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Katherine Gambir

Camille Garnsey

Kelly Ann Necastro

Thoai Ngo
Population Council

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Effectiveness, safety, and acceptability of medical abortion at home vs. in the clinic: an updated systematic review in response to COVID-19

Protocol

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Authors: Katherine Gambir[1], Camille Garnsey[1], Kelly Ann Necastro[2], Thoai D. Ngo[1, 3]

Affiliations:

[1]Poverty, Gender and Youth Program, Population Council, New York, New York, USA [2]Massachusetts General Hospital, Boston, Massachusetts, USA. [3]The GIRL Center, Population Council, New York, New York, USA

Corresponding author:

Katherine Gambir
Poverty, Gender, and Youth Program
kgambir@gmail.com

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New York, NY 10017
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Description: This document describes the protocol for an updated systematic review of the evidence comparing medical abortion practiced at home and in clinics in terms of effectiveness, safety and acceptability. We are updating Ngo et al.'s 2011 review given the importance of access to home-medication abortion during the COVID-19 pandemic. We will conduct a systematic search for randomized controlled trials and prospective cohort studies comparing home-based and clinic-based medical abortion. Successful abortion is the main outcome of interest. Side-effects, complications, and acceptability are secondary outcomes. Risk Ratios (RRs) and their 95% confidence intervals (CIs) will be calculated. Estimates will be pooled using a random-effects model.

INTRODUCTION

Rationale

Medical abortion is a non-surgical pregnancy termination option that involves using a combination of mifepristone and misoprostol, or misoprostol only, to end a pregnancy. The current World Health Organization (WHO) guidelines advise a combination protocol for abortions less than 12 weeks of gestation that involves an initial dose of mifepristone followed by a dose of misoprostol 24-48 hours later (1). Of the estimated 55 million abortions that occur worldwide each year, 25 million (45%) are estimated to be unsafe, with most unsafe abortions occurring in low-resource settings (2). However, an increasing reliance on medical abortion methods worldwide have been associated with an increase in the rates of safe abortion, and a decline in the rates of morbidity and mortality associated with abortion (3–5). Additionally, in the thirty years since mifepristone was first approved as an abortifacient, research has shown the method to be safe, effective, and acceptable to women in a range of settings (6–10). A growing body of evidence also suggests that women with access to adequate information, high-quality drugs, and facility based care can manage their own abortions with little or no healthcare provider supervision, yet access to medical abortion continues to be limited by laws, regulations, and medical guidelines that restrict who can administer the drugs, where administration can take place, and how the drugs can be administered (11–15).

On March 11, 2020, the WHO declared COVID-19, a viral disease that began spreading in Wuhan, China in January of 2020, a global pandemic (16). Following the declaration, governments across the world moved aggressively: instituting nationwide lockdowns and extensive travel restrictions, and urging citizens to practice social distancing to slow the spread of the disease (17). Health systems worldwide have been burdened by the pandemic as facilities have struggled to keep pace with the rate of virus-related hospitalizations, the rapid spread of the disease among healthcare professionals, and shortages of personal protective equipment (18–20). The necessary but drastic restrictions on movement and daily life have the unintended consequence of further limiting access to other essential healthcare services, including abortion. To reduce the spread of coronavirus and alleviate burdens on health care systems and frontline healthcare workers, it is critical to limit physical interactions between individuals seeking abortions and providers as much as possible.

Expanding access to home-based abortion care is an important strategy for protecting abortion access while slowing the spread of the deadly virus and reducing burdens on healthcare systems, especially in settings where capacity and workforces are already strained and limited. Home-based medical abortion most often entails a health-care provider administering mifepristone at the clinic, and the pregnant person taking misoprostol later in the privacy of their own home with any desired members of their support network. The model requires fewer clinic visits, alleviating burdens on health care facilities and providers, and limiting points of contact (14,21).

