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Original article

Could second-trimester medical abortion be offered as a day service? Assessing the feasibility of a 1-day outpatient procedure using pooled data from six clinical studies☆

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ABSTRACT

Objectives: Current service delivery models for second-trimester medical abortion typically include routine inpatient admission and overnight stays. To assess the feasibility of a day-service model, we evaluated outpatient administration of abortion medications and analyzed the proportion of clients who could avoid an overnight stay. We also examined additional key elements of medical abortion care to evaluate the practicality of this model.
Study design: We pooled data from six clinical studies of second-trimester medical abortion conducted by Gynuity over the past 10 years. We include 868 individuals receiving mifepristone–misoprostol abortion between 13 and 22 weeks' gestation.
Results: At 8 h post misoprostol initiation, 309/521 (59.3%) participants at 13-18 weeks' gestation had a successful abortion; by 10 h, 382/521 (73.3%) were successful. Taking the mifepristone at home lowered neither the efficacy of the method nor satisfaction with the experience. Nonphysician providers played a significant role in the provision of care. Needed interventions were relatively rare; serious complications were very rare.
Conclusions: Our findings support the provision of second-trimester medical abortion in a day-clinic setting, especially at ≤18 weeks' gestation. Such a model could increase access to quality care in many settings.
Implications: Second-trimester medical abortion can safely and effectively be offered as a day service. Nonphysician providers are well suited to provide the majority of care. Developing guidelines for a 1-day model could increase access to quality care in many settings worldwide.

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1. Introduction

Medical abortion is one of the most important reproductive health technologies to emerge in recent history [1]. Modern regimens combining mifepristone and misoprostol offer a safe and effective option for termination of pregnancy and an alternative to surgical methods [2,3]. Over time, evidence-based changes to clinical regimens and service delivery have improved efficacy and facilitated greater access, autonomy, flexibility and privacy for individuals seeking abortion in the first trimester. The cumulative body of evidence establishing the effectiveness, safety and acceptability of mifepristone and misoprostol for medical abortion in the second trimester demands similar innovation in delivery of services [4,5]. Yet, in many settings, delivery of second-trimester medical abortion typically includes routine inpatient admission and prolonged hospital stays. Such requirements appear out of line with current safety and efficacy evidence.

Historically, a number of medications have been used to induce second-trimester abortion. Compared to mifepristone and/or misoprostol, use of these methods was associated with increased risk for infection, hemorrhage, cervical damage, uterine rupture and other complications [6–8]. In addition, earlier prostaglandin formulations induced severe pain and pronounced side effects to the gastrointestinal system (nausea, vomiting, diarrhea), as well as rare but serious respiratory or cardiovascular effects. So while it was prudent with these earlier interventions to require hospital admission and physician supervision, given the safety and side effect profiles of current regimens, that may no longer be the case. In some settings, such as Eastern Europe/Central Asia, hospitalization requirements are based on surgical abortion guidelines and do not reflect the realities of the medical abortion process.

Recommended regimens of mifepristone and misoprostol are highly effective, well tolerated and associated with shorter times to abortion success compared to misoprostol alone [4,9–13]. Complications are rare [4,9–13]. Service delivery guidelines should be modified to reflect this evidence, as out-of-date practices limit the availability of services

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and introduce excessive burdens for those seeking care. Updated protocols would be useful in all settings where medical abortion is offered, including but not limited to low- and middle-income countries. Such a day service might also be more cost-effective [14,15].

We posited that it may be possible to remove some of these burdens by offering second-trimester medical abortion with mifepristone and misoprostol as an outpatient day service. We identified a 1-day model and evaluated its potential.

2. Materials and methods

Drawing from the conclusions of our earlier second-trimester clinical trials, we envisioned a model in which individuals, following a clinical evaluation, take mifepristone at home followed 24–48 h later by an initial dose of misoprostol, also at home, before presenting at an outpatient clinic. Upon arrival at the clinic, additional doses of misoprostol would be administered until successful abortion is achieved. Individuals not completing the process by a set time in the day (corresponding to the closing of daily outpatient services) would be transferred to an inpatient facility/ward for overnight ongoing care.

