



## Commentary: No-test medication abortion: A sample protocol for increasing access during a pandemic and beyond ☆☆☆



Elizabeth G. Raymond<sup>a,\*</sup>, Daniel Grossman<sup>b</sup>, Alice Mark<sup>c</sup>, Ushma D. Upadhyay<sup>b</sup>, Gillian Dean<sup>d</sup>, Mitchell D. Creinin<sup>e</sup>, Leah Coplon<sup>f</sup>, Jamila Perritt<sup>g</sup>, Jessica M. Atrio<sup>h</sup>, DeShawn Taylor<sup>i</sup>, Marji Gold<sup>j</sup>

<sup>a</sup> Gynuity Health Projects, New York, NY, United States

<sup>b</sup> Advancing New Standards in Reproductive Health (ANSIRH), Bixby Center for Global Reproductive Health, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California San Francisco, Oakland, CA, United States

<sup>c</sup> National Abortion Federation, Washington DC, United States

<sup>d</sup> Planned Parenthood Federation of America, New York, NY, United States

<sup>e</sup> Department of Obstetrics and Gynecology, University of California, Davis, Sacramento, CA, United States

<sup>f</sup> Maine Family Planning, Augusta, ME, United States

<sup>g</sup> Reproductive Health and Family Planning Specialist, Washington DC, United States

<sup>h</sup> Society of Family Planning, Clinical Affairs Subcommittee and Department of Obstetrics and Gynecology, Montefiore Hospital and Albert Einstein College of Medicine, Bronx, NY, United States

<sup>i</sup> Department of Obstetrics and Gynecology, University of Arizona College of Medicine Phoenix, AZ, United States

<sup>j</sup> Department of Family and Social Medicine, Albert Einstein College of Medicine, Bronx, NY, United States

### 1. Introduction

The COVID-19 pandemic is acutely threatening access to essential health services, including abortion [1]. Across all fields of medicine, changes in practice models are occurring rapidly. For patients seeking abortion, urgent modifications of current protocols are needed to ensure that patients can continue to obtain this time-sensitive treatment while limiting transmission of infection by maintaining distance between and among patients and providers. Remote delivery of care, which has recently been endorsed by local, state, and federal authorities as a key epidemic control measure [2], will be indispensable to accommodate patients and staff who are navigating quarantines, stay-at-home directives, lack of transportation, new family or work obligations, or other unavoidable circumstances that impede their ability to go in person to a health facility.

Fortunately, medication abortion (MA) using mifepristone and misoprostol can address many of these challenges. At present,

MA typically entails a visit to a clinician or facility that provides abortion where an ultrasound or pelvic examination and often blood tests are performed to evaluate eligibility before pills are dispensed. Many abortion providers require a follow-up ultrasound or blood test after treatment to confirm abortion completion. However, research and experience have demonstrated that these tests, which inherently involve physical contact between patient and health care worker, are usually unnecessary for safe and effective MA [3–7]. Indeed, over the past 15 years, international organizations have provided mifepristone and misoprostol by mail to tens of thousands of patients screened only by history [8–11]. A prospective study conducted in 2015–2016 in the United States, Mexico, and Moldova provided 406 MAs without screening ultrasound or pelvic examination [12]. No serious adverse events were reported that resulted from the omission of the tests, and participants were highly satisfied.

To assist abortion providers with the current crisis, we present a sample protocol (Box. 1) for providing a “no-test” MA that includes recommendations for patient selection, Rh status evaluation and management, the treatment regimen, and follow-up. Although FDA-imposed restrictions on mifepristone dispensing may require patients to go to the abortion provider or facility to obtain the drug [13], this protocol would enable every other part of the MA process to be implemented without any in-person encounter. The protocol is intended to serve as a guidance; abortion providers should use clinical judgment when adapting it for their practice settings and patient populations. Below we summarize the data that we considered in developing this protocol and our rationales for and comments on selected provisions.

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\* Corresponding author.

