First-trimester pregnancy termination: Medication abortion

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INTRODUCTION

Medication abortion (also referred to as medical abortion) is the termination of pregnancy by using medications to induce a process similar to a miscarriage. It is an alternative to uterine aspiration (also known as aspiration abortion, suction curettage, dilation and curettage, dilation and evacuation, or surgical abortion). Medication abortion and uterine aspiration are both safe and effective procedures for appropriately selected patients seeking pregnancy termination [1,2].

As abortion provision has streamlined and improved, several resource-rich countries have experienced increased utilization of medication abortion as compared with uterine aspiration, improved access to medication abortion methods, and a decline in medication abortion complications [3]. Similarly, in countries where abortion medications are available directly from pharmacies rather than requiring in-person dispensation by a clinician, abortion provision occurs at substantially earlier gestations [4-6] and is just as safe as taking the medications in a clinic with a doctor [7].

Use of a combination of mifepristone (an antiprogesterone) and misoprostol (a prostaglandin) is the primary method of medication abortion in the United States in pregnancies through 77 days (11+0 weeks) of gestation and is the preferred method of pregnancy termination in all patients where these medications are available. A survey of transgender, nonbinary, and gender-expansive people in the United States demonstrated a preference for medication abortion over uterine aspiration at a rate of three to one [8].

First-trimester medication abortion is reviewed here. An overview of pregnancy termination, including a discussion on how to choose between a medication abortion and uterine aspiration; first-trimester surgical abortion; and management of second-trimester pregnancy terminations are discussed separately.

- (See "Overview of pregnancy termination".)
- (See "First-trimester pregnancy termination: Uterine aspiration".)
- (See "Overview of second-trimester pregnancy termination".)
- (See "Second-trimester pregnancy termination: Induction (medication) termination".)
- (See "Second-trimester pregnancy termination: Dilation and evacuation".)

PATIENT SELECTION

Candidates — In the United States, mifepristone is approved for medication termination of intrauterine pregnancy through 70 days of gestation [9]. Use in patients beyond this gestational age is off-label.

Planned Parenthood Federation of America (PPFA), the largest provider of medication abortions in the United States, has extended the gestational age for mifepristone/misoprostol abortion through 77 days (11+0 weeks) [10,11]. First-trimester medication abortion beyond 70 days may also result in lower efficacy (and more significant bleeding and cramping) [10-13]. Thus, this increased gestational age limit approved by PPFA is accompanied by a recommendation for an automatic second dose of misoprostol to be provided to patients at 9+0 to 11+0 weeks of gestation, three to six hours after the first dose. This is further discussed below. (See 'Misoprostol' below.)

According to the manufacturer of mifepristone, pregnancy is dated from the first day of the last menstrual period in a presumed 28-day cycle with ovulation occurring at midcycle. Confirmation of an intrauterine pregnancy is **not** an absolute requirement prior to initiating the medication abortion regimen; evaluation of pregnancy of unknown location (for patients without symptoms or risk factors for ectopic pregnancy (table 1)) can occur at the same time medication abortion is initiated. This is discussed in more detail below. (See 'Pregnancy of unknown location' below.)

Contraindications — There are few contraindications to medication abortion, which include:

- **Allergy or drug interaction** – Allergy to, or concomitant use of medications that interact with, mifepristone or misoprostol.

- Mifepristone is a glucocorticoid receptor antagonist and is therefore contraindicated in patients with chronic adrenal failure or who are on concurrent long-term corticosteroid therapy.

- Mifepristone is also porphyrinogenic and is thus contraindicated in patients with porphyrias [14].

- Asthma is **not** a contraindication to use of misoprostol. Although some prostaglandins result in bronchoconstriction, misoprostol is a bronchodilator and therefore not associated with the onset, or exacerbation, of asthma.

- **Ectopic pregnancy** – An ectopic pregnancy is a potentially life-threatening condition and should not be managed with mifepristone/misoprostol. (See "Ectopic pregnancy: Choosing a treatment".)

  Rarely, ectopic pregnancy is present but is not detected prior to the medication abortion. This occurs in approximately 7 to 20 per 100,000 cases [15,16]. In one study including over 200,000 medication abortions, there were 8 ectopic pregnancies, 1 of which resulted in death [15].

  Thus, patients with risk factors for ectopic pregnancy (table 1), abdominal pain, vaginal bleeding that is inconsistent with typical patterns seen during medication abortion, or no intrauterine gestation and symptoms of ongoing pregnancy should be evaluated urgently for an ectopic pregnancy. (See "Ectopic pregnancy: Clinical manifestations and diagnosis".)

- **Anemia or anticoagulation therapy** – Due to the blood loss associated with first-trimester medication abortion and the potential for heavy bleeding at home, patients with known anemia (typically with hemoglobin levels below 9.0 g/dL), hemorrhagic disorders, or taking anticoagulant therapy may be directed toward uterine aspiration, particularly at a gestational age later in the first trimester.

- **Current IUD use** – Medication abortion is contraindicated in patients with an intrauterine device (IUD) in place. If the IUD is removed, the patient may then be a candidate for medication abortion.

PROVIDER REQUIREMENTS

When a medication abortion is supervised by a clinician, the provider must be able to:

- Assess that gestational age is within eligibility guidelines.

- Identify patients who have a suspected ectopic pregnancy and be able to facilitate further medical or surgical care for such patients.
- Provide uterine aspiration in cases of severe bleeding or incomplete abortion or refer a patient to another clinician to provide this care.
- Identify and refer patients to facilities equipped to perform blood transfusions and resuscitation, if needed.
- Sign the prescriber agreement with the distributor of mifepristone. This is a private, confidential agreement between the provider or practice and the distributor, and this signed form is not available for public viewing or reporting. Often a single person can sign on behalf of an entire practice or department; we encourage this practice.
- Require that patients read the manufacturer's medication guide and sign the patient agreement form [17].
- Report any patient deaths that may be attributed to the medication abortion (rare).

In the United States, providers of first-trimester medication abortion may be physicians or advanced-practice clinicians (APCs; nurse practitioners, physician assistants, and certified nurse midwives) in settings in which these professionals have appropriate training and practice privileges. APCs comprise between 28 and 49 percent of providers of medication abortion in the United States [18,19]. Studies have shown that APCs safely provide medication abortion services with equivalent clinical outcomes to procedures administered by physicians [20-22], and their provision may improve access to these services. Despite these safety data, many states require that an abortion be performed by a licensed physician [23,24].

PROTOCOLS BY SETTING

Traditionally, mifepristone was administered during an in-person clinic visit with an abortion provider; however, the prevalence of telemedicine services [25], postal mail delivery of mifepristone and misoprostol [26], direct pharmacy dispensation [4,7,20,27], and self-managed abortion (SMA) is increasing. Based on accumulated evidence, the American College of Obstetricians and Gynecologists (ACOG) and the National Abortion Federation (NAF) support these alternative approaches to evaluation, counseling, and medication provision, including elimination of in-person visits for many patients [28-33].

In-person — The first encounter has traditionally been an in-person office or clinic visit and is used to provide counseling, assess a patient's eligibility for medication abortion, provide the

mifepristone tablet (200 mg orally), and give instructions regarding misoprostol self-administration 24 to 48 hours after taking mifepristone. (See 'Mifepristone plus misoprostol' below.)

Counseling and informed consent — After deciding to have an abortion, a patient is counseled about the following:

- Options of either medication abortion or uterine aspiration and the risks and benefits of each method. (See "Overview of pregnancy termination", section on 'First trimester'.)
- Steps of the medication abortion procedure, including expected medication effects (eg, vaginal bleeding, pain, passing the gestational tissue (see 'Patient experience' below)). As the process involves multiple steps, and patients may be anxious during the clinic visit, we write down the dates and times to take each premedication and misoprostol. (See 'Pain control' below and 'Misoprostol' below.)