To assess the feasibility of this 1-day service, we utilized data from all our previously published second-trimester mifepristone–misoprostol medical abortion studies (and those currently under review) to evaluate one's ability to take abortion medications outside of the clinic setting and, if starting the process at home, the likelihood of achieving a successful abortion soon enough to avoid an overnight stay. We examined other key elements of care to evaluate the practicality on implementing such a model, including the likelihood of receiving an intervention, frequency of serious adverse events, pain management, the referral process and provider type.

We pooled primary data from six clinical studies of second-trimester medical abortion conducted by Gynuity Health Projects in five countries (Vietnam, Tunisia, Armenia, Uzbekistan and Ukraine) between August 2007 and May 2016. Four of these studies have been published [10–13]; the other two are unpublished. The 6 studies included 868 participants between 13 and 22 weeks' gestation who received mifepristone 200 mg orally followed 24 h later by misoprostol 400 mcg administered either buccally or sublingually at 3-h intervals (Tables 1 and 2). These studies all took place at tertiary-level urban hospitals. Success was defined as complete uterine evacuation (fetus and placenta) without surgical intervention or oxytocin during the measured time frame. Variables utilized included gestational age, abortion outcome, time to success from misoprostol initiation, location where mifepristone was taken, self-reports of symptoms and side effects, interventions received, serious adverse events and medications provided to prevent/relieve pain. In addition, we communicated with the Principal Investigators from each study to determine provider type at each step of the abortion process. All studies received ethical approval prior and were registered on clinicaltrials.gov. No ethics approval was needed for this review of existing, deidentified data.

Table 2
Background characteristics of study participants included in the pooled analysis of six second-trimester medical abortion studies

	N=868
Age, in years: median (range)	26 (13–46)
Parity: *n* (%)	
0	448 (51.6%)
1	204 (23.5%)
2	155 (17.9%)
3+	61 (7.0%)
Gestational age: *n* (%)	
13–14 weeks (85–98 days)	152 (17.5%)
15–16 weeks (99–112 days)	190 (21.9%)
17–18 weeks (113–126 days)	190 (21.9%)
19–20 weeks (127–140 days)	167 (19.2%)
21–22 weeks (141–154 days)	169 (19.5%)
Took mifepristone at home	592 (68.2%)

3. Results

3.1. Will a significant proportion of individuals have a successful abortion in 1 day (and thus not require an overnight stay)?

We estimated that individuals could attend a day service for approximately 8 h before being transferred to an overnight facility. Using the pooled data, we found that at 8 h post misoprostol initiation, around half (401/846, 47.4%) had achieved a successful abortion. However, the proportion who had expelled both fetus and placenta decreased substantially with increasing gestational age (Fig. 1). At the 8-h mark, 59.3% of those at 13–18 weeks' gestation (85–126 days) vs. 28.3% of those at 19–22 weeks' gestation (127–154 days) had successful abortion ($p<.001$). But if the first dose of misoprostol was taken at home 2 h before returning to the clinic (as discussed above), that would allow 10 total hours following misoprostol: at 10 h, 73.3% of those 13–18 weeks vs. 44.3% at 19–22 weeks ($p<.001$) had successful abortions. Further, a clinic that is set up to allow for a more extensive outpatient clinic, say 10 h in clinic before transfer, would allow for 12 total hours postmisoprostol, which according to our pooled data would result in a successful abortion for 85.0% (13–18 weeks) and 67.4% (19–22 weeks) of participants.

3.2. Can individuals safely administer abortion medications on their own outside of the clinic setting?

There is extensive evidence in our data that individuals can administer mifepristone at home or elsewhere without supervision. In three of the six studies we reviewed, participants were instructed to take the

Table 1
Overview of the six second-trimester medical abortion studies included in this pooled analysis[a]

	Ngoc 2011	Abbas 2016	Dabash 2015	Louie 2017	Platais (in review)	Platais (in review)
Country	Vietnam	Vietnam	Tunisia	Armenia	Uzbekistan	Ukraine
Type of study	RCT	RCT	RCT	Open label	Open label	Open label
Gestational age range (weeks)	14–21	13–22	14–21	13–22	13–22	13–22
N (868 total)	130	252	60	120	134	172
Mifepristone dose	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg
Misoprostol dose & route	400 mcg buccal	400 mcg buccal	400 mcg buccal	400 mcg buccal	400 mcg sublingual	400 mcg sublingual
Misoprostol schedule	q3h; max 5 doses in 24 h	q3h; no max	q3h; max 5 doses in 24 h × 2[b]	q3h; no max	q3h; no max	q3h; no max
Outcome time point	15 h	48 h	48 h	No cutoff	No cutoff	No cutoff

RCT = randomized controlled trial.

