

Commentary

# If we can do it for misoprostol, why not for mifepristone? The case for taking mifepristone out of the office in medical abortion<sup>☆</sup>

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Received 29 May 2015; revised 8 June 2015; accepted 12 June 2015

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## Abstract

Given the highly political nature of abortion in the United States, the provision of medical abortion with mifepristone (Mifeprex<sup>®</sup>) and misoprostol has always occurred under a unique set of circumstances. The Food and Drug Administration-approved regimen requires clinicians to administer the mifepristone in the office and also requires women to return to the office for the misoprostol. In the US, where off-label drug use is an accepted practice when supportive evidence exists, most clinicians give women the misoprostol at the initial visit for her to take at home, eliminating an unnecessary visit to the office. This commentary suggests that, based on current studies, there is also enough evidence to offer women the option to self-administer mifepristone out of the office and that this is just another feature of off-label use. Six studies, enrolling over 1800 women, found that the option of taking mifepristone out of the office was popular and acceptable among women and providers. Given that it is safe, highly acceptable and not burdensome on providers, outside-office-use of mifepristone should be offered to all women as part of routine medical abortion services.

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Given the highly political nature of abortion in the United States, the provision of medical abortion with mifepristone (Mifeprex<sup>®</sup>) and misoprostol has always occurred under a unique set of circumstances. Even though mifepristone is an extremely safe drug, the Food and Drug Administration (FDA) required that the manufacturer agree to a Risk Evaluation and mitigation strategy mandating the drug be dispensed only in the provider's office and not in pharmacies. Correspondingly, the FDA-approved label for mifepristone (the first drug taken in the most commonly used regimen) stipulates that the medication must be administered in the provider's office. In addition to the requirement for direct administration of mifepristone, the FDA label also describes the process for using misoprostol, the second medication in the regimen, although it is extremely uncommon for a drug label to include requirements for

follow-up. In the 15 years since the FDA approval of mifepristone, many improvements have been made to the regimen listed in the label to make medical abortion more effective, acceptable and accessible [1]; this commentary focuses on regimen changes that would allow women to take the mifepristone out of the office. While some papers on this topic have referred to this practice as “home-use,” we use “outside-office-use” to emphasize the point that the woman does not need to be home when taking the mifepristone. We believe that ample evidence exists to demonstrate that women can follow directions and safely take the mifepristone out of the office, and we advocate that this option should be offered to all women as a part of routine medical abortion services.

The FDA-approved medical abortion regimen requires women to return to the office for the misoprostol. Once Hausknecht [2] demonstrated that women could leave the office as soon as misoprostol was administered and handle the expulsion on their own, subsequent studies explored dispensing misoprostol to women for home use. These studies demonstrated that women were able to follow

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<sup>☆</sup> Conflicts of interest: none.

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instructions and take the misoprostol as directed and led to the elimination of a clinic visit. In some situations that arise in clinical practice, allowing women to take the mifepristone out of the office can actually eliminate a visit as well. For example, some clinics do not administer mifepristone if an Rh result is not available (as Rh-negative patients typically receive RhD immunoglobulin in the US). If women were given mifepristone and the blood type drawn on the same day, Rh-positive women (approximately 85% of women in the US) would not need to come back to get the mifepristone, since they could take it at home at a time agreed on during the office visit; for most women, this process would eliminate an additional visit.

Overall, a strong rationale exists for allowing women to self-administer mifepristone out of the office. Mifepristone is an extremely safe drug (see Cleland commentary) with moderate (and manageable) side effects [3,4]. Most of the cramping and bleeding during medical abortion comes after use of misoprostol [4], which women have safely been self-administering for over 20 years. Giving women the mifepristone in the office for later use (if that is the option they choose) would enable them to better schedule their bleeding and cramping around their other responsibilities. For example, if a patient who normally had weekends off had her appointment on a Tuesday, she could wait to take the mifepristone on Friday, and then take the misoprostol on Saturday, so she would not have to miss any work or school. Self-administration of mifepristone allows for greater patient autonomy and privacy. Lastly, eliminating the requirement to take the mifepristone at the clinic disabuses the notion that there is something dangerous about this drug that requires it to be taken in the presence of a provider. Concerns about redistribution of the drug ignore that most women coming for an abortion do not wish to be pregnant and so are highly motivated to take the medication. In addition, in the US, almost all patients receive one tablet of mifepristone following evidence-based off-label use guidelines (rather than the three tablets recommended in the label), so she is receiving only enough medication for her own abortion.

There is a widespread belief among providers that patients must take the mifepristone in the clinic. Except for those states that have laws requiring medical abortion be provided in accordance with the FDA-approved protocol (currently North Dakota, Texas and Ohio have such laws in effect) — outside-office-use of mifepristone is currently permissible under guidelines for off-label use. While it is true that the label for Mifeprex<sup>®</sup> states that the drug should be administered at the clinic on Day 1, it also states that the dosage is 600 mg, that patients must return to the clinic to take the misoprostol and that the misoprostol dosage is 400 mcg orally. As off-label drug use is a common and accepted practice in the US when supportive evidence exists, the most commonly used regimen in the US is 200-mg mifepristone followed by 800 mcg of misoprostol used buccally at home. Taking mifepristone out of the office is just another feature of off-label use.

