English

PROVIDING MEDICAL ABORTION IN LOW-RESOURCE SETTINGS

An Introductory Guidebook

Second Edition

Providing Medical Abortion in Low-Resource Settings: An Introductory Guidebook

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Preface to the Second Edition

The availability and use of medical abortion has increased rapidly since the publication of the first edition of this guidebook in 2004. We wrote the second edition of *Providing Medical Abortion in Developing Countries: An Introductory Guidebook* to incorporate important scientific developments and innovations in clinical practice. These changes have informed the emergence of protocols that can be used in a variety of low-resource settings worldwide. The new title *Providing Medical Abortion in Low-Resource Settings* reflects these broader applications.
The guidebook follows the same chapter and topic sequence as the first edition. The second edition includes updated information on routes of misoprostol administration, infection and medical abortion, use of medical abortion for late first trimester abortion induction, telemedicine and medical abortion, professional and international clinical guidelines for use of mifepristone-misoprostol medical abortion, and a list of additional resources now available.

Table of Contents

I. Introduction

The term medical abortion refers to pregnancy termination with abortion-inducing medications in lieu of a surgical procedure.[1] Although the idea of using medications to induce abortion has been around for centuries, evidence-based regimens for use in the first trimester of pregnancy only became a reality in the last 25 years. Mifepristone (commonly referred to as RU-486) was developed in France in the 1970s and 80s by researchers investigating glucocorticoid receptors. The first clinical study of the drug as an abortifacient began in Geneva in 1981. In 1985, investigators reported that in combination with a prostaglandin analog (now, almost universally misoprostol) increased the efficacy of mifepristone. In 1988, France became the first country (outside of China) to license mifepristone for use in combination with a prostaglandin analog for early abortion. Since that time, the method has slowly spread around the globe, and millions of women have used the method worldwide.

Mifepristone is now registered in over 40 countries. In 2005, mifepristone was included in the World Health Organization's (WHO) Essential Medicines List. In recent years, several new mifepristone and prostaglandin analog (misoprostol) products have entered the market increasing the availability and reducing the cost of both drugs. New simplified regimens are making medical abortion more acceptable to women and providers. Together these developments are helping an increasing number of women access a non-surgical option for termination of pregnancy. Medical abortion has the potential to increase access to safe abortion services because it can be offered by providers in settings where surgical abortion may not be safe or widely available.

The first edition of this guidebook (2004) grew out of a meeting held in Bellagio, Italy in July 1998, where a group of researchers, healthcare providers, women's health advocates, donors, and representatives of ministries of health discussed the potential of medical abortion in the international arena. After much debate, the group came to consensus that a regimen of mifepristone followed by a suitable prostaglandin can feasibly be delivered in a manner that is safe, effective, and acceptable for women in developing countries.[2] Harnessing the momentum gained from this initial meeting, a small group of medical abortion experts from around the world assembled in July 2000 to develop recommendations for use in low-resource

settings. The goal of this second meeting was to provide comprehensive, easy to understand guidelines for new providers and policymakers worldwide.

In 2009, the guidebook was revised, reflecting recent scientific and programmatic developments in the use of mifepristone-misopostol for early abortion. The new title "Providing Medical Abortion in Low-Resource Settings" underscores how these developments have encouraged the creation of simplified medical abortion protocols relevant in low-resource settings worldwide.

How to use this guidebook

This guidebook is geared to providers and policy makers who are interested in learning about medical methods for safe termination of early pregnancy. The information in this guidebook is meant for readers with a basic knowledge of reproductive biology and women's health services. The guidebook may also serve as an introduction to those with no prior knowledge about medical abortion. Topics mentioned more than once are cross-referenced.

II. Overview

Chapter themes

- What mifepristone is and how it works
- Efficacy when used with a prostaglandin for early medical abortion
- Safety and acceptability of the method

A. What mifepristone is and how it works

Mifepristone is an antiprogestin licensed for pregnancy termination in many countries around the world. In some European countries, mifepristone is also licensed for cervical softening prior to first trimester abortions, cervical softening for second trimester abortion, and induction of labor following intra-uterine fetal death. It is currently under study for a number of other potential applications. Mifepristone blocks progesterone receptors, and, if taken in early pregnancy, the uterus can no longer sustain the growing embryo. Mifepristone also triggers an increase in endogenous prostaglandins and dilates the cervix, facilitating abortion.

When used alone, mifepristone has been shown to be from 60 to 80% effective in inducing abortions in pregnancies of less than 49 days since the last menstrual period (LMP). Because the drug makes the uterus more sensitive to the muscle contracting effects of prostaglandins, the combination of mifepristone with a prostaglandin analog increases the efficacy of the regimen. Initially, sulprostone (an injectable prostaglandin) and gemeprost (a vaginal suppository) were used with mifepristone in Europe. Sulprostone was associated with a number of cardiovascular incidents, including one fatal myocardial infarction, and its use was supplanted by misoprostol (an oral prostaglandin analog). Gemeprost is still used occasionally in the second trimester in the United Kingdom and Sweden. Worldwide, misoprostol is currently the favored prostaglandin for use with

mifepristone because of its safety, low cost, wide availability, stability at room temperature, and easy administration.[3] Misoprostol may be administered orally, vaginally, buccally, or sublingually and is generally taken 24-48 hours after ingestion of mifepristone.

B. Efficacy

A successful medical abortion is defined as complete termination of pregnancy without the need for a surgical procedure. Mifepristone-misoprostol medical abortion for early first trimester pregnancies has a high success rate, generally around 95% (see Appendix A for success rates reported in clinical trials), although even higher in some service delivery systems (98.5% in the Planned Parenthood Federation of America).[4,5] Failure, defined as recourse to a surgical procedure, may be the result of an ongoing pregnancy, incomplete expulsion, heavy bleeding, judgment of the provider that the medical process should be terminated surgically, or the request of the woman. Fewer than 5% of women expel the products of conception after mifepristone but before taking misoprostol.[6] The majority of women expel within 24 hours of misoprostol administration but the process may take up to 2 weeks to complete.

Factors that may affect efficacy:

- ***Gestational age of pregnancy:*** Medical abortion is less effective as gestational age increases. Regimens using buccal, sublingual and vaginal misoprostol are highly effective at gestational ages up to nine weeks' LMP. Oral misoprostol is also highly effective at gestational ages up to eight weeks' LMP but declines slightly at later gestational ages (see Appendix A). The method remains effective in the late first trimester and many different regimens are equally feasible (see Chapter VII).

- ***Regimen:*** Regimens for mifepristone-misoprostol medical abortion vary in terms of misoprostol dose, timing of the doses, and misoprostol route of administration. Although the efficacy of regimens does not appear to vary widely at gestational ages less than eight weeks there is evidence that regimen variations may have an effect on efficacy in gestations greater than eight weeks' LMP (see Chapter IV, Section A) but provider practices are probably more important than what regimen is chosen.

- ***Provider:*** Success rates for providers using the same regimen often vary considerably. A provider may decide to complete the abortion surgically for convenience when not medically necessary or may mistakenly believe the abortion was not complete and intervene surgically. Factors that may lead a provider to intervene unnecessarily include incorrect clinical judgment, provider impatience, and inexperience with the method. As providers become more comfortable with the method, they tend to achieve higher success rates because they are willing to wait longer for the medical abortion to complete.[7,8] Additionally, as staff gain confidence and experience, they may be better able to provide support and counseling to women who otherwise might request surgical intervention despite an underlying wish to abort without surgery.

- ***Visit schedule:*** Protocols that allow more time between drug administration and the follow-up visit and/or allow for multiple follow-up visits may have higher success rates since some women's abortions are not complete for several days or even several weeks after use of the drugs. Many women want to know as soon as possible if the abortion is finished, so early follow-up consultations for women who want to confirm that the abortion is complete may increase satisfaction levels. On the other hand, excessive follow up may lead to needless interventions, inflating the failure rate.

C. Safety

Early medical abortion with mifepristone and misoprostol is extremely safe. There is less risk associated with properly used modern methods of abortion, including medical abortion, than with the continuation of pregnancy.[4,9,10,11,12] Millions of women worldwide have safely and successfully used mifepristone for early medical abortion. Neither drug has been associated with long term effects on women's health.[13]

Frequently cited safety concerns:

- ***Excessive bleeding:*** Bleeding can best be managed if women are counseled on what to expect and when to seek treatment if bleeding becomes very heavy or persists for a long time (see Chapter IV, Section C). Bleeding excessive enough to warrant a blood transfusion is extremely rare; less than one woman per 2,000 who use medical abortion experience it.[4,14,15]

- ***Ectopic pregnancy:*** Medical abortion with mifepristone neither exacerbates nor ends an ectopic pregnancy. Careful evaluation before treatment and careful monitoring for symptoms after treatment can help to identify women with ectopic pregnancies so that they may be referred for appropriate treatment.

- ***Teratogenic effects:*** A very small percentage of pregnancies may continue after administration of mifepristone-misoprostol. In such cases, if a woman changes her mind about her abortion, or in the rare instance that the clinician fails to diagnose an ongoing pregnancy at a follow-up visit, the pregnancy may continue to term. Although it is possible that either drug could have teratogenic effects on the fetus, there is no evidence that mifepristone causes deformities. Limb defects and Mobius syndrome have been reported after misoprostol use but prospective data show no association with birth defects.[16] Overall, data on misoprostol suggest a possible association between birth defects and *in utero* exposure to misoprostol at a narrow sensitive window very early in gestation. While the relative risk of malformations appears real, epidemiological studies indicated that the absolute risk is low (less than 10 malformations per 1,000 live births exposed to misoprostol *in utero*).[17,18] During counseling, it is important to emphasize to the woman the need for follow up and completion of the abortion if the pregnancy is ongoing. All women should be informed of the possibility of birth defects if they elect to continue a pregnancy to term after exposure to misoprostol.