[a] We only included study arms with mifepristone followed approximately 24 h later by misoprostol. For all six studies, only those in good health with a live fetus, presenting without evidence of labor (e.g., closed os, intact membranes and no contractions) were included; menstrual history and clinical assessment with or without ultrasound informed determinations of gestational age. Exclusions included any persons with allergies or contraindications to mifepristone or misoprostol, contraindications to vaginal delivery, including evidence for placenta previa, or (in all studies except Ukraine) a history of cesarean section or other transmural uterine scar.

[b] Those who did not complete the abortion in 24 h were allowed a second 24-h period, again with a 5-dose maximum.

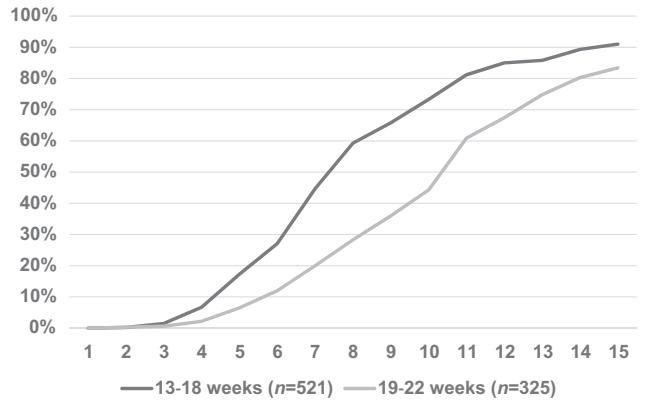

Fig. 1. Proportion of women with successful abortion in the six pooled second-trimester medical abortion studies, by hour post misoprostol initiation. *Twenty-two participants were excluded from this analysis due to missing data: outcome information is unavailable for 2 users, and an additional 20 had no recorded time of expulsion. The first successful abortion (fetal and placental expulsion) among participants 13–18 weeks occurred at 1.3 h after misoprostol initiation; among those 19–22 weeks, the first success occurred 1.8 h after misoprostol initiation.

mifepristone at home; in two studies, they were given that option. Of those given a choice, half (150/306, 49.0%) chose to take the mifepristone at home. Overall satisfaction did not differ between those who took the mifepristone in the hospital vs. those who took it at home (89.0% vs. 90.7% satisfied or very satisfied; p=.71). Method success was, in fact, higher among those who took mifepristone at home (100% vs. 93.6%; p<.01). There were no expulsions or serious side effects between mifepristone ingestion and initial misoprostol dose.

Given the ease and acceptance of taking mifepristone at home, we also considered whether individuals could also take their initial dose of misoprostol at home and how this might impact service delivery. One concern might be pain, bleeding and/or other side effects between the first and second doses prior to clinic arrival. The pooled dataset demonstrates that both pain and bleeding are fairly minimal in the early hours following misoprostol initiation (Table 3). At the time of the initial misoprostol dose, only 3/846 (0.4%) reported pain greater than a 3 on a 0–7 or 1–7 scale. Bleeding was also minimal at that time, with most participants (591/615; 96.1%) reporting no bleeding and none reporting moderate or severe bleeding. Nausea was noted by 23/309 (7.4%). Few reported vomiting, diarrhea or chills at this time. None of the symptoms or side effects differed significantly by gestational age group.

Three hours later, at the time of the second dose, 102/853 (12.0%) reported pain greater than 3, a small portion of whom (10/853, 1.2%) reported pain at 6 or 7. At this time, most (583/611, 95.4%) reported no or mild bleeding; 27 participants (4.4%) reported moderate and 1 (0.2%) reported heavy bleeding. Other side effects were more apparent, with 130/309 (42.1%), 33/309 (10.7%), 22/309 (7.1%) and 21/309 (6.8%) reporting nausea, vomiting, diarrhea and chills, respectively. Again, none of these effects differed significantly by gestational age group.

