



# Medical management of abortion



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# Medical management of abortion

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# Acknowledgements

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WHO is grateful for the contributions of staff and consultants to the Department, members of the Guideline Development Group and the external peer reviewers who participated in initial online consultations, subsequent technical consultations and the review of this guideline.

A complete list of contributors and their specific roles can be found in Annex 1.

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## Acronyms and abbreviations

<b>B</b>	buccal (in the cheek) <i>(route of administration of medication)</i>	<b>IUD</b>	intrauterine device
<b>COI</b>	conflict of interest	<b>IUFD</b>	intrauterine fetal demise
<b>DMPA</b>	depot medroxyprogesterone acetate	<b>LMP</b>	last menstrual period
<b>DOI</b>	declaration of interest	<b>NGO</b>	nongovernmental organization
<b>ERG</b>	External Review Group	<b>PAHO</b>	Pan American Health Organization
<b>EST</b>	Evidence Synthesis Team	<b>PICO</b>	population, intervention, comparator, outcome
<b>EtD</b>	Evidence to Decision	<b>PO</b>	oral <i>(route of administration of medication)</i>
<b>GDG</b>	Guideline Development Group	<b>PV</b>	vaginal <i>(route of administration of medication)</i>
<b>GRADE</b>	Grading of Recommendations Assessment, Development and Evaluation	<b>RCT</b>	randomized controlled trial
<b>hCG</b>	human chorionic gonadotrophin	<b>SL</b>	sublingual (under the tongue) <i>(route of administration of medication)</i>
<b>IM</b>	intramuscular	<b>WHO</b>	World Health Organization

# Glossary

**Duration of pregnancy (gestation):** Size of the uterus, estimated in weeks, based on clinical examination, that corresponds to a pregnant uterus of the same gestational age dated by last menstrual period (LMP).

**Medical methods of abortion (medical abortion):** Use of pharmacological drugs to terminate pregnancy. Sometimes the terms “non-surgical abortion” or “medication abortion” are also used.

## Routes of misoprostol administration:

- oral** pills are swallowed;
- buccal** pills are placed between the cheek and gums and swallowed after 30 minutes;
- sublingual** pills are placed under the tongue and swallowed after 30 minutes;
- vaginal** pills are placed in the vaginal fornices (deepest portions of the vagina) and the individual is instructed to lie down for 30 minutes.

**Surgical methods of abortion (surgical abortion):** use of transcervical procedures for terminating pregnancy, including vacuum aspiration and dilatation and evacuation (D&E). See Chapter 2, section 2.2.4 in the WHO *Safe abortion* guideline (2012)<sup>1</sup> for a more detailed description of methods of surgical abortion.

## Human rights terminology

**International human rights treaty/covenant/convention:** adopted by the international community of States, normally at the United Nations General Assembly. Each treaty sets out a range of human rights, and corresponding obligations which are legally binding on States that have ratified the treaty. Annex 7 in the 2012 *Safe abortion* guideline includes a list of these treaties.

**Regional human rights treaties:** States adopted human rights treaties in Africa, the Americas, Europe and the Middle East. Regional human rights bodies, such as the African Union, the Organization of American States, the Council of Europe, the European Union, and the League of Arab States monitor States’ compliance with the treaties. To date, there are no regional human rights treaties in South-East Asia or the Western Pacific. Annex 7 in the 2012 *Safe abortion* guideline includes a list of regional human rights treaties.

**Human rights standards:** the meaning and scope of human rights as interpreted and applied by the human rights bodies tasked with this work, e.g. international, regional and national courts, and human rights committees.

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<sup>1</sup> Safe abortion: technical and policy guidance for health systems, second edition. Geneva: World Health Organization; 2012 ([http://apps.who.int/iris/bitstream/handle/10665/70914/9789241548434\\_eng.pdf](http://apps.who.int/iris/bitstream/handle/10665/70914/9789241548434_eng.pdf)).

# Executive summary







Medical abortion care encompasses the management of various clinical conditions including spontaneous and induced abortion (both viable and non-viable pregnancies), incomplete abortion and intrauterine fetal demise, as well as post-abortion contraception.

Medical management of abortion generally involves either a combination regimen of mifepristone and misoprostol or a misoprostol-only regimen. Medical abortion care plays a crucial role in providing access to safe, effective and acceptable abortion care. In both high- and low-resource settings, the use of medical methods of abortion have contributed to task shifting and sharing and more efficient use of resources. Moreover, many interventions in medical abortion care, particularly those in early pregnancy, can now be provided at the primary-care level and on an outpatient basis, which further increases access to care. Medical abortion care reduces the need for skilled surgical abortion providers and offers a non-invasive and highly acceptable option to pregnant individuals.

## Rationale for this guideline

Recommendations for the use of mifepristone and misoprostol for inducing abortion and for managing incomplete abortion are contained within the 2012 WHO guideline *Safe abortion: technical and policy guidance for health systems*. Evidence related to home use of medication and self-assessment is included in the 2015 WHO guideline *Health worker roles in providing safe abortion and post-abortion contraception*. However, a number of new studies have been published in more recent years providing evidence related to the timing, dosage, dosing intervals and routes of administration of medications to manage abortion, and also the timing of contraception initiation following a medical abortion. Hence it was critical for WHO to review the evidence and update its own recommendations.

## Guideline development process

The guideline was developed according to the principles set out in the *WHO handbook for guideline development* and under the oversight of the WHO Guidelines Review Committee. The core team at WHO (the Steering Group) was complemented by an Evidence Synthesis Team (EST) of experts (including two guideline methodologists) and by a multidisciplinary group of external technical experts who constituted the Guideline Development Group (GDG).

The WHO 2012 *Safe abortion* guidance will be updated during 2019–2020. The contents of this 2018 guideline represent prioritized thematic areas that need to be updated more urgently, based on input from a pre-scoping online survey, conducted in mid-2016 among a group of experts in the field, and from a technical consultation and scoping meeting held in February 2017. Based on input received, the WHO Steering Group drafted an initial list of thematic issues and associated questions in PICO (population, intervention, comparator, outcome) format. These thematic issues included surgical management of abortion; however, the focus of this clinical guideline is medical management of abortion. A systematic literature search was conducted followed by review of the evidence; eight separate systematic reviews were undertaken. Data that informed the recommendations in this guideline came from a total of 140 studies carried out in a wide variety of settings ranging from high- to low-income economies. Figure 1 shows the geographical spread and number of studies per indication for medical management of abortion that served as the evidence base. The certainty of the evidence on safety, effectiveness and user satisfaction was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.<sup>2</sup>

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<sup>2</sup> Further information is available at: <http://www.gradeworkinggroup.org/>

Recommendations were finalized in consultation with the GDG and using Evidence to Decision (EtD) frameworks that considered benefits, harms, values, equity, feasibility and acceptability, as well as implications for resource use, where available. Where there was limited evidence, supplemental programmatic information provided by experts from the field was considered. The guideline was prepared by the WHO Steering Group with input from the GDG. In addition to the GDG, several external peer reviewers who were unconnected to the guideline development process also reviewed and critically appraised the draft guideline prior to its finalization. Declarations of interest (DOIs) were managed according to standard procedures.

**FIGURE 1**

**Evidence base informing the recommendations**

RESOLUTION OF INCOMPLETE ABORTION	24 studies	Australia, Burkina Faso, China, Denmark, Egypt, Finland, Ghana, India, Madagascar, Mauritania, Mozambique, Niger, Nigeria, Republic of Moldova, Senegal, South Africa, Sweden, Thailand, Turkey, Uganda, United Kingdom, United Republic of Tanzania, United States of America (USA), Viet Nam
INDUCED ABORTION FOR FETAL DEMISE	16 studies	Australia, India, Iran, Netherlands, Pakistan, Sudan, Thailand, Turkey, USA, Viet Nam
INDUCED ABORTION < 12 WEEKS	49 studies	Armenia, Canada, China, Cuba, Georgia, Hong Kong SAR, Hungary, India, Iran, Kazakhstan, Mongolia, Mozambique, Nepal, Republic of Moldova, Romania, Scotland, Serbia, Slovenia, South Africa, Sweden, Thailand, Tunisia, Ukraine, United Kingdom, USA, Viet Nam
INDUCED ABORTION ≥ 12 WEEKS	44 studies	Australia, Armenia, Canada, China, Cuba, Finland, Georgia, Hungary, Hong Kong SAR, India, Nepal, New Zealand, Singapore, Slovenia, South Africa, Sweden, Thailand, Tunisia, Turkey, United Kingdom, USA, Uzbekistan, Viet Nam
TIMING OF POST-ABORTION CONTRACEPTION	7 studies	Finland, Mexico, Portugal, Sweden, United Kingdom, USA

## Overview of recommendations:

This guideline focuses exclusively on medical management of abortion. It provides *new* recommendations related to the following indications: medical management of incomplete abortion at  $\geq 13$  weeks of gestation<sup>3</sup> (Recommendation 1b), medical management of intrauterine fetal demise at  $\geq 14$  to  $\leq 28$  weeks of gestation (Recommendation 2), timing of post-abortion hormonal contraception initiation (Recommendation 4a) and timing of post-abortion IUD placement (Recommendation 4b).

In addition, this guideline includes *updated* recommendations related to the following indications: medical management of incomplete abortion at  $< 13$  weeks of gestation (Recommendation 1a), and medical management of induced abortion at  $< 12$  weeks (Recommendation 3a) and at  $\geq 12$  weeks (Recommendation 3b).

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<sup>3</sup> Duration of pregnancy (gestation): Size of the uterus, estimated in weeks, based on clinical examination, that corresponds to a pregnant uterus of the same gestational age dated by last menstrual period (LMP).

**TABLE 1**
**Summary chart of recommendations on medical management of abortion**

RECOMMENDATIONS	COMBINATION REGIMEN (RECOMMENDED <sup>a</sup> )		MISOPROSTOL-ONLY (ALTERNATE)
	MIFEPRISTONE	» 1–2 DAYS » MISOPROSTOL	MISOPROSTOL
<b>1A. INCOMPLETE ABORTION</b> < 13 WEEKS	None	Use misoprostol-only regimen	600 µg PO <sup>b</sup> or 400 µg SL <sup>b</sup>
<b>1B. INCOMPLETE ABORTION</b> ≥ 13 WEEKS	None	Use misoprostol-only regimen	400 µg B, PV or SL every 3 hours <sup>b</sup>
<b>2. INTRAUTERINE FETAL DEMISE</b> ≥ 14–28 WEEKS	200 mg PO once	400 µg PV or SL every 4–6 hours <sup>b</sup>	400 µg SL (preferred) or PV every 4–6 hours <sup>b</sup>
<b>3A. INDUCED ABORTION</b> < 12 WEEKS	200 mg PO once	800 µg B, PV or SL <sup>b</sup>	800 µg B, PV or SL <sup>b</sup>
<b>3B. INDUCED ABORTION</b> ≥ 12 WEEKS	200 mg PO once	400 µg B, PV or SL every 3 hours <sup>b</sup>	400 µg B, PV or SL every 3 hours <sup>b</sup>
<b>TIMING OF POST-ABORTION CONTRACEPTION</b>			
<b>IMMEDIATE INITIATION</b>			
<b>4A. HORMONAL CONTRACEPTION</b>	Immediately after the first pill of the medical abortion		
<b>4B. IUD</b>	With assessment of successful abortion		

B: buccal; PO: oral; PV: vaginal; SL: sublingual

<sup>a</sup> Combination regimen is recommended because it is more effective.

<sup>b</sup> Repeat doses of misoprostol can be considered when needed to achieve success of the abortion process. In this guideline we do not provide a maximum number of doses of misoprostol. Health-care providers should use caution and clinical judgement to decide the maximum number of doses of misoprostol in pregnant individuals with prior uterine incision. Uterine rupture is a rare complication; clinical judgement and health system preparedness for emergency management of uterine rupture must be considered with advanced gestational age.

## Notable differences between this guideline and previous guidance

There are several notable differences between this guideline and previous (2012) WHO guidance, including the time period between mifepristone and misoprostol dosing, the use of a loading dose, and the maximum number of doses of misoprostol.