E-mail addresses: [eraymond@gynuity.org](mailto:eraymond@gynuity.org) (E.G. Raymond), [Daniel.Grossman@UCSF.edu](mailto:Daniel.Grossman@UCSF.edu) (D. Grossman), [amark@prochoice.org](mailto:amark@prochoice.org) (A. Mark), [Ushma.Upadhyay@ucsf.edu](mailto:Ushma.Upadhyay@ucsf.edu) (U.D. Upadhyay), [gillian.dean@ppfa.org](mailto:gillian.dean@ppfa.org) (G. Dean), [mdcreinin@ucdavis.edu](mailto:mdcreinin@ucdavis.edu) (M.D. Creinin), [lcoplon@mainefamilyplanning.org](mailto:lcoplon@mainefamilyplanning.org) (L. Coplon), [jatrio@montefiore.org](mailto:jatrio@montefiore.org) (J.M. Atrio), [d.taylor@desertstarfp.org](mailto:d.taylor@desertstarfp.org) (D. Taylor), [mgold@montefiore.org](mailto:mgold@montefiore.org) (M. Gold).

## Sample Protocol for No-Test Medication Abortion

### PURPOSE

To enable safe and effective provision of medication abortion without a mandatory pre-treatment ultrasound, pelvic examination or laboratory tests when medically appropriate, given that these tests may be significant barriers to access and, in the setting of a pandemic, may increase transmission of infection to patients and health care workers.

### CRITERIA

- Pregnancy confirmed by patient report of urine or serum test or prior ultrasound
- Last menstrual period started  $\leq 77$  days before anticipated date of mifepristone ingestion
- Certain of last menstrual period onset date  $\pm 1$  week
- None of the following symptoms or risk factors for ectopic pregnancy:
  - Vaginal bleeding or spotting within the past week
  - Unilateral pelvic pain or significant bilateral pelvic pain within the past week
  - Prior ectopic pregnancy
  - Prior permanent contraception or other tubal surgery
  - IUD in uterus at conception or currently
- None of the following contraindications to medication abortion, assessed by history:
  - Hemorrhagic disorder or concurrent anticoagulant therapy
  - Chronic adrenal failure
  - Concurrent long-term systemic corticosteroid therapy
  - Inherited porphyria
  - Allergy to mifepristone, misoprostol, or other prostaglandin
- No strong preference for pre-treatment ultrasound, pelvic examination or laboratory tests

### RH TYPING AND ADMINISTRATION OF ANTI-D IMMUNOGLOBULIN

- Not needed if the gestational age on the anticipated mifepristone ingestion date will be  $< 70$  days or if the patient reports positive Rh type, wants no future children, or declines anti-D immunoglobulin.
- Should be considered for patients not meeting above criteria

### TREATMENT

Provide the following:

- Mifepristone 200 mg orally
- Misoprostol 800 mcg x 2
- Analgesics, antiemetics per health facility protocol
- Patient instruction sheet and health facility emergency contact information
- Two high sensitivity pregnancy tests (HSPTs)

The patient should take mifepristone 200 mg orally followed by misoprostol 800 mcg buccally or vaginally 24–48 hours later. Patients with estimated GA  $> 63$  days should take a second dose of misoprostol 800 mcg 4 hours after the first. Patients with estimated GA  $\leq 63$  days should take the second dose if no bleeding occurs within the first 24 hours after the first misoprostol dose or if instructed to take it by a clinician. Review the instruction sheet with the patient.

### FOLLOW-UP

1. Plan a follow-up contact with the patient one week after dispensing treatment.
2. If the patient reports indicators of continuing or ectopic pregnancy (e.g., any of the symptoms on the instruction sheet), evaluate with ultrasound or serum HCGs.
3. Otherwise, instruct the patient to perform the first HSPT 4 weeks after taking misoprostol (not earlier) and to contact the abortion provider if the result is positive.
4. If the patient has indicators of continuing or ectopic pregnancy, evaluate with ultrasound or serum HCGs
5. If the first HSPT result is positive but the patient has no such indicators, instruct the patient to perform the second HSPT in 1 week.
6. If second HSPT result is also positive, evaluate with ultrasound, serum HCGs, additional urine testing, or uterine aspiration.