Table 3
Results from our pooled analysis of six second-trimester medical abortion studies: pain, bleeding and additional side effects at dose 1 and 2 of misoprostol: *n* (%)

	At first miso dose	At second miso dose
Reported side effect		
Pain >3 (on 0–7 or 1–7 scale)	3/846 (0.4%)	102/853 (12.0%)
Bleeding		
None	591/615 (96.1%)	411/611 (67.3%)
Mild	24/615 (3.9%)	172/611 (28.2%)
Moderate or heavy	0/615 (0.0%)	28/611 (4.6%)
Nausea[a]	23/309 (7.4%)	130/309 (42.1%)
Vomiting[a]	5/309 (1.6%)	33/309 (10.7%)
Diarrhea[a]	5/309 (1.6%)	22/309 (7.1%)
Chills[a]	9/309 (2.9%)	21/309 (6.8%)

[a] Three of the 6 studies only collected data on side effects at the end of the abortion process and not at each dose.

Another concern raised has been the possibility of fetal and placental expulsion prior to arrival at the clinic. To address this issue, we used the pooled data to examine fetal and placental expulsion rates in the first few hours following the first dose of misoprostol among 846 individuals with recorded expulsion times. At 1, 2 and 3 h after initiation of misoprostol, few [1 (0.1%), 5 (0.6%) and 13 (1.5%), respectively] had experienced fetal expulsion. Among those 13, 0 (0.0%), 2 (0.2%) and 10 (1.2%), respectively, had also expelled the placenta. The gestational age of these 13 participants ranged from 91 to 133 days.

3.3. What types of interventions are likely to be needed, and what frequency should we expect?

In the pooled data, 11 of 868 (1.3%) had an intervention (other than additional misoprostol) prior to fetal expulsion. These interventions included oxytocin (*n*=3), forceps removal (*n*=3) and/or aspiration (*n*=8). To facilitate placental expulsion, 41 (4.7%) had an intervention other than additional misoprostol. These interventions included forceps removal (*n*=23), oxytocin (*n*=14), uterine massage (*n*=6), manual exploration/curettage with fingers (*n*=4) and/or aspiration (*n*=12). The rate of intervention did not differ significantly by gestational age. The only type of intervention that varied significantly by gestational age was massage to facilitate placental expulsion, which was more common in those at 19–22 weeks' versus 13–18 weeks' gestation (2.8% vs. 0.0%; p=.001).

Many of these interventions occurred after a substantial number of hours had passed. Precise intervention times were not documented, but 9/11 (81.8%) and 22/41 (53.7%) of those who had an intervention to facilitate fetal or placental expulsions, respectively, received at least 5 doses of misoprostol, indicating that the interventions took place at least 12 h after misoprostol initiation. In our hypothetical day service, all of these people would have been transferred for inpatient care prior to intervention.

Placental management typically did not require intervention. Our data show that, for most individuals, the placenta typically expels fairly quickly after the fetus: among the 802 clients (92.4%) with successful abortion and no intervention, the median time between fetal and placental expulsion was 10 min (range=0–560).

3.4. How common are serious complications?

In our studies, 2/868 people (0.2%) had heavy bleeding and 2/868 (0.2%) had an infection that resulted in hospitalization. There were no fatalities among individuals enrolled in these trials.

3.5. Is pain management feasible in a day-service setting?

The vast majority of those who received pain medication in our studies received acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs). In Armenia, Vietnam and Tunisia, these medications were given as orally administered tablets. In Uzbekistan and Ukraine, they were provided NSAIDs either as oral tablets or via intramuscular injection. Very few participants received medication intravenously. In three of the studies, participants were asked how acceptable their pain had been. The majority (474/556, 85.3%) reported that their overall pain was acceptable or highly acceptable. Only 25/556 (4.5%) said that their overall pain was unacceptable or highly unacceptable.

3.6. What type of processes would need to be in place for individuals needing additional care?

People who do not have a successful abortion within the day-service time frame