- ***Infection:*** Serious infection following medical abortion (defined as an infection requiring intravenous (IV) antibiotics and hospitalization) is rare.[19] In the United States, where there is a well-functioning reporting system for adverse events following early medical abortion, the frequency of reported infections is about 2 per 1,000 uses.[20] Fatal infection associated with *C. sordellii and C. perfringens* has been reported, however, this phenomenom is extremely rare, occurring in less than 0.5 per 100,000 uses.[21,22] Overwhelmingly, infections reported following medical abortion are not serious and are treated with a single course of oral antibiotics in an outpatient setting.

- ***Fertility:*** Medical abortion with mifepristone and misoprostol has no effect on a woman's fertility.[13]

D. Acceptability

Overall, studies have shown that medical abortion is very acceptable to both women and providers worldwide. For example, studies conducted in China, Cuba, India, Vietnam, Nepal, South Africa, Turkey and Tunisia found that over 90% of women were "satisfied" or "very satisfied" with their medical abortions.[14,23,24,25,26,27,28,29] Research from France, Scotland, and Sweden indicates that 60-70% of eligible women opt for medical methods of abortion if given a choice.[30,31] In one study that queried women who had experienced both medical and surgical abortion, the majority preferred medical abortion to surgical abortion.[32] It is important to note that a woman's view of her abortion experience is often linked to the context in which the abortion is provided.

Table 2.1 Advantages and disadvantages of early abortion methods as cited by women and providers[33]

	Medical abortion	Surgical abortion
Advantages	• Avoids surgery, anesthesia • More natural, like menses • Less painful to some women • Easier emotionally for some women • Can be provided by mid-level staff • Woman can be more in control, involved	• Quicker • More certain • Less painful to some women • Easier emotionally for some women • Can be provided by mid-level staff in some settings • Provider controlled • Woman can be less involved
Disadvantages	• Bleeding, cramping, nausea (actual or feared) • Waiting, uncertainty • Depending on protocol, more or longer clinic visits • Cost	• Invasive • Small risk of uterine or cervical injury • Risk of infection • Loss of privacy, autonomy

Summary points

- The success rate of mifepristone and misoprostol medical abortions early in the first trimester up to 9 weeks' LMP, is high, generally around 95%.
- Mifepristone has been used safely, effectively, and with high acceptability by millions of women around the world since 1988.

III. Deciding to Use Medical Abortion

Chapter themes

- Who can use medical abortion?
- Dating gestational age

A. Who can use medical abortion?

Most women with early pregnancies are able to choose mifepristone-misoprostol medical abortion. Very few women are excluded by labeling instructions in most countries.

Mifepristone contraindications:

- Suspected ectopic pregnancy or undiagnosed adnexal mass
- Chronic adrenal failure
- Concurrent long-term corticosteroid therapy
- History of allergy to mifepristone
- Hemorrhagic disorders or concurrent anticoagulant therapy (i.e. blood thinner medications)
- Inherited porphyrias (rare genetic blood diseases)

If an IUD is in place, it must be removed before medication is administered.

Misoprostol contraindications:

- History of allergy to prostaglandins, including misoprostol

Previously, medical abortion was advised against for women over 35 who also smoked more than 10 cigarettes per day. This exclusion criterion was later determined to be unnecessary after misoprostol replaced sulprostrone as the prostaglandin component of the regimen. Despite contraindications for use of some prostaglandins in women with asthma, medical abortion with mifepristone and misoprostol is not contraindicated for use in asthmatic women. In fact, unlike some prostaglandins, misoprostol relaxes the smooth muscles of the tracheo-bronchial tree, and so is not known to have adverse effects in asthmatic women.

Other conditions to consider:

- ***Severe anemia:*** Although women using medical abortion experience more prolonged bleeding than women having a surgical abortion, the total amount of blood loss and decrease in hemoglobin levels is typically modest for both methods. Anemia is not a contraindication for the method, but all women with severe anemia should initiate treatment for anemia as soon as it is diagnosed.

- ***Breastfeeding:*** There is no evidence that mifepristone or the prostaglandins used for medical abortion are harmful to nursing infants. Given that the doses are few and fairly rapidly metabolized, it is unlikely these drugs would be found in large quantities in breast milk. However, most drugs in women's blood do get into breast milk in small amounts. For this reason, women are sometimes advised to discard the breast milk produced for four to six hours after ingestion of each dose of misoprostol.[34,35]

- ***Access to emergency back-up care:*** Although severe complications following medical abortion requiring emergency treatment or blood transfusions are rare, women should have adequate access to emergency back-up facilities during the abortion process.

B. Gestational age dating for determining eligibility

The following tools can be used to calculate the gestational duration of a woman's pregnancy.[36,37,38]

- ***Last menstrual period:*** Studies have shown that almost all women are able to date their pregnancies reliably (i.e. within +/- 2 weeks of provider assessment using ultrasound) by calculating from the first day of their last menstrual period.[39,40]

- ***Physical Exam:*** Experienced providers can assess gestational age by conducting a physical exam to estimate the size of the woman's uterus. Special care should be taken with obese women because it may be difficult to conduct an accurate exam.

- ***Ultrasonography:*** Ultrasound, as recorded and interpreted by an experienced sonographer, is a useful tool to date a woman's pregnancy but other methods of dating pregnancies are also acceptable. If a provider suspects an ectopic or multiple pregnancy, ultrasound may help to confirm the diagnosis.

Precise dating of pregnancy is not needed for medical abortion. The estimate has to rule out pregnancies beyond 9 weeks mostly for service delivery and administrative reasons. Even after 9 weeks, the method still has a high probability of success (See Chapter VII).

Additional factors to consider when determining gestational age limits:

- Legal and programmatic restrictions as applicable
- Medical abortion drug regimen used and its efficacy at later gestational ages
- Women's desire to have a medical abortion
- Provider experience and comfort with the method

Medical abortion and off-label use

In countries where mifepristone is licensed for use in medical abortion, the license will specify the regimen and gestational age limit for which the drug can be marketed. Yet, in many countries, licensed medicines can also be used in ways and for indications that are not included in the original registration. This is called "off-label use." According to the United States Food and Drug Administration (FDA), "Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgment. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects." Early mifepristone registrations specified the use of 600 mg mifepristone and limited use of the method up to seven weeks gestation (49 days' LMP). Later evidence demonstrated that a reduced dose of 200 mg mifepristone was as effective (and less costly) up to 63 days' LMP when combined with vaginal, buccal, or sublingual doses of misoprostol. Today, most protocols in the United States clinics and other countries provide for use off-label to 63 days' LMP with a single 200 mg dose of mifepristone.

Summary points

- Most women can use mifepristone for early medical abortion.
- Early mifepristone misoprostol protocols were cautious; the safety and efficacy results of numerous clinical trials have enabled more women at later gestational duration access to the method.
- There is no evidence to show that mifepristone stops working or becomes dangerous at a certain gestational age; it appears to be more effective for earlier pregnancies.
- The gestational age of most pregnancies can be assessed by menstrual history and physical exam.

IV. Medical Abortion Protocols with Mifepristone and Misoprostol

Chapter themes

- Dose, route, and timing of administration
- Schedule of visits
- Side effects and complications
- Follow up

A. Dose, route, and timing of administration

Although the registered regimen is similar in most countries, local standards of care have introduced variants into many medical systems. Each of these regimens appears to be highly effective. Variations of the dose, timing, and route of administration and the evidence for these are discussed below.

Dose

- ***Mifepristone dose:*** A low dose of mifepristone (200 mg) has proven to be as effective as the originally used 600 mg dose and can greatly reduce costs.[41,42,43,44]

- ***Misoprostol dose:*** Most recommended medical abortion regimens use 400-800 mcg misoprostol. Doses of 800 mcg vaginally and buccally (in the cheek) have been shown to be highly effective up to 63 days' LMP. When administered sublingually (under the tongue) or buccally, even 400 mcg doses have been shown to be highly effective up to 9 weeks' LMP (See Appendix A). Higher doses of prostaglandin may result in slightly higher success rates and/or shorter mean time to expulsion, but they are also linked to increased side effects. Some providers believe that repeat dosing of misoprostol for women who do not expel the products of conception in the first 24 hours or have incomplete abortions or heavy bleeding improves success rates. Studies in which participants repeat the

misoprostol dose following mifepristone tend to have higher efficacy rates than do studies in which women were given a single dose of prostaglandin, but the results are inconclusive.[45,46]

Route of administration

- ***Mifepristone:*** Mifepristone is administered orally. There is no evidence to suggest that alternative routes of administration may be more effective or convenient.

- ***Misoprostol:*** Studies have examined oral, vaginal, buccal, and sublingual administration of misoprostol for medical abortion. For buccal and sublingual administration, women are generally advised to hold the pills in their cheeks or under their tongue for 20-30 minutes and then swallow any remaining fragments. Buccal, sublingual, and vaginal administration of misoprostol have been shown to be highly effective up to 9 weeks' LMP.[47,48,49,50,51,52,53] Methods of delayed swallowing, such as buccal and sublingual administration, offer a safe and effective alternative at later gestational ages and may avoid the discomfort and distaste associated with vaginal administration. There may also be a difference in side effects by route of administration, but these findings may be confounded by the effect of different dosing schemes.

Timing

- ***Gestational age:*** Mifepristone-misoprostol medical abortion appears to be most effective in early pregnancy. As gestational age increases, efficacy tends to decrease, although this decline is small and gradual.

- ***Timing of misoprostol administration:*** Most recommended medical abortion regimens require women to administer the misoprostol 24-48 hours after mifepristone. Studies demonstrate that the method is also successful when misoprostol is taken between 12-72 hours after mifepristone.[54,55] Regimens employing shorter intervals (i.e. less than 12 hours) between mifepristone and misoprostol or simultaneous administration appear to be slightly less effective.[56,57,58] Expanding the range of time in which misoprostol may be taken could increase the flexibility of this regimen, making it more accommodating for women's and clinic's schedules.