TABLE 2

### Notable differences between information in this guideline and previous guidance

TOPIC	THIS GUIDELINE (2018)	SAFE ABORTION GUIDELINE (2012) <sup>4</sup>
TIME PERIOD BETWEEN MIFEPRISTONE AND MISOPROSTOL DOSING	Time period is in days rather than hours	Time was provided in hours (i.e. 36–48) for induced abortion regimens with pregnancies beyond nine weeks
LOADING DOSE	The use of a loading dose of misoprostol is not necessary	Previous guidance recommended a loading dose that differed from subsequent doses of misoprostol for induced abortion regimens with pregnancies beyond nine weeks
MAXIMUM NUMBER OF DOSES OF MISOPROSTOL	In this guideline we do not provide a maximum number of doses of misoprostol	Previous guidance recommended a maximum number of five doses

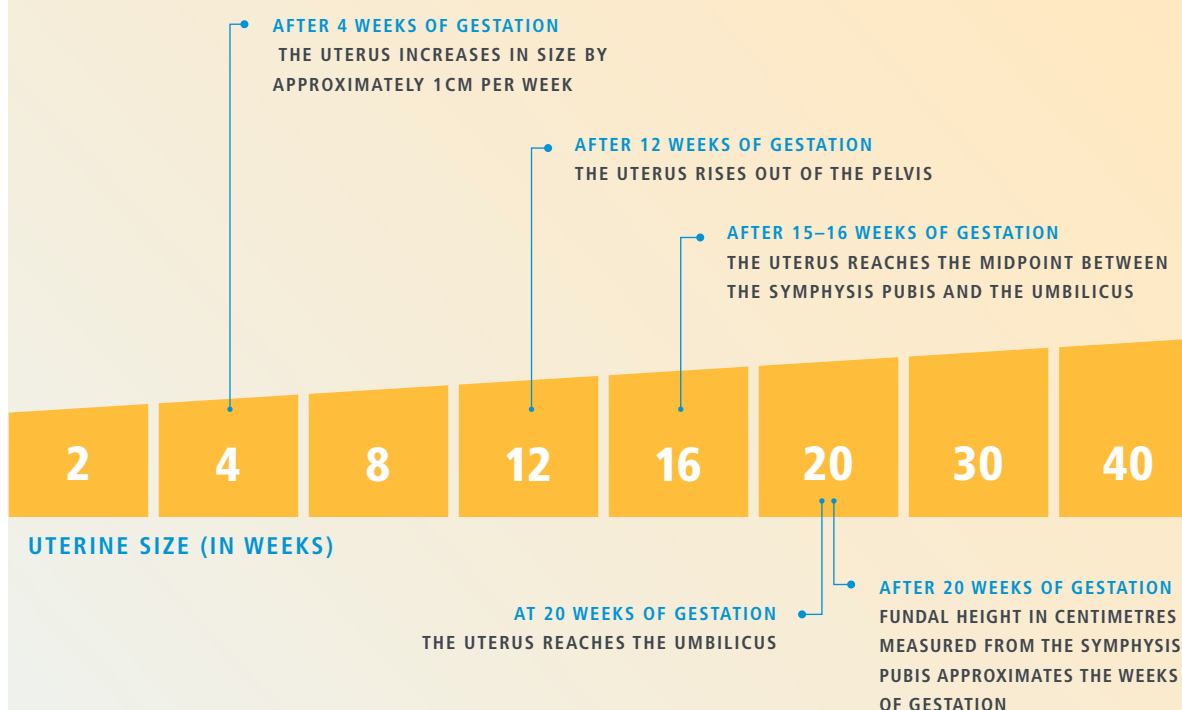
<sup>4</sup> Safe abortion: technical and policy guidance for health systems, second edition. Geneva: World Health Organization; 2012 ([http://www.who.int/reproductivehealth/publications/unsafe\\_abortion/9789241548434/en/](http://www.who.int/reproductivehealth/publications/unsafe_abortion/9789241548434/en/)).

## Estimation of duration of pregnancy (gestation)

In this guideline, duration of pregnancy (gestation) is the size of the uterus, estimated in weeks, based on clinical examination, that corresponds to a pregnant uterus of the same gestational age dated by last menstrual period (LMP). Where it is difficult to determine uterine size based on clinical examination, alternate methods of pregnancy dating can be used (i.e. LMP or ultrasound).

**FIGURE 2**

### Pregnancy dating by physical examination (bimanual pelvic and abdominal examination)



#### LIMITATIONS TO DATING BY UTERINE SIZE ON PHYSICAL EXAMINATION

- uterine malformations/ fibroids
- multiple gestation
- marked uterine retroversion
- obesity
- molar pregnancy

#### KEY CONSIDERATIONS

##### A UTERUS THAT IS SMALLER THAN EXPECTED MAY INDICATE:

- the woman is not pregnant
- inaccurate menstrual dating
- ectopic pregnancy or abnormal intrauterine pregnancy, e.g. spontaneous or missed abortion

##### A UTERUS THAT IS LARGER THAN EXPECTED MAY INDICATE:

- inaccurate menstrual dating
- multiple gestation
- uterine abnormalities, such as fibroids
- molar pregnancy

Source: Clinical practice handbook for safe abortion. Geneva: World Health Organization; 2014, p. 17 ([http://www.who.int/reproductivehealth/publications/unsafe\\_abortion/clinical-practice-safe-abortion/en/](http://www.who.int/reproductivehealth/publications/unsafe_abortion/clinical-practice-safe-abortion/en/)); adapted from Goodman S, Wolfe M; TEACH Trainers Collaborative Working Group. Early abortion training workbook, third edition. San Francisco (CA): UCSF Bixby Center for Reproductive Health Research and Policy; 2007 (<http://www.teachtraining.org/trainingworkbook/earlyabortiontrainingworkbook.pdf>).

# 1. Introduction







## 1.1 Background

Mifepristone and misoprostol in combination or misoprostol alone are the medications generally used to induce abortion and to manage incomplete abortion or intrauterine fetal demise (IUFD).

These medications are increasingly available globally, and they are on the World Health Organization (WHO) List of Essential Medicines (1). Mifepristone is an anti-progestin which binds to progesterone receptors, inhibiting the action of progesterone and hence interfering with the continuation of pregnancy. Treatment regimens entail an initial dose of mifepristone followed by administration of a synthetic prostaglandin analogue, misoprostol, which induces cervical softening and dilation and enhances uterine contractions, which aids in expelling the products of conception (2,3).

Misoprostol is a prostaglandin E1 analogue that can be used either in combination with mifepristone or on its own (4–6). Misoprostol has a wide range of reproductive health applications, including induction of labour, management of spontaneous and induced abortion, and prevention and treatment of postpartum haemorrhage (7). Due to the ease of handling and storing it, as well as its non-invasiveness and proven cost-effectiveness, the use of misoprostol within abortion care – either in combination with mifepristone or alone – offers several advantages. It reduces the need for skilled surgical abortion providers, equipment, sterilization and anaesthesia, while offering a non-invasive and highly acceptable option to pregnant individuals (8). For these reasons, and because it is stable at room temperature within its packaging, misoprostol is particularly useful in low-resource settings (7).

Medical abortion plays a crucial role in providing access to safe, effective and acceptable abortion care. Previous guidance published by WHO, including *Safe abortion: technical and policy guidance for health systems* (2012), provided recommendations for the use of mifepristone and misoprostol in combination or misoprostol alone for the management of medical abortion (6). The 2012 guidance stated that many interventions in medical abortion care, particularly those

in early pregnancy, can be provided at the primary care level and on an outpatient basis, which further increases access to care (6). In both high- and low-resource settings, the use of medical methods of abortion have contributed to task shifting and sharing and more efficient use of resources (9). Given the nature of the medical abortion process, it is also possible for individuals to play a role in managing some of the components by themselves, outside of a health-care facility. Another existing WHO guideline, *Health worker roles in providing safe abortion and post-abortion contraception* (2015), recommends that in specific circumstances, individuals may self-manage their mifepristone and/or misoprostol medication without direct supervision of a health-care provider, as well as self-assess the success of the abortion process using pregnancy tests and checklists (10) (see Box 1). It should be noted that pregnancy tests used to self-assess the success of the abortion process are low-sensitivity urine pregnancy tests, which are different from those tests commonly used to diagnose pregnancy. Such self-assessment and self-management approaches can be empowering for individuals and help to triage care, leading to a more optimal use of health-care resources.

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All individuals who can become pregnant, including women, girls and those with varying gender identities, and who seek medical abortion care should be provided with all of the necessary information to make an informed decision to ensure the promotion of their health and human rights, including sex and gender equality and non-discrimination.

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All individuals who can become pregnant, including women, girls and those with varying gender identities, and who seek medical abortion care should be provided with all of the necessary information to make an informed decision to ensure the promotion of their health and human rights, including sex and gender equality and non-discrimination. With this information, individuals can decide freely and responsibly the number, spacing and timing of their children (11). It is the right of every person, regardless of marital status, to enjoy the benefits of scientific progress and its applications (11).

Depending upon the context, unmarried individuals, adolescents, those living in extreme poverty, individuals from ethnic minorities, refugees and other displaced persons, people with disabilities, and those facing violence in the home may be vulnerable to inequitable access to safe abortion services. Adolescents, in particular, are less likely than adults to be able to obtain legal and safe abortions to terminate their pregnancies. Some of the barriers adolescents face include requirements for third party authorizations (including parental consent) and financial constraints (inability to pay the required fees) (6, 12). Additional considerations related to the care of adolescents can be found in section 4 (General implementation considerations), and in the WHO adolescent job aid (13).

Where geographic inequities exist, people must travel greater distances for care, thereby raising costs and delaying access (14). Financing mechanisms should ensure equitable access to good-quality services (15). Where individuals are charged fees for abortion, such fees should be matched to their ability to pay,

and procedures should be developed for exempting the poor and adolescents from paying for services. As far as possible, abortion services should be mandated for coverage under insurance plans. Abortion should never be denied or delayed because of inability to pay. Providers of abortion services should ensure that all individuals are treated with respect and without discrimination.

Health-care providers, health managers, policy-makers and other stakeholders need up-to-date, evidence-based recommendations to inform clinical policies and practices, to enable improved health-care outcomes and to provide information that is complete, accurate and easy to understand. Expansion of medical abortion and new studies related to the timing, interval and routes of administration of medical abortion medications, necessitated a review of the evidence and the development of new recommendations as well as updates to the WHO recommendations issued in 2012 (6).

## BOX 1

### Other relevant WHO guidance on safe abortion

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PREVIOUS WHO RECOMMENDATIONS RELATED TO MEDICAL ABORTION CARE WERE PRESENTED IN TWO WHO GUIDELINES, WHICH REMAIN CURRENT AND APPLICABLE:

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#### › *Safe abortion: technical and policy guidance for health systems*

This guideline was first issued in 2003 and the second edition was released in 2012 (updated based on evidence available for review in 2010). It provides recommendations for clinical care while addressing policy, programmatic and health systems considerations in the provision of safe abortion (6). Specific thematic areas related to medical abortion regimens contained within the 2012 edition have been updated in this 2018 guideline on the medical management of abortion; however, guidance on aspects of care provision (such as the service location and determination of success of medical abortion regimens) still apply, as presented in the 2012 guideline. These considerations have been placed in this 2018 guideline either in the "Additional considerations" subsections for each recommendation or in the "General implementation considerations" section, which follows the "Recommendations" section.

#### › *Health worker roles in providing safe abortion and post-abortion contraception*

This guideline was issued in 2015 (with evidence up until 2015). It contains recommendations on the roles of various health workers involved in abortion care, as well as on self-management of medical abortion (10). These 2015 recommendations remain applicable, since this 2018 guideline on the medical management of abortion focuses solely on the medication regimens.

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## 1.2 Goal and objectives

**Goal:** To provide evidence-based recommendations on the safety and effectiveness of abortion medications for the clinical management of abortion, as well as the satisfaction of users.