  The patient is also given a telephone number to call with questions or in case of an emergency (eg, bleeding that does not decrease after pregnancy tissue is passed, soaking two maxi pads per hour for two consecutive hours [31]).
- If the medication abortion is unsuccessful (by the presence of an ongoing pregnancy or clinically significant retained gestational tissue), additional misoprostol or an aspiration procedure is required to complete the procedure, as an ongoing pregnancy will have an increased risk of severe fetal abnormalities. (See 'Incomplete or failed abortion' below and 'Teratogenicity' below.)
- Effects of medication abortion cannot be reversed once mifepristone has been taken [34,35]. Despite a lack of evidence, in some legal contexts, it has been theorized that the pregnancy interruption effects of mifepristone could be "reversed" through post-mifepristone administration of progesterone [34].

The patient is given the Medication Guide and Patient Agreement to review; these forms are available for download in multiple languages from the mifepristone distributor.

Informed consent is documented, including consent for uterine aspiration in the setting of continued pregnancy or symptomatic retained tissue following administration of the medication abortion.

Legal requirements regarding pregnancy termination, parental consent, and preprocedure counseling vary by state in the United States. Information regarding these requirements is provided by the state government or through multiple reproductive health websites.

Counseling for patients undergoing abortion is discussed in more detail separately. (See "Counseling in abortion care".)

Plan for contraception — If the patient has an intrauterine device (IUD) in place, it must be removed before initiation of medication abortion. (See 'Contraindications' above.)

As ovulation can occur soon after medication abortion, we encourage contraception counseling prior to the medication abortion procedure. Types of contraceptive methods and timing of initiation following medication abortion are discussed in detail separately. (See "Contraception: Postabortion", section on 'Initiation of contraception'.)

Role of additional testing — While laboratory testing and imaging are not required prior to medication abortion, the following may be performed in selected patients.

Ultrasound and laboratory testing

- **Ultrasound** – Determining that the gestational age is not more than the recommended limit (ie, ≤77 days [11+0 weeks] of gestation) is critical in deciding whether a patient is a candidate for misoprostol/mifepristone abortion. While gestational age is often determined from menstrual history alone (see 'Contraindications' above), in some cases (eg, irregular menses, risk factors for ectopic pregnancy (table 1)), clinical examination and/or pelvic ultrasound (if available) may be helpful. However, assessment of gestational age by last menstrual period (LMP) is accurate in most patients. In a systematic review of five eligible studies evaluating the accuracy of assessing gestational age prior to first trimester medication abortion, only 2.5 to 11 percent of patients who were eligible for medication abortion by LMP were ineligible by ultrasound evaluation [36].

- **Quantitative hCG** – A quantitative human chorionic gonadotropin (hCG) level should be obtained in patients who have an initial ultrasound that does not demonstrate a definitive intrauterine pregnancy, however, we do not wait for the hCG result to perform the medication abortion (see 'Pregnancy of unknown location' below).

  While no specific hCG level corresponds exactly to a gestational age, a value that is unusually high for the clinical setting of very early pregnancy (eg, >3500 international units [IU]/L) should prompt further work-up for an ectopic or molar pregnancy.

  A quantitative hCG is also needed for those patients who will utilize serial serum quantitative hCG values or semiquantitative urine pregnancy tests as a means of follow-up to confirm pregnancy expulsion. (See 'Follow-up' below.)

- **Other** – Laboratory testing for hemoglobin or hematocrit, Rh typing (and administration of Rhogam to Rh negative individuals), and chlamydia and/or gonorrhea are described in detail separately. (See "Overview of pregnancy termination", section on 'Laboratory testing'.)

Pregnancy of unknown location — Some patients may present for termination before an intrauterine pregnancy can be seen on ultrasound. In our practice, we provide medication abortion for patients with pregnancy of unknown location who meet all of the following criteria [37]:

- Positive pregnancy test
- No symptoms of ectopic pregnancy
- No ultrasound evidence of ectopic pregnancy
- Baseline quantitative hCG and agreement to have follow-up serial hCG levels until termination is confirmed
- Accept the possible risk of delay in diagnosis of a clinically significant ectopic pregnancy

In a meta-analysis of studies comparing initiation of abortion before versus after definitive evidence of an intrauterine pregnancy, performing the abortion before definitive evidence did not significantly increase the risk of missed ectopic pregnancy, ongoing pregnancy, or need for surgical intervention in patients without symptoms of ectopic pregnancy, but the quality of evidence was low [38]. A subsequent study including 5619 pregnancies below 49 days gestation, immediate initiation of medication abortion compared with delay until diagnosis of confirmed intrauterine pregnancy provided faster treatment with no increase in emergency room visits [39].

Limited role of prophylactic antibiotics — Most clinicians do **not** administer prophylactic antibiotics for first-trimester medication abortion, although practice varies. The Society of Family Planning (SFP) states that, although individual practitioners may decide to use antibiotics with provision of medication abortion, the SFP does not recommend antibiotics for all patients having a medication abortion [40], a guidance shared by the NAF [33], Planned Parenthood Federation of America (PPFA), ACOG [31], and the World Health Organization (WHO) [22].

There are no randomized trials regarding whether prophylactic antibiotics should be used for first-trimester medication abortion [41].

Use of prophylactic antibiotics also has several potential disadvantages, including side effects, cost, increased complexity of the regimen, and promotion of antibiotic resistance [42].

Implications for future pregnancy — First-trimester medication termination of pregnancy does not appear to be associated with an increased risk of adverse outcomes in subsequent pregnancies [43,44]. In a retrospective study from Denmark evaluating subsequent pregnancy outcomes in almost 12,000 patients with a history of first trimester pregnancy termination, those with a history of medication abortion compared with uterine aspiration had similar rates of miscarriage, ectopic pregnancy, preterm birth, and low birth weight in the first pregnancy after their abortion [45].

Telemedicine and hybrid models — During the coronavirus disease 2019 (COVID-19) pandemic when access to health care was limited and given increasingly restrictive abortion policies in the United States, utilization of alternative methods to in-person medication abortion (eg, telemedicine, hybrid models) increased. These models utilize a patient history-only approach (also called "history-based" or "no-test" abortion) to medication abortion candidate selection without relying on ultrasound, physical examination, or laboratory assessment. The provider-patient interaction occurs online, or by video or phone, and the clinician remotely dispenses the medications once counseling is complete. (See "Overview of pregnancy termination", section on 'Telemedicine' and 'Mifepristone plus misoprostol' below.)

In this telehealth model, effectiveness is comparable [46] or higher [47] to that of in-person visits, patient satisfaction is excellent (94 to 96 percent) [48-51], but follow-up rates may be lower (60 versus 77 percent) [30]. In a large, 14-center retrospective cohort study of 3779 geographic-, racial-, and ethnic-diverse patients who received history-based screening and medication abortion was dispensed either in person (66 percent) or through postal mail (34 percent), rates of effectiveness (adjusted, 94.8 percent; 95% CI, 93.6-95.9 percent) and major adverse events (0.54 percent; 95% CI, 0.18- 0.9 percent) were similar to published rate of models involving ultrasound and physical examination [52].

Self-managed — In settings where abortion is illegal or functionally inaccessible, the prevalence of self-managed abortion (SMA), where patients purchase medication abortion medications without the direct assistance of the formal medical system [53,54], is also increasing. (See "Overview of pregnancy termination", section on 'Self-managed'.)

