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