**Objectives:** To review the evidence and develop (or update) recommendations related to the following focus areas.

1. Medical management of incomplete abortion at < 13 weeks and at  $\geq 13$  weeks of gestation (updating the recommendations in the 2012 WHO *Safe abortion* guideline (6) based on new evidence)
2. Medical management of intrauterine fetal demise (IUID) at  $\geq 14$  to  $\leq 28$  weeks of gestation (new recommendation as no previous recommendations existed)
3. Medical management of induced abortion at < 12 weeks and at  $\geq 12$  weeks of gestation (updating the recommendations in the 2012 WHO *Safe abortion* guideline (6) based on new evidence)
4. Timing of initiation of contraception after medical abortion (new recommendation as no previous recommendations existed).

In this guideline, duration of pregnancy (gestation) is the size of the uterus, estimated in weeks, based on clinical examination, that corresponds to a pregnant uterus of the same gestational age dated by last menstrual period (LMP). Where it is difficult to determine uterine size based on clinical examination, alternate methods of pregnancy dating can be used (i.e. LMP or ultrasound). See also Figure 2 in the Executive summary.

### 1.3 Target audience and relevance

The guideline is expected to be useful for:

- ▶ health-care providers;
- ▶ national and subnational policy-makers;
- ▶ implementers and managers of national and subnational reproductive health programmes; and
- ▶ nongovernmental and other organizations and professional bodies involved in the planning and management of medical abortion services.

While legal, policy and regulatory contexts vary, abortion is legal at least to save the life of the pregnant individual in most countries and more than two thirds of countries have one or more additional grounds for legal abortion (16). The provision of post-abortion care is always legal (10). These recommendations will be relevant across a diverse range of settings as the need to make care more accessible and rationalize the use of available health resources exists in both high- and low-resource settings.

# 2. Guideline development process





This guideline was developed by the WHO Department of Reproductive Health and Research in accordance with procedures outlined in the *WHO handbook for guideline development, second edition, 2014 (17)* and under the oversight of the WHO Guidelines Review Committee.

Individuals from other organizations who contributed to this guideline did so in their capacity as individual experts. Donors to the Department who fund work on abortion issues were not included among the members of the Guideline Development Group (GDG) and were not present at any of the GDG meetings. Commercial entities were not involved in developing the guideline, nor was funding from such sources used.

## **2.1 Contributors and their roles**

The guideline was produced by the WHO Department of Reproductive Health and Research and the work of developing the guideline was coordinated by the WHO Steering Group, comprising WHO staff and consultants. The Secretariat was formed of members of the Steering Group from the Department of Reproductive Health and Research. The Secretariat developed the guideline questions, oversaw and participated in the evidence retrieval and synthesis, developed the Evidence to Decision (EtD) frameworks and drafted the recommendations, while also managing the day-to-day activities of developing the guideline.

The Evidence Synthesis Team (EST) consisted of several researchers, who conducted the systematic reviews, and guideline methodologists, who were responsible for evidence retrieval, synthesis and appraisal, including assisting the Steering Group to develop the EtD frameworks. The guideline methodologists were experts from the Global Health Unit, Norwegian Institute of Public Health, Oslo, Norway, and

Cochrane, Portland, United States of America (USA). They worked closely with the WHO Steering Group and researchers from the EST to appraise the evidence from the systematic reviews using Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.<sup>6</sup>

The Guideline Development Group (GDG) was composed of 11 members (5 women, 6 men) from various regions who possessed expertise on a diverse range of relevant issues. GDG members were selected on the basis of their particular knowledge of clinical care for abortion, service delivery and health systems and their work in regions of the world where the need for medical guidance on abortion care is a high priority. The GDG members provided input into the development of the scope of the guideline, the formulation of the population-intervention-comparator-outcome (PICO) questions, the review of the evidence and the development of the recommendations. They also reviewed and approved the final guideline.

A technical consultation and scoping meeting for this guideline was held in Geneva, Switzerland, in February 2017. Further consultation was conducted via email, and four subsequent GDG webinar meetings were held, in December 2017, March 2018, June 2018 and August 2018.

Eight individuals, external to the guideline development process and chosen to reflect the views of end-users who will be impacted by these recommendations, served as an External Review Group (ERG) for the draft guidelines.

A complete list of all contributors, their affiliations and roles is provided in Annex 1.

## 2.2 Declarations of interests

In accordance with the *WHO handbook for guideline development (17)*, all members of the GDG, EST and ERG were required to complete the standard WHO Declaration of Interests (DOI) form. GDG members completed the form prior to each meeting they attended and were also instructed to let the Secretariat know of any changes to their declared interests over time. In addition, experts were requested to submit an electronic copy of their curriculum vitae and their biographies (which were posted online for a minimum of two weeks) along with the completed DOI form prior to each meeting. The WHO Steering Group evaluated the responses and discussed them with the Director of the WHO Department of Reproductive Health and Research. At the GDG meetings, the Chair presented a summary of the DOIs and all participants had the opportunity to confirm, append or amend any interests already declared.

<sup>6</sup> Further information is available at: <http://www.gradeworkinggroup.org/>



One individual being considered for the GDG declared an interest that was perceived to be a potential conflict of interest for the purpose of this guideline. This was discussed with the WHO Office of Compliance, Risk Management and Ethics (CRE). Based on the advice of the CRE, this individual was allowed to participate in the meetings as a technical resource person but did not participate in the development of the recommendations. No additional conflicts of financial interests or involvement with commercial entities were declared. The DOI forms and curriculum vitae have been electronically archived to ensure that confidentiality is maintained.

### 2.3 Scoping and formulation of the guideline questions

The issues to be addressed by this guideline were carefully scoped and refined. The initial list of concepts to be considered was developed on the basis of the results of a pre-scoping online survey conducted in mid-2016, which over 60 experts from all regions of the world were invited to participate in. This survey aimed to identify relevant research gaps and possible interventions (the survey form is provided in Annex 2). A total of 40 responses were received. Further discussions were held via telephone or videoconference with the respondents. Based on input received, the WHO Steering Group drafted an initial list of thematic issues and associated questions in PICO format. The draft list of PICO questions was presented at the technical consultation and scoping meeting in February 2017. Most of those who contributed to the development of the guideline, as listed in Annex 1, also attended this meeting.

Preliminary PICO questions were identified, discussed, reviewed, modified and finalized during the scoping meeting. The final PICO questions for this guideline represent prioritized thematic areas that needed to be updated most urgently, based on input during the technical consultation and scoping meeting. The finalized priority PICO questions covered the following thematic areas:

- ▶ medical management of incomplete abortion at  $\geq 13$  weeks of gestation;
- ▶ medical management of intrauterine fetal demise (IUFD) at  $\geq 14$  to  $\leq 28$  weeks of gestation;
- ▶ medical management of induced abortion at 9–12 weeks of gestation;
- ▶ medical management of induced abortion at  $\geq 12$  weeks of gestation;
- ▶ timing of initiation of contraception after a medical abortion.

Several other thematic areas were noted as important, two of which were re-addressed in an effort to provide a more comprehensive set of

recommendations:

- ▶ medical management of incomplete abortion at < 13 weeks of gestation; and
- ▶ medical management of induced abortion at < 9 weeks of gestation.

The primary outcomes of interest were:

- ▶ benefits and harms
  - effectiveness (specific to the task) and
  - safety, i.e. serious adverse events and complications (specific to the task).

The secondary outcomes of interest were:

- ▶ side-effects (specific to the intervention) and
- ▶ satisfaction of users (specific to the intervention).

## 2.4 Evidence retrieval and synthesis

Evidence of safety, effectiveness and satisfaction related to the interventions of interest included relevant randomized controlled trials (RCTs) as well as non-randomized controlled trials, controlled before-and-after studies, interrupted time-series and cohort studies. The following databases were searched from inception to June 2017, without language filters.

- ▶ **International databases:** ClinicalTrials.gov, Cochrane database, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Global Index Medicus (GIM), Population Information Online (POPLINE), PubMed.
- ▶ **Regional databases:** African Index Medicus (AIM), Chinese Biomedical Literature Database, Index Medicus for the South-East Asian Region (IMSEAR), Index Medicus for the Eastern Mediterranean Region (IMEMR), Latin American and Caribbean Health Sciences Literature (LILACS), Western Pacific Regional Index Medicus (WPRIM).

In addition, a search of trial registry sites and organizational websites, as well as information from experts in the field, were used to identify any major ongoing or completed but unpublished trials that could be relevant to the guideline and the recommendations.

### 2.4.1 Assessment of confidence in the evidence

The certainty (i.e. the extent to which one can be confident that an estimate of the effect or association is correct) of the evidence on the benefits and harms outcomes was assessed using the GRADE approach; two GRADE methodologists were responsible for different thematic issues. Five criteria – study limitations, consistency of effect, imprecision, indirectness and publication bias – were used to assess the certainty for each outcome. The level of certainty in the evidence was downgraded by one level for serious limitations and by two levels for

very serious limitations. Information about the certainty of evidence can be found in the justification section for each recommendation.

#### **2.4.2 Moving from evidence to recommendations**

Various factors that inform decisions on recommendations were assessed using the Evidence to Decision (EtD) framework method developed by the DECIDE collaboration (18). Developing an EtD framework requires explicit and systematic consideration of evidence on interventions in terms of specified domains: effects (benefits/harms), values, equity, resources required, acceptability (as distinct from the secondary outcome of satisfaction) and feasibility.

Additional evidence of potential harms or unintended consequences is described in the “Additional considerations” subsection of each evidence summary. Such considerations include programmatic data that did not directly address the priority PICO question but provided pertinent information in the absence of direct evidence, and additional data extracted from other relevant sources including qualitative studies.

### **2.5 Use of the frameworks for decision-making**

Draft EtD frameworks were prepared by the WHO Steering Group and the EST. These were reviewed by the GDG and recommendations were subsequently drafted and then were finalized during the four GDG webinar meetings. In addition to the EtD frameworks, the GDG also had access to all the supporting materials.


Decision-making (formulation of recommendations) was based on the EtD frameworks and discussion of the synthesized evidence. The final adoption of each recommendation was consensus-driven, defined as full agreement among all GDG members, where possible. The final decision was based on majority opinion, provided the GDG members with opposing views were willing to agree to this outcome; voting to reach a final decision was unnecessary. An option for noting dissenting opinions was available, but at no time was it necessary to exercise this option.

### **2.6 Document preparation, revision and peer review**

Responsible officers at WHO wrote the draft guideline. The GDG reviewed the draft and their feedback was incorporated. The guideline was also reviewed by the members of the ERG who were unconnected with the process of guideline development. They provided structured feedback on accuracy, presentation, implementation considerations and the overall usefulness of the guideline.

# 3. Recommendations, rationale and evidence summary





Recommendations in this guideline focus on four thematic areas and are presented here accordingly in subsections, as follows.

Recommendations on medical regimens for the management of:

1. incomplete abortion
2. intrauterine fetal demise (IUFD)
3. induced abortion.

Recommendations on the timing of:

4. initiation of contraception after medical abortion.

Following each recommendation, the rationale and evidence summary are provided, followed by additional considerations and research gaps. The research gaps were identified using a survey that was circulated among the members of the Guideline Development Group (GDG) to indicate topics requiring further research.

Considerations relating to care provision, including location of services, provider type, assessment of success of the medical abortion regimen, and the role of ultrasound, are derived from the 2012 WHO publication, *Safe abortion: technical and policy guidance for health systems (6)*. Information on these considerations has been included in this guideline under the “Additional considerations” subsections for each recommendation and in the “General implementation considerations” section, which follows this section on recommendations.

Recommendations in this guideline are presented using one of the following phrases:

- ▶ *We recommend* the intervention (strong recommendation in favour of the intervention)
- ▶ *We suggest* the intervention (weak, conditional, discretionary or qualified recommendation in favour of the intervention)

Justifications for each recommendation are provided. The certainty of the underlying body of evidence (high, moderate, low or very low) is also specified.

### 3.1 Guiding principles

Principles underlying the process of improving the access to and quality of abortion care include the right of access to relevant evidence-based health information, so that individuals who can become pregnant can have control over and decide freely and responsibly on matters related to their sexuality and reproduction (including their sexual and reproductive health) free of coercion, discrimination and violence (11). These principles also include the provision of additional services, for the holistic care of the patient.

