or more cesareans (RR 17.55; 95% CI, 3.00–102.8) [92], the CI is very wide. In patients with one or more prior cesarean deliveries, the use of PGE1 was also associated with higher retained placenta risk (RR, 1.21; 95% CI, 1.03–1.43) and blood transfusion compared to those without a uterine scar. It seems plausible that this risk may be similar in the setting of other prior uterine surgery, such as open myomectomy.

History of more than one prior cesarean delivery is not a contraindication to medication abortion regimens using misoprostol. Particularly when the alternative may be hysterotomy for individuals with later gestations, a potentially morbid procedure especially in the setting of prior abdominal surgery, it is reasonable to counsel patients using a shared decision-making model. There is insufficient evidence to conclusively support a change in medication abortion regimen in the setting of prior uterine incision. Given increased uterine rupture risk in the multiply-scarred uterus, lower misoprostol doses can be considered. Expert opinion suggests reducing misoprostol doses at higher gestational durations [93]. Mifepristone administration may lower total abortion time, thereby effectively reducing the total misoprostol dose, but there are no data on whether mifepristone affects uterine rupture rates.

2.6. What is the recommended pain management approach for patients undergoing medication abortion between 14 0/7 and 27 6/7 weeks of gestation?

The uterine expulsion process relies on uterine contractions and cervical dilation, which usually results in pain that culminates with expulsion. Studies of pain, pain control, and medication abortion focus on gestations < 12 weeks. As such, these recommendations are extrapolated from the literature on earlier medication abortion and obstetric care.

Of note, racial and ethnic inequities in health outcomes and care—including the assessment and pain treatment—are prevalent and persistent. There is ongoing need for clinical guidance to directly address these disparities and to promote equitable pain management [94–96].

The World Health Organization recommends routinely offering pain medication for medication abortion at any gestational duration [97]. For pain management for medication abortion at or > 12 weeks of gestation, they suggest consideration of methods in addition to nonsteroidal anti-inflammatory medication for control pain or discomfort, including antiemetics and epidural anesthesia, where available [97]. Where available, other pain management techniques—including moderate sedation, nitrous oxide, intravenous opiates, or patient-controlled analgesia—should be considered.

Post-abortion, patients may experience discomfort. In most cases, over-the-counter medications or topical management for vaginal and vulvar swelling (ice, sitz baths, topical analgesic) should be sufficient to provide pain relief. A multimodal, step-wise approach using a combination of agents with different mechanisms of action is recommended to individualize pain control regimens using shared decision-making with patients [94]. If opioids are required, a short course of low-dose opioids can be considered. However, severe pain following medication abortion is unusual and should prompt an evaluation for potential complications [98].

2.7. What are counseling considerations for medication abortion 14 0/7 to 27 6/7 weeks of gestation?

Patients deciding between procedural and medication abortion should be counseled on the nature of both options, in addition to the

risks and benefits. Medication abortion has a lower completion rate than procedural abortion. On the other hand, medication abortion at 14 0/7 to 27 6/7 weeks of gestation may offer patients a chance to hold the fetus, an intact fetus for autopsy or genetic diagnosis, and a potential option to avoid a procedure. Patients should be informed about what options are available in their health care setting and should be counseled on how to access their preferred option if it is not available.

Inducing fetal asystole before medication abortion at near-viable gestational durations to avoid signs of life at time of expulsion is practiced widely for legal considerations as well as patient and provider comfort. For more information, please see the Society of Family Planning clinical guidelines on induction of fetal asystole [99].

Lactation suppression: Lactation is likely after abortion at 18 weeks of gestation or later. Without intervention, 4 days after abortion, 97% of patients report some breast symptoms, and 33.3% report significant bother [100]. Managing these symptoms should be included routinely both in anticipatory guidance and treatment. Supportive measures, such as ice packs, may be helpful, although evidence for the effectiveness of such measures is inconsistent. If pharmacologic management is chosen, cabergoline is effective and generally safe, with few adverse effects (though contraindicated in patients with uncontrolled hypertension or history of cardiac valvular disorders). A recent Cochrane review reported that cabergoline 1 mg given within 1 day of term delivery was effective, well tolerated, and superior to bromocriptine for suppressing lactation and minimizing adverse effects [101]. Cabergoline has also proven effective in preventing bothersome breast symptoms after uterine evacuation at 18 to 28 weeks of gestation [100].