SMA is part of an overall culture shift toward "direct-to-consumer" medical services, though this shift is being driven more urgently by restrictive abortion bans. The WHO endorses SMA [55] and healthcare providers should familiarize themselves with resources to provide patients who may benefit from these services; examples of such resources include:

- Women Help Women, Self-Managed Abortion: Safe & Supported (https://abortionpillinfo.org/)
- AidAccess (https://aidaccess.org/)
- If When How (https://www.ifwhenhow.org/)
- Repro Legal Helpline (https://www.reprolegalhelpline.org/)
- Miscarriage and Abortion Hotline (https://www.mahotline.org/)

In a meta-analysis comparing the efficacy, acceptability, and safety of early medication abortion (≤9 weeks of gestation), those utilizing self-administered versus provider-administered mifepristone methods had similar rates of successful abortion (approximately 96 percent in each group; two randomized trials); results were also similar for the 16 prospective cohort studies [56]. When data from the randomized trials and nonrandomized studies were combined, 91 percent of patients in both groups were satisfied or highly satisfied with their procedure. The authors were unable to conclude whether there was a difference between groups in complications requiring surgical intervention; neither of the randomized trials reported this outcome.

MEDICATIONS

Mifepristone plus misoprostol — The US Food and Drug Administration (FDA) approved mifepristone for medication abortion with the required combined regimen of mifepristone and misoprostol [9,57,58].

Mifepristone — Mifepristone is a progesterone receptor antagonist that results in decidual necrosis, placental separation, softening and dilation of the cervix, and sensitization of the myometrium to uterotonics such as misoprostol. When used alongside misoprostol for first trimester medication abortion, the combined effect results in enhanced and expeditious expulsion of the products of conception [59-61]. As a result, combined mifepristone-misoprostol is more effective than either drug alone [62]. (See 'Efficacy' below.)

In the United States, mifepristone is available only with Risk Evaluation and Mitigation Strategy (REMS) restrictions and must be dispensed by an abortion provider. (See "Overview of pregnancy termination", section on 'Legal issues'.)

- **Dose** – The dose of mifepristone for first-trimester medication abortion is 200 mg orally. Doses lower than 200 mg do not offer a benefit and may be less effective [63-65], and

higher doses are unnecessary. Ingestion of a single dose in the range of 200 mg up to 800 mg produces approximately the same serum concentration [66-68], and a meta-analysis of four randomized trials demonstrated 200 mg is equally effective for pregnancy termination as the originally approved 600 mg dose (risk ratio 1.07, 95% CI 0.87-1.32) [62,69,70].

- **Administration** – The patient is typically instructed to take mifepristone along with a beverage and some crackers to ease any gastrointestinal symptoms that can occur, more from the anxiety of the experience than from the mifepristone itself. If a patient vomits within 30 minutes of the mifepristone administration, the dose should be repeated. Vomiting after 30 minutes of taking mifepristone is not likely to impact absorption and clinical effect.

Rarely, patients will experience bleeding or cramping during the 24 to 48 hours after taking mifepristone but before the misoprostol dose (see 'Patient experience' below). In most cases, if these symptoms are present, the patient should still take the misoprostol since mifepristone alone is not highly effective; the exception is that misoprostol should not be taken if expulsion of the gestation has been confirmed through an emergency visit. Approximately 1 to 5 percent of patients will expel the conceptus after a single dose of mifepristone only, without misoprostol [71].

Misoprostol — Misoprostol, a synthetic prostaglandin E1, is widely available and can be stored at room temperature, making it an ideal prostaglandin complement to mifepristone for first-trimester medication abortion. Other prostaglandins such as gemeprost and sulprostone have been used in combination with mifepristone for termination of pregnancy but have lower treatment success than the misoprostol regimen [72] or are associated with worse adverse effects [73].

After taking misoprostol, the patient is likely to abort within several hours. The typical time to abortion with buccal misoprostol has not been well studied, but for other routes, the proportion of patients who abort within four hours after taking misoprostol are vaginal (93 percent) [74] and oral (44 to 78 percent (figure 1)) [71].

- **Dose** – We dispense four pills of misoprostol 200 mcg (a total dose of 800 mcg) to be self-administered buccally at 24 to 48 hours after the mifepristone is taken. Over 90 percent of United States abortion practices use the 800 mcg dose for this procedure [18]. In one randomized trial, 400 mcg was found to be equally as effective as 800 mcg, but this dose is not widely used [75].

- **Second dose for selected patients** – For patients at 9+0 to 11+0 weeks, an automatic second dose of misoprostol is administered three to six hours after the first dose to decrease the risk of ongoing pregnancy, especially at these later gestational ages [76-78].

  For patients <9 weeks of gestation, automatic additional doses of misoprostol are not routinely utilized. However, during the COVID-19 pandemic, it has become routine practice to also provide a second dose to such patients; in this scenario, patients do not take the dose automatically, but rather await instruction from their provider and self-administer the second dose only if there is concern for an incomplete abortion.

- **Timing** – In the 2016 FDA regimen, the interval from mifepristone to misoprostol is 24 to 48 hours [79]. This flexibility in dosing increases convenience for patients, allowing them a window of time in which to take the misoprostol and experience the resulting effects of vaginal bleeding and cramping within the context of their other scheduled activities or when a support person is available as needed.

  The mifepristone-misoprostol interval has been evaluated, and any interval from 24 to 72 hours appears to result in similar efficacy, but <24 hours does not appear to be as effective. We are not aware of data on misoprostol administration >72 hours after mifepristone [80]. Representative studies include:

  - A meta-analysis of randomized trials included pooled data from three studies that showed similar rates of complete abortion when the interval was decreased from 48 to 24 hours [70].

  - A systematic review compared six studies that used a 24-hour interval with 15 studies that used a 24-to-48-hour interval and found that a longer interval resulted in improved procedure success (94.2 versus 96.8 percent, respectively) [81]. One trial including 2295 patients showed similar efficacy for a 24-, 48-, or 72-hour interval [82].

  - A systematic review found increased medication abortion failure rates with intervals of <23 hours as compared with intervals within 23 to 72 hours (odds ratio [OR] 2.1, 95% CI 1.4-3.2) [83].

- **Route –** Misoprostol is manufactured and approved by the FDA for use as an oral tablet, but several routes of administration (buccal, oral, vaginal, sublingual) have been used for first-trimester medication abortion. For most patients, buccal has become the preferred route based on safety, side effects, and patient preference and is the route we prescribe in our practice. For patients with gestations ≤49 days, oral administration is also reasonable. Representative studies supporting our practice include the following:

- In a randomized trial evaluating the pharmacokinetics of misoprostol, buccal dosing was more effective than oral dosing [84]. A subgroup analysis based on gestational age found that for gestations >49 days, buccal dosing had lower rates of incomplete abortion (5 versus 13 percent, relative risk [RR] 0.37, 95% CI 0.18-0.73) [85]. For gestations ≤49 days, oral and buccal dosing had similar rates of incomplete abortion. Rates of gastrointestinal side effects and patient satisfaction were also similar for both routes.

- While vaginal dosing is effective and has a low rate of side effects, it is no longer routinely used as it has been proposed as a contributing factor to infection complications with medication abortion [86-88].

- Buccal compared with vaginal dosing appears to have less patient-to-patient variability in absorption and resulting serum concentration [89].

- In some studies, patients have reported a preference for oral rather than vaginal administration [90,91], but appear to find both oral and buccal dosing acceptable [85]. However, oral compared with vaginal dosing is associated with more side effects and possibly lower efficacy [70,92].

- Buccal and vaginal dosing have similar pharmacokinetics and, compared with oral dosing, result in greater bioavailability; a later, lower peak serum concentration at 60 to 80 minutes; and a longer duration of bioactivity [74,93-97]. These pharmacokinetics are likely responsible for the decrease in side effects with vaginal and buccal dosing as compared with sublingual dosing [2,70,96], as nausea and vomiting are likely related to a higher peak level of the pharmacokinetic curve [97]. By contrast, one randomized trial found comparable efficacy and side effects for sublingual and buccal administration [98].