Governments in the UK and Northern Ireland have already recognized the potential for home use of medical abortion to reduce the burden on healthcare systems in light of COVID-19 and shifted regulation to allow for home-based care (22,23). On the other hand, legislators in six states in the United States have sought to freeze abortion services indefinitely by including abortion on the list of "non-essential healthcare" that must be delayed until shut-down orders are lifted (24). Similarly, activists in Slovakia

and Italy are urging their governments to make similar designations and a bill in Poland aimed at further restricting abortion was recently re-introduced in the parliament there(25). These policies and efforts, many of which continue to be challenged in court, ignore global public health expertise and medical guidance that clearly designate abortion as a time sensitive and essential service (26).

In 2011, Ngo et. al published a systematic review of the evidence on the efficacy, safety, and acceptability of home-administered medical abortion compared to clinic-based medical abortion. The review suggested that there is no difference in the effectiveness or acceptability of home-based medical abortion compared to clinic-based medical abortion, and that home-based abortion is safe (27). Since the publication of this review, the evidence on home-based medical abortion has grown. A recently published systematic review found no difference in effectiveness between self-administered and provider-administered abortions, where all participants who self-administered did so at home (28). Additionally, recent studies have demonstrated that women prefer home-administration to clinic-based care for reasons related to control and privacy (29–35), and it is likely that such preferences are more pronounced due to concerns around contracting or spreading COVID-19. However, the WHO and the majority of health officials around the world have not yet issued guidelines on the option of home-/self-administration of medical abortion to protect healthcare workers and ensure access to abortion care.

Given the growing body of evidence from the past decade and the importance of access to home-based medical abortion in the context of the COVID-19 global health and economic crisis, it is critically important to reexamine and update this body of literature to provide a conclusive evidence base for health officials across the globe to refer to during and post pandemic.

Objective

This review examines published literature on the evidence on the effectiveness, safety, and acceptability of medical abortions performed at home in comparison to medical abortions performed in clinics or other health care facilities.

METHODS

Eligibility Criteria

We will search for published studies on home-based administration of medical abortion that test different regimens (e.g. mifepristone, or misoprostol, or both), routes of administration, and doses. Randomized and non-randomized controlled trials (RCTs and NRCTs) (clustered or non-clustered) and prospective cohort studies with a concurrent comparison group, that compare the safety, or effectiveness, or both, of home-based medical abortions to clinic-based medical abortion, will be eligible for inclusion. We will search without language restrictions.

The inclusion criteria for studies include:

1. a comparison between home-based administration of medical abortion and clinic-based administration of medical abortion;

2. a prospective assessment of outcomes; and

3. recruitment of women who are seeking an abortion.

Types of participants

Studies recruiting women of any age, in any setting, who are seeking an induced abortion, and provide informed consent, are eligible for the review. We will exclude studies recruiting women with missed, incomplete abortion, or intrauterine fetal death from the review. Studies will be eligible irrespective of the gestational age of the fetus, and we will explore the possible impact of this variable on the results by subgroup analysis, as gestational age has been identified as a known confounder, with higher gestational ages indicating lower efficacy of medical abortion (27,36).

Types of interventions

Studies comparing induced medical abortion with mifepristone-misoprostol or misoprostol-only administered at home versus induced medical abortion with mifepristone-misoprostol or misoprostol-only in the clinic. The only administration route (for home and clinic-based administration) for mifepristone is oral. Possible home and clinic-based administration routes for misoprostol include oral, sublingual, buccal, and vaginal. Repeat doses of misoprostol may occur.

Primary outcomes

The primary outcome is success of medical abortion (with success defined as uterine evacuation without the need for surgical intervention).

Secondary outcomes

The secondary outcomes are:

1. serious complications;

2. side effects of medical abortion, which may include nausea, heavy bleeding, diarrhea, fever/chills, pain/cramps, and vomiting; and

3. acceptability, as defined by women's level of satisfaction with the medical abortion process, likelihood of selecting the same medical abortion method again, likelihood of recommending method to a friend, and likelihood of selecting home use or clinic use for future medical abortion; and

4. companionship during home administration of misoprostol.

Serious complications are rare (27) however, complications have been reported on, and therefore are important to document.