#### 3.1.1 Provide information

Information is a necessary component of any medical care and should always be provided to individuals considering abortion. At a minimum, this should include (6):

- ▶ the available options for abortion methods and pain management;
- ▶ what will be done before, during and after the procedure, including any tests that may be performed;
- ▶ what they are likely to experience (e.g. pain and bleeding) and how long the procedure and the recovery are likely to take (vaginal bleeding for two weeks is normal after medical abortion – such bleeding can last up to 45 days in rare cases);
- ▶ how to recognize potential complications, and how and where to seek help, if required (individuals should return to the hospital or clinic if they experience increased intensity of cramping or abdominal pain, heavy vaginal bleeding and/or fever);
- ▶ when normal activities can be resumed, including sexual intercourse (the return of fertility can occur within two weeks following abortion);
- ▶ where and how to access additional services and follow-up care (see section 3.1.4 on the right).

#### 3.1.2 Offer counselling

Counselling is a focused, interactive process through which one voluntarily receives support, additional information and guidance from a trained person, in an environment that is conducive to openly sharing thoughts, feelings and perceptions. When providing counselling, it is essential to:

- ▶ communicate information in simple language;
- ▶ maintain privacy;
- ▶ support the individual and ensure they receive adequate responses to their questions and needs; and
- ▶ avoid imposing personal values and beliefs (6).

### 3.1.3 Additional services

Additional services may need to be provided to individuals seeking medical abortion (19).

- ▶ Provide iron tablets for anaemia, if needed.
- ▶ Provide any necessary pain medications.
- ▶ Provide emotional support, if needed.
- ▶ Refer the individual to other services as determined by an assessment of their needs; these services may include: counselling and testing for sexually transmitted infections (STIs, including HIV), abuse support services, psychological or social services, or other specialist health or medical services.

### 3.1.4 Follow-up care

Routine follow-up is not necessary following an uncomplicated surgical or medical abortion using mifepristone and misoprostol. However, an optional follow-up visit 7–14 days after their procedure may be offered to provide further contraceptive counselling and services, further emotional support, or to address any medical concerns.

A routine follow-up visit is recommended only in the case of medical abortion using misoprostol alone, to assess success of the abortion.

At the follow-up appointment:

- ▶ assess the individual's recovery and inquire about any signs or symptoms of ongoing pregnancy;
- ▶ review any available medical records and referral documents;
- ▶ ask about any symptoms experienced since the procedure;
- ▶ perform a focused physical examination in response to any complaints; and
- ▶ assess the individual's fertility goals and need for contraceptive services.
  - If no method was started prior to discharge from the facility, provide information and offer counselling and the appropriate contraceptive method, if desired by the client.
  - If a contraceptive method was already started, assess the method used and note any concerns – where there are no concerns, resupply as needed; where there are concerns, help with selection of another appropriate method (19).

## 3.2 Incomplete abortion

### 3.2.1 Diagnosis of incomplete abortion

Incomplete abortion is defined by clinical presence of open cervical os and bleeding, whereby all products of conception have not been expelled from the uterus. Common symptoms include vaginal bleeding and abdominal pain. Incomplete abortion should also be suspected if, upon visual examination, the expelled tissue is not consistent with the estimated duration of pregnancy.

### 3.2.2 Medical management of incomplete abortion: Recommendations 1a and 1b

Incomplete abortion may be managed expectantly, or treated surgically or medically. The mode of management to be used should be selected based on the individual's clinical condition and preference for treatment.

#### RECOMMENDATION 1A

#### Medical management of incomplete abortion at < 13 weeks of gestation<sup>7</sup>

RECOMMENDATIONS	COMBINATION REGIMEN		MISOPROSTOL-ONLY
	MIFEPRISTONE	» 1-2 DAYS »	MISOPROSTOL
INCOMPLETE ABORTION < 13 WEEKS	None	Use misoprostol-only regimen	600 µg PO <sup>a</sup> or 400 µg SL <sup>a</sup>

PO: oral; SL: sublingual

**For the treatment of incomplete abortion at < 13 weeks uterine size, we suggest the use of 600 µg misoprostol administered orally or 400 µg misoprostol administered sublingually.<sup>a</sup>**

**RECOMMENDATION TYPE: NEW OR UPDATED**

Recommendation 1a is an updated recommendation from the WHO 2012 *Safe abortion* guidance (6). The option of 400–800 µg vaginal misoprostol has been removed from this updated recommendation.

<sup>a</sup> Repeat doses of misoprostol can be considered when needed to achieve success of the abortion process. In this guideline we do not provide a maximum number of doses of misoprostol. Health-care providers should use caution and clinical judgement to decide the maximum number of doses of misoprostol in pregnant individuals with prior uterine incision. Uterine rupture is a rare complication; clinical judgement and health system preparedness for emergency management of uterine rupture must be considered with advanced gestational age.

<sup>7</sup> In this guideline, duration of pregnancy (gestation) is the size of the uterus, estimated in weeks, based on clinical examination, that corresponds to a pregnant uterus of the same gestational age dated by last menstrual period (LMP).



### 3.2.3 Evidence summary and rationale for Recommendations 1a and 1b

A Cochrane review served as the evidence base for the medical management of incomplete abortion; the review assessed the effectiveness, safety and acceptability of various management options (20). There were 24 studies included in the review that focused on incomplete abortion at < 13 weeks of gestation. Of those 24 studies, 22 compared different doses and routes of misoprostol in misoprostol-only regimens and options of expectant, medical or surgical management.

**Effects (benefits and harms)** Two studies focused on misoprostol dosage regimens; these studies found higher rates of successful abortion and fewer unplanned surgical interventions with 600 µg repeat oral dosing. In the studies that compared misoprostol routes, there was no clear evidence of one route being superior to another. In the studies that compared medical management with surgical or expectant management, the incidence

RECOMMENDATION 1B

### Medical management of incomplete abortion at ≥ 13 weeks of gestation

RECOMMENDATIONS	COMBINATION REGIMEN	MISOPROSTOL-ONLY
	MIFEPRISTONE >> 1-2 DAYS >> MISOPROSTOL	MISOPROSTOL
<b>INCOMPLETE ABORTION ≥ 13 WEEKS</b>	None	Use misoprostol-only regimen 400 µg B, PV or SL every 3 hours <sup>a</sup>

B: buccal; PV: vaginal; SL: sublingual

**For the treatment of incomplete abortion at ≥ 13 weeks uterine size, we suggest the use of repeat doses of 400 µg misoprostol administered sublingually, vaginally or buccally every 3 hours.<sup>a</sup>**

△

RECOMMENDATION TYPE: NEW OR UPDATED

Recommendation 1b is a new recommendation.

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<sup>a</sup> Repeat doses of misoprostol can be considered when needed to achieve success of the abortion process. In this guideline we do not provide a maximum number of doses of misoprostol. Health-care providers should use caution and clinical judgement to decide the maximum number of doses of misoprostol in pregnant individuals with prior uterine incision. Uterine rupture is a rare complication; clinical judgement and health system preparedness for emergency management of uterine rupture must be considered with advanced gestational age.

of successful abortion was found to be slightly lower with medical and expectant management, but all methods achieved high success rates. In all 22 studies that looked at the relevant regimens, there were few data on serious adverse events.

There were no studies that focused exclusively on incomplete abortion at  $\geq 13$  weeks. One study set in Finland evaluated the management of incomplete abortion in pregnancies up to 24 weeks of gestation, but it included only three women whose pregnancies fell within the gestational age between 13 and 24 weeks by menstrual dating (21). Of these three women, one received medical treatment and the other two received surgical intervention.

**Values** There was no evidence identified in the Cochrane review that looked directly at how women value medical abortion procedures. However, generally, women describe avoidance of surgery as a positive feature of medical management, while some women value the shorter abortion process and minimal bleeding associated with surgical management (22,23). Some women dislike the side-effects associated with medical management, including bleeding, fevers and chills (22,23).

**Equity** We were unable to identify research on aspects of equity relating to the relative effectiveness of the intervention in different subgroups; no assumptions were made.

**Resources** We attempted to collect programmatic data from organizations involved in service delivery in order to inform the decision on how resources factor into the recommendation. However, we were only able to collect limited information, and the available data varied considerably in its reporting (e.g. definition of terms), thus these data were not used in the decision-making. In cases where additional hospital resources are required, such as blood transfusion, inpatient management or analgesic measures, we assume that the costs associated with this care will be higher.

**Acceptability** Women generally find medical management of incomplete abortion with misoprostol alone acceptable and would recommend the procedure to a friend (24–27).

**Feasibility** We were unable to identify research on the feasibility of implementing the use of misoprostol alone or in combination with mifepristone for the management of incomplete abortion. However, the Cochrane review included 22 studies conducted across 24 countries, providing information related to the varying country contexts in which such services may be provided. Of these 24 countries, seven were in low-income economies, seven were in lower-middle-income economies, four were in upper-middle-income economies and six were in high-income economies (20).

**Rationale for Recommendation 1a (on incomplete abortion at < 13 weeks):** Women treated with 600 µg oral misoprostol had higher rates of successful abortion and lower occurrence of additional surgical interventions; this is based on low-certainty evidence. Low-certainty evidence also suggests that the use of 400 µg sublingual misoprostol leads to high rates of successful abortion. Acceptability of these regimens also appears high.

**Rationale for Recommendation 1b (on incomplete abortion at ≥ 13 weeks):** Due to the lack of direct evidence on medical management of incomplete abortion at ≥ 13 weeks of gestation, this recommendation is based on information extrapolated from data related to the medical management of abortion at > 12 weeks using misoprostol alone. Individuals presenting with incomplete abortion at ≥ 13 weeks may present with varying amounts of residual tissue or products of conception. Thus, the GDG members took the view that since the regimen utilized for medical abortion at > 12 weeks is safe, effective and acceptable, then this regimen can also be applied to those being treated for incomplete abortion where expulsion of uterine contents has begun, as evidenced by bleeding, cramping or contractions.

### 3.2.4 Additional considerations

Ultrasound scanning is not routinely required for the provision of abortion (4,28,29). Ultrasound is useful to detect ongoing pregnancy; measuring endometrial thickness, however, is not generally useful for diagnosing incomplete abortion and may lead to inappropriate surgical interventions (30).

The following health worker cadres can provide medical management of uncomplicated incomplete abortion, given task-specific training and functioning systems for monitoring and supportive supervision: auxiliary nurses, auxiliary nurse midwives, nurses, midwives, associate/advanced associate clinicians, and non-specialist and specialist doctors (10).

### 3.2.5 Research gaps

*General:*

- ▶ Identification of the most effective medical abortion regimen for incomplete abortion at ≥ 13 weeks of gestation (including the use of mifepristone in combination with misoprostol versus misoprostol alone) is still needed. Recommendations have been made for this regimen using indirect evidence. Results from the survey on research gaps (completed by GDG members) noted the lack of evidence for effective regimens in this clinical scenario and, therefore, further research on this topic should be pursued.

### 3.3 Intrauterine fetal demise

#### 3.3.1 Diagnosis of intrauterine fetal demise (IUFD)

Fetal demise refers to situations in which the fetus is no longer alive, but the uterus has not yet started to expel its contents and the cervical os remains closed (31). The diagnosis is made by ultrasound scan following the clinical findings, which can include vaginal bleeding, absent fetal heart sounds on electronic auscultation, a failure to feel fetal movements or a uterus that is significantly smaller than the expected size (31).

#### 3.3.2 Medical management of IUFD at $\geq 14$ to $\leq 28$ weeks of gestation: Recommendation 2

IUFD may be managed expectantly, or treated surgically or medically. The decision about the mode of management of IUFD should be based upon the individual's clinical condition and preference for treatment.

Medical management of IUFD includes the use of mifepristone in combination with misoprostol (recommended) or misoprostol alone (alternate).

#### 3.3.3 Evidence summary and rationale for Recommendation 2

A systematic review assessed the effectiveness, safety and acceptability of misoprostol treatment of IUFD at  $\geq 14$  to  $\leq 28$  weeks of gestation (32). A total of 16 RCTs were identified for inclusion in the review. Studies were included in the review if they included cases of IUFD at  $\geq 14$  to  $\leq 28$  weeks and if these cases were evenly distributed between the study arms. Studies that included IUFD at  $< 14$  weeks or  $> 28$  weeks of gestation were considered only if the mean gestational age of participants was within the range of  $\geq 14$  to  $\leq 28$  weeks.