B. Schedule of clinic visits

Most medical abortions in the United States and elsewhere require just two visits (see Figure 4.1). The approved regimen used in the United States specifies that a woman make three clinic visits: one to swallow the mifepristone, a second (1-3 days after mifepristone ingestion) to swallow the misoprostol, and a third (approximately 2 weeks later) to confirm that the abortion is complete. Yet, several studies have tested the safety and efficacy of home administration of misoprostol thereby reducing the number of clinic visits.[23-25,27-29,59-62] Most women find this option preferable, and providers may find it easier and more feasible for service delivery. Home administration of misoprostol has become the standard of care in the United States, where over one million women have used the method in this way,[20] and many other countries have also adopted this option.

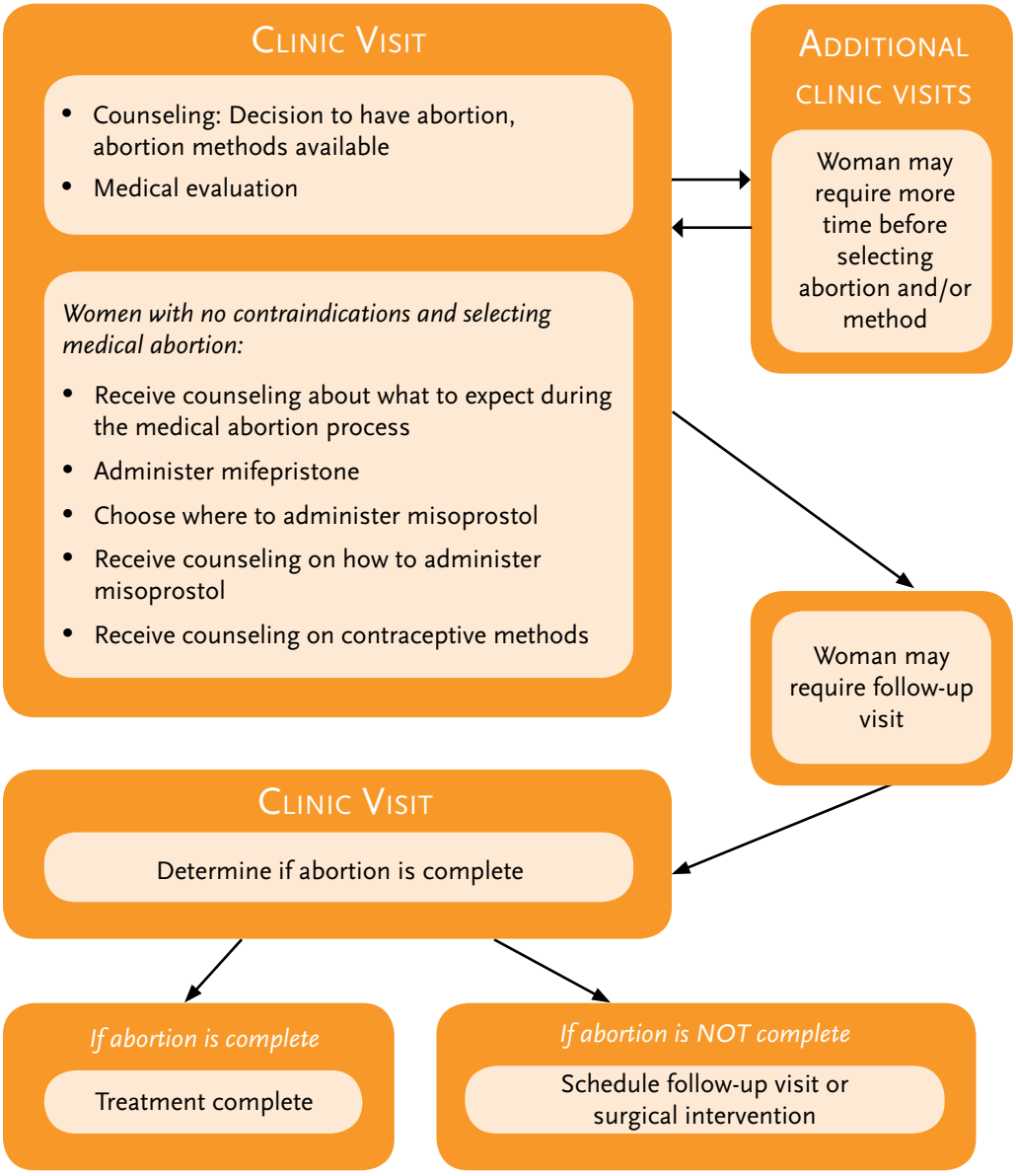
Most recommended medical abortion regimens require women to take mifepristone in the clinic. Yet, there are no data to substantiate the medical necessity of taking mifepristone, which has few to no side-effects for most women, under direct medical supervision. Data on home use of mifepristone are scant. One recent descriptive study of home use of both mifepristone and misoprostol by women who acquired the pills from the Women on the Web website and self-administered the tablets reported a success rate similar to those reported for other outpatient settings (93.2%).[63]

In addition, researchers are exploring how the follow-up visit could be omitted, or handled in ways other than through a personal appearance at a clinic. Potential alternatives include a self-administered patient assessment and low-sensitivity pregnancy test.[64] To date, however, an effective pregnancy test is not commercially available, and further research is required to identify appropriate diagnostic tools for women.[65]

The following are potential scenarios in which the number of visits would increase:

- A woman presents to a clinic with an unwanted pregnancy and after being given information about surgical and medical abortion, requests additional time before selecting a method.

Figure 4.1 Typical series of medical abortion clinic visits



- A woman returns for her two-week follow-up visit and learns that, though her pregnancy is not ongoing, her abortion is not complete. The decision is made to either administer additional doses of misoprostol or simply wait to see if the abortion completes without further intervention. In either case, an additional follow-up visit would be recommended.

C. Managing side effects and complications

Most of the side effects associated with medical abortion are well-known and easy to manage. In the clinic, the person attending the woman (such as counseling staff, nurse, midwife, or a trained support person) should be able to describe possible side effects and their management and to address women's concerns. In rare instances, a physician may be needed to manage side effects.

The two most common intended effects are the pain (associated with uterine cramping) and vaginal bleeding. These symptoms are expected, as they are part of the abortion process and not really "side effects." Women can be given either pain medication tablets or a prescription for pain medication before leaving the clinic. They should also be instructed to seek additional care (either at the clinic or an emergency facility) if they are bleeding excessively (see definition below) or have a persistent fever. See Table 4.1 for a description of common effects, complications, and suggestions for management of these problems.

Table 4.1 Treatment and management of side effects and complications

	Description	Management
Pain	Reports of pain and perceived need for analgesia vary greatly from culture to culture, clinic to clinic, and person to person. For instance, in places where surgical terminations are performed with no anesthesia, medical abortion is often rated as almost painless. Most women report at least some pain, however, and roughly half perceive a need for analgesia. Pain rarely indicates the need for a surgical intervention and tends to improve rapidly once the expulsion takes place.	• Hot water bottle or heating pad • Sitting or lying comfortably • Support of friends/family • Soothing music, television, tea (where available) • Paracetamol/acetaminophen • Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen • Weak opioids such as codeine (and one of the above)
Bleeding	All women who experience a successful medical abortion will experience vaginal bleeding. Bleeding is likely to be more abundant and prolonged than normal menstruation but typically does not adversely affect hemoglobin levels. The total amount of blood loss is related to gestational age.[66] Bleeding is often heaviest three to six hours after the prostaglandin administration and usually lasts about a week but may last as long as a month for some women.	• Set reasonable expectations about bleeding during pre-abortion counseling • Give clear instructions about how to decide if bleeding is excessive and where to go for additional care
Heavy or prolonged bleeding	Excessive or prolonged bleeding causing a clinically significant change in hemoglobin concentration is uncommon.[49,67,68] Approximately 1% of women will require uterine evacuation for hemostatic control. The need for transfusion is even rarer (0.1% to 0.2%). There are no reports in the medical literature of hysterectomy for hemostasis after medical abortion. While it is important to explain to the woman that most medical abortions take place without incident, it is equally important to encourage the woman to call her provider if she experiences excessively heavy bleeding. Establishing a sanitary pad count (or local equivalent) will help make bleeding measurement concrete. In the United States, for instance, women are told that if they soak more than two super-size sanitary pads per hour for two consecutive hours they should call a provider.	• If there is evidence of hemodynamic compromise, intravenous fluids should be administered • If bleeding is particularly profuse or prolonged, surgical intervention may be required • Transfusion should be provided only if clearly medically required

Table 4.1 Treatment and management of side effects and complications (*continued*)

	Description	Management
Fever/chills	Misoprostol can sometimes cause temperature elevations. These temperature elevations do not usually last more than two hours or so. Although uterine/pelvic infections are rare in medical abortion, a fever that persists over several days or that starts days after prostaglandin administration could signal an infection.	• Provide anti-pyretics and reassurance • If fever persists for more than four hours or develops more than a day after misoprostol administration, the woman should be instructed to contact the clinic
Nausea and vomiting	Nausea has been documented in approximately half of all women undergoing medical abortion and vomiting may occur in fewer than a third. These symptoms are usually related to pregnancy and administration of the medical abortifacients. They may appear or increase in intensity after mifepristone administration and usually decline hours after misoprostol intake.	• Reassure women that nausea and vomiting are commonly associated with pregnancy and are also a possible side effect of the medication • Provide women with anti-nausea or anti-emetic medication for severe symptoms if the drugs are available
Diarrhea	Transient diarrhea appears in fewer than a quarter of all women after misoprostol administration. Since the diarrhea is almost always short-lived, treatment is rarely necessary.	• Reassure the woman that diarrhea is sometimes associated with misoprostol and usually passes rapidly
Headache and faintness or dizziness	These symptoms have been documented in fewer than a quarter of all women. They are usually self-limited, resolve spontaneously, and are best managed symptomatically.	• Provide reassurance and analgesia as needed

Table 4.1 *(continued)*

	Description	Management
Infection	Serious infection following medical abortion (defined as an infection requiring IV antibiotics and hospitalization) is rare.[19] In the United States, where there is a well-functioning reporting system for adverse events following early medical abortion, the frequency of reported infections is about 2 per 1,000 uses.[20] Fatal infection associated with *C. sordellii and C. perfringens* has been reported, however, this phenomenom is extremely rare, occurring in less than 0.5 per 100,000 uses.[21 22] Overwhelmingly, infections reported following medical abortion are not serious and are treated with a single course of oral antibiotics in an outpatient setting.	• If infection is suspected (see fever) the woman should be evaluated • If there is evidence of endometritis and the abortion is incomplete, a surgical abortion should be performed and antibiotics provided • Any severe infection could require hospitalization and parenteral antibiotics • Antibiotic administration (either prophylactically or with screen and treat protocols) is used in some settings, including the United Kingdom and Sweden and clinics of the Planned Parenthood Federation of America. However, routine antibiotic use may not be feasible in all settings, for all women, and is not without its own risks of side effects and serious adverse events, such as serious and fatal allergic reactions. Neither the United States FDA nor the WHO recommend routine antibiotics for medical abortion procedures.