Why is this misconception so prevalent? First, many providers (and women) still believe that abortion is risky, and thus, women must be supervised during the process since they “can’t handle it” on their own. In addition, many still consider medical abortion a “procedure” that is “done” by a provider, although in reality medical abortion is a treatment with medication and not actually a procedure. Third, many providers are not aware that evidence exists to support a change in the medical abortion process, and the relevant clinical guidelines are either silent on the matter (i.e., neither the American College of Obstetricians and Gynecologists’ Practice Bulletin [1] nor the National Abortion Federation’s Clinical Policy Guidelines [5] have mentioned the current evidence supporting a change), or explicitly state that the mifepristone should be given in the clinic (i.e. Planned Parenthood’s Medical Standards and Guidelines). Lastly, the unique mechanisms for Mifeprex<sup>®</sup> distribution and dispensing add confusion to what is and is not allowable, and the extremely contentious atmosphere in which abortion is provided in the US make providers reluctant to do anything that seems remotely out of the ordinary.

In fact, research studies in settings as varied as Armenia, Azerbaijan, Nepal, the US and Kazakhstan have demonstrated that the outside-office-use option is popular and acceptable among women [6–10]. The proportion of women choosing to take the mifepristone at home ranged from 46%–74%, and among these users, 92%–99% would choose to take it out of the office again for a future abortion (Fig. 1). A newly published study (in this issue) conducted in Planned Parenthood centers found that 32% chose home-use of mifepristone, and 99% would choose it again [11]. Some countries (including Armenia, the Republic of Georgia, Azerbaijan, and Uruguay) explicitly allow this option in their clinical guidelines. Australia allows for pharmacy distribution of mifepristone (described in a commentary in this issue), which results in out-of-office use. In addition, telemedicine medical abortion services such as Women on Web (which has been operating since 2006) and the Willow Women’s Clinic in Vancouver have demonstrated the feasibility of outside-office use of mifepristone or methotrexate in regular clinical services as they send the medical abortion drugs to women through the mail after consultation [12,13].

Given that it is safe, highly acceptable, and not burdensome on staff, outside-office-use of mifepristone should be offered to all women as a part of routine medical abortion services. In addition, clinical guidelines should explicitly state that the practice is evidence based, and the manufacturer should include this change among the other changes to the label it is requesting. Changing the guidelines for mifepristone use has major implications for new service delivery models such as pharmacy distribution of mifepristone or telemedicine medical abortion models that are direct-to-consumer. These innovations have the potential to greatly increase access to abortion by increasing the number

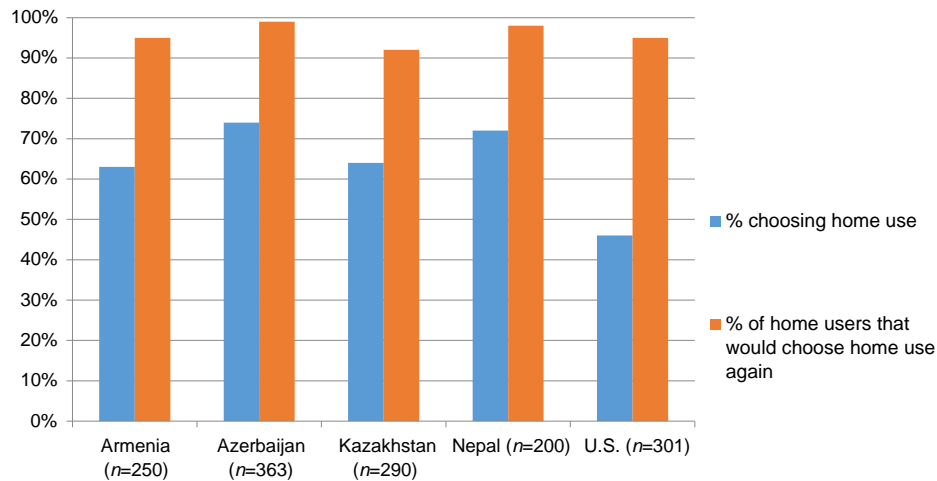


Fig. 1. Uptake and satisfaction of home use of mifepristone in research studies. Sources: Louie et al. 2015 [6]; Louie et al. 2014 [7]; Platais et al. 2015 [10]; Conkling et al. 2015 [8]; Swica et al. 2013 [9].

and geographical distribution of providers offering medical abortion and, thus, will be critical in improving the lives of women moving forward.

### Acknowledgements

This work was supported by an anonymous donor.

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