The review included studies that compared regimens of mifepristone used in combination with misoprostol versus misoprostol alone, as well as those that compared different doses of misoprostol after administration of mifepristone, different doses of misoprostol with or without a loading dose, different routes of administration of misoprostol and different preparations of misoprostol (i.e. moistened or dry).

#### Effects (benefits and harms)

The reviewed studies showed that women treated with a combination of mifepristone and misoprostol had higher rates of complete abortion within 24 hours and a shorter expulsion time than those treated with misoprostol alone. For both combination regimens and misoprostol-only regimens, women treated with 400  $\mu\text{g}$  misoprostol had higher rates of complete abortion within 24 hours and lower rates of serious adverse events than women treated with alternative dosages of misoprostol. In the studies that compared routes of

## RECOMMENDATION 2

### Medical management for intrauterine fetal demise at $\geq 14$ to $\leq 28$ weeks of gestation<sup>8</sup>

RECOMMENDATIONS	COMBINATION REGIMEN (RECOMMENDED <sup>a</sup> )		MISOPROSTOL-ONLY (ALTERNATE)
	MIFEPRISTONE	» 1–2 DAYS » MISOPROSTOL	MISOPROSTOL
INTRAUTERINE FETAL DEMISE $\geq 14$ –28 WEEKS	200 mg PO once	400 $\mu$ g PV or SL every 4–6 hours <sup>b</sup>	400 $\mu$ g SL (preferred) or PV every 4–6 hours <sup>b</sup>

PO: oral; PV: vaginal; SL: sublingual

We suggest the use of 200 mg mifepristone administered orally, followed 1–2 days later by repeat doses of 400  $\mu$ g misoprostol administered sublingually or vaginally every 4–6 hours.<sup>b</sup> The minimum recommended interval between use of mifepristone and misoprostol is 24 hours.

For the misoprostol-only regimen, we suggest the use of repeat doses of 400  $\mu$ g misoprostol administered sublingually every 4–6 hours.<sup>b</sup>

Where sublingual misoprostol is not used, we suggest the use of repeat doses of 400  $\mu$ g misoprostol administered vaginally every 4–6 hours.<sup>b</sup>

#### Notes:

- Data related to gestational ages over 24 weeks of gestation were more limited.
- The use of a loading dose of misoprostol is not necessary. There is no advantage to the use of moistened over dry misoprostol.



#### RECOMMENDATION TYPE: NEW OR UPDATED

Recommendation 2 is new.

<sup>a</sup> Combination regimen is recommended because it is more effective.

<sup>b</sup> Repeat doses of misoprostol can be considered when needed to achieve success of the abortion process. In this guideline we do not provide a maximum number of doses of misoprostol. Health-care providers should use caution and clinical judgement to decide the maximum number of doses of misoprostol in pregnant individuals with prior uterine incision. Uterine rupture is a rare complication; clinical judgement and health system preparedness for emergency management of uterine rupture must be considered with advanced gestational age.

administration for misoprostol, there was no strong evidence of one route being superior to another.

**Values** We were not able to identify research addressing the value placed on management of IUFD. Generally, we made the assumption that individuals would value shorter induction to expulsion times, and would value avoiding additional surgical intervention, serious adverse events and minor side-effects. However, there may be important variability in how much individuals value these outcomes, particularly in relation to each other. For example, a person may choose a longer induction to expulsion time if it is associated with a lower risk of serious adverse events and minor side-effects.

<sup>8</sup> In this guideline, duration of pregnancy (gestation) is the size of the uterus, estimated in weeks, based on clinical examination, that corresponds to a pregnant uterus of the same gestational age dated by last menstrual period (LMP).

**Equity** We were unable to identify research on aspects of equity related to the relative effectiveness of the intervention in different subgroups; no assumptions were made.

**Resources** We were unable to identify research that explored the costs involved or the cost-effectiveness of the intervention among the studies included in the systematic review. However, serious adverse events related to medical management of IUFD are rare. In cases where additional hospital resources are required, such as blood transfusion, inpatient management or analgesic measures, we assume that the costs associated with this care will be higher. We were unable to determine the impact that the use of mifepristone has on costs. While there may be an increased upfront cost in the delivery of a combination regimen (mifepristone and misoprostol), the overall resource use (and cost) may be decreased due to a shorter abortion process and higher success rates.

**Acceptability** Several factors impacting acceptability were considered in the development of this recommendation, including tolerability of medication. Overall, women were satisfied with their treatment (33–35) and found the pain associated with the induction less than or the same as they expected (35).

**Feasibility** We were unable to identify research on the feasibility of implementing the use of misoprostol alone or in combination with mifepristone for the management of IUFD at  $\geq 14$  to  $\leq 28$  weeks specifically. However, the 16 studies were conducted across 17 countries (one study was conducted across sites in two countries) providing information on the varying country contexts in which such services may be provided. Of these 17 countries, six were lower-middle-income economies, seven were upper-middle-income economies and four were high-income economies (32).

**Rationale for Recommendation 2:** Women treated with a combination of mifepristone and misoprostol had higher rates of successful abortion within 24 hours and a shorter expulsion time than those treated with misoprostol alone. The certainty of the evidence ranged from low to very low. Evidence suggests that in both combination regimens and misoprostol-only regimens, the use of 400  $\mu\text{g}$  misoprostol leads to higher rates of successful abortion within 24 hours and lower rates of serious adverse events compared with other doses.

### 3.3.4 Additional considerations

For the health-care providers managing IUFD at  $\geq 14$  to  $\leq 28$  weeks of gestation, the recommendations for cadres who can manage medical abortion at  $> 12$  weeks can be followed. Alongside non-specialist and specialist doctors, additional cadres – including nurses, midwives and associate/advanced associate clinicians – can provide care

where there is access to appropriate surgical backup and the proper infrastructure is available to address incomplete abortion or other complications (10). Patient preference should be considered when determining the route of misoprostol administration in medical management.

### **3.3.5 Research gaps**

*General:*

- ▶ Identification of the most effective medical regimen for IUFD management is needed. In particular, future research can investigate the efficacy of lower doses of misoprostol, such as 200 µg, when used with mifepristone.
- ▶ Misoprostol dosage for management of IUFD at <20 weeks versus 20–28 weeks of gestation should be investigated.

### 3.4 Induced abortion

#### 3.4.1 Indication for induced abortion

People with an unplanned, mistimed or unwanted pregnancy may choose to have a medical abortion. Medical abortion refers to the sequential use of mifepristone followed by misoprostol or, in settings where mifepristone is not available, the use of misoprostol alone, to induce abortion, as an alternative to surgical management of abortion. An enabling regulatory and policy environment is needed to ensure that every individual who can become pregnant and who is legally eligible has ready access to safe abortion care. Laws and policies on abortion should protect health and human rights (6).

#### RECOMMENDATION 3A

#### Medical management of induced abortion at < 12 weeks of gestation<sup>9</sup>

RECOMMENDATIONS	COMBINATION REGIMEN (RECOMMENDED <sup>a</sup> )		MISOPROSTOL-ONLY (ALTERNATE)
	MIFEPRISTONE	>> 1–2 DAYS >>	MISOPROSTOL
INDUCED ABORTION < 12 WEEKS	200 mg PO once	800 µg B, PV or SL <sup>b,c</sup>	800 µg B, PV or SL <sup>b,c</sup>

B: buccal; PO: oral; PV: vaginal; SL: sublingual

We recommend the use of 200 mg mifepristone administered orally, followed 1–2 days later by 800 µg misoprostol administered vaginally, sublingually or buccally.<sup>b,c</sup> The minimum recommended interval between use of mifepristone and misoprostol is 24 hours.

For the misoprostol-only regimen, we recommend the use of 800 µg misoprostol administered vaginally, sublingually or buccally.<sup>b,c</sup>

Notes:

- There is limited evidence to suggest that simultaneous dosing of mifepristone and misoprostol is efficacious (39,40).

**RECOMMENDATION TYPE: NEW OR UPDATED**

Recommendation 3a has been updated from the WHO 2012 *Safe abortion* guidance (6). This updated recommendation applies to pregnancies up to 12 weeks of gestation, whereas in the prior guidance, different regimens were recommended for pregnancies up to 7 weeks, 9 weeks and 12 weeks. For the recommended misoprostol-only regimen, buccal route of administration has been added and the maximum number of doses has been removed. Interval dosing has been removed and a note has been added that repeat doses of misoprostol can be considered to achieve success of the abortion process.

<sup>a</sup> Combination regimen is recommended because it is more effective.

<sup>b</sup> Consideration for patient and provider preference suggests the inclusion of all routes, including buccal administration.

<sup>c</sup> See note on next page (for Recommendation 3b).

<sup>9</sup> In this guideline, duration of pregnancy (gestation) is the size of the uterus, estimated in weeks, based on clinical examination, that corresponds to a pregnant uterus of the same gestational age dated by last menstrual period (LMP).



### 3.4.2 Medical management of induced abortion: Recommendations 3a and 3b

The decision about abortion management should be based on the individual's preference for treatment. The WHO guideline, *Safe abortion: technical and policy guidance for health systems* (2012), recommends manual or electric vacuum aspiration, dilation and evacuation, or medical management, either using a combination regimen (mifepristone followed by misoprostol) or misoprostol alone (6). Mifepristone followed by a prostaglandin analogue has been shown to be safe and effective (36). Limited evidence also suggests that a regimen with repeated doses of misoprostol between 9 and 12 weeks of gestation is safe and effective (4,28,37,38); however, use of misoprostol alone is less effective than its use in combination with mifepristone.

#### RECOMMENDATION 3B

#### Medical management of induced abortion at $\geq 12$ weeks of gestation

RECOMMENDATIONS	COMBINATION REGIMEN (RECOMMENDED <sup>a</sup> )		MISOPROSTOL-ONLY (ALTERNATE)
	MIFEPRISTONE	» 1–2 DAYS »	MISOPROSTOL
INDUCED ABORTION $\geq 12$ WEEKS	200 mg PO once	400 $\mu$ g B, PV or SL every 3 hours <sup>bc</sup>	400 $\mu$ g B, PV or SL every 3 hours <sup>bc</sup>

B: buccal; PO: oral; PV: vaginal; SL: sublingual

We suggest the use of 200 mg mifepristone administered orally, followed 1–2 days later by repeat doses of 400  $\mu$ g misoprostol administered vaginally, sublingually or buccally every 3 hours.<sup>bc</sup> The minimum recommended interval between use of mifepristone and misoprostol is 24 hours.

For the misoprostol-only regimen, we suggest the use of repeat doses of 400  $\mu$ g misoprostol administered vaginally, sublingually or buccally every 3 hours.<sup>bc</sup>

#### Notes:

- The use of a loading dose of misoprostol is not necessary. There is no advantage to the use of moistened over dry misoprostol.

#### RECOMMENDATION TYPE: NEW OR UPDATED

Recommendation 3b has been updated from the WHO 2012 *Safe abortion* guidance (6). For this recommendation, the combination regimen (mifepristone and misoprostol) does not have the loading dose of 800  $\mu$ g misoprostol as in the prior guidance. For both the combination regimen and the misoprostol-only regimen, the buccal route has been added as an option. Maximum number of doses has been removed and the time period between mifepristone and misoprostol dosing is given in days.

<sup>a</sup> Combination regimen is recommended because it is more effective.

<sup>b</sup> Evidence suggests that vaginal route is the most effective. Consideration for patient and provider preference suggests the inclusion of all routes, including buccal administration.

<sup>c</sup> Repeat doses of misoprostol can be considered when needed to achieve success of the abortion process. In this guideline we do not provide a maximum number of doses of misoprostol. Health-care providers should use caution and clinical judgement to decide the maximum number of doses of misoprostol in pregnant individuals with prior uterine incision. Uterine rupture is a rare complication; clinical judgement and health system preparedness for emergency management of uterine rupture must be considered with advanced gestational age.

This guideline provides updated information related to specific dosages, routes and regimens for medical abortion, which differ for pregnancies of different gestational ages.

### 3.4.3 Evidence summary and rationale for Recommendations 3a and 3b

Three systematic reviews served as the evidence base for the effectiveness, safety and acceptability of medical management of induced abortion regimens using mifepristone plus misoprostol (the combination regimen) or misoprostol alone: the first was for induced abortions at  $\leq 63$  days of gestation (41); the second was for induced abortions at  $> 63$  days and up to 84 days (42); and the third was for induced abortions at  $\geq 12$  weeks of gestation (43).

