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ADVANCING NEW STANDARDS IN REPRODUCTIVE HEALTH

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U.S. studies on medication abortion without in-person clinician dispensing of mifepristone

Key Findings or Implications

- Between 2000-2021, the Food and Drug Administration's Risk Evaluation and Mitigation Strategy (REMS) for mifepristone required the drug to be dispensed only in clinics, medical offices, or hospitals.
- After temporarily removing the in-person dispensing requirement during the COVID-19 public health emergency, in 2021 the FDA reviewed the evidence and decided to make the change permanent and allow for certified pharmacies (both brick-and-mortar and mail-order) to dispense mifepristone. FDA issued guidance about pharmacy certification in 2023.
- Seven studies, each with more than 100 participants, have been published on medication abortion provided without in-person clinician dispensing of mifepristone in the United States (U.S.).
- In all 7 studies, medication abortion effectiveness was high and serious adverse events were uncommon. Results were similar to what has been reported in prior studies of medication abortion when mifepristone was dispensed in person by a clinician.
- The evidence indicates that in-person dispensing is not necessary to ensure medication abortion effectiveness or safety.

Background

- Studies of medication abortion through 10 weeks' gestation with mifepristone dispensed in person by a clinician have found an overall effectiveness of 97.4%[1], and a prevalence of serious adverse events (SAEs)† of less than 0.5% of patients.[1,2]
- From 2000 to 2021, the FDA mandated that mifepristone be dispensed in person at healthcare facilities, as codified in the drug's Risk Evaluation and Mitigation Strategy (REMS).[3]
- In April 2021, the FDA temporarily suspended the in-person dispensing requirement for mifepristone for the remainder of the COVID-19 public health emergency.[4]
- In December 2021, after reviewing the evidence, the FDA decided to permanently remove the in-person dispensing requirement for mifepristone and allow certified brick-and-mortar and mail-order pharmacies to dispense the drug.[5] In January 2023, FDA issued guidance about pharmacy certification to dispense mifepristone.[6]

†SAEs included death, hospitalization, surgery (not including uterine evacuation), and blood transfusion.

Research conducted on the safety and effectiveness of medication abortion without in-person clinician dispensing

This issue brief summarizes published results of U.S. studies of medication abortion in which mifepristone was mailed to patients, rather than having a clinician dispense the medication in person in a clinic, medical office, or hospital setting. Seven publications met our inclusion criteria for this review. The effectiveness of medication abortion ranged from 93.5% to 97.8% (Table 1). There were no deaths in any of the studies. Other serious adverse events, which included hospitalization, blood transfusion, or surgery (not including uterine evacuation), were uncommon and ranged from zero to 1.5% (Table 1).

- Chong et al.[7] describes results from a direct-to-patient telemedicine abortion service. Study participants obtained screening tests as necessary (ultrasound, pelvic exam, and blood tests)[§] and had a videoconference with a study clinician to confirm eligibility. Study sites mailed mifepristone and misoprostol to the participant's preferred address. The study took place between 2016-2020 and had abortion outcome data for 1,157 abortions (13.8% loss to follow-up).
- In a study by Grossman et al., participants were assessed by a clinician in person for eligibility and dispensed mifepristone and misoprostol at a nearby brick-and-mortar pharmacy. The study took place between 2018-2020 and had abortion outcome data for 260 participants (1.5% loss to follow-up).[8]
- In a second study by Grossman et al., clinicians dispensed mifepristone and misoprostol via mail-order pharmacy to participants after an in-person eligibility assessment. The final analysis includes abortion outcome data for 510 medication abortions among participants recruited in 2020-2022 (3.8% loss to follow-up).[9]
- Ralph et al.[10] conducted a prospective observational study to evaluate the effectiveness and safety of no-test medication abortion screening and mailing of medications as compared to in-person care with ultrasonography. Participants were recruited from 2021 to 2023 across six states. The final sample of patients with abortion outcome data in the no-test, telehealth with mailing of medications group included 204 participants (10.5% loss to follow-up).[10]
- Raymond et al.[11] assessed the feasibility, safety, and acceptability of asynchronous screening for medication abortion eligibility using a programmed questionnaire in Minnesota and Colorado. The sample includes abortion outcome data for 115 patients who received abortion medications by mail and took the mifepristone and misoprostol (15% loss to follow-up).
- A retrospective cohort study by Upadhyay et al. evaluated effectiveness and safety of a history-based screening, no-test approach to medication abortion care in 2020-2021. The analysis includes abortion outcome data for 727 patients who received abortion medications by mail without ultrasonography or pelvic examination (43% loss to follow-up).[12]
- A prospective cohort study by Upadhyay et al. assessed effectiveness and safety of telehealth medication abortion care from three virtual clinics operating in 20 states and Washington, DC, in 2021-2022. The analysis includes 4,454 abortions among participants who received medications via mail-order pharmacy and reported taking both medications (26% loss to follow-up).[13]

§75% of enrollments had a pre-abortion ultrasound.