2.8. What are considerations for service delivery of medication abortion between 14 0/7 and 27 6/7 weeks of gestation?

Medication abortion between 14 0/7 and 27 6/7 weeks of gestation continues to primarily be a facility-based process (ambulatory and hospital based) [102]. This standard is based on current practice patterns and not evidence. A facility-based process enables access to a wide range of pain control options and expedient management of common problems associated with medication abortion at 14 0/7 to 27 6/7 weeks of gestation, such as retained placenta. Facility-based care may also provide access to related resources, such as spiritual care, bereavement services, and fetal remains disposition. However, facility-based care is costly, is less private, and may not be necessary for all patients. Patients do not need to be directly observed for the entire process. Mifepristone can be ingested prior to facility presentation. Initial doses of misoprostol can also be started for patients at low risk for extramural delivery. Since abortion in some instances can occur within a few hours of first misoprostol dose, and cramping and bleeding may also occur shortly after misoprostol dosing, the decision to do this should be taken carefully.

Appropriately trained and credentialed clinicians can provide medication abortion after 13 6/7 weeks of gestation with appropriate backup, especially as the care is similar to obstetric delivery care that is routinely provided by advanced practice clinicians.

The role of self-managed abortion (SMA) may depend as much on the legal context as on medical risks. For guidance on SMA, please see Society of Family Planning Interim Recommendations: Self-managed abortion [103]. There is still need for additional research and evidence-based guidance for SMA at later weeks of gestation, specifically.

Two studies found acceptability is high for both mifepristone plus misoprostol and misoprostol-only regimens [20,104]. Dabash et al. found similar high overall acceptability (90% vs 81.7%) and side effect acceptability (90% vs 83%) for mifepristone plus misoprostol and misoprostol only. Those given the misoprostol-only regimen had lower satisfaction with the duration of their hospital stay than those in the mifepristone group (78% vs 91.7%, $p = 0.04$) [16].

2.9. When can contraception be started after medication abortion between 14 0/7 and 27 6/7 weeks of gestation?

The Society of Family Planning endorses the Centers for Disease Control US Medical Eligibility for Contraceptive Use [105]. As for all patients, contraception counseling should take into account the potential reproductive coercion experienced by the patient [106]. If contraception is desired, patients can initiate almost all methods when the medication abortion is started (first medication of regimen) or after expulsion is complete (in particular, intrauterine devices [IUDs]). Exceptions are fertility awareness methods, diaphragm, or cervical cap. Incision planning for permanent contraception via minilaparotomy may depend on the uterine size postexpulsion. IUD placement or permanent contraception should be delayed if postabortion hemorrhage occurs or infection is confirmed or suspected. An IUD can be placed or permanent contraception performed once symptoms have resolved and antibiotic treatment has been completed. Per the US Medical Eligibility for Contraceptive Use, combined hormonal contraceptives are category 1 (no restriction) for immediate initiation after second-trimester abortion [105]. After 24 weeks of gestation, it may be reasonable to delay estrogen-containing method initiation due to thromboembolism risk in line with practices after term deliveries.

3. Conclusions and recommendations

Please see Appendix 1 for a key to interpreting GRADE.

- We recommend mifepristone 200 mg orally (where available) 24 to 48 hours before misoprostol, followed by misoprostol 400 mcg every 3 hours vaginally, sublingually, or buccally for medication abortion between 14 0/7 and 23 6/7 weeks of gestation (GRADE 1A).
- When mifepristone 200 mg orally is not available 24 to 48 hours prior to the first misoprostol dose, we recommend administering mifepristone and vaginal misoprostol simultaneously (GRADE 1B).
- If mifepristone is unavailable, we recommend misoprostol 400 mcg vaginally, sublingually, or buccally every 3 hours for medication abortion between 14 6/7 and 23 6/7 weeks of gestation. A loading dose is not recommended, as it does not hasten abortion times or improve outcomes (GRADE 1B).
- We suggest mifepristone 200 mg (where available) plus misoprostol 200 mcg vaginally or buccally every 3 hours for medication abortion between 24 0/7 and 27 6/7 weeks of gestation (GRADE 2C).
- If mifepristone is unavailable, we suggest misoprostol 200 mcg vaginally or buccally every 3 hours for medication abortion between 24 0/7 and 27 6/7 weeks of gestation (GRADE 2C).
- We do not suggest oxytocin-based regimens for medication abortion unless misoprostol with or without mifepristone is unavailable or contraindicated (e.g., allergy; GRADE 2C).
- We suggest against osmotic dilator use prior to or concurrent with misoprostol (with or without mifepristone), gemeprost, or high-dose oxytocin, with the possible exception of fetal demise (GRADE 2B).
- We suggest considering Foley catheter placement with misoprostol-only regimens (GRADE 2B). There is insufficient evidence to make a recommendation for Foley catheter placement when used with mifepristone in combination with misoprostol.
- There is insufficient evidence to recommend a change in misoprostol regimen for people with more than one prior cesarean in high-resource settings. Expert opinion suggests reducing