In the first systematic review, 41 studies were included towards the development of this recommendation comparing the combination regimen to the use of misoprostol alone, and comparing different routes, doses and dosing intervals for misoprostol after administration of mifepristone, and different doses of misoprostol in misoprostol-only regimens (41).

In the second systematic review, five studies were included towards the development of these recommendations comparing different routes of misoprostol administration after use of mifepristone, different doses of misoprostol administration in misoprostol-only regimens, and comparing the management of induced abortion in a health-care facility to self-management by the pregnant individual (42).

In the third systematic review, a total of 44 RCTs were identified for inclusion. The review included studies that compared the combination regimen with misoprostol alone. Studies also compared different doses of misoprostol after administration of mifepristone, different doses of misoprostol with or without a loading dose, different routes of administration of misoprostol, and different preparations of misoprostol (i.e. moistened or dry) (43).

**Effects (benefits and harms)** The first review, on induced abortions at  $\leq 63$  days of gestation (41), revealed that the combination regimen had higher rates of successful abortion and lower rates of ongoing pregnancy than the misoprostol-only regimen. In the studies comparing misoprostol doses and interval of misoprostol administration in the combination regimen, there were higher rates of successful abortion and lower rates of ongoing pregnancy with 800  $\mu\text{g}$  of misoprostol and an interval of at least 24 hours between use of mifepristone and misoprostol. Studies comparing the different routes of misoprostol administration revealed the vaginal and sublingual routes to be more effective. In the few studies that compared misoprostol dosages in misoprostol-only regimen, 800  $\mu\text{g}$  of misoprostol had lower rates of ongoing pregnancy and higher rates of successful abortion.

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An enabling regulatory and policy environment is needed to ensure that every individual who can become pregnant and who is legally eligible has ready access to safe abortion care.

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The second systematic review revealed that medical abortion is effective in the late first trimester (>63 days and up to 84 days of gestation) (42). A combination regimen is significantly more effective than a misoprostol-only regimen. Success rates were higher with repeat dosing of misoprostol both in combination regimens and when misoprostol was used alone, and they were also higher with vaginal rather than oral administration for repeat dosing. Two studies addressed outpatient medical abortion, showing no significant difference in effectiveness, safety or acceptability between the two groups.

The third systematic review, on induced abortion at  $\geq 12$  weeks, showed that combination regimens had lower rates of ongoing pregnancy at 24 and 48 hours when compared with misoprostol-only regimens. Dosing of mifepristone 24 hours before misoprostol had lower rates of ongoing pregnancy when compared to simultaneous dosing of both medications. In misoprostol-only regimens, dosing intervals of 3 hours had lower rates of ongoing pregnancy at 24 and 48 hours compared to other dosing intervals. For both combination and misoprostol-only regimens, sublingual and vaginal misoprostol routes of administration had better efficacy and lower rates of side-effects than the oral route (43).

**Values** We were unable to identify research on values relating to the management of medical abortion. We made the assumption that individuals value outcomes of effectiveness and safety, but it is unclear how they would value those outcomes when weighed against side-effects and markers of acceptability.

Women may also strongly value certain interventions over others, with preferences for route and timing of medication administration, and type of intervention (medical or surgical) differing significantly between one woman and another, or one region of the world and another (44–46). Consideration should also be given to the value women place on the timing and cost of abortion services as well as opportunities to take part in managing their own abortion care in situations where at-home dosing or abortion self-management are available (47–49).

**Equity** We were unable to identify research on aspects of equity around relative effectiveness of the interventions in different subgroups. However, in 4 studies, participants ranged in age from 16 to 44 years, demonstrating inclusion of people across age groups (50–53).

**Resources** In the studies included in the three systematic reviews, we were unable to identify research that explored the costs involved or the cost-effectiveness. Studies on medical abortion include analgesic options ranging from oral to parenteral administration, including opiates, depending on gestational age. In cases where additional

hospital resources are required, such as blood transfusion, inpatient management, analgesic measures or foeticide, we assume that the costs associated with these services will be higher. We were unable to determine the impact that the use of mifepristone has on costs. While there may be an increased upfront cost with the use of a combination regimen, the overall resources used may be decreased due to a shorter abortion process and a higher success rate.

**Feasibility** We were unable to identify research on the feasibility of implementing the use of misoprostol alone or in combination with mifepristone for the management of medical abortion. However, four studies conducted in women with pregnancies 9–12 weeks of gestation reported that the medical abortion service was provided as outpatient care indicating feasibility of offering the service through outpatient health-care facilities (33,50,51,53). Additionally, studies related to management of medical abortion at < 12 weeks of gestation were conducted across 10 countries: two high-income, three upper-middle-income, four lower-middle-income and one low-income economy (41). Studies related to management of medical abortion at ≥ 12 weeks of gestation were conducted across 23 countries (four studies were conducted across sites in multiple countries): one was a low-income economy, six were lower-middle-income economies, five were upper-middle-income economies, and 11 were high-income economies (43).

**Acceptability** Generally, women find various routes of misoprostol administration acceptable (48,49,54–59). Additionally, women found the side-effects to be acceptable (47,49). Women receiving care for management of medical abortion at < 12 weeks of gestation reported that the ability to predict timing of the bleeding was the best feature of taking the medicines at home (51). Home use of medical abortion at < 12 weeks gestation following an interaction with a health-care provider enabled women to keep working or reduced opportunity costs (51).

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Women receiving care for management of medical abortion at < 12 weeks of gestation reported that the ability to predict timing of the bleeding was the best feature of taking the medicines at home (51).

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**Rationale for Recommendation 3a (on medical abortion at < 12 weeks of gestation):** The combination mifepristone and misoprostol regimen is based on moderate certainty of evidence for induced abortion at < 12 weeks. In combination regimens, misoprostol dosage of 800 µg administered vaginally, sublingually or buccally is recommended based on moderate certainty of evidence. Evidence is limited regarding the use of misoprostol-only regimens, especially between 9 and 12 weeks of gestation. Thus, the GDG members took the view that when using misoprostol-only regimens, the dose of 800 µg administered vaginally, sublingually or buccally is safe, effective and acceptable.

**Rationale for Recommendation 3b (on medical abortion at ≥ 12 weeks of gestation):** The combination mifepristone and misoprostol regimen is based on moderate certainty of evidence for induced

abortion at  $\geq 12$  weeks. Mifepristone 200 mg is suggested based on success, women's values and cost (given the higher price of 600 mg of mifepristone) based on low to very low certainty of evidence. Misoprostol dosage of 400  $\mu\text{g}$  administered every 3 hours is suggested based on overall very low certainty of evidence and is conditional upon resources available in different settings. Evidence on use of the buccal route was inconclusive, but it should be considered as an acceptable option if an individual prefers this route of administration. This is based on low to very low certainty of evidence.

#### **3.4.4 Additional considerations**

Given the nature of the medical abortion process when using the combination regimen, it is possible for individuals to play a role in managing some of the components by themselves outside of a health-care facility. Where there is access to a source of accurate information and to a health-care provider (should one be needed or wanted at any stage of the process), the abortion process can be self-managed with pregnancies  $< 12$  weeks of gestation without the direct supervision of a health-care provider (10) (evidence is limited for pregnancies  $> 10$  weeks [53,60–64]).

For provision of medical abortion of pregnancies  $< 12$  weeks, the following cadres have been recommended: auxiliary nurses, auxiliary nurse midwives, nurses, midwives, associate/advanced associate clinicians, and non-specialist and specialist doctors. Doctors of complementary systems of medicine can be providers of this service in health system contexts with an established mechanism for the participation of such doctors in other tasks related to maternal and reproductive health (10).

Alongside non-specialist and specialist doctors, the following cadres can provide medical abortion for pregnancies  $\geq 12$  weeks in contexts where appropriate surgical backup and proper infrastructure is established and easily accessible to address incomplete abortion or other complications: nurses, midwives, associate/advanced associate clinicians (10).

#### **3.4.5 Research gaps**

*General:*

- ▶ The various next steps that individuals can take, if needed, after medical abortion should be further evaluated. This includes self-assessment of the success of medical abortion, in particular for misoprostol-only regimens, which tend to be used in more restrictive settings and which are less effective.
- ▶ For those with uterine scars, the safety and efficacy of medical abortion regimens is an area requiring more research. In particular, the misoprostol dosage when used in combination with mifepristone and when used in misoprostol-only regimens for pregnancies 13–20 weeks versus 20–28 weeks of gestation can be investigated.

- ▶ Additional evidence is needed on the cost-effectiveness of all medical abortion interventions.
- ▶ Qualitative research is needed on individuals' values and preferences relating to all medical abortion interventions.

*Medical abortion at < 12 weeks of gestation:*

- ▶ Studies are needed on the efficacy, safety and acceptability of medical abortion (combination mifepristone and misoprostol regimens and misoprostol-only regimens) in the outpatient setting for pregnancies 9–12 weeks of gestation. This includes the follow-up care for medical abortion when self-assessment is used to determine eligibility for and success of the medical abortion.

*Medical abortion at  $\geq$  12 weeks of gestation:*

- ▶ Studies are needed to determine the gestational age limit within which it is safe to carry out medical abortion without hospital admission.
- ▶ In connection to the research gap noted above, qualitative research will also be needed on the acceptability of outpatient medical abortion.

## 3.5 Post-abortion contraception

### 3.5.1 Provision of post-abortion contraception

Contraception can be initiated at the time of administration of the first pill of the medical abortion regimen or after assessment of successful medical abortion. All contraceptive options may be used. Criteria laid out in the WHO publications *Medical eligibility criteria for contraceptive use* and *Ensuring human rights in the provision of contraceptive information and services* should be adhered to (65,66).

**TABLE 3**

**Post-abortion medical eligibility recommendations for contraceptive methods**

CONTRACEPTIVE METHOD	POST-ABORTION CONDITION		
	FIRST TRIMESTER	SECOND TRIMESTER	IMMEDIATE POST-SEPTIC ABORTION
COMBINED ORAL CONTRACEPTIVES (COCs)	1	1	1
COMBINED INJECTABLE CONTRACEPTIVES (CICs)	1	1	1
PATCH & VAGINAL RING	1	1	1
PROGESTERONE-ONLY PILLS (POPs)	1	1	1
PROGESTOGEN-ONLY INJECTABLES: DMPA, NET-EN (depot medroxyprogesterone acetate, norethisterone enanthate)	1	1	1
PROGESTOGEN-ONLY IMPLANTS: LNG, ETG (levonorgestrel, etonogestrel)	1	1	1
COPPER-BEARING INTRAUTERINE DEVICE (IUD)	1	2	4
LNG-RELEASING IUD	1	2	4
CONDOMS	1	1	1
SPERMICIDE	1	1	1
DIAPHRAGM	1	1	1

#### DEFINITION OF CATEGORIES

1. A condition for which there is no restriction for the use of the contraceptive method.
2. A condition where the advantages of using the method generally outweigh the theoretical or proven risks.
3. A condition where the theoretical or proven risks usually outweigh the advantages of using the method.
4. A condition that represents an unacceptable health risk if the contraceptive method is used.

Source: WHO (2015) (65)

### 3.5.2 Timing of post-abortion contraception: Recommendations 4a and 4b

The following recommendations provide further clarification on the timing of initiating contraception after a medical abortion.

### 3.5.3 Evidence summary and rationale for Recommendations 4a and 4b

Three systematic reviews served as the evidence base for the timing of post-abortion contraception. The first systematic review assessed the efficacy and safety of non-IUD hormonal contraception initiation after abortion (including medical abortion) (68). Three RCTs (67,69,70) and one cohort study (71) compared immediate versus delayed initiation of implants or DMPA after medical abortion with mifepristone and misoprostol. No studies assessed hormonal contraception initiation after medical abortion with a misoprostol-only regimen.