**Box. 1.** Sample protocol for no-test medication abortion.

## 2. Patient selection

The three key goals of clinical evaluation before MA are (1) to confirm that the gestational age (GA) is within accepted limits for effective and safe outpatient treatment, (2) to identify ectopic pregnancy, and (3) to establish that the patient has no other contraindications to MA.

The sample no-test MA protocol specifies an upper GA limit of 77 days as estimated from the first day of the last menstrual period (LMP). The LMP-based GA should be  $\leq 77$  days on the day of mifepristone ingestion, which may be later than the day the drug is dispensed if the patient plans to take the pills home for later use or if the medication is mailed or dispensed to a patient intermediary. The patient should be certain within one week of the LMP onset date.

We chose a 77-day limit because recent data have indicated that outpatient MA is safe and effective through that GA [14,15] and because this limit is consistent with current guidelines of the National Abortion Federation [16] and Planned Parenthood Federation of America (personal communication, Gillian Dean, MD, MPH, Planned Parenthood Federation of America). We note, though, that 2014 guidelines issued by the American College of Obstetricians and Gynecologists (ACOG) and the Society for Family Planning [17] as well as the mifepristone label approved by the US Food and Drug Administration in 2016 specify a 70-day limit. In response to the pandemic, ACOG has recently issued a statement acknowledging that LMP-based gestational dating without ultrasound is acceptable, although no specific GA limit was specified [18].

Regardless of the precise GA limit selected, use of the no-test approach will inevitably result in treatment of some fraction of patients whose true GAs exceed 77 days. Data from studies that compared LMP-based GA estimates to ultrasound-based estimates suggest that this fraction tends to be higher in patient populations that include more patients with advanced GA [19,20] and that it may be reduced by decreasing the LMP-based GA cutoff [19]. Reassuringly, the largest study, which was conducted in the United States in 2005–2007 [21], found that only 31 (1%) of 3012 MA patients who were certain that their LMPs had started  $\leq 77$  days prior had GAs  $> 77$  days by ultrasound examination. Furthermore, international studies that included more than 1600 patients treated with mifepristone and one or more misoprostol doses at 13–24 weeks of gestation reported efficacy and safety similar to that expected in earlier gestation:  $>93\%$  of patients aborted without further intervention, 0.7–4% required transfusion, and no patient required hysterectomy or died [22]. Therefore, we expect that serious adverse health consequences of GA underestimation based on LMP will be rare. Nevertheless, clinicians using the no-test approach to MA should have a plan for managing or referring patients who may need a second trimester procedure to complete the abortion.

When assessing GA, providers may incorporate other historical information reported by the patient that, for simplicity, we do not mention in the sample protocol but that may indicate that the GA is greater than the proposed limit. For example, a patient who reports a positive pregnancy test  $>7$  weeks before presentation is unlikely to have a GA of  $\leq 77$  days. The sample protocol does not exclude patients who report menstrual irregularity or recent use of hormonal contraceptives. Although these conditions may signal ovulatory dysfunction, we expect that they would more likely lead to overestimation of GA than to underestimation, which is the primary concern for MA eligibility, and excluding patients with these conditions may therefore unnecessarily limit access by eligible patients.