D. Follow up

The following tools can be used to evaluate whether or not the abortion was a success.[36]

- ***Physical exam:*** Woman's report of symptoms of abortion (see Chapter IV, Section C for information on pain/bleeding patterns) with physical examination demonstrating return of uterus to pre-pregnant size.

- ***Ultrasonography:*** Ultrasound examination can be a useful tool for evaluation of success if the provider has expertise in the technique. It is important to differentiate between blood clots/debris, true incomplete abortion and an ongoing pregnancy.[69] Evacuation of the uterus in a clinically well woman is not indicated even if some debris can be seen on ultrasound exam. As with spontaneous abortion, expectant management is often sufficient for all but ongoing pregnancies.

Persistent gestational sac

Even after fetal demise, a non-viable gestational sac may be retained in the uterus. If the woman has no symptoms of infection, no worrisome bleeding, and wishes to wait for expulsion, she may do so. Additional doses of misoprostol may induce uterine activity to expel the pregnancy tissue.[70]

Management:

- Consider administration of additional doses of misoprostol
- Provide reassurance to the woman: If there are no signs of clinical danger (e.g. fever, heavy bleeding) it is safe to wait for expulsion or to take another course of misoprostol.
- Research on the optimal dose of misoprostol for this indication is under investigation.[70]

Serum β-hCG decline after medical abortion

The serum concentration of β-hCG (human chorionic gonadratropin) rises exponentially during the first six weeks of pregnancy, with reported doubling times of approximately 1.3 to 2 days.[36] Although mean serum levels have been shown to be highly correlated with gestational age during early pregnancy, a wide range of values is compatible with normal progression of pregnancy at early gestational ages. Only readings outside a wide range indicate a problem, as do serial readings that do not change appropriately.

A single hCG reading cannot be used to date a pregnancy with precision. To document a change in hCG, a comparison of sequential serum samples is necessary. A decline in serum hCG levels can indicate that the pregnancy has ended. Increase of hCG levels can indicate ongoing pregnancy. If hCG levels have declined 50% in 24 hours, the pregnancy is likely to have ended.[71,72] In women with complete medical abortion, hCG serum concentration should be below 1,000 IU/L two weeks after mifepristone administration.[73] Time to reach very low levels (below 50 IU/L) is directly related to the initial hCG level.[74]

Summary points:

- Many mifepristone-misoprostol regimens work well for early first trimester pregnancy termination.
- The vast majority of women make two clinic visits during their medical abortion procedures. However, the number of visits a woman makes to her health care provider can range from one (one for medical evaluation, counseling and mifepristone administration) to four or more, depending on individual circumstances and the protocol followed.
- Primary effects (i.e. pain and bleeding) and side effects are expected and well tolerated by women.
- It is important to confirm that each medical abortion is complete. However, a clinic visit may not be required to confirm whether the procedure is complete.

V. Counseling and Information Provision

Chapter themes

- Choosing a method
- Screening for suitability
- Preparing the woman for what to expect
- Contraception after the abortion

Information is a crucial component of medical abortion.[75,76] Counseling provides the opportunity to inform women about what to expect and to ensure that women know the warning signs of the need for additional help. Clinical experience has shown that medical abortion counseling may be closely related to the efficacy and acceptability of the method. If women are properly informed about what to expect after taking the drugs, they are better prepared for their experiences and less likely to request a medically unnecessary surgical termination to end the process. In addition, women who are more confident about and comfortable with the method may find it more satisfactory.

If providers and women are less familiar with medical abortion methods, counseling may take longer than prior to surgical abortions. As providers gain more experience, the amount of time required for counseling tends to decrease. For a detailed counseling checklist, please see Appendix B.

A. Choosing a method

If both medical and surgical abortion methods are available, a brief description of both of these options should be given to women. Below is a sample of a description of medical abortion:

> Medical abortion is a method of abortion that uses pills to end a pregnancy. Two different medications are needed for a medical abortion. To use this

method, women take the first kind of pill, called mifepristone, to start the abortion. Later, they take a second set of pills, called misoprostol, to complete the treatment, at home or in the clinic. Following the second set of pills, women may experience cramping, bleeding, nausea, vomiting, and diarrhea. Most of these side effects generally go away after a few hours, but bleeding similar to a heavy period can continue for a week or longer. Studies have found this regimen effective about 95% of the time and very acceptable to most women.

It is important to provide complete, accurate and unbiased information to enable each woman to select the most appropriate method for herself. Women should not be coerced into selecting either a medical or surgical abortion. Providers should take time to inform the woman that if the medical abortion fails, she may need to have a surgical intervention to complete the procedure. Issues such as personal beliefs, privacy preferences and social context should be considered.

B. Screening for suitability

Each woman should be screened to assess her eligibility for medical abortion. From the medical standpoint, it is important to determine whether or not the method is appropriate for the woman, including that a pregnancy is not greater than 9 weeks' LMP and if the woman has any known contraindications. In addition, it is useful for the provider to discuss the various options available to each woman so the woman can determine if medical termination fits well with her needs and expectations. For example, each user needs to be comfortable with the waiting time to completion. The following list highlights areas that should be incorporated into standard screening for medical abortion.

- Medical history (see Chapter III, Section A)
- Personal characteristics and preferences
- Social circumstances: family/partner support, job and household responsibilities
- Access to adequate back-up facilities
- Ability to return to clinic for a follow-up visit as or if necessary

C. Preparing the woman for what to expect

Counseling allows the provider to help women develop realistic expectations about the abortion. To assist with this process, the following issues should be discussed:

- ***Mifepristone and misoprostol:*** Explain what they are, how they work, and how they should be taken.

- ***Misoprostol administration:*** Explain how women should administer the misoprostol tablets. For example, for buccal (and sublingual) administration, women are advised to place the misoprostol tablets in the cheek cavity for the buccal route (or under the tongue for the sublingual route) for 20-30 minutes and then swallow the pill remnants.

- ***Success rate:*** Explain that between 2 - 8% of women will require a surgical intervention. If the drugs fail, the woman should be prepared to complete the abortion surgically.

- ***Understanding of the method:*** Rumors or misconceptions about the method should be dispelled, and all of the woman's questions or concerns should be thoroughly reviewed.

- ***Expectations about primary and secondary effects:*** Discuss the amount of pain, bleeding and side effects that are commonly experienced.

- ***Products of conception:*** Women should be informed that it is possible, though not likely, that they will see the products of conception. Some clinics find it useful to show women pictures of expelled products of conception at different gestational ages to enable women to have a realistic idea of what they might see.

- ***Possible complications:*** Women should be given a detailed description of possible complications and how they can be managed (see Chapter IV, Section C). In addition, if feasible within the local context, providers may want to give women a telephone number to call if they have any questions or concerns.

- ***Follow-up care:*** Although the woman may believe that her abortion is complete (i.e. if she believes she has seen the expulsion or bleeding has ceased), best current clinical advice is that each woman should return for her follow up to confirm that her abortion is complete. Future protocols may develop mechanisms by which a woman can assess her abortion status on her own, without having to make an additional clinic visit for this purpose.[64] Low-sensitivity pregnancy tests and self-administered questionnaires may help women and providers assess whether additional post-medical abortion care is required.

- ***Cost:*** In places where abortion services must be covered by the woman, the costs of each abortion method should be discussed.

- ***Informed consent:*** Depending on local regulations and practices, women may be required to sign a consent form. Informed consent should include an explanation of the process, a statement indicating that risks, benefits, complications and potential side effects have been fully explained and that the woman has had the opportunity to ask questions and received satisfactory answers. The consent form should also indicate that the woman has received detailed information about the procedures for emergency care, if needed. A sample informed consent form is included as Appendix C.

Best and worst features of medical abortion as reported by women participating in clinical studies[13,23-29]

Best features	Worst features
• No surgery and/or injections and/or anesthesia • Non-invasive • Natural, like menses or miscarriage • Less pain, cramping • Easier emotionally, less frightening or traumatic • Easier, simpler, faster	• Pain, cramping (feared or actual) • Waiting, uncertainty, fear of unknown • Nausea, vomiting, diarrhea (feared or experienced) • Amount of bleeding • Fear of failure, true failure • Takes too long

D. Contraception after the abortion

Contraception should be discussed with every woman. All women should be reminded that fertility returns quickly following early first trimester abortion. For this reason it is critical that women understand the subsequent risk of pregnancy. Information about contraception should be provided at the first clinic visit. Women having medical abortions can begin using oral contraceptives, injectables and implants the day of misoprostol administration. Condoms, contraceptive jellies and foams, the cervical cap, and the diaphragm should be used with the first sexual relations. It is best for women requesting intrauterine devices to wait until their abortions are complete before insertion. An appropriate contraceptive method will depend on local availability and the needs and preferences of each woman.

Summary points:

- Providing women with complete information is critical to ensure success, safety, and acceptability.
- Most contraceptive methods can be used immediately after medical abortion.