misoprostol doses at higher gestational durations (at or over 24 weeks of gestation or uterine size). We suggest mifepristone pretreatment when it is available, although this does not eliminate uterine rupture risk. We suggest individualizing care and reduced misoprostol dosing in low-resource settings or at 24 0/7 weeks of gestation or later (or equivalent uterine size; GRADE 2C).
- We recommend routinely offering pain management to people undergoing medication abortion (GRADE 1B).
- We recommend a step-wise multimodal approach to address pain. We recommend using shared decision-making with the patient to determine whether opioid medications are indicated (GRADE 1B).
- We suggest that appropriately trained and credentialed advanced practice clinicians can provide medication abortion between 14 0/7 and 27 6/7 weeks of gestation with appropriate backup within the confines of local regulations and licensure (GRADE 2B).
- We recommend the initiation of most contraceptive methods immediately following medication abortion per patient preference. Surgical considerations may affect permanent contraception timing, and in cases of infection, IUD placement and permanent contraception should be deferred until resolution (GRADE 1A).

4. Recommendations for future research

Research is needed to inform evidence-based recommendations for self-managed abortion after 11 weeks of gestation. In addition, further research could inform recommendations for more effective pain control and side effect management, as well as examining the safety of these regimens outside of medical facilities. Future recommendations could also incorporate a shared decision-making guide for clinicians around medication abortion for patients at increased complication risk, such as prior uterine scar.

5. Search strategy

We searched PubMed for all articles on induced abortion at 13 weeks of gestation or greater. Complete search terms, available in appendix, included “abortion,” “mifepristone,” “misoprostol,” and “randomized clinical trial”. We reviewed reference lists of included articles to identify additional publications. For studies included in tables, we adapted those presented in Whitehouse et al., “Medical regimens for abortion at 12 weeks and above: a systematic review and meta-analysis.” This systematic review included articles published between January 2008 (January 2008 was chosen as the start date to identify eligible publications not included in the 2011 Cochrane Review by Wildschut et al.) and May 2017. In addition, we recreated the search to include articles published between June 2017 and June 2022.

We reviewed references and abstracts for inclusion. We reviewed the full text of all potentially relevant articles where available. We included RCTs reporting a mean gestational duration of 12 weeks of gestation or greater and that compared one of the following methods of medication abortion: (1) combination mifepristone-misoprostol (i.e., “combination regimens”) vs misoprostol only, (2) various dosages and timings in combination regimens, (3) various routes of misoprostol in combination regimens, (4) various dosages and timings in misoprostol-only regimens, and (5) various routes in misoprostol-only regimens. We excluded studies with other designs or those in which participants had spontaneous abortion (incomplete, threatened, or missed abortion), septic abortion, and studies not reporting the primary outcome. We also reviewed references used in prior relevant Society of Family Planning guidelines.

6. Intended audience

These Clinical Recommendations are intended for Society of Family Planning and Society for Maternal-Fetal Medicine members, family planning and maternal-fetal medicine clinicians, reproductive health service clinicians, family planning and reproductive health researchers, and policy makers.

Authorship

This Clinical Recommendation was prepared by Blake Zwerling, MD, MSc; Alison Edelman, MD, MPH; Anwar Jackson, MD, MS; and Anne Burke, MD, MPH, with assistance from Malavika Prabhu, MD. It was reviewed and approved by the Clinical Affairs Committee on behalf of the Board of Directors of the Society of Family Planning and by the Publications Committee, Document Review Committee, and Executive Committee of the Society for Maternal-Fetal Medicine.

Disclaimer

This publication is designed as a resource to assist clinicians in providing family planning care. It should not be considered inclusive of all proper treatments or serve as the standard of care. It is not intended to substitute for the independent professional judgment of the treating clinician. Variations, taking into account individual circumstances, may be appropriate. This publication reflects the best-available evidence at the time of publication, recognizing that continued research or major changes in the practice environment may impact future recommendations and should be evaluated for incorporation into care. Any updates to this document can be found at https://www.societyfp.org/clinical-guidance/. The Society and its contributors provide the information contained in this publication "as is" and without any representations or warranties, express or implied, of any kind, whether of accuracy, reliability, or otherwise.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.contraception.2023.110143.

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