MA with mifepristone and misoprostol is contraindicated in patients with ectopic pregnancy not because the drugs are dangerous for such patients but because the regimen is not a proven treatment for this condition. The sample no-test protocol excludes patients with significant symptoms of or risk factors for ectopic pregnancy; recent vaginal bleeding or pelvic pain, prior permanent contraception, prior ectopic pregnancy, or intrauterine device in place at conception [23,24]. We do not exclude patients who report prior pelvic inflammatory disease because unconfirmed diagnoses of this condition are associated with only a mildly increased risk [24]. We recognize that the listed criteria will not identify every patient with ectopic pregnancy; an estimated half of all patients with this condition have no risk factors [25]. However, published and emerging data suggest that the incidence of ectopic pregnancy among patients seeking MA is very low,  $<1\%$  [26,27]. Moreover, substantial data [28–32] and current clinical MA guidelines [16,33] support treatment of patients in whom ectopic pregnancy

has not been definitively excluded because the condition can be detected and managed afterwards. Thus, this aspect of the protocol is consistent with the standard of care.

The medical contraindications in the sample protocol are those listed in the FDA-approved mifepristone label. Patient history is sufficient for assessing these conditions.

### 3. Rh typing and other pre-treatment laboratory testing

Recent research has suggested that the risk of Rh sensitization after early abortion is negligible [34–36]. Consequently, the National Abortion Federation has concluded that forgoing Rh typing and administration of anti-D immunoglobulin is reasonable for Rh-negative patients having aspiration abortion before 56 days of gestation and may be considered for all patients having MA at less than 70 days [16,37]. The sample protocol is consistent with this conclusion. In addition, it specifies that testing is unnecessary for patients who can report a Rh-positive blood type or who are certain that they want no future children after the planned abortion. Any patient may opt out of Rh typing; the recent statement from ACOG notes that Rh testing and RhD immunoglobulin administration should not be a barrier to the provision of medication abortion [18].

Hemoglobin/hematocrit and other laboratory tests are not routinely needed before first-trimester abortion but may be performed as indicated by medical history and patient symptoms [16].

### 4. Treatment regimen

The sample protocol specifies that patients should receive a standard regimen of mifepristone 200 mg orally and misoprostol 800 mcg vaginally or buccally [16]. In addition, each patient should be provided with an extra dose of misoprostol 800 mcg. Those with estimated GA  $> 63$  days should be instructed to take this second misoprostol dose 4 hours after the first to improve effectiveness [16,38]. Patients with estimated GA  $< 63$  days may be instructed to take the second dose if no bleeding occurs within the first 24 hours after the first dose or to retain it for use if recommended by the provider. Alternatively, all patients may be told to take two misoprostol doses 4 hours apart. Although this specific regimen has not been studied, trials of repeated doses of misoprostol in the first and second trimester suggest that it will be safe [39–43].

### 5. Scheduled follow-up

The primary goals of follow-up are to confirm absence of continuing pregnancy, to detect ectopic pregnancies not diagnosed before treatment, and to identify complications that need evaluation and treatment. To accomplish these goals, the sample protocol relies on patient symptoms and high sensitivity urine pregnancy tests (HSPTs) that the patient performs at home. This strategy has been validated in several studies [44,45], is consistent with current MA guidelines for follow-up of patients who have documented intrauterine pregnancies [16,17], and is increasingly used by MA providers.

The sample instruction sheet (Box. 2), which includes a list of symptoms that may need in-person evaluation, is derived from studies of symptoms used to assess outcomes in MA patients with intrauterine pregnancies documented by ultrasound [44–47] and from experience in managing patients with ectopic pregnancies. The instruction sheet directs patients to contact the abortion provider if specified symptoms occur or the HSPT result is positive. Research has shown that patients can safely use these tools on their own to recognize when follow-up is needed [48,49], and

### Sample Instructions for Patients Receiving No-Test Medication Abortion

1. **Call your abortion provider if:**
  - ☐ You vomit within the first 30 minutes after taking mifepristone.
  - ☐ You have a fever of 100.4°F or higher more than 24 hours after you take the misoprostol.
  - ☐ One week after taking misoprostol, you have any of the following:
    - You have not had cramping and bleeding heavier than a period.
    - Your bleeding is not getting lighter.
    - You do not feel that you passed the pregnancy.
    - Your pregnancy symptoms (such as nausea and breast tenderness) are not resolving.
  - ☐ At any time, you have any of the following:
    - An increase in pain/cramps or bleeding more than 24 hours after taking misoprostol.
    - Severe pain or cramps that don't get better with pain medicine, rest, or heating pads.
    - Enough bleeding to soak 2 maxi pads an hour for more than 2 hours.
    - Dizziness or vomiting lasting more than 2 hours.
    - Weakness, nausea, or diarrhea lasting more than 24 hours.
2. Perform one urine pregnancy test 4 weeks after taking misoprostol (not earlier). **Call your abortion provider if the result is positive or invalid.** Use the second test if instructed to do so by your abortion provider.