VI. Bringing Mifepristone to New Settings

Chapter themes

- Staff training
- Service delivery components
- Dissemination of information
- Medical abortion myths
- Confronting abortion stigma

The basic requirements for medical abortion service delivery include trained staff and the required medications (mifepristone and misoprostol). Staff should include skilled counselors and providers who are able to determine eligibility, confirm success, refer and/or provide women with emergency back-up care.

A. Staff training

Staff at facilities offering medical abortion should be trained in each of the following:

- ***Protocols for medical abortion:*** Staff should be knowledgeable about mifepristone and misoprostol and the protocol being used in the clinic.

- ***Counseling:*** Staff should receive comprehensive training on counseling for medical abortion (see Chapter V).

- ***Dating gestational age:*** Staff should be able to assess gestational duration by review of pertinent history, symptoms, and physical exam (see Chapter III, Section B). Since the effectiveness of medical abortion does not decrease dramatically with each day of increasing gestational length, it may not be necessary to date gestational age precisely. Lab tests to detect hormone levels and ultrasonography may aid in determining gestational age but are not requirements for service provision.

- ***Identifying rare pregnancy abnormalities:*** Staff should be knowledgeable about warning signs for rare pregnancy abnormalities such as ectopic pregnancies and hydatiform mole. Since women presenting for medical abortion usually seek care early in their pregnancies, providers have an opportunity to diagnose rare conditions early. Mifepristone and misoprostol have no effect on ectopic and molar pregnancies.
- ***Determining success:*** Abortion status can be assessed at follow up by clinical history and exam (see Chapter IV, Section D). For example, if the clinician is able to detect an increase in uterine size compatible with additional weeks of fetal growth or if the woman is having prolonged bleeding problems, additional intervention is likely needed.
- ***Values clarification:*** Discussion with staff about values may be useful, especially in instances where some of the staff members are ambivalent about providing abortion services.

Regardless of whether new providers are physicians or other health care providers, adequate medical abortion training will greatly improve their comfort and skill with the method. Recent studies have demonstrated that success and satisfaction with the method tends to increase as provider experience and skills increase.

A basic training course should include the following elements:

- Mifepristone and misoprostol: Pharmacology and mechanism of action
- Eligibility and contraindications
- Protocols for medical abortion
- Diagnosing completed abortion, incomplete abortion and ongoing pregnancy
- Managing side effects and adverse events
- Ultrasound: Its advantages and disadvantages in various settings
- Counseling

Experience has shown that use of case studies in training is quite helpful, especially when discussing management of side effects and diagnosis of abortion status. In addition, role plays and group activities have proven extremely effective means of training on eligibility and counseling. Several international organizations have developed training curricula for medical abortion (see Appendix E Additional Resources).

B. Service delivery components

Providers who currently offer family planning, pre-natal care or other reproductive health services can add medical abortion to their current services. In particular, surgical abortion providers can easily offer medical abortion services once they receive appropriate training. Studies have also shown that introduction of medical abortion is feasible in settings that previously had not provided abortion services. Providers can offer the method safely and effectively using existing referral mechanisms for management of miscarriage and without introducing a radical reconfiguration of services.[26,77]

Medications

- ***Mifepristone and misoprostol:*** Both drugs can be administered either at home or in the clinic. Regardless of where the drugs are administered, women should be carefully counseled on how and when to take each drug and on potential complications, expected and adverse effects, and management of these occurrences.

Emergency care facilities/referral services

- ***Surgical termination:*** Since the method is not 100% effective, medical abortion providers should be able to perform or refer women for surgical completion, when needed.

- ***Emergency care:*** Women need to know where to go for emergency care. Most back-up care is similar to that needed by women following spontaneous abortion, and many communities have a health care facility already in place to provide such care.

Additional service delivery components

- ***Waiting area:*** If misoprostol is taken at the clinic, it is convenient to have an area where women can wait after taking the medication. A sufficient number of toilets should be nearby. Beds are rarely necessary, but comfortable chairs can be useful. Ideally, clinics provide space for a woman's companion to stay with her during the abortion process.

- ***Ultrasonography:*** As explained above, ultrasonography can be useful in determining gestational age, identifying pregnancy complications, and confirming abortion completion, if providers skilled in imaging and its interpretation are available.

- ***Pain and anti-nausea medications:*** These products can be given to women in advance to be used as needed to help to ease side effects (see Chapter IV, Section C).

- ***Anti-D globulin:*** While most guidelines recommend using anti-D globulin for Rh negative women with gestations of more than seven weeks, its use before seven weeks' gestation is debated. It is possible that at this very early stage of pregnancy there is little, if any, opportunity for an exchange of blood between the woman and the fetus.[78] More research is needed to determine exactly when such precautions are necessary. If the local standard of care indicates anti-D globulin for Rh negative women undergoing surgical or spontaneous abortion, this care also should be provided for women undergoing medical abortion until further evidence becomes available.

C. Dissemination of information

As with all new technologies, information dissemination is critical to building local and national support. International experience suggests that the following dissemination strategies have worked well:

- Promoting the method as a component of comprehensive reproductive health services.

- Increasing women's awareness and understanding of medical abortion through media and women's organizations or groups.

- Communicating information among providers via medical journals.

- Introducing medical abortion at local, national and regional professional meetings, especially where the technology is relatively unknown and/or underutilized.

- Educating health workers at all levels, including physicians, mid-level providers, reception personnel, counselors and telephone operators.

- Creating networks of service providers through which they can share their experiences.

D. Medical abortion myths

It is important to respond to common myths regarding the method. The following are some common myths about medical abortion and factual evidence.

Myth #1: Ultrasound is necessary for all medical abortion services.

Many providers are concerned about offering medical abortion, especially in rural areas where ultrasound may not be available. While ultrasound is a useful tool both for gestational age dating and for identifying ectopic pregnancies, it is not irreplaceable. It is useful to identify a location where women can be referred for an ultrasound exam, if needed.

Myth #2: Medical abortion is dangerous because it does not resolve ectopic pregnancies.

Medical abortion is contraindicated for women with known ectopic pregnancies because mifepristone will not end an ectopic pregnancy. Medical abortion providers must be trained to diagnose ectopic pregnancy. Early contact between pregnant women seeking medical abortion and health care providers creates an opportunity to diagnose the condition sooner than would have been possible if the woman had chosen to continue her pregnancy.

Myth #3: Only physicians can administer medical abortion.

Given the nature of medical abortion – women simply ingest two sets of pills – trained non-physician providers can be effective medical abortion providers. Provision of medical abortion by non-physician providers also may increase the pool of providers and build on the skills of staff such as nurse-midwives. Mid-level clinicians play a crucial role in the provision of pregnancy-related care in many settings, particularly in rural or remote settings where physicians are scarce. Evidence suggests that various health care providers, including midwives and nurses specialized in pregnancy-related care, are either successfully engaged in the provision of medical abortion services or possess the skills needed to provide medical abortion with additional training.[79]

Myth #4: Medical abortion is not appropriate for women in rural areas.

If a health care facility offering medical abortion is not able to provide back-up care, such as surgical aspiration, the facility should be located in reasonable proximity to a center that can provide this care. For instance, rural hospitals and primary health care facilities can act as nodal points and provide back-up services to primary health care facilities in the geographic vicinity. This "hub and spoke" referral system is commonly used throughout much of the world for other types of health care delivery.

E. Confronting abortion stigma

While many countries, particularly in Sub-Saharan Africa and Latin America, have strict abortion laws, there are almost always limited circumstances in which abortion is permitted. If abortion is legally permitted, women should ideally be able to choose either surgical or medical abortion.

Below are suggestions for promoting the method in areas where abortion is highly stigmatized and restricted.

- Emphasize that medical abortion is safe for women.
- Introduce the idea that medical abortion is similar to miscarriage.
- Some countries have had success launching medical abortion services by beginning to use misoprostol for treatment of incomplete abortion and miscarriage.

Summary points:

- It is simple and straightforward to train providers to offer medical abortion in almost any setting.
- Medical abortion can be safely offered by many types of providers once they are trained.
- It is essential to disseminate information to women and to health care providers at all levels.
- Many of the barriers mentioned in relation to development of medical abortion services are myths.

VII. Mifepristone and Misoprostol for Late First Trimester Abortion

Medical abortion with mifepristone and misoprostol is a standard of care throughout the first trimester in the United Kingdom and has been recommended by the Royal College of Obstetricians and Gynaecologists (RCOG).[80] Research has documented success rates after 9 weeks' LMP comparable to earlier gestations, with some modifications to the procedure. However, there are no studies that directly compare outcomes of earlier versus later procedures. Therefore, the information below is based on comparing observations across multiple studies.

A. Similarities to Early Medical Abortion:

1. ***The method is successful in more than 90% of cases***. The published experience with use of this method beyond 9 weeks' LMP (nearly 3,000 cases) demonstrates a cumulative efficacy of greater than 93%.[81,82,83,84,85,86,87] The largest case series, published by Hamoda, et al., demonstrated a decrease in efficacy non-significant in their series, with increasing gestational age: from 97.3% success in women 10 weeks' LMP to 92.0% in women 13 weeks' LMP.[87]

2. ***The time to expulsion is similar to time to expulsion in early medical abortion,*** between 4 and 5 hours on average, compared to between 3 and 4 hours with earlier inductions.[84,87]

3. ***Reported side effects are generally mild and transient.*** As in earlier inductions, after misoprostol administration, women report experiencing nausea, vomiting, diarrhea, fever, chills and headache. Most of these effects are transient and managed when necessary with anti-emetic and anti–diarrheal medications.

4. ***When offered the option between medical and surgical abortion, women are highly satisfied with the procedure***.[83,88]

B. Differences from Early Medical Abortion:

1. ***Procedure is usually performed in-clinic.*** Women presenting for early medical abortion (through 9 weeks' LMP) can take misoprostol, and subsequently abort, at home. All of the studies and routine use of this treatment beyond 9 weeks' LMP involve either in-clinic or in-patient misoprostol administration. Research is currently under way to determine whether these later procedures could be provided outside the clinic setting; however, until further investigations are complete only in-clinic or in-patient procedures are recommended.