Given the rare use of buccal medications, we describe this process at length, telling patients to place two pills in the lower right cheek and two pills in the lower left cheek, dosing all four pills in the buccal mucosa at once. We also utilize an image to help patients understand correct placement (figure 2). Experts vary in terms of whether they instruct the patient to swallow or spit out whatever remains of the pills after 30 minutes of buccal exposure.

- **Efficacy of self-administration** – Misoprostol self-administration is effective and has high rates of patient satisfaction. In a systematic review of nine prospective studies including 4522 patients undergoing first-trimester medication abortion, misoprostol self-administration at home compared with administration by a clinician had similar rates of

complete abortion, but self-administration was associated with higher patient satisfaction [99]. While there was a slight increase in the duration of pain and vomiting (0.3 days longer) with self-administration, patient contact with health services was similar between groups.

Efficacy — First-trimester mifepristone plus misoprostol abortion is successful in 95 to 98 percent of procedures [71,73,74,76,81,93,100-103]. By contrast, lower efficacy may be achieved when mifepristone or misoprostol are used alone. In a meta-analysis including randomized trials, those receiving misoprostol alone compared with a combined regimen (eg, mifepristone plus misoprostol) had higher rates of failed abortion (relative risk [RR] of failure 2.4, 95% CI 1.9-3; 18 trials; 3471 patients), however the certainty of evidence was low [62]. Failed abortion rates also trended higher in patients receiving mifepristone alone compared with a combined regimen (three studies, 273 patients), but these results were not statistically significant. (See 'Misoprostol-only' below.)

Factors associated with decreased efficacy include increased gestational age, increased parity, and prior abortion [71]. While the mechanism for the latter is unclear, it is theorized that pregnancy is more successfully established at an earlier gestational age in parous patients than in nulliparous patients [77,104,105]. Prior cesarean birth is not associated with increased failure of medication abortion [106].

Teratogenicity — In cases where complete abortion is not achieved, exposure to misoprostol may result in severe fetal abnormalities. In a review of 71 cases of continuing pregnancy after mifepristone-based medication abortion, malformations occurred in eight cases, and all but one included exposure to the prostaglandin gemeprost [107]. Other retrospective studies have also shown an association between prostaglandins, notably misoprostol, and congenital abnormalities [108]. Such malformations include scalp or skull defects, cranial nerve palsies (Moebius syndrome), and limb deficiencies (eg, equinovarus) [109-112]. The rise in uterine pressure related to uterine contractions or vascular spasm may be the mechanism contributing to these teratogenic effects [109-112].

We are unaware of data to suggest that exposure to mifepristone alone is teratogenic.

Less commonly used regimens

Misoprostol-only — Misoprostol given alone, whether by the vaginal or the buccal route, is less effective than when given in combination with mifepristone [113,114]. (See 'Efficacy' above.)

However, the use of misoprostol alone is a reasonable option in settings where mifepristone is not available. (See "Misoprostol as a single agent for medical termination of pregnancy".)

Methotrexate-based regimens — Prior to FDA approval of mifepristone, methotrexate (50 mg/m^2) followed by vaginal misoprostol (800 mcg) three to seven days later was used for medication abortion. In Canada, before mifepristone was approved in 2015, 85 percent of clinics that provided medication abortion utilized a methotrexate-based regimen [18]. However, compared with mifepristone/misoprostol, a methotrexate/misoprostol regimen is less effective and requires a longer time to complete abortion [115-118]. In one study, 23 percent of patients who aborted after methotrexate and misoprostol did so after a mean delay of 24 days [115]. While some United States medical practices continue to use this method to induce abortion, we strongly recommend that medical practices that provide early pregnancy care incorporate mifepristone into their practice, thus, eliminating the need for methotrexate-based regimens.

Other — Letrozole, a third-generation selective aromatase inhibitor, along with misoprostol has been described by the World Health Organization (WHO) as an alternative to misoprostol plus mifepristone or misoprostol alone regimens [55]. However, there is no high-quality evidence supporting this regimen and we do not use this regimen in our practice.

PATIENT EXPERIENCE

Expected symptoms — Patients can expect vaginal bleeding, abdominal pain, and other symptoms (eg, nausea, vomiting, fevers) following first-trimester medication abortion (table 2) [81]; while bothersome, these symptoms are typically self-limited but may be more severe with increasing duration of gestation [59,119].

- **Vaginal bleeding** – The bleeding pattern after medication abortion is typically bimodal, with moderate to heavy bleeding within the first few hours and days after misoprostol administration (ie, expulsion of pregnancy tissues) followed by a repeat heavier bleeding episode approximately 30 to 60 days later (ie, resumption of menses) [120].

  Vaginal bleeding is typically heavier and longer (mean duration 8 to 17 days) than a menstrual period (figure 3). The perception among patients is that the bleeding is more pronounced after medication abortion than after uterine aspiration because of the duration of bleeding, rather than the volume of blood loss. Representative studies include:

  - In one prospective study including 185 patients undergoing medication abortion, the mean decrease in hemoglobin was 0.7 g/dL, and fewer than 8 percent of patients had a loss exceeding 2 g/dL [121]. When objectively measured, blood loss ranged from 84 to 101 mL compared with a mean loss of 53 mL in patients undergoing uterine aspiration [122]. Blood loss was greater in pregnancies of longer duration [123].

- In one prospective study including over 2000 patients undergoing first-trimester medication abortion, 9 percent of patients still reported mild bleeding after 30 days and 1 percent after 60 days [71].

Blood loss is usually not severe enough to require additional interventions. As an example, in large series, less than 1 percent of patients undergoing first-trimester medication abortion required emergency curettage for excessive bleeding [31]. In another large study, blood transfusion was required in only 0.05 percent of procedures [15]. Because of the possibility of heavy bleeding with misoprostol administration at home, patients with bleeding disorders, anemia, or on anticoagulation therapy may not be candidates for medication abortion. (See 'Contraindications' above.)

Attempts to reduce the duration of bleeding by administration of an oral contraceptive or methotrexate have been ineffective [124,125].

- **Abdominal pain** – Abdominal pain and cramps are experienced by nearly all patients undergoing medication abortion, and patients should be counseled about this as part of the decision-making process between medication abortion and uterine aspiration options. (See "Overview of pregnancy termination", section on 'How to choose'.)

  Increasing patient age and higher gravity and parity correlate with less pain, while dysmenorrhea and increased gestational age correlate with increased pain with medication abortion [126]. The pain is usually self-limited and typically is most severe from shortly after misoprostol is taken until the expulsion of the pregnancy. In a real-time pain study monitoring patients undergoing medication abortion, the mean time to maximum pain was 3.7 ± 2.4 hours after misoprostol, with a mean maximum pain sore of 5.5 ± 2.2 on an 11-point numerical rating scale [127]. At 12, 24, and 72 hours after misoprostol 61, 77, and 82 percent of patients no longer experienced pain.

  If a patient calls with pain that is unrelieved with usual measures (eg, pain medicines, hot water bottle, heating pad) or with pain that increases in severity after the bleeding has begun to subside, medical evaluation is required to assess for complication from a medication abortion. (See 'Complications' below.)

- **Other** – Other symptoms may include gastrointestinal discomfort (eg, nausea, vomiting, diarrhea), thermoregulatory effects (eg, fever, chills), headache, and dizziness. Fever in the absence of infection is a common effect of misoprostol and is reported in 23 to 69 percent of patients undergoing first-trimester abortion [31].

Pain control — Many patients require one or more medications for pain relief. Typically, nonsteroidal anti-inflammatory drugs (NSAIDs) are sufficient [128], but some patients experience a degree of pain that is relieved only with opioids.

- **NSAIDs** – For prophylaxis against crampy abdominal pain and gastrointestinal side effects, we advise patients to premedicate with an NSAID (eg, ibuprofen 600 or 800 mg) and antiemetic (eg, promethazine 25 mg orally) shortly before or after misoprostol. Although concerns have been raised that pretreatment with NSAIDs may decrease the efficacy of exogenous misoprostol [129], abortion success is not affected [130].