**Box. 2.** Sample instructions for patients receiving no-test medication abortion.

indeed patient-controlled follow-up is widely used for MA follow-up by provider organizations in multiple European countries [50–52]. However, the sample no-test protocol recommends a planned follow-up contact with the provider one week after dispensing the abortifacient medications to confirm absence of symptoms of ongoing or undiagnosed ectopic pregnancy or other potential complications. This contact may be conducted by videoconference, telephone, patient portal, email, text, or other telehealth modalities [53,54].

MA failures are often detectable based on symptoms alone [6,44,47–49]. Nevertheless, the sample no-test protocol recommends a HSPT 4 weeks after misoprostol use to confirm pregnancy termination. Available data indicate that 5–25% of HSPTs performed about a month after MA treatment produce positive results, nearly all of which are “false positives” in patients who no longer have viable pregnancies [44,45]. Therefore, the sample protocol recommends that two HSPTs be provided initially to each patient. The patient should be instructed to contact the provider if the result of the initial 4-week test is positive. If the patient is asymptomatic, a repeat test one week later may be appropriate. If the patient has symptoms of ongoing or ectopic pregnancy or the second HSPT result is positive, further evaluation is indicated. The specific procedures for this evaluation should address the patient's individual clinical situation and may include ultrasound, serial serum HCG levels, additional urine pregnancy testing, or aspiration and tissue examination.

Patients receiving a no-test MA may remain at risk for having ectopic pregnancy until a negative HSPT result is obtained. Therefore, vigilant attention on the part of both provider and patients to

symptoms such as increased pelvic or abdominal pain, continued vaginal bleeding, or dizziness is imperative.

### 6. Counseling

Patients requesting a no-test MA should receive standard pre-abortion counseling about pregnancy options, the risks and benefits of MA, expected results, side effects, and warning signs. In addition, each patient should be explicitly informed that LMP-based dating may underestimate GA, in which case efficacy may be lower than expected, bleeding and cramping may be heavier, and, rarely, fetal tissue may be visible. Moreover, patients should understand that without ultrasound, ectopic pregnancy will not be definitively excluded before treatment. To increase the chance of abortion success and reduce the time to diagnosis of ectopic pregnancy or MA complications, patients should be advised to diligently follow all instructions provided. However, patients should also be advised that serious adverse events of no-test abortion are expected to be rare and that side effects of MA can often be managed remotely. To avoid unnecessary infectious exposure during a pandemic as well as excess cost and inconvenience, patients should contact the abortion provider before seeking in-person care.

### 7. Conclusion

Although the COVID-19 crisis prompted the development of this sample protocol, we recognize that the pandemic is only one of many longstanding, serious impediments to abortion access in



the United States. Omitting unnecessary use of ultrasound, examination, and laboratory tests before MA can reduce barriers to this essential service by decreasing cost and enhancing convenience and comfort. The no-test approach can enable provision of abortion in new venues and by new categories of providers, and it can facilitate new service delivery models, such as synchronous or asynchronous telehealth, stationary or mobile “mini-clinics”, pill pick-up arrangements, or dispensing via lockboxes or, potentially, by mail [7,54]. If the no-test strategy results in earlier treatment, it may increase MA success rates [14,43,55]. Details of the no-test MA protocol will certainly need to be revised as new evidence emerges, but we anticipate that this approach to providing the service will continue to be beneficial for both patients and abortion providers even after the current epidemic resolves.

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