2. ***To have a successful procedure, women usually take multiple misoprostol doses.*** Typical regimens for early abortion require one dose of misoprostol, usually between 400 and 800 mcg, taken by one of several routes. For women undergoing medical abortion beyond 9 weeks' LMP, serial doses are given at 3 to 4 hour intervals, until the woman has expelled the fetus. Studies indicate that on average women administer two to three doses. The regimen recommended by the RCOG is: 200 mg mifepristone followed 36 to 48 hours later by 800 mcg vaginally. After the initial misoprostol dose, a maximum of four additional 400 mcg doses, orally or vaginally (depending on whether the patient is bleeding), given every three hours is recommended.

3. ***Risk of bleeding requiring transfusion may be higher among women inducing with mifepristone and misoprostol beyond 9 weeks.*** In the literature there are 8 reported transfusions out of approximately 3,000 procedures (2.8 per 1,000 procedures). This rate is higher than with inductions before 9 weeks' LMP, which is about 1 per 2,000 procedures. A similar trend of increasing bleeding complications is seen with later surgical procedures.[89]

4. ***Women generally require more pain medication than with earlier inductions.*** A review of over 4,000 medical abortion procedures from 5 through 22 weeks' LMP demonstrated that analgesia requirement significantly increased with lower maternal age, higher gestation, longer induction-to-abortion interval, and with increased misoprostol doses.[90] At the same time, there is variation among clinics and providers as well as among cultures. Regardless, research indicates more women will require stronger analgesics during a procedure after 9 weeks' LMP compared to earlier procedures.

Summary points:

- Mifepristone-misoprostol medical abortion is safe and effective in the late first trimester (10-12 weeks' LMP).
- Regimens for mifepristone-misoprostol medical abortion in the late first trimester use 200 mg mifepristone followed 36-48 hours later by misoprostol.
- Most studied regimens use multiple misoprostol doses and require women to remain in the clinic for misoprostol administration. Research on outpatient alternatives is ongoing.

VIII. Where there is no Mifepristone

Chapter themes

- Methotrexate and misoprostol for medical abortion
- Misoprostol-alone abortions

Regimen	Advantages	Disadvantages
Mifepristone + misoprostol	• >95% effective • Acts rapidly	• Mifepristone can be costly • Not available worldwide
Methothrexate + misoprostol	• >90% effective	• Acts slowly • Potential to cause fetal malformations for ongoing pregnancies
Misoprostol alone	• Mid-80's% effective • Least costly • Widely available	• More side effects • May be associated with fetal malformations for ongoing pregnancies

A. Methotrexate and misoprostol

Methotrexate is a folic acid antagonist that interferes with DNA synthesis. When used as an abortifacient both alone and in combination with a prostaglandin, methotrexate can successfully end early intra-uterine and ectopic pregnancies.[91] For induced abortion, use of a complementary prostaglandin, such as misoprostol, induces uterine contractions, causing the expulsion to take place more quickly.[92,93]

Regimens

Methotrexate and misoprostol have been used for medical abortion up to 63 days' LMP. The most commonly used regimen is 50 mg methotrexate orally, followed 5 to 7 days later by 800 mcg misoprostol vaginally. The misoprostol dose is usually repeated after 24 hours if abortion has not occurred.

Methotrexate is currently available as both a solution and oral tablets. The solution can either be taken orally or injected intramuscularly. Intramuscular methotrexate is most commonly administered in a dose relative to the woman's body surface area. Researchers have explored the possibility of administering the misoprostol 4, 5, or 6 days after methotrexate and have found that each of these regimens is effective.[94,95]

Safety

Methotrexate is used for a number of indications other than medical abortion. The drug is not known to have any effect on future fertility or to increase the risk of abnormalities in future pregnancies.[96,97,98] Pharmacokinetic studies indicate that the typical 50 mg oral dose is safe, as blood serum levels do not reach sustained toxic levels.[99]

Contraindications for methotrexate-misoprostol

- Severe anemia
- Known coagulopathy
- Active liver or renal disease
- Uncontrolled seizure disorder
- Acute inflammatory bowel disease

It may be advisable for women who are taking folate-containing medications, including vitamins, to discontinue these medications for one week following methotrexate administration. Some clinicians advise against eating foods high in folate such as dark green leafy vegetables, broccoli, beans, brewers' yeast, whole grains, wheat germ, oranges, and organ meats for two weeks after methotrexate, but there is no evidence that such precautions are necessary. Because methotrexate is excreted in breast milk, breast-feeding women who are able to provide alternative nutrition to their children should discard breast milk for 72 hours after taking methotrexate.

Teratogenicity

Women should be advised about the possible teratogenic effects of methotrexate and misoprostol and counseled regarding the importance of surgical completion if the drugs do not successfully end the pregnancy. Anecdotal reports of a pattern of anomalies among infants born to women treated with methotrexate during pregnancy indicate that methotrexate is potentially teratogenic.[100,101,102] Most reports of teratogenicity associated with methotrexate involve high doses used for chemotherapy. See Chapter II, Section C for information on misoprostol and teratogenicity.

Efficacy

The overall success rate of methotrexate-misoprostol medical abortion reported in the clinical trial literature varies between 88% to 97%[103,104] (See Appendix A for success rates reported in clinical trials). Although these rates can be similar to those achieved with mifepristone, medical abortion with methotrexate takes longer to complete.

As described in Chapter II, the efficacy of medical abortion is associated with the protocol used and provider experience; success rates increase when women wait longer to expel the products of conception before recourse to surgical evacuation. There is some evidence that methotrexate and misoprostol may be more effective at earlier gestational ages. However, the data are inconclusive and studies of abortion up to 63 days' LMP report success rates above 90%.[103,104]

Acceptability

Between 83% and 89% of participants in methotrexate medical abortion studies stated that they would choose the same method again.[105,106] A study that compared the acceptability of mifepristone and methotrexate regimens found that acceptance was higher for mifepristone with significant differences in pain and waiting time between the two drugs.[107]

Side effects and complications

The side effects of methotrexate-misoprostol medical abortion are similar to those experienced with mifepristone-misoprostol regimens. A study comparing the side effects of mifepristone and methotrexate medical abortion regimens found that headaches were significantly more common after mifepristone and that diarrhea, fever, chills, and high "worst" pain scores were significantly more common after methotrexate.[108] Management of side effects is similar to that recommended with mifepristone (see Chapter IV, Section C for recommendations). Differences in recommendations regarding failed or incomplete abortion and ectopic pregnancy are discussed below.

Failed or incomplete abortion
In most protocols, ongoing viable pregnancy has been defined as the presence of gestational cardiac activity on transvaginal ultrasonography two weeks after methotrexate administration. Intervention for a nonviable pregnancy is not necessary and expulsion will occur with time, on average 22 to 29 days after methotrexate. Current recommendations in the United States for medical abortion with methotrexate regimens suggest waiting at least 29 to 45 days before offering a surgical evacuation, though some women do not want to wait this long and may request a surgical intervention earlier.[109]

B. Misoprostol alone

Misoprostol used alone for abortion is a promising alternative where mifepristone-misoprostol regimens are not available. Studies have evaluated the efficacy of misoprostol used alone for both first and second trimester abortions. Given its wide availability, low price, and ease of use, women around the world have begun to use misoprostol without medical supervision as a means of abortion induction.

Regimen

Most studies have assessed the efficacy of an 800 mcg dose of misoprostol repeated up to three times. A regimen of 800 mcg either vaginally every 3-12 hours or sublingually every three hours repeated up to three times has been shown to be effective (85%).[110]

Safety

Millions of women have used misoprostol (both alone and in combination with mifepristone or methotrexate) for safe termination of pregnancy.

Uterine rupture
Misoprostol may increase the risk of uterine rupture, especially in later gestations and in women with a scarred uterus. The exact risk of uterine rupture with early medical abortion is unknown, but has not occurred in hundreds of thousands of recorded uses of mifepristone-misoprostol for early first trimester abortion. Anecdotal evidence exists of uterine rupture in women undergoing second trimester medical abortion using misoprostol (both alone[111,112,113] and with mifepristone[112]).

Teratogenicity
Although some studies conclude that there is no clear evidence of teratogenicity,[114,115,116] others have found a connection between attempted unsafe abortion with misoprostol and congenital defects.[117,118,119,120] Doctors and women need to be aware that failed termination in early pregnancy after exposure to misoprostol may lead to an abnormal fetus. Surgical termination is recommended if pregnancy is ongoing after exposure to misoprostol.

Clandestine use of misoprostol

Self-administration of misoprostol to induce an abortion has been documented in settings both where abortion is widely available and highly restricted.[121,122] This phenomenon has been observed in Brazil since the 1990's and more recently in other Latin American countries. Use of misoprostol to induce abortion in this way appears to have decreased abortion-related mortality and morbidity.[123] Recent research conducted in the United States in three large urban centers showed that knowledge about misoprostol for abortion self-induction is limited (about 4%).[124]

Efficacy

In areas where mifepristone is not available, use of misoprostol alone may be a good, safe alternative. Good regimens in the most recent studies have success rates in the mid-80's percent range (See Appendix A for success rates reported in clinical trials).

Acceptability

Most studies do not explicitly investigate the acceptability of misoprostol alone, but available data suggest that acceptability is high.

Side effects

As with other forms of medical abortion, the most commonly reported primary and secondary side effects are uterine cramping and pain, bleeding, and nausea. Management of side effects is the same as for mifepristone medical abortion (see Chapter IV, Section C).

Mode of administration

Sublingual or vaginal administration of misoprostol are recommended. A large study conducted by the WHO found that when used vaginally the interval between doses could be either 3 or 12 hours. With sublingual, the 3-hour dosing led to more side effects but the 12-hour dosing interval was associated with lower efficacy.[110] Buccal administration is also being used for this purpose.