Methods

- We conducted a systematic review of published, U.S.-based quantitative studies examining effectiveness and safety outcomes when mifepristone was not dispensed in person by a clinician in a clinic, medical office, or hospital.
- We searched PubMed on June 26, 2024, with the following search terms: ((mail OR (mail-order) OR pharmacist OR pharmacy) AND mifepristone AND abortion) OR ((medication abortion) AND (telehealth OR telemedicine OR synchronous OR asynchronous)). In total, 11 of 447 publications met inclusion criteria. Of those 11, Kerestes et al.[14], Upadhyay et al.[15], Grossman et al.[16], and Raymond et al. 2019[17] were removed as most or all participants who received medications by mail in these studies were included in Chong et al.[7], Upadhyay et al.[12], or Grossman et al.[9]
- Two researchers independently reviewed each publication and extracted key study design, measurement, and outcome data. The unit of analysis was individual abortions. Cases where patients were known to not have taken mifepristone were excluded. Loss to follow-up was defined as the number of abortions with no information on abortion outcome divided by the number of total abortions, not including cases where it was known the participant did not take mifepristone.
- We extracted overall effectiveness and safety outcome measures from each study but applied our own definitions to the data from each study. Effectiveness was defined as the proportion of abortions that were complete with medications only, regardless of misoprostol dosage. For safety, we extracted information on serious adverse events including death, hospitalization, surgery (not including uterine evacuation), or blood transfusion that were at least possibly related to the medication abortion and that occurred after mifepristone was taken. When this information was not available in published sources, we followed up directly with study authors.

Implications

- Seven recent U.S.-based studies demonstrate that medication abortion provided without in-person dispensing of mifepristone is effective and safe, with findings similar to in-person clinician dispensing. These findings, as well as data from other countries,[18] indicate that the in-person dispensing requirement of the REMS is not necessary to ensure medication abortion effectiveness or safety. These data support FDA's decision to permanently remove the in-person dispensing requirement for mifepristone.

Table 1. Abortion outcome data on effectiveness and safety among all participants for whom outcome was known

Study	Abortion outcome known	Abortion complete with medications alone			Abortion incomplete with medications alone*		SAE related to MA†		
	N	n	Proportion	95% CI	n	Proportion	n	Proportion	95% CI
Chong et al., *Contraception 2021*	1,157	1,103	95.3%	94.0% - 96.5%	54	4.7%	9	0.8%	0.3% - 1.5%
Grossman et al., *Obstet Gynecol 2021*	260	243	93.5%	89.7% - 96.1%	17	6.5%	0	0	-
Grossman et al., *JAMA Intern Med 2024*	510	499	97.8%	96.2% - 98.9%	11	2.2%	3	0.6%	0.1% - 1.7%
Ralph et al., *JAMA 2024*	204	194	95.1%	91.2% - 97.6%	10	4.9%	3	1.5%	0.3% - 4.2%
Raymond et al., *Contraception 2024*	115	110	95.6%	90.1% - 98.6%	5	4.3%	0	0	-
Upadhyay et al., *JAMA Intern Med 2022*	727	688	94.6%	92.7% - 96.2%	39	5.4%	5	0.7%	0.2% - 1.6%
Upadhyay et al., *Nature Med 2024*	4,454	4,358	97.8%	97.4% - 98.3%	96	2.2%	15	0.3%	0.2% - 0.6%

**Includes those who had ongoing pregnancies or aspiration / dilation & curettage / procedural abortion for any reason.*

†Serious adverse events related to medication abortion included death, hospitalization, surgery (not including uterine evacuation), and blood transfusion. No deaths were reported in any of the studies.

References

1. Danco Laboratories, LLC. MIFEPREX (mifepristone) tablets label. U.S. Food and Drug Administration; 2016. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf [accessed 29 April 2024].