- **Opioids** – We rarely provide a prescription for two to four doses of an oral narcotic analgesic as needed for discomfort unrelieved by NSAIDs, consistent with more than half of United States abortion practices [18]. In two randomized trials, pain control scores at the time of medication abortion did not improve with the use of narcotics compared with NSAIDs [131,132]. In one trial, 172 patients undergoing medication abortion at <10 weeks of gestation received either oxycodone or placebo; all patients also received ibuprofen and ondansetron [131]. The addition of oxycodone (10 mg at the onset of pain with an additional six 5 mg tablets to be taken as needed with a maximum dose of 15 mg) did not improve pain scores or reduce the duration of pain. The lack of benefit may be the result of the relatively low doses of narcotic being used (10 mg of oxycodone is equivalent to 5 mg intravenous morphine sulphate) and that patients undergoing medication abortion may actually require a larger opioid dose in order to improve pain scores [133]. Further discussion about the use of opioids for acute pain can be found elsewhere. (See "Prescription of opioids for acute pain in opioid naïve patients" and "Management of acute pain in the patient chronically using opioids for non-cancer pain".)

- **Other** – Other pain medications, such acetaminophen or pregabalin, do not appear to improve pain control more than NSAIDs [134].

  Some patients report the use of marijuana prior to undergoing their abortion procedure as an adjuvant to the pain medications provided by their health care provider; however, marijuana has not been shown to provide additional benefit. In a randomized trial of 70 patients undergoing medication abortion at ≤70 days of gestation, patients that were given ibuprofen plus 5 mg of oral dronabinol (a synthetic form of tetrahydrocannabinol [THC]) compared with ibuprofen alone had similar maximum pain scores and reported similar satisfaction rates with their overall pain management [135]. Other secondary outcomes, such as anxiety and nausea, were also similar between groups. Limitations of this study include that it used an FDA-approved derivative of marijuana available by

prescription only and did not evaluate higher doses or smoked products, which may provide different results [136].

FOLLOW-UP

While the goal of follow-up is to confirm that the abortion is complete and without complications (eg, continued pregnancy, retained products of conception), it is no longer a required part of medication abortion. Further contraceptive counseling or provision may also be provided during follow-up, if desired by the patient and not previously undertaken (see 'Complications' below and 'Plan for contraception' above). Once a complete abortion has been confirmed, the patient does not need further follow-up for the abortion procedure. If new patient concerns arise (eg, heavy bleeding, pain), the patient should contact their regular provider for evaluation.

Remote follow-up with urine hCG — Historically, patients were seen in clinic within 5 to 14 days of mifepristone administration [18]. However, with increasing rates of abortion restriction and the desire to minimize contact in healthcare institutions that accompanied the COVID-19 pandemic, more patients are being offered remote follow-up in conjunction with a home urine pregnancy test [137-139]. In our urban practice within a community that has overall good access to abortion and other medical care, we have prioritized phone follow-up at one to two weeks with an at-home pregnancy test at four weeks. The phone follow-up is conducted by our nursing staff; the patient is asked about their experience during the abortion process and whether the cramping, bleeding, and passage of tissue were consistent with a complete abortion. Patients are also asked about fever or discharge, which may be suggestive of infection.

Protocols that utilize urine human chorionic gonadotropin (hCG) in conjunction with patient symptoms result in high false positive rates (85.2 to 88 percent at four- to five-week follow-up intervals after medication abortion), but they provide a follow-up option that avoids the inconvenience of returning to clinic for many patients who test negative (low false-negative rate of 0.2 percent) [140,141]. Gestational age at time of mifepristone does not affect urine pregnancy results in this follow-up [141]. In a systematic review including eight comparative studies evaluating self-assessment follow-up protocols, the sensitivity for detecting an ongoing pregnancy was ≥90 percent [142]. It is important to note that all but one of the studies in the systematic review utilized a low sensitivity urine pregnancy test (a positive result requires a urine hCG >1000 milli-international units [mIU]/mL). Most over-the-counter pregnancy tests are high-sensitivity tests (a positive result requires a urine hCG >25 mIU/mL [140]), and, thus, there

is a small chance they will be positive four weeks after the procedure even if the abortion was completed.

A semiquantitative multilevel pregnancy test (MLPT) has been developed, largely to improve the convenience and service delivery of medication abortion follow-up. The test is easily interpreted by patients [143] and measures hCG levels in concentrations of <25, 25 to 99, 100 to 499, 500 to 1999, 2000 to 9999, and >10,000 (figure 4). In a systematic review including seven studies evaluating urine pregnancy testing after medication abortion, the MLPT assessment instrument was highly reliable and efficient for allowing the patient to test hCG levels at home [144]. If put into practice, such tests could be performed as a baseline on the day of mifepristone administration and then as a follow-up.

Patient's report of symptoms of vaginal bleeding and cramping alone (without a negative urine hCG) is not sufficient evidence that the pregnancy has been terminated, though more study is needed [145,146]. Research evaluating self-assessment for medication abortion outcomes found that the risk of an undiagnosed ongoing pregnancy increases with increasing gestational age and decreases when standardized questions and criteria are used in telephone follow-up [137,142,145,147].

Role of ultrasound or serum hCG — Prior to COVID-19 and increased abortion restrictions, complete abortion was typically confirmed by measurement of serum human chorionic gonadotropin (hCG) or by transvaginal ultrasound; a pelvic examination may also be performed, though we find this to be rarely needed.

While there is no evidence that one method is superior to the other, we prefer ultrasound in patients who have concerning symptoms of retained tissue (eg, pain, prolonged or heavy bleeding [148,149]), and serum hCG for patients at an early gestational age because an intrauterine gestational sac or yolk sac can be difficult to visualize in such patients.

- **Transvaginal ultrasound** – When transvaginal ultrasound is used in patients with a prior ultrasound with visualization of a gestational sac:
  - The absence of a gestational sac is confirmation of a complete abortion.
  - If there is no gestational sac and the patient has no abnormal symptoms, sonographic findings of heterogeneous echoes, Doppler flow, or a thickened endometrial stripe are **not** evidence of incomplete expulsion and should **not** prompt repeat misoprostol or uterine evacuation without correlation with symptoms that suggest further management is needed [149]. Measurement of endometrial thickness on transvaginal ultrasound is not a clinically useful predictor for the subsequent need for surgical

intervention [150-154]. Typically, if asymptomatic patients are incidentally found to have a modestly thickened endometrial stripe (eg, 2 to 3 cm), they should be alerted to this finding and to symptoms (eg, fever, chills, pain, heavy bleeding, lack of resumption of menses six to eight weeks after medication abortion) that might represent the need for further evaluation and potential uterine aspiration. (See "Retained products of conception in the first half of pregnancy", section on 'Asymptomatic patients with suspected RPOC'.)

- **Serum hCG** – When hCG is used to confirm complete abortion, a baseline serum quantitative hCG is usually drawn on the day mifepristone is administered. The hCG is then repeated, typically within 5 to 14 days; some flexibility is helpful to patients if the second blood draw is done at a laboratory separate from the abortion clinic, which may be remote from, and inconvenient for, the patient [155]. In our practice, if the value has dropped by at least 80 percent and the patient's symptoms are reassuring, we discontinue further lab draws.

  For patients with early gestations, we use a more rapid follow-up sequence and measure a repeat hCG three to five days after the baseline measurement on the day of mifepristone administration. This is to exclude any possibility of an ectopic pregnancy. If the hCG plateaus or increases, the patient should be evaluated for ectopic pregnancy. (See "Ectopic pregnancy: Clinical manifestations and diagnosis", section on 'Diagnostic evaluation'.)