Telemedicine and mifepristone and misoprostol

Women on Web is a service that uses telemedicine to help women access mifepristone and misoprostol in countries with restrictive abortion laws and little to no safe abortion care. After an online consultation, women with an unwanted pregnancy of up to 9 weeks' LMP consult with a physician. If there are no contraindications, mifepristone and misoprostol are mailed to the woman.
http://www.womenonweb.org/

Summary points:

- Where mifepristone is not available, methotrexate and misoprostol are good medical abortion options.
- Telemedicine may help to make medical abortion more available in settings where mifepristone and misoprostol are not available.

IX. Looking Forward

This guidebook was made possible by the enormous progress in medical abortion technology over the last two decades. Finally, we have available a powerful tool that can be used widely to help solve a difficult and painful problem that is all too common in the lives of millions of women. The purpose of this guidebook is to show how the technology can be provided even where resources are scarce and medical services are not necessarily sophisticated.

The promise of medical abortion to ensure access to needed services, to increase the comfort and autonomy of women, and to improve health outcomes will not be fully realized until the technology is accessible in all places where women can choose to end unwanted pregnancies. Using the suggestions provided by this guidebook can help to advance the goal of making medical abortion a real choice for more women.

At the time the contraceptive pill was developed, it was almost unimaginable that we would also be able to address the problem of abortion with medicines and avoid surgery. But indeed, we are really there. The method has been used by tens of millions of women in dozens of countries, and it is incontrovertibly safe, effective, acceptable, and feasible to introduce into services.

Nonetheless, we are not at the end of the line in improving the technology – and especially in re-thinking and re-designing aspects of services. We now know, for example, that fewer visits to the clinic are completely compatible with safety and efficacy of the method. The minimum visit mode of service delivery is also highly desirable to most women and to providers. One challenge, therefore, is to convince policymakers, regulatory agencies, health systems, and individual clinicians to provide medical abortion with the fewest possible visits.

At the moment, we have a lot of positive experience with services that allow women to take the misoprostol at home and not return to the clinic for this purpose. Since it is the misoprostol, and not the mifepristone, that causes most of the uncomfortable side effects of the method, it is logical to explore the idea of allowing women to take the mifepristone at home as well. In the future, we can consider

mechanisms of allowing a woman to buy the mifepristone in the pharmacy (a situation that already exists in some places) and even to have it on hand should she need it at a later date.

Since many women feel perfectly well and tend to avoid re-visits to clinics after abortion, we need more research on ways to help eligible women safely skip return visits after completion of their medical abortions. We do know that women are very good at determining whether they might require additional care for medical complications, and with appropriate counseling, they should be able to self-refer back to facilities for this purpose. Documentation exists showing that women are unlikely to think that their abortion has succeeded when it is not yet complete and that they are more likely to believe that the pregnancy has not been ended when it already has terminated.[125] In the future, there can be a place for inexpensive low-sensitivity pregnancy tests to aid women in deciding when they may need care for a pregnancy that continues after medical abortion.

A great many services, in both more and less developed parts of the world, that provide medical abortion have discovered on their own that the method is simple to provide and that it can be provided very well by non-physicians. This insight is critical to making the method more accessible in low-resource environments. Another challenge for the future is to ensure that the message is widely known and understood by those who design services and develop norms for health services.

As for the science and technology itself, we look forward to a way to make the process of medical abortion even more comfortable for women, reducing what are now considered as the inevitable consequences of use of the method: bleeding and pain. For this goal, we will need to engage with the basic scientists to begin to explore alternative molecules and formulations. But why not? The past has been instructive and productive: the technology is here, and it works. The promise for the future is enormous, with dividends in the health and productivity of women all over the world. We look forward to being part of this exciting prospect.

X. Appendices

Appendix A: Efficacy of mifepristone and misoprostol, methotrexate and misoprostol and misoprostol alone for early medical abortion

Table 1 Efficacy of mifepristone and misoprostol for early medical abortion

Reference	N	Gestational age	Dose mifepristone (mg)	First dose misoprostol (mcg)	Additional doses misoprostol (mcg)	Success (%)
Raghavan S, *et al.*[51]	240	≤ 63 days	200	400 sublingual on day 2		99
	239	≤ 63 days	200	400 oral on day 2		94
von Hertzen H, *et al.*[55]	529	≤ 63 days	100	800 vaginal on day 2		93
	534	≤ 63 days	100	800 vaginal on day 3		91
	531	≤ 63 days	200	800 vaginal on day 2		94
	532	≤ 63 days	200	800 vaginal on day 3		93
Winikoff B, *et al.*[53]	421	≤ 63 days	200	800 buccal on day 2	800 buccal on day 8-14 if needed	96
	426	≤ 63 days	200	800 oral on day 2	800 oral on day 8-14 if needed	91
Coyaji K, *et al.*[46]	147	≤ 56 days	200	400 oral on day 3		86
	150	≤ 56 days	200	400 oral on day 3	400 oral 3 hrs later	92
Guest J, *et al.*[58]	210	≤ 63 days	200	800 vaginal on day 1 (6 hrs after mife)	800 vaginal on day 3 to 8 if needed	89
	215	≤ 63 days	200	800 vaginal on day 3	800 vaginal on day 5 to 10 if needed	96
Creinin MD, *et al.*[57]	554	≤ 63 days	200	800 vaginal on day 1 (0-15 min after mife)	800 vaginal on day 8 if needed	95
	546	≤ 63 days	200	800 vaginal on day 2	800 vaginal on day 8 if needed	97

Table 1 (*continued*)

Middleton T, *et al.*[126]	216	≤ 56 days	200	800 buccal on day 2-3		95
	213	≤ 56 days	200	800 vaginal on day 2-3		93
Creinin MD, *et al.*[56]	525	≤ 63 days	200	800 vaginal on day 1 (6-8 hrs after mife)	800 vaginal on day 8 if needed	96
	531	≤ 63 days	200	800 vaginal on day 2	800 vaginal on day 8 if needed	98
Tang OS, *et al.*[52]	112	≤ 63 days	200	800 vaginal on day 3		94
	112	≤ 63 days	200	800 sublingual on day 3		98
von Hertzen H, *et al.*[127]	740	≤ 63 days	200	800 oral on day 3	400 oral twice daily on days 4-10	92
	741	≤ 63 days	200	800 vaginal on day 3	400 oral twice daily on days 4-10	95
	738	≤ 63 days	200	800 vaginal on day 3		94
Schaff EA, *et al.*[128]	220	≤ 63 days	200	400 oral on day 3	800 vaginal on day 4-8 if needed	91
	269	≤ 63 days	200	800 oral on day 3	800 vaginal on day 4-8 if needed	95
	522	≤ 63 days	200	800 vaginal on day 3	800 vaginal on day 4-8 if needed	98
Bartley J, *et al.*[129]	453	≤ 63 days	200	800 vaginal on day 3		99
Schaff *et al.*[47]	548	≤ 63 days	200	400 oral on day 2	400 oral 2 hrs later, 800 vaginal on day 3-8 if needed	95
	596	≤ 63 days	200	800 vaginal on day 2	800 vaginal on day 3-8 if needed	99
Schaff EA, *et al.*[54]	734	≤ 56 days	200	800 vaginal on day 1		98
	766	≤ 56 days	200	800 vaginal on day 2		98
	755	≤ 56 days	200	800 vaginal on day 3		96

Table 1 Efficacy of mifepristone and misoprostol for early medical abortion (*continued*)

Schaff EA, *et al.*[60]	933	≤ 56 days	200	800 vaginal on day 3		97
Spitz I, *et al.*[6]	827	≤ 49 days	600	400 oral on day 3		92
	678	50-56 days	600	400 oral on day 3		83
	510	57-63 days	600	400 oral on day 3		77
Winikoff B, *et al.*[14]	1,373	≤ 56 days	600	400 oral on day 3		84-95
Aubeny E, *et al.*[130]	1,108	≤ 63 days	600	400 oral on day 3	200 oral 3 hrs later if needed	93
Baird DT, *et al.*[131]	386	≤ 63 days	200	600 oral on day 3		95
El-Refaey H, *et al.*[132]	130	≤ 63 days	600	800 oral on day 3		87
	133	≤ 63 days	600	800 vaginal on day 3		95
El-Refaey H, *et al.*[133]	150	≤ 56 days	200	800 oral on day 3		93
Guo-wei S, *et al.*[134]	149	≤ 49 days	150	600 oral on day 3		95
McKinley C, *et al.*[135]	110	≤ 63 days	200	600 oral on day 3		94
	110	≤ 63 days	600	600 oral on day 3		94
Peyron R, *et al.*[136]	488	≤ 49 days	600	400 oral on day 3		97
	385	≤ 49 days	600	400 oral on day 3	200 oral 4 hrs later if needed	99

Table 2 Efficacy of methotrexate and misoprostol for early medical abortion

Reference	N	Gestational age	Dose methotrexate (mg)	Dose misoprostol (mcg)	Dosing Interval	Success (%)
Wiebe, *et al.*[137]	154	≤ 49 days	50 mg/m2 IM	600 vaginal q 24 hrs x2	4-6 days	94
	155	≤ 49 days	50 mg/m2 IM	600 buccal q 24 hrs x2	4-6 days	90
Creinin, *et al.*[138]	26	≤ 49 days	50 mg/m2 IM	800 vaginal	3-7 days	93
Borgatta, *et al.*[139]	1,973	≤ 49 days	50 mg/m2 IM	800 vaginal q 24 hrs x2 if needed	5-7 days	84
Carbonell, *et al.*[140]	148	≤ 56 days	25 mg oral	800 vaginal q 24 hrs if needed	7 days	91
Wiebe, *et al.*[141]	99	≤ 49 days	50 mg/m2 IM	None	5-6 days	83
	256	≤ 49 days	50 mg/m2 IM	800 vaginal	5-6 days	89
Carbonell, *et al.*[94]	300	≤ 63 days	50 mg oral	800 vaginal, repeated at 48 and 96 hrs if needed	3-5 days	91
Carbonell, *et al.*[142]	287	≤ 63 days	50 mg/m2 IM	800 vaginal q 48 hrs x3 if needed (self-administered)	3-5 days	92-93
Wiebe, *et al.*[143]	289	≤ 49 days	50 mg/m2 IM	750 vaginal	4-5 days	91
	241	≤ 49 days	50 mg/m2 IM	600 vaginal q 8 hrs x3	4-5 days	88
	289	≤ 49 days	50 mg/m2 IM	750 vaginal	4-5 days	91
	226	≤ 49 days	60 mg/m2 IM	750 vaginal	4-5 days	85
	145	≤ 49 days	50 mg/m2 IM	500 vaginal	4-5 days	93
	144	≤ 49 days	50 mg/m2 IM	750 vaginal	4-5 days	90
Creinin, *et al.*[144]	99	≤ 49 days	75 mg IM	800 vaginal	5-6 days	95
	202	≤ 49 days	50 mg/m2 IM	800 vaginal	5-6 days	89
	299	≤ 49 days	50 mg/m2 oral	800 vaginal	5-6 days	91