Reporting of the secondary outcomes listed here will not be an inclusion criterion for the review and we will include studies regardless of the whether they assessed the secondary outcomes.

Data Collection

Search Strategy

Our search strategy for this review will build on the search Ngo et al. conducted for the original home-administration review, as well as a recently conducted search for a review of self-administered vs.

provider administered medical abortion (27,28). We will adapt the search terms used in these reviews to ensure we find all relevant studies. We will search the following electronic databases for relevant trials: the Cochrane Central Register of Controlled Trials via the Cochrane Register of Studies Online (CRSO) web platform (from inception on-wards) (MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations Ovid (from inception onwards) Embase Ovid (1980 onwards) (and CINAHL (Cumulative Index to Nursing and Allied Health Literature) Ebsco (from 1982 onwards).

We will search the following trial registers for ongoing and registered trials: ClinicalTrials.gov and WHO ICTRP (who.int/ictrp). We will also search Google Scholar for recent trials not yet indexed in the major databases.

We will also hand search reference lists of relevant trials and systematic reviews retrieved by the search to identify eligible RCTs and prospective cohort studies of home-administration of medical abortion with a concurrent comparison group and contact experts in the field to obtain additional data. We will also hand search the following websites for relevant articles: Guttmacher Institute, Gynuity, International Consortium for Medical Abortion, Ipas, Marie Stopes International, and the Population Council.

Draft of Search Terms

Below is a preliminary draft of the search strategy we will use when searching the Cochrane Central Register of Controlled Trials:

1 exp Abortion, induced/ or Abortion, legal/ or Abortion, criminal/ or Abortion, septic/ or Abortion, therapeutic/ or Abortion applicants/

2 (abortion* or ((medical* or trimester* or gestation* or pregnan*) adj5 terminat*) or "uterine evacuation*").tw.

3 or/1-2

4 Abortifacient agents/ or Abortifacient agents, nonsteroidal/ or Abortifacient agents, steroidal/ or Mifepristone/ or Misoprostol/

5 (Abortifacient* or Mifepristone* or Misoprostol* or RU486 or RU-486 or "abortion pill" or Cytotec or GyMiso or Korlym or Mifegyne or Mifeprex or Misodel).tw.

6 or/4-5

7 Self administration/ or Self medication/ or Nurse Midwives/ or Pharmacies/ or Physicians/ or exp Health personnel/

8 (self* or herself or themselves or chemist or chemists or clinic or clinician* or drugstore* or "drug store*" or home or home-use or home-based or

midwife or midwives or nurse* or OTC or "over the counter" or pharmacies or pharmacist* or pharmacy* or physician* or provider*).tw.

9 or/7-8

10 and/3,6,9

Selection process

After two independent reviewers conduct an initial screen of titles and abstracts retrieved by the search, we will retrieve the full texts of all potentially eligible studies. We will correspond with study investigators, as necessary, to clarify study eligibility. Disagreements will be resolved by discussion. If any reports require translation, we will describe the process used for data collection. We will document the selection process with a PRISMA diagram (37,38).

Data extraction and management

Two review authors will independently screen and extract data from eligible studies using a data extraction form designed and pilot-tested by the authors. Any disagreements will be resolved by discussion. Data extracted will include study design and key features of studies.

Data items

We will extract the following data during our review:

1. Population. Mean gestational age; mean patient age; percentage married; primigravida measured by percentage; percentage of women who experienced their first abortion in this study; and mean years of education will be extracted from the studies. We will also extract data on the percentage and number of women who were lost to follow-up and the number and percentage of women who self-selected into each group for non-randomized studies.

2. Intervention. We will record the description of the intervention including the drugs used, dosage, number of doses, and routes of administration, as well as each study's inclusion and exclusion criteria. Drug regimens include either mifepristone-misoprostol or misoprostol-only. We will extract data on each dose of each drug measured in mcg or mg, as well as the route of administration for each dose (e.g. oral, sublingual, buccal, or vaginal). We will include administration in a health facility followed by administration at home.