#### RECOMMENDATION 4A

#### Timing of post-abortion hormonal contraception initiation, except for intrauterine device (IUD)

##### TIMING OF POST-ABORTION CONTRACEPTION

##### IMMEDIATE INITIATION

##### HORMONAL CONTRACEPTION

Immediately after the first pill of the medical abortion

For individuals undergoing medical abortion with the combination mifepristone and misoprostol regimen or the misoprostol-only regimen who desire hormonal contraception (oral contraceptive pills, contraceptive patch, contraceptive ring, contraceptive implant or contraceptive injections), we suggest that they be given the option of starting hormonal contraception immediately after the first pill of the medical abortion regimen.

##### Notes:

- All individuals who can become pregnant should be provided with all of the necessary information to make an informed decision regarding the use of contraception. Immediate initiation of intramuscular (IM) depot medroxyprogesterone acetate (DMPA) is associated with a slight decrease in the effectiveness of medical abortion regimens (67). However, immediate initiation of DMPA should still be offered as an available contraceptive method after an abortion.
- Indirect evidence was used as a basis for decision-making on initiation of hormonal contraception as an option for individuals undergoing medical abortion with misoprostol alone.
- No data were available on the use of combined hormonal contraception (pills or injections) by those undergoing medical abortion.



RECOMMENDATION TYPE: NEW OR UPDATED

Recommendation 4a is a new recommendation.



The second systematic review assessed contraceptive continuation at six months (implants, DMPA and IUD) and unintended pregnancies after the index abortion (72). This review included the same three RCTs (67,69,70) and one cohort study (71) that were included in the first review.

The third systematic review assessed the effectiveness and safety of initiation of IUD after abortion (73). In this review, three studies compared immediate versus delayed IUD insertion after medical abortion with mifepristone and misoprostol (74–76). The included studies assessed copper-bearing and levonorgestrel-releasing IUDs. No studies assessed IUD initiation after medical abortion with a misoprostol-only regimen.

**Effects (benefits and harms)**

The findings of the three RCTs and one cohort study in the first systematic review (68) showed that there was little difference in the rates of successful abortion between the two groups (immediate versus delayed initiation of implants or DMPA after medical abortion) and satisfaction regarding the timing of their contraception initiation was high. Findings from the same studies, which were also reviewed in the second systematic review (72), showed that continuation rates at six months were higher for the women in the immediate initiation group. Contraceptive failure rates were lower among women who initiated the implant, DMPA or the IUD immediately. The studies on immediate versus delayed IUD insertion after medical abortion in the third systematic review (73) showed that there was no difference between the immediate and delayed insertion groups with regard to adverse events or the need for further intervention after IUD

RECOMMENDATION 4B

### Timing of post-abortion intrauterine device (IUD) placement

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TIMING OF POST-ABORTION CONTRACEPTION

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IMMEDIATE INITIATION

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IUD	With assessment of successful abortion
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For individuals undergoing medical abortion with the combination mifepristone and misoprostol regimen or the misoprostol-only regimen who wish to have an IUD inserted, we suggest IUD placement at the time that success of the abortion procedure is determined. The use of clinical signs with bimanual examination, serum human chorionic gonadotrophin (hCG) levels or ultrasonography (if available), and an assessment of the individual’s current symptoms can be used to determine whether or not there is an ongoing pregnancy.

>

RECOMMENDATION TYPE: NEW OR UPDATED

Recommendation 4b is a new recommendation.

placement. There were fewer expulsions of the IUD at 12 months among women who had undergone immediate IUD placement.

**Values** Women placed high value on accepting a contraceptive method to prevent a future pregnancy. Two studies looking at DMPA and implants reported that women undergoing an abortion placed high importance on preventing a pregnancy in the next six months (67,70).

**Resources** In regard to resource requirements and cost-effectiveness, there was no direct research evidence that explored these domains. The cost of the IUD and implant versus pills and injections in various country contexts could not be determined. While there may be increased upfront costs of the IUD and implant, related to the cost of the devices, provider training and additional placement and removal visits, costs may decrease over time compared with the repeated need for pills and injections (77).

**Equity** There was no research evidence identified on aspects of equity around the relative effectiveness of the intervention in different subgroups. However, three studies included adolescents (67,70,71) and three studies included nulliparous women (74–76).

**Acceptability** Women reported high satisfaction with immediate initiation of their implant or DMPA administration (67,70). Acceptability and satisfaction were also reported by women in the immediate-start group based on fewer visits made to the health-care provider compared with the delayed-start group (70). Immediate initiators of implants had higher attendance at follow-up appointments (69,71).

For the IUD studies, similar considerations were taken into account. None of the included studies specifically addressed acceptability of the service to women. However, timing of insertion can be used as a proxy indicator for acceptability; more women had the IUD placed at the time that successful abortion was determined compared with the number of women who opted for delayed insertion (74,76). The rate of loss to follow-up at six months was reportedly lower for the early-insertion group as compared with the delayed insertion group (75).

**Feasibility** Initiation of post-abortion contraception appears feasible to implement. The included studies for both IUD and hormonal contraception were conducted through outpatient clinics, indicating feasibility of offering the service through outpatient health-care facilities.

**Rationale for Recommendation 4a (on post-abortion hormonal contraception initiation, except for IUD):** There was little difference in the successful abortion rates between women who started non-IUD hormonal contraception after receiving mifepristone versus those who started after receiving both mifepristone and misoprostol. This difference was based on low certainty of evidence. Women placed value on accepting a contraceptive method and they placed value on preventing future pregnancies. Satisfaction with and acceptability of immediate initiation of a contraceptive method was high. Continuation rates for the implant at six months were higher for the women in the immediate-initiation group. The certainty of the evidence was very low.

**Rationale for Recommendation 4b (on post-abortion IUD placement):** Placement of an IUD at the time the abortion process has been deemed successful leads to lower rates of contraceptive failure and higher continuation rates at 6 and 12 months. The 6-month continuation rates are based on moderate certainty of evidence while the contraceptive failure rates are based on low certainty of evidence and the continuation rates at 12 months are based on very low certainty of evidence. There is no difference in the number of women requiring further intervention post-IUD placement due to retained tissue or bleeding, but the certainty of the evidence was low. There is no difference in the side-effect of pain at IUD insertion between the two groups, based on moderate certainty of evidence. Serious adverse events are rare and there was no difference between the two groups for uterine perforation or death, but this was based on very low certainty of evidence. Acceptability and feasibility of immediate placement of the IUD was high.

#### **3.5.4 Additional considerations**

All individuals who can become pregnant should be informed that ovulation can return within two weeks following abortion, putting them at risk of pregnancy unless an effective contraceptive method is used. Those who are interested in contraception should be provided with accurate information to assist them with choosing the most appropriate contraceptive method to meet their needs. Some prefer to discuss options for contraception after the abortion is completed. For those seeking an abortion following a reported contraceptive failure, it is important to discuss whether the method may have been used incorrectly and how to use it correctly, or whether it may be appropriate to change to a different method. Ultimately, the final decision about whether to use contraception, and which method to use, is up to the individual alone (19).



**IMPORTANT NOTE:** Acceptance of a contraceptive method must never be a precondition for providing an abortion.

For the health workforce, task sharing guidelines have offered options for various cadres to conduct different aspects of the provision of contraception counselling and services (10,78).

For injectable contraception administration, the following cadres have been recommended: auxiliary nurses, auxiliary nurse midwives, nurses, midwives, pharmacists, associate/advanced associate clinicians, and non-specialist and specialist doctors. Doctors of complementary systems of medicine can be providers of this service in health system contexts with an established mechanism for the participation of such doctors in other tasks related to maternal and reproductive health. Pharmacy workers can administer the injectable contraceptive under direct supervision of a pharmacist. Lay health workers as administrators of injectable contraception can be an option if conducted under targeted monitoring and evaluation (10).

For implant insertion and removal, the following cadres have been recommended: nurses, midwives, pharmacists, associate/advanced associate clinicians, and non-specialist and specialist doctors. Auxiliary nurses and auxiliary nurse midwives may perform implant insertion/removal within the context of targeted monitoring and evaluation. Doctors of complementary systems of medicine can be providers of this service in health system contexts with an established mechanism for the participation of such doctors in other tasks related to maternal and reproductive health and where training in implant removal is given along with training in insertion (10).

For IUD placement, the following cadres have been recommended: auxiliary nurse midwives, nurses, midwives, associate and advanced associate clinicians, non-specialist and specialist doctors. Doctors of complementary systems of medicine can be providers of this service in health system contexts with an established mechanism for the participation of such doctors in other tasks related to maternal and reproductive health (10).

Self-administration of injectable contraception is an option in contexts where mechanisms to provide appropriate information and training exist, referral linkages to health-care providers are strong, and monitoring and follow-up can be ensured (10).

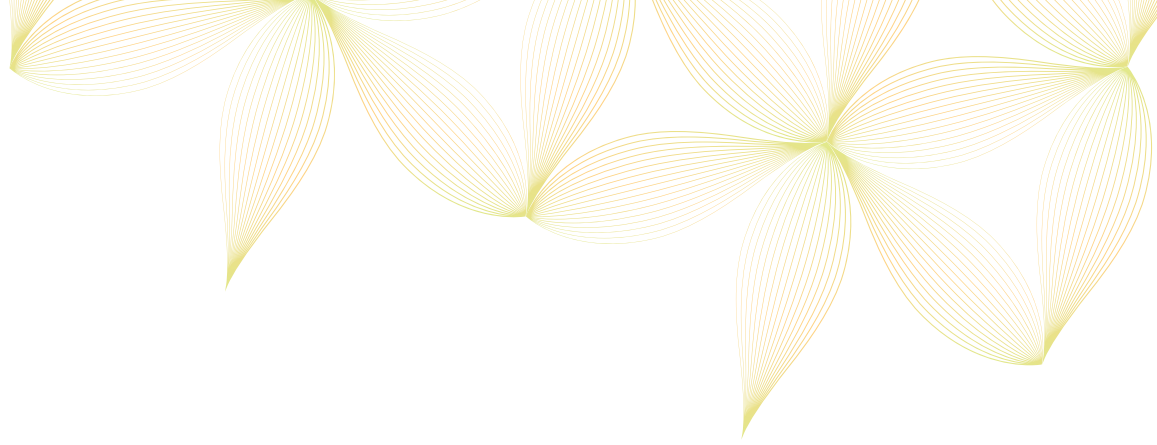
### 3.5.5 Research gaps

*General:*

- ▶ Studies are needed on the efficacy, safety and acceptability of immediate initiation of contraception with misoprostol-only regimens.
- ▶ Studies on the efficacy, safety and acceptability of the initiation of combined hormonal contraception at the time of mifepristone administration are also lacking.
- ▶ Recommendations on the timing of post-abortion contraception are inclusive of combined hormonal contraception and misoprostol-only regimens, based on indirect evidence. Results from the survey on research gaps (completed by GDG members) noted the lack of direct evidence for these clinical scenarios and, therefore, further research on this topic should be pursued.

# 4. General implementation considerations





General implementation considerations for the recommendations in this guideline are outlined below through a question-and-answer format.



**IMPORTANT NOTE:** The quality of medicines used is an important factor that can influence the process and overall success of a medical abortion. Substandard mifepristone and/or misoprostol products that do not contain the right active ingredients in the right dosages, and those that are not manufactured, transported or stored under the specified conditions, can affect the outcomes of a medical abortion. It is critical that mifepristone and misoprostol used for medical abortion are properly manufactured in line with specifications and are handled appropriately through the supply chain until use at the point of care. Ensuring use of quality-assured mifepristone and misoprostol that has been transported and stored correctly according to the specified conditions can contribute to the overall quality of a medical abortion process.

**Q: Where should medical abortion services be available?**

A: Services should be available at the primary-care level, with referral systems in place for all required higher-level care.

**Q: Who can provide these medical abortion services?**

A: In addition to non-specialist doctors and specialist doctors, with task-specific training and functioning systems for monitoring and supportive supervision, a wide range of health worker cadres – such as auxiliary nurses, auxiliary nurse midwives, nurses, midwives, associate/advanced associate clinicians, pharmacists and

doctors of complementary medicine – can provide various aspects of medical abortion services. In addition, indirect evidence from a qualitative systematic review on factors affecting implementation of task sharing in abortion identified that some providers in a middle-income setting where abortion is legal saw medical abortion as having a number of benefits for health services (9). These reported benefits included that it was safe and effective; it would reduce the burden on health services; and it may make it easier for people involved to act in accordance with their conscience. A discussion of general considerations for task shifting in maternal health and family planning can be found in the 2012 OptimizeMNH guideline: *WHO recommendations: optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting* (78).