  Serum hCG levels fall rapidly after complete medication abortion. In both prospective and retrospective studies, serum hCG levels dropped by 50 to 70 percent on average within 72 hours of mifepristone administration in those patients who had a successful medication abortion [156,157] and more than 50 percent within 24 hours after pregnancy expulsion [150,156].

  In rare cases, a heterotopic pregnancy or gestational trophoblastic disease may be suspected if the hCG plateaus or increases and subsequent ultrasound shows that the intrauterine pregnancy was completely expelled.

COMPLICATIONS

First-trimester pregnancy termination is a safe procedure and major adverse events are uncommon. In a study of over 200,000 medication abortion procedures, a major adverse event (hospital admission, blood transfusion, emergency department treatment, intravenous antibiotics administration, infection, and death) occurred in 0.16 percent of cases, with

emergency department treatment or hospital admission in 0.1 and 0.06 percent of patients, respectively [15].

Incomplete or failed abortion — Incomplete abortion refers to the incomplete expulsion of the products of conception. Failed abortion is defined as an ongoing pregnancy (ie, continued pregnancy growth on ultrasound, an increasing human chorionic gonadotropin [hCG] level). This may be suspected if the patient has persistent pelvic cramping or vaginal bleeding (eg, spotting persists for more than two weeks, bleeding increases rather than decreases) or ongoing pregnancy symptoms (eg, nausea).

Because of the potential teratogenic risk of prostaglandins (see 'Teratogenicity' above), either should be treated with an additional dose of misoprostol or surgical evacuation (ie, uterine aspiration) [2]:

- Suction aspiration is required if there are signs or symptoms of infection and/or the pregnancy has continued to grow and is now beyond 11+0 weeks of gestation. (See "First-trimester pregnancy termination: Uterine aspiration".)

- For patients with no infection at ≤11+0 weeks, either uterine aspiration or a subsequent dose of misoprostol may be offered. If a subsequent dose of misoprostol is given, we give 800 mcg vaginally or buccally, though lower doses (eg, 400 or 600 mcg) may also be effective [158]. Follow-up (preferably in-person) is then arranged to confirm complete abortion. Most patients (91 to 100 percent) who receive a subsequent dose of misoprostol for incomplete expulsion do expel the gestation [81].

An increasing hCG also raises concern for an ectopic pregnancy. (See 'Contraindications' above.)

Excessive or prolonged bleeding — For patients with excessive or prolonged bleeding, incomplete abortion and infection (eg, postabortal endometritis) should be excluded. (See 'Incomplete or failed abortion' above and 'Infection' below.)

Rarely, a previously undiagnosed uterine arterial-venous malformation or bleeding diathesis may result in bleeding that requires fluid resuscitation, transfusion, uterine artery embolization, or hysterectomy. For patients in whom no other bleeding source is diagnosed, uterine atony alone (without retained tissue) is a rare cause of prolonged or heavy bleeding in pregnancies <11+0 weeks of gestation, but uterotonics (eg, additional misoprostol, carboprost, methergine) may provide benefit. These medications are discussed in detail separately. (See "Postpartum hemorrhage: Medical and minimally invasive management", section on 'Administer additional uterotonic medications'.)

Infection — Patients with the following symptoms or signs should be evaluated for infection: persistent fever, chills, body aches, excessive or prolonged vaginal bleeding, moderate to severe pelvic pain that persists for a day or more after expulsion of the pregnancy, or a purulent vaginal discharge [159-162].

While fever is common (see 'Expected symptoms' above), the incidence of infection is low as medication abortion does not involve instrumentation of the uterus. In a systematic review including more than 46,000 patients undergoing medication abortion, the incidence of infection was 0.9 percent [163]. The incidence of severe infection is even lower. In large, retrospective studies of patients who underwent first-trimester medication abortion, the incidence of serious infection (defined as administration of intravenous antibiotics, hospitalization, sepsis, or death) was 0.006 to 0.093 percent. Infection may include:

- **Postabortal endometritis** – Postabortal endometritis may present with or without fever. Because retained tissue is a risk factor for endometritis, patients diagnosed with endometritis should be evaluated for retained tissue. (See "Retained products of conception in the first half of pregnancy", section on 'Diagnostic evaluation'.)

  Postabortal endometritis is treated in the same manner as other types of postpartum endometritis. (See "Postpartum endometritis".)

- **Clostridial sepsis** – Clostridial sepsis following medication abortion has been reported [159-162]. In general, fulminant lethal clostridial sepsis is rare, and cases are disproportionately higher in pregnant patients, particularly those with spontaneous and induced abortion or cervical or uterine procedures [88,164].

  Clinicians should be aware of the presenting symptoms of clostridial sepsis. Patients with *Clostridium sordellii* sepsis following abortion generally present with dramatic leukocytosis with a marked left shift, hemoconcentration, tachycardia, hypotension, crampy abdominal pain, pleural/peritoneal effusion, and general malaise (weakness, nausea, vomiting, and diarrhea). Other symptoms (eg, fever, bacteremia, rash, significant findings on pelvic examination or gas gangrene by imaging) are absent.

  Optimal therapy is unproven but probably includes surgical debridement, removal of infected organs (eg, hysterectomy), and antibiotics with good anaerobic activity [88]. (See "Toxic shock syndrome due to Clostridium sordellii", section on 'Treatment'.)

Mortality — The overall death rate from all legal abortions is far less than the maternal mortality ratio among patients with term pregnancies in the United States. (See "Overview of pregnancy termination", section on 'Maternal mortality'.)

In the largest series performed to assess safety of medication abortion provision at Planned Parenthood Federation of America (PPFA)'s national affiliates in 2009 to 2010 and including 233,805 patients, the mortality rate for medication abortion was 0.41 per 100,000; only one maternal death was reported and was secondary to ectopic pregnancy [15]. This is similar to the mortality rate of all United States legal induced abortions from 2008 to 2013 (0.62 per 100,000) [165] and significantly lower than the maternal mortality rate for patients with pregnancies at term (16 per 100,000) [166]. Risks of fatal complication in both medication abortion and uterine aspiration increase with increased gestational age [167].

In North America, the majority of deaths associated with first-trimester medication abortion have been due to clostridial sepsis or ectopic pregnancy. (See 'Infection' above and 'Contraindications' above.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Pregnancy termination".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Abortion (The Basics)")
- Beyond the Basics topics (see "Patient education: Abortion (pregnancy termination) (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Clinical significance** – First-trimester medication abortion is the termination of pregnancy by using medications to induce a process similar to a miscarriage and is an alternative to uterine aspiration. Mifepristone (a progesterone antagonist), in combination with misoprostol (a synthetic prostaglandin E1), is approved for this use in the United States for the termination of pregnancies up to 70 days of gestation but is used routinely through 77 days (11+0 weeks) of gestation. (See 'Introduction' above.)

- **Contraindications** – Contraindications to first-trimester medication abortion include a gestation >77 days, suspected ectopic pregnancy, intrauterine device (IUD) in place, known anemia, some hemorrhagic disorders, anticoagulant therapy, chronic adrenal failure, long-term corticosteroid therapy, inherited porphyrias, and inability to comply with the regimen or lack of access to emergency care in the case of a complication. (See 'Contraindications' above.)

- **Medications** – For first-trimester medication abortion, we suggest mifepristone plus misoprostol rather than either medication alone (**Grade 2C**). (See 'Efficacy' above.)

  - The steps of the procedure vary by patients setting (eg, in-person, telemedicine, self-managed) but typically includes a single dose of mifepristone (oral, 200 mg) followed by misoprostol (800 mcg) 24 to 48 hours after taking mifepristone. We suggest misoprostol be taken buccally rather than by other routes (**Grade 2C**). We instruct our patients to place misoprostol in the buccal space between the cheek and the gum for 30 minutes (figure 2). (See 'Protocols by setting' above.)