3. Comparison groups. Comparison groups will include those who underwent a medical abortion in a health facility. We will record the number of women recruited to each comparison group and the number of complete abortions and extract the same data points for both intervention and comparison groups.

Outcomes and Prioritization

The proportion of women with successful medical abortion (uterine evacuation without the need for surgical intervention) is the primary outcome, and therefore, the most important outcome in this review. We will extract data on serious complications and side effects (including nausea, heavy bleeding, diarrhea, fever/chills, pain/cramps, and vomiting) reported in the studies, describe how each were defined and documented, and summarize the findings. We will also extract data on acceptability, including the number and proportion of women who were satisfied or highly satisfied with the method; the number and proportion of women who would choose the method again; the number and proportion of women who would select home use or clinic use for future medical abortion; and the number and

proportion of women who would recommend the method to a friend. Finally, we will extract data on companionship among home-use participants.

Where studies have multiple publications, we will collate multiple reports of the same under a single study ID with multiple references. We will correspond with study investigators for further data on methods, results, or both, as required.

Data Analysis

Risk of bias in included studies

Two review authors will independently assess included RCTs and NRCTs for quality of the evidence and risk of bias using the GRADE criteria (e.g., risk of bias, consistency of effect, imprecision, indirectness, and publication bias). We will assess the risk of bias for our primary outcome of successful abortion (39). Two review authors will work independently to judge the evidence quality (e.g. high, moderate, low, or very low) and disagreements will be resolved by discussion. The review authors will justify, document, and incorporate their judgments into reporting the results for the successful abortion outcome. We will analyze the risk of bias for high-quality and low-quality studies in combination and separately to minimize risk of bias. We will also address risk of bias for NRCTs by controlling for gestational age in our analysis, as it has been found to be an important confounder of successful abortion; previous reviews found lower efficacy in more advanced pregnancies (36).

Measures of treatment effect

For dichotomous outcomes (e.g. successful abortion, any complication requiring hospitalization, among others), we will use the number of events in the control (clinic-based) and intervention (home-based) groups of each study to calculate Mantel-Haenszel risk ratios (RRs). We will present 95% confidence intervals (CIs) for all outcomes in our main effects analysis and for two secondary outcomes-complications and acceptability. We will calculate the risk of having a successful abortion using the number of women recruited for each study and an intention-to-treat approach where possible. Where data to calculate RRs or mean differences (MDs) are not available, we will use the most detailed numerical data available that may facilitate similar analyses of included studies (e.g. test statistics, P values). We will assess whether the estimates calculated in the review for individual studies are compatible in each case with the estimates reported in the study publications. We will also control for gestational age in our analysis of non-randomized studies (28.)

Assessment of heterogeneity

We will assess statistical heterogeneity with Chi^2 and I^2 statistics, using a cut-off point of $P < 0.10$ to indicate statistical heterogeneity, and we will use the I^2 statistic to quantify heterogeneity. We will use the Cochrane Handbook criteria for interpreting I^2 values (38).

Data synthesis

For studies determined to be sufficiently similar regarding participants, interventions, comparisons, and outcomes, we will conduct a meta-analysis. We will combine data using a random-effects model to obtain an overall summary. We are selecting this model a priori to incorporate the effect of trial

heterogeneity among prospective studies from different settings (27). We will present a forest plot showing a RR and 95% CI for the primary outcome of successful abortion. We will group RCTs and NRCTs separately when summarizing the effect size of our primary outcome, and in combination for our secondary outcomes related to side effects, complications, and acceptability. We will report a narrative synthesis for any outcomes for which insufficient data are found for meta-analysis, including incomplete reporting on the outcomes of interest. We will document and summarize data on dosage, number of doses of mifepristone/misoprostol, and route of administration (e.g. oral, sublingual, buccal, or vaginal) to compare by mode of administration (home versus clinic).

We will combine the results to find a common effect across those studies by conducting a meta-analysis. We will perform statistical analysis using RevMan Web (41).