Table 3 Efficacy of misoprostol alone for early medical abortion

Reference	N	Gestational age	First dose misoprostol (mcg)	Additional doses misoprostol (mcg)	Success (%)
von Hertzen, *et al.*[110]	512	≤ 63 days	800 sublingual	q 3 hrs x3	84
	509	≤ 63 days	800 sublingual	q 12 hrs x3	78
	513	≤ 63 days	800 vaginal	q 3 hrs x3	85
	512	≤ 63 days	800 vaginal	q 12 hrs x3	83
Aldrich, *et al.*[103]	2,444	≤ 56 days	800 vaginal	800 vaginal if needed	77
Blanchard, *et al.*[145]	36	≤ 56 days	400 oral	q 3 hrs x4	39
	24	≤ 56 days	800 oral	q 6 hrs x2	5
	40	≤ 56 days	600 vaginal		43
	35	≤ 56 days	800 oral	q 3 hrs x2	46
	25	≤ 56 days	800 vaginal		60
	51	≤ 56 days	800 vaginal	800 vaginal at 24 hrs if needed	80
	50	≤ 56 days	800 vaginal	q 24 hrs x2	66
Borgatta, *et al.*[146]	440	≤ 56 days	800 vaginal	q 24 hrs x2	91
Carbonell, *et al.*[147]	452	≤ 63 days	800 vaginal	q 8 hrs (self-administered) x3	91
Cheung, *et al.*[148]	50	≤ 49 days	400 sublingual	q 3 hrs x3	86
Singh, *et al.*[149]	150	≤ 56 days	800 vaginal	400 vaginal q 3 hrs up to x3	85
Jain, *et al.*[150]	125	≤ 56 days	800 vaginal	q 24 hrs up to x3	88
Tang, *et al.*[151]	50	≤ 83 days	600 sublingual	q 3 hrs up to x5	86
Tang, *et al.*[152]	25	≤ 83 days	Varying doses sublingual		93
Zikopoulos, *et al.*[153]	160	≤ 56 days	800 vaginal	q 24 hrs up to x3	91
Carbonell, *et al.*[154]	300	42-63 days	1,000 vaginal	q 24 hrs up to x3	93
Carbonell, *et al.*[155]	150	63-84 days	800 vaginal	q 24 hrs up to x3	84

Table 3 (*continued*)

Bugalho, *et al.*[156]	103	≤ 42 days	800 vaginal	800 vaginal 7 days afterward if needed	92
Ngai, *et al.*[157]	80	≤ 63 days	800 vaginal	q 48 hrs up to x3	75
Velazco, *et al.*[158]	150	35-63 days	800 vaginal	q 24 hrs up to x3	89
Carbonell, *et al.*[159]	180	64-91 days	800 vaginal	q 12 hrs up to x3	85
Esteve, *et al.*[160]	720	35-63 days	800 vaginal	q 24 hrs up to x3	89
Jain, *et al.*[161]	150	≤ 56 days	800 vaginal	q 24 hrs x2 + 800 vaginal 8 days afterward if needed	91
Jain, *et al.*[162]	100	≤ 56 days	800 vaginal	800 vaginal 24 hrs afterward if needed	88
Ozeren, *et al.*[163]	36	≤ 63 days	800 vaginal	800 vaginal on day 4 if needed	58
Tang, *et al.*[164]	20	≤ 63 days	800 vaginal	400 vaginal q 3 hrs x4	70
Carbonell, *et al.*[165]	120	64-84 days	800 vaginal	q 24 hrs up to x3	87
Carbonell, *et al.*[166]	175	≤ 63 days	800 vaginal	q 48 hrs up to x3 + 400-600 vaginal if needed	92
Carbonell, *et al.*[167]	141	≤ 69 days	800 vaginal	q 48 hrs up to x3	94
Bugalho, *et al.*[168]	101	35-77 days	200 vaginal	q 12 hrs up to x4	46
	133	35-77 days	400 vaginal	q 12 hrs up to x4	66
Creinin, *et al.*[169]	61	≤ 56 days	800 vaginal	800 vaginal 24 hrs afterward if needed	47

Appendix B: Counseling checklist for medical abortion

1. Discuss the differences between medical and surgical abortion:

Medical Abortion	Surgical Abortion
• High success rate	• High success rate
• Surgical intervention required in small percentage	• Very small percentage may require re-evacuation
• Avoids invasive procedures	• Instruments inserted into the uterus
• Avoids sedation and anesthesia	• Typically includes sedation with or without anesthesia
• Severe complications are rare	• Complications are rare. Infection from surgical instrumentation and injury to the genital tract can occur.
• Time to completion uncertain	• Time to completion is predictable
• Involves multiple steps	• Involves a single step
• Woman has greater control	• Provider has greater control

2. Ask the woman to choose the method that she would like.

3. If medical abortion is selected, confirm that the woman is eligible for this method.

4. Be sure that all women are:
    - certain about the abortion decision
    - at appropriate gestational age
    - able to follow treatment protocol

- willing to attend follow-up appointment, if needed
- willing to have surgical completion, if needed
- able to access emergency care

5. Explain the regimen:
    - Instruct how and when to administer misoprostol (if home use is chosen).
    - Explain what to expect during the expulsion process.

6. Describe commonly experienced side effects:
    - Vaginal bleeding comparable to or heavier than a normal heavy period
    - Cramping
    - Nausea, vomiting, and/or diarrhea
    - Fatigue
    - Each of these symptoms is normal and should not last a very long time
    - Stock up on sanitary pads (or local equivalent)

7. Describe how to manage side effects:
    - Analgesics

8. Explain when to contact the clinic:
    - Severe pain not relieved by analgesics
    - Soaking at least 2 extra large sanitary pads (or local equivalent) per hour for 2 consecutive hours
    - Fever lasting 6 hours or more

9. Provide emergency contact information for the clinic.

10. Offer contraceptive information.

11. Be sure that the woman leaves the clinic with the following:
    - Misoprostol tablets (if home use regimen is chosen)
    - Analgesia or a prescription for analgesia
    - Instruction sheet that includes:
        - Details on how and when to administer misoprostol (if home use regimen is chosen)
        - Description of side effects and how to manage them
        - Instructions for when to call the clinic
        - Date and time of follow-up visit

Appendix C: Sample informed consent form

The medical abortion procedure has been fully explained to me. I understand that I will be given mifepristone to take by mouth in the clinic and that I will need to take misoprostol from one to three days later. I understand that I will be asked to return to the clinic for a follow-up visit approximately two weeks after my first visit. I can also come to the clinic at any other time as well if I have any concerns or questions. I realize that I can request and receive a surgical abortion at any point in time.

I understand that many women experience some side effects with medical abortion. I may feel some nausea and may vomit or have diarrhea. I realize that I will probably have abdominal pain or cramping, and bleeding. The bleeding may be heavier than I usually experience with my menses. I understand that all of these side effects are temporary.

I also understand that the medical abortion regimen may fail to terminate my pregnancy. I have been told that this occurs in about five out of every one hundred cases.

There are several reports of fetal abnormalities from women who have taken the combined regimen of mifepristone-misoprostol and then continued their pregnancies to term. Therefore, if the treatment fails, I realize that it is strongly recommended that I should have a surgical abortion.

If I have a medical emergency, or any concerns about my medical abortion, I may call _____ at telephone number: _____.

I, _____ (print name), would like to terminate my pregnancy with a medical abortion regimen. I have read and understand this informed consent form. All of my questions have been answered, and I have received the name and telephone number to call in case of emergency.

Signed: _____ Date: _____

Appendix D: Bellagio meeting participants

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Dr. Christian Fiala Gynmed Ambulatorium Mariahilfer Gürtel 37 A-1150 Vienna, Austria	

* deceased

Appendix E: Additional Resources

Concept Foundation
www.medabon.info

Early Option Pill
www.earlyoptionpill.com

Ibis Reproductive Health - Medication Abortion Website
http://www.medicationabortion.com

International Consortium for Medical Abortion
http://www.medicalabortionconsortium.org

Ipas
http://www.ipas.org

Misoprostol Org
http://www.misoprostol.org

National Abortion Federation (NAF) - Educational Resources
http://www.prochoice.org

Royal College of Obstetricians and Gynaecologists
http://www.rcog.org.uk/files/rcog-corp/uploaded-files/NEBInducedAbortionfull.pdf

United States FDA - MIFEPREX™ (mifepristone) Label
http://www.accessdata.fda.gov/drugsatfda_docs/label/2000/20687lbl.pdf

Women on Web
http://www.womenonweb.org

World Health Organization - Safe Abortion: Technical and Policy Guidance for Health Systems
http://www.who.int/reproductivehealth/publications/unsafe_abortion/9241590343/en/index.html

World Health Organization - Frequently Asked Clinical Questions about Medical Abortion
http://www.who.int/reproductivehealth/publications/unsafe_abortion/9241594845/en/index.html

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