The specific cadres able to provide medical abortion services have been outlined in the additional considerations section for each recommendation.

**Q: Can medical abortion processes be self-managed?**

A: When using the combination mifepristone and misoprostol regimen, the medical abortion process can be self-managed for pregnancies up to 12 weeks of gestation, including the ability to take the medications at home, without direct supervision of a health-care provider (10); it should be noted that there was limited evidence for pregnancies beyond 10 weeks (53,60–64). This is an option in circumstances where individuals have a source of accurate information and access to a health-care provider should they need or want it at any stage during the process (10).

**Q: What general considerations should be taken into account when providing care to adolescents/youth?**

A: Ensure that you are fully aware of the national and local laws and policies. In your work with adolescents, you may find that in some situations, prevailing laws and policies may not permit you to do what is in the best interests of your adolescent patient (e.g. in some places, the provision of contraceptives to unmarried adolescents is illegal). In such situations, you may need to draw upon your experience and the support of caring and knowledgeable people to find the best way to balance your legal obligations with your ethical obligations (13).

Provide information on the implications of each treatment option and help the adolescent choose the one best suited to his/her needs. While doing this:

- ▶ present all the relevant information;
- ▶ respond to questions as fully and honestly as you can;



- ▶ help them choose; and
- ▶ respect their choice, even if it is not the one you would have wanted them to make.

Adolescents may be reluctant to disclose information on sensitive matters if their parents, guardians or spouses are also present.

Reduce the stigma around the issue by normalising it: an adolescent who has an unwanted pregnancy or a sexually transmitted infection may feel embarrassed or even ashamed. You can reduce the stigma around the issue by saying to the adolescent, "I have treated a number of young people with the same problem you have."

**Q: What considerations should be taken into account when conducting a clinical interview and examination with adolescents/youth?**

A: Following is list of considerations and steps.

- ▶ Respect local sensitivities regarding gender norms (e.g. whether it is appropriate for a male health worker to examine a female patient). If needed, ensure the presence of a female colleague during the examination (13).
- ▶ Ensure privacy (e.g. make sure that curtains are drawn, doors are shut and that no unauthorized person enters the room during the examination).
- ▶ Start the clinical interview with issues that are the least sensitive and least threatening; it is often best to ask first about the activities of their peers and friends rather than directly about their own activities.
- ▶ If the adolescent is with an accompanying person, reach an agreement as to whether they want this person to be present during the examination.
- ▶ Inform the adolescent about what examination you want to carry out and the purpose of the examination.
- ▶ Explain the nature of the examination.
- ▶ Obtain the consent of the adolescent.

**Q: How does one determine duration of pregnancy (gestation)?**

A: Physical examination to assess uterine size (i.e. bimanual pelvic and abdominal examination), assessment of last menstrual period (LMP) and recognition of symptoms of pregnancy are usually adequate. Laboratory or ultrasound testing may also be used, if needed. Laboratory testing is needed when typical signs of pregnancy are not clearly present and the provider is unsure whether there is an ongoing pregnancy. Obtaining tests should not hinder or delay uterine evacuation. Ultrasound scanning is not routinely required. Where it is available, it can help identify an intrauterine pregnancy and exclude an ectopic pregnancy (6, 19).

**Q: How can success of the medical abortion be determined?**

A: Success of medical abortion is determined by signs and symptoms as experienced by the individual. These may include heavy bleeding with clots, passage of the products of conception, and pain that may be significantly stronger than normal menstrual cramps. If ongoing symptoms of pregnancy are reported and/or there has only been minimal or no bleeding after taking the medications as directed, ongoing pregnancy should be suspected and further evaluation could include pelvic examination (demonstrating a growing uterus) or an ultrasound scan (demonstrating an ongoing pregnancy) (19).

**Q: What is the role of ultrasound in these recommendations?**

A: Ultrasound scanning is not routinely required for the provision of abortion (6). Successful abortion may be confirmed by pelvic examination, pelvic ultrasound or a repeat hCG measurement. If serum hCG measurements are used, it should be remembered that in some cases low hCG levels can be detectable for up to four weeks after successful expulsion. Ultrasound is useful to detect ongoing pregnancy by measuring endometrial thickness; it should be noted, however, that endometrial thickness is not useful for diagnosing incomplete abortion and its use as an indicator for this purpose may lead to inappropriate surgical interventions (6).

For initiation of contraception, an ultrasound is not needed. Non-IUD methods can be started immediately. IUDs can be inserted whenever the medical abortion has been deemed successful (19).

**Q: Is there a maximum number of doses of misoprostol that can be used in the medical management of abortion?**

A: Repeat doses of misoprostol can be considered when needed to achieve success of the abortion process. In this guideline we do not provide a maximum number of doses of misoprostol. Health-care providers should use caution and clinical judgement to decide the maximum number of doses of misoprostol in pregnant individuals with prior uterine incision. Uterine rupture is a rare

complication; clinical judgement and health system preparedness for emergency management of uterine rupture must be considered with advanced gestational age.

**Q: What is the best way to store misoprostol?**

A: Aluminium blister packs are the best way to store misoprostol (79). Cutting the blister pack and storing misoprostol outside the aluminium blister may increase the risk of damage to the packaging (i.e. the inner seal), leading to exposure to environmental conditions (80).

Store misoprostol in dry conditions at temperatures at or below 25 °C (77 °F) (79,81).

Exposure to heat and humidity during manufacturing, packaging and storage may compromise the quality of misoprostol (81).

**Q: What is the best way to store mifepristone?**

A: Store at 25 °C (77 °F); excursions permitted between 15 ° and 30 °C (59 ° and 86 °F) (82).

**Q: When does return to ovulation occur after a medical abortion?**

A: Ovulation can occur as few as eight days after a medical abortion (83).

# 5. Dissemination and adaptation

# 6. Guideline impact evaluation and future updates



## Dissemination and adaptation

Translation of this guideline into Spanish (in collaboration with PAHO), French and Portuguese is planned. Versions in other United Nations languages will be developed as needed. Third-party translations into additional non-United Nations languages will be encouraged, provided they comply with WHO guidance on such translations.

The digital versions of the guideline in all languages will be available via the WHO website<sup>10</sup> and through the WHO Reproductive Health Library (RHL) website.<sup>11</sup> Print versions of this guideline will be distributed to WHO regional and country offices, nongovernmental organization (NGO) partners, professional associations and other networks and partners.

WHO regional offices are expected to be active partners in the dissemination and adaptation of these guidelines. A number of other interested agencies and NGOs are encouraged to partner with WHO in the dissemination and local adaptation of the guidelines and in developing derivative informational materials.

The guideline will be launched in WHO regions through regional dissemination meetings and specific knowledge transfer and adaptation activities and implementation research will take place in select countries based on need and interest to move ahead with implementation of the recommendations. Derivative products will be developed, such as simple pocket-sized charts.

## Guideline impact evaluation and future updates

Two years after publication of the guideline, an online survey will be conducted through WHO regional and country offices and selected respondents representing other user groups (e.g. professional societies, NGOs). The purpose of the survey will be to gauge in-country progress in utilization of the guideline, implementation of the recommendations and any influence on policy decisions. It will also help in gathering feedback relevant to future modifications of the guidance.

Evidence will be reviewed and the guideline updated in four years, or earlier if new evidence warrants an update.

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<sup>10</sup> The webpage for this guideline, all language versions and related products is: <http://www.who.int/reproductivehealth/publications/medical-management-abortion/en/>

<sup>11</sup> Available at: [www.who.int/rhl](http://www.who.int/rhl)

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ANNEX 1:

# WHO staff and external experts involved in the guideline development process



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## WHO Steering Group

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\* WHO/RHR is based at WHO headquarters, Geneva, Switzerland.

Note: The Secretariat includes all members of the Steering Group who are affiliated with WHO/RHR (or were at the time of guideline development).

## MEMBERS

## Guideline Development Group (GDG)

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<b>Josaphat K. Byamugisha</b> Associate Professor, Makerere University, Department of Obstetrics and Gynecology, Mulago National Referral Hospital	M	Uganda (African Region)	Clinical and reproductive health research	None
<b>Laura Castleman</b> Medical Director, Ipas, Adjunct Clinical Assistant Professor, Department of Obstetrics and Gynecology, University of Michigan	F	United States of America (Region of the Americas)	Reproductive health research and clinical care	None
<b>Munir Kassa Eshetu</b> Director for Reproductive Health Service Quality, Center for International Reproductive Health Training (CIRHT)	M	Ethiopia (African Region)	Reproductive health	None
<b>Anibal Faúndes</b> General Coordinator, International Federation of Gynecology and Obstetrics (FIGO) Initiative on Prevention of Unsafe Abortion	M	Brazil (Region of the Americas)	Clinical care, obstetrics and gynaecology	None
<b>Selma Hajri</b> Coordinator, African Network for Medical Abortion	F	Tunisia (Eastern Mediterranean Region)	Women's health, clinical and reproductive health research	None
<b>Kirti Iyengar</b> Founder, Action Research & Training for Health (ARTH)	F	India (South-East Asia Region)	Public health	None
<b>Hiromi Obara</b> Health Policy Advisor, Japan International Cooperation Agency (JICA)	F	Lao People's Democratic Republic (Western Pacific Region)	Clinical care, women's health	None
<b>Patricio Sanhueza</b> Head of Reproductive Health, Mexico City Secretariat of Health	M	Mexico (Region of the Americas)	Public health, women's health	None
<b>Paul Van Look (CHAIR)</b> Independent consultant	M	Geneva (European Region)	Sexual and reproductive health	None
<b>Beverly Winikoff</b> President, Gynuity Health Projects	F	United States of America (Region of the Americas)	Clinical research, women's health	None
<b>Ann Yates</b> Midwifery Advisor, International Confederation of Midwives	F	The Netherlands (European Region)	Clinical care, women's health	None

## GDG meeting observers

<b>Jennifer Blum</b> Vice President, Programs and Strategic Initiatives, Gynuity Health Projects	F	United States of America (Region of the Americas)	Clinical research on post-abortion care, medical abortion and postpartum haemorrhage	None
<b>Kristina Gemzell-Danielsson</b> Professor and Chair, Division of Obstetrics and Gynecology, Department of Women's and Children's Health, Karolinska Institutet	F	Sweden (European Region)	Clinical research on contraception and abortion, guideline development	Declared

\* Conflict of interest (COI)

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<b>Laura Laursen</b> University of Chicago Medical Center	F	Abortion, family planning	None
<b>Antonella Lavelanet</b> WHO/RHR	F	Abortion, family planning, policy	None
<b>Karthik Srinivasan</b> Independent consultant	M	Abortion, family planning	None
<b>Katherine Whitehouse</b> Independent consultant (former Medical Officer at WHO/RHR)	F	Abortion, family planning	None

## Guideline methodologists

<b>Maria Rodriguez</b> Cochrane Fertility Regulation Group at Oregon Health & Science University	F	Quality appraisal using GRADE <sup>1</sup> methodology, and translation of evidence into recommendations	None
<b>Marita Sporstøl Fønhus</b> Norwegian Knowledge Centre	F	Quality appraisal using GRADE <sup>1</sup> methodology, and translation of evidence into recommendations	None

\* Conflict of interest (COI)

<sup>1</sup> GRADE: Grading of Recommendations Assessment, Development and Evaluation. Further information is available at: <http://www.gradeworkinggroup.org/>

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<b>Helena Kopp Kallner</b> Karolinska Institutet	F	Sweden <i>(European Region)</i>	Medical abortion care	None
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<b>Mariana Romero</b> Center for the Study of State and Society	F	Argentina <i>(Region of the Americas)</i>	Women's health	None
<b>Stephen Rulisa</b> University of Rwanda	M	Rwanda <i>(African Region)</i>	Women's health	None
<b>Shahida Zaidi</b> National Committee for Maternal and Neonatal Health	F	Pakistan <i>(Eastern Mediterranean Region)</i>	Abortion care	None

\* Conflict of interest (COI)





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