2. Upadhyay US, Desai S, Zlidar V, Weitz TA, Grossman D, Anderson P, et al. Incidence of emergency department visits and complications after abortion. Obstet Gynecol 2015; 125(1): 175-83.

3. Center for Drug Evaluation and Research. Risk Evaluation and Mitigation Strategy (REMS), SINGLE SHARED SYSTEM FOR MIFEPRISTONE 200MG. U.S. Food and Drug Administration; 2021. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/rems/Mifepristone_2021_05_14_REMS_Full.pdf [accessed 14 May 2024].

4. Woodcock J, Acting Commissioner of Food and Drugs. Letter to the American College of Obstetricians and Gynecologists and Society for Maternal-Fetal Medicine. U.S. Food and Drug Administration; 2021. Available from: https://www.aclu.org/sites/default/files/field_document/fda_acting_commissioner_letter_to_acog_april_12_2021.pdf [accessed 14 May 2024].

5. Cavazzoni PA, Director of Center for Drug Evaluation and Research. Response Letter from FDA CDER to American Association of Pro-Life Obstetricians and Gynecologists and American College of Pediatricians. U.S. Food and Drug Administration; 2021. Available from: https://www.regulations.gov/document/FDA-2019-P-1534-0016 [accessed 14 May 2024].

6. Food and Drug Administration. Questions and Answers on Mifepristone for Medical Termination of Pregnancy Through Ten Weeks Gestation. Content current as of 09/01/2023. Available from: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation [accessed 13 May 2024].

7. Chong E, Shochet T, Raymond E, Platais I, Anger HA, Raidoo S, et al. Expansion of a direct-to-patient telemedicine abortion service in the United States and experience during the COVID-19 pandemic. Contraception 2021; 104(1):43-8.

8. Grossman D, Baba CF, Kaller S, Biggs MA, Raifman S, Gurazada T, et al. Medication Abortion with Pharmacist Dispensing of Mifepristone. Obstet Gynecol 2021; 137(4):613-22.

9. Grossman D, Raifman S, Morris N, Arena A, Bachrach L, Beaman J, et al. Mail-order pharmacy dispensing of mifepristone for medication abortion after in-person screening. JAMA Intern Med 2024; doi: 10.1001/jamainternmed.2024.1476. Epub ahead of print.

10. Ralph LJ, Baba CF, Biggs MA, McNicholas C, Miller AH, Grossman D. Comparison of No-Test Telehealth and In-Person Medication Abortion. JAMA. 2024 Jun 24:e2410680. doi: 10.1001/jama.2024.10680.

11. Raymond EG, Frye LJ, Tocce K, Gingras S, Almquist A, Firstenberg A, et al. Evaluation of a “smart” screening tool for asynchronous assessment of medication abortion eligibility: A pilot study. Contraception 2024(131): 110340.

12. Upadhyay UD, Raymond EG, Koenig LR, Coplon L, Gold M, Kaneshiro B, et al. Outcomes and Safety of History-Based Screening for Medication Abortion: A Retrospective Multicenter Cohort Study. JAMA Intern Med 2022;182(5):482-491.

13. Upadhyay U, Koenig LR, Meckstroth K, Ko J, Valladares ES, Biggs MA. Effectiveness and safety of telehealth medication abortion in the USA. Nature Medicine. Feb 15 2024.

14. Kerestes C, Murayama S, Tyson J, Natavio M, Seamon E, Raidoo S, et al. Provision of medication abortion in Hawai’I during COVID-19: Practical experience with multiple care delivery models. Contraception 2021; 104(1):49-53.

15. Upadhyay UD, Koenig LR, Meckstroth KR. Safety and Efficacy of Telehealth Medication Abortions in the US During the COVID-19 Pandemic. JAMA Netw Open 2021;4(8):e2122320.

16. Grossman D, Raifman S, Morris N, Arena A, Bachrach L, Beaman J, et al. Mail-order pharmacy dispensing of mifepristone for medication abortion after in-person clinical assessment. Contraception 2022;107:36-41.

17. Raymond E, Chong E, Winikoff B, Platais I, Mary M, Lotarevich T, et al. TelAbortion: evaluation of a direct to patient telemedicine abortion service in the United States. Contraception 2019;100(3):173-177.

18. Aiken A, Lohr PA, Lord J, Ghosh N, Starling J. Effectiveness, safety and acceptability of no-test medical abortion (termination of pregnancy) provided via telemedicine: a national cohort study. BJOG Int J Obstet Gynaecol 2021; 128(9):1464-74.