Subgroup analysis and investigation of heterogeneity

If we detect substantial heterogeneity, we will explore possible explanations in subgroup analyses. When interpreting the results, we will take any statistical heterogeneity into account, especially if there is any variation in the direction of the effect.

As applicable, we will conduct subgroup analyses for the primary outcome measure within the following subgroups (where data are available).

1. By gestational age (e.g. < 9 weeks, 9 to 12 weeks, and ≥ 12 weeks).

2. Low- to middle-resource settings versus high-resource settings (as defined by the study authors).

Sensitivity analysis

We will conduct sensitivity analyses to assess heterogeneity and the effect of risk of bias in the included studies, comparing studies rated at high or low risk of bias for each assessed item. We will also conduct a separate analysis of high-quality studies (i.e., RCTs) to explore the effect of biases on study heterogeneity.

Overall quality of the body of evidence

We will use the GRADE to assess the overall quality of the evidence (39). Given that standard practice is to take the lowest quality of evidence from all the critical outcomes assessed, and we are only using GRADE to assess one outcome (our primary outcome of successful abortion), the overall quality rating we provide will mirror our quality assessment for the outcome of successful abortion.

Results

Proposed Tables and Figures

Table 1. List of databases and search terms used in systematic review comparing home-based and clinic-based medical abortion

Search	Cochrane	MEDLINE	Ovid	CINAHL	Ebsco
1					
2					
Results					

Table 2. Rates of successful abortion in studies comparing home-based and clinic-based medical abortion included in systematic review

Study	Mifepristone dose (mg); misoprostol dose (µg), [supplementary dose]; route	No. of women recruited (no. lost to follow-up)		Complete abortion, no. (%)		Complete abortion RR (95% CI)	Max. Gestational age	Contact with health services	Women accompanied during home administration of misoprostol (%)	Comparative participant characteristics at baseline
		H	C	H	C					

*C, clinic; CI, confidence interval; H, home; RR, risk ratio; *$P < 0.05$.

Table 3. Side-effects, their duration and the proportion of women who reported them among those who underwent home-based and clinic-based medical abortion

Study	Side-effect										
	Pain/Cramps		Nausea		Vomiting		Fever/chills		Heavy bleeding[a]	
	Mean # of days (SD)	% who reported	Mean # of days (SD)	% who reported	Mean # of days (SD)	% who reported	Mean # of days (SD)	% who reported	Mean # of days (SD)	% who reported
	H	C		H	C		H	C		H	C	

*C, clinic; H, home; NR, not reported; SD, standard deviation; *$P < 0.05$.

[a]Bleeding heavier than a normal menstrual bleed.

Table 4. Acceptability of home-based and clinic-based medical abortion (MA) in studies included in systematic review comparing home-based and clinic-based medical abortion

Study	Satisfied or highly satisfied with method (%)			Would choose method again (%)			Would recommend method to a friend (%)			Would select home use of miso for future MA (%)			Would select clinic use for future MA (%)		
	H	C	MD	H	C	MD	H	C	MD	H	C	MD	H	C	MD

* C, clinic; H, home; MD, mean difference; NR, not reported; *P < 0.05.

Table 5. Characteristics of studies

Study	Methods	Participants	Interventions	Outcomes	Funding	Notes

Figure 1. Summary of study selection for systematic review of studies comparing home-based and clinic-based medical abortion (PRISMA flow diagram)

Figure 2. Forest plot comparing rates of successful abortion in women who underwent home-based compared to clinic-based medical abortion

IMPLICATIONS

Unsafe abortion is an important cause of global maternal mortality and morbidity. The COVID-19 global health crisis's impact on health systems, movement, and travel globally have the unintended consequences of restricting access to safe abortion care. One strategy to expand access to safe abortion and alleviate stress on already overburdened health facilities is to expand access to home-based medical abortion. This review updates the evidence on the effectiveness, safety, and acceptability of medical abortion performed at home. The results will have implications for health systems and legislators who may use the evidence to expand access to home-based medical abortion in the context of the COVID-19 emergency.

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