  - For gestations from 9+0 to 11+0 weeks, a second dose of misoprostol 800 mcg should be given for the patient to self-administer buccally three to six hours after the first dose; this dose should be administered, even if bleeding has occurred, to decrease the risk of an incomplete abortion. (See 'Misoprostol' above.)

- **Follow-up** – Final follow-up to confirm complete abortion, is not required. If done, it can be performed with a phone screen at two weeks and a home urine pregnancy test performed at four weeks. Ultrasound and hCG may be performed in selected patients. (See 'Follow-up' above.)

- **Efficacy** – First-trimester medication abortion is successful in 95 to 98 percent of procedures. Failed medication abortion is treated with repeat misoprostol or surgical uterine evacuation. (See 'Efficacy' above.)

- **Expected symptoms** – Side effects following administration of mifepristone and misoprostol primarily consist of crampy abdominal pain, vaginal bleeding, gastrointestinal discomfort (eg, nausea), and fever. (See 'Expected symptoms' above.)

- **Complications** – Major adverse events after medication abortion are uncommon. Potential complications include incomplete abortion, hemorrhage, infection, or death (rare). (See 'Complications' above.)

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Topic 3296 Version 53.0

GRAPHICS

Risk factors for ectopic pregnancy compared with pregnant controls

Degree of risk	Risk factors	Odds ratio
High	Previous ectopic pregnancy	2.7 to 8.3
	Previous tubal surgery	2.1 to 21
	Tubal pathology	3.5 to 25
	Sterilization	5.2 to 19
	IUD	
	- Past use	1.7
	- Current use	4.2 to 16.4
	- Levonorgestrel IUD	4.9
	In vitro fertilization in current pregnancy	4 to 9.3
Moderate	Current use of estrogen/progestin oral contraceptives	1.7 to 4.5
	Previous sexually transmitted infections (gonorrhea, chlamydia)	2.8 to 3.7
	Previous pelvic inflammatory disease	2.5 to 3.4
	In utero DES exposure	3.7
	Smoking	
	- Past smoker	1.5 to 2.5
	- Current smoker	1.7 to 3.9
	Previous pelvic/abdominal surgery	4
	Previous spontaneous abortion	3
Low	Previous medically induced abortion	2.8
	Infertility	2.1 to 2.7
	Age ≥40 years	2.9
	Vaginal douching	1.1 to 3.1

	Age at first intercourse <18 years	1.6
	Previous appendectomy	1.6

IUD: intrauterine device; DES: diethylstilbestrol.

Data from:

- *Clayton HB, Schieve LA, Peterson HB, et al. Ectopic pregnancy risk with assisted reproductive technology procedures. Obstet Gynecol 2006; 107:595.*
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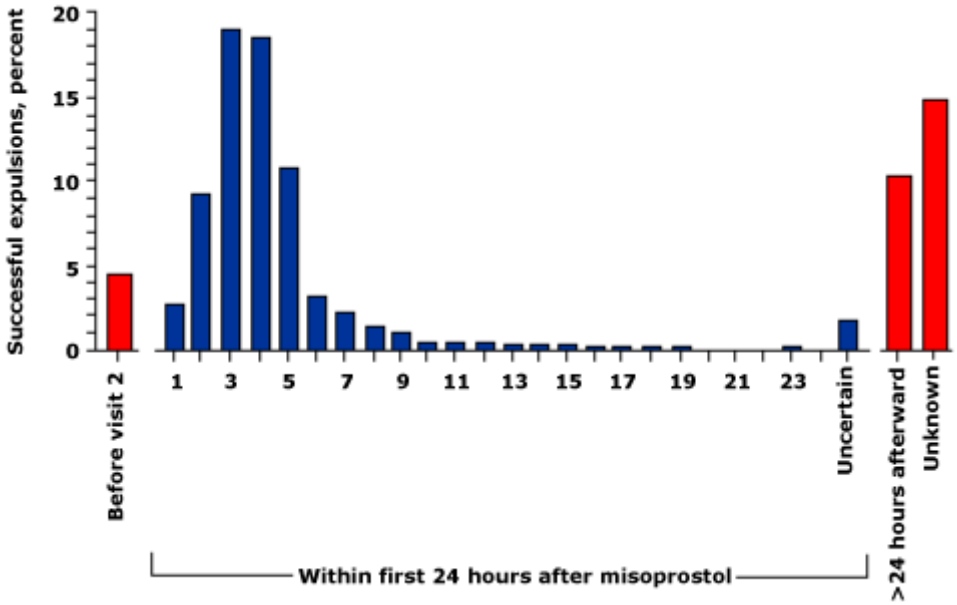
Graphic 82282 Version 9.0

Time of expulsion of conceptus in 1720 women with successful medical termination of pregnancy

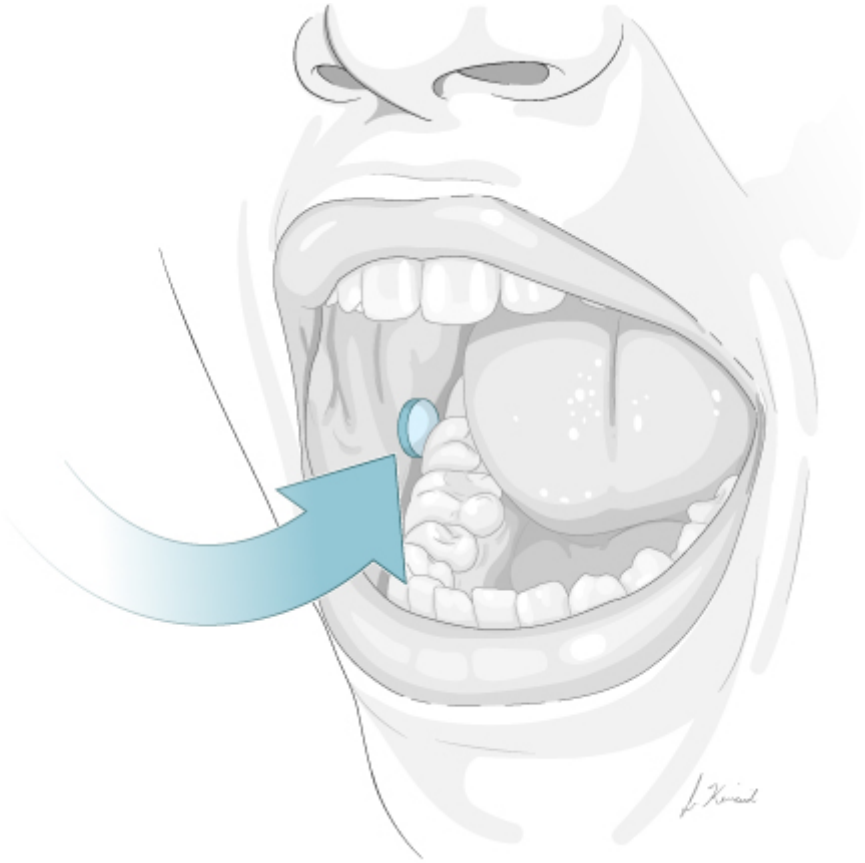


The women received oral mifepristone 600 mg at visit 1 and oral misoprostol 400 mcg 2 days later (visit 2). "Uncertain" indicates that expulsion occurred within the first 24 hours after misoprostol was given, but the exact time was not known.

Data from Spitz IM, Bardin CW, Benton L, Robbins A. N Engl J Med 1998; 388:1241.

Graphic 79736 Version 3.0

Buccal administration of medication



For buccal administration, the tablet is placed in the space between the cheek and the gum of the lower jaw.

Modified from: Tropical and inhalant medications. In: Fundamental Nursing Skills and Concepts, 11th ed, Timby BK (Ed), Lippincott Williams and Wilkins, Philadelphia 2016.

Graphic 119194 Version 2.0

Adverse effects in selected North American trials of medical abortion regimens

Trial	Incidence of adv						
	Nausea		Vomiting		Diarrhea		
	Mifepristone	Misoprostol	Mifepristone	Misoprostol	Mifepristone	Misoprostol	
Schaff (1997)¶	36	36	14	14	8	22	
Schaff (1999)Δ	45	43	13	26	11	23	
Wiebe (2002)◇	45	39	13	15	5	16	
Creinin (2004)§	20	44	5	23	1	27	
	39	52	14	30	7	25	
Creinin (2007)¥	N/R	58	N/R	31	N/R	35	
	29	51	9	31	5	26	
Winikoff (2008)‡	N/R	64	N/R	40	N/R	35	
	N/R	66	N/R	40	N/R	34	

N/R: not reported.

* Fever, warmth, hot flushes, or chills.

¶ Mifepristone, 600 mg, followed by misoprostol, 800 mcg vaginally, 36 to 48 hours later.[1]

Δ Mifepristone, 200 mg, followed by misoprostol, 800 mcg vaginally, 48 hours later.[2]

◇ Mifepristone, 600 mg, followed by misoprostol, 400 mcg orally, 36 to 48 hours later.[3]

§ Mifepristone, 200 mg, followed by misoprostol, 800 mcg vaginally, 6 to 8 hours later (first row) or 24 hours later (second row).[4]

¥ Mifepristone, 200 mg, followed by misoprostol, 800 mcg vaginally, 0 to 15 minutes later (first row) or 24 hours later (second row).[5]

‡ Mifepristone, 200 mg, followed by misoprostol, 800 mcg orally (first row) or buccally (second row), 24 to 36 hours later.[6]

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1. *Schaff EA, Stadalius LS, Eisinger SH, Franks P. Vaginal misoprostol administered at home after mifepristone (RU486) for abortion. J Fam Pract 1997; 44:353.*
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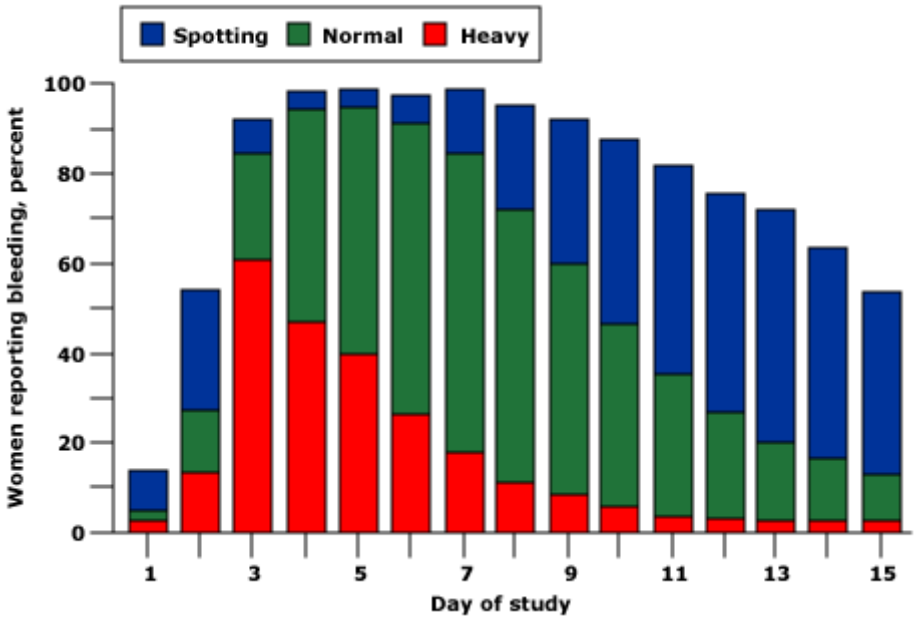
Graphic 119196 Version 1.0

Types of vaginal bleeding as recorded by women from day 1 (administration of mifepristone) to day 15

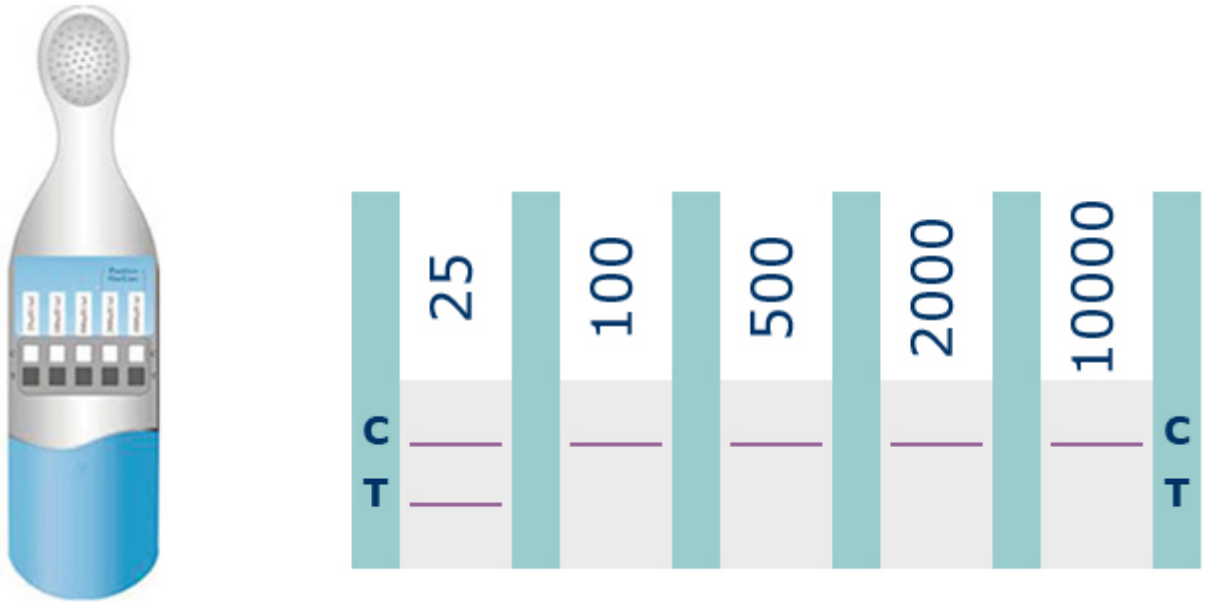


The data are from 1506 women who did not undergo surgical termination of pregnancy and who recorded the types of bleeding they had from study day 1 to day 15 on menstrual diary cards. Bleeding was characterized as spotting, as similar to normal menstrual bleeding (normal), or as heavier than normal menstrual bleeding (heavy).

Data from Spitz IM, Bardin CW, Benton L, Robbins A. N Engl J Med 1998; 388:1241.

Graphic 56315 Version 2.0

Semiquantitative multi-level urine hCG test



- The dBest multilevel pregnancy test with reading of at least 25 mIU/mL of hCG.
- A control line indicates that the test strip has been properly saturated with urine and that the test is functioning properly. A control line must appear in all 5 columns for the test to be considered valid.
- A test line indicates a positive test result.
- A column with 1 line (a C line but no shading in the T line) is indicative of a negative test reading. A column consisting of 2 lines (a C line and a T line) indicates a positive test reading for the specific level of hCG.

hCG: human chorionic gonadotropin; C: control line; T: test line.

Graphic 119675 Version 1.0

Contributor Disclosures

Deborah A Bartz, MD, MPH No relevant financial relationship(s) with ineligible companies to disclose. **Paul D Blumenthal, MD, MPH** No relevant financial relationship(s) with ineligible companies to disclose. **Jody Steinauer, MD, MAS, PhD** Consultant/Advisory Boards: Modern Fertility[Contraceptive decision-making, education and support for patients and clinicians. This includes unbiased information about all methods of contraception.]. All of the relevant financial relationships listed have been mitigated. **Alana Chakrabarti, MD** No relevant financial relationship(s) with ineligible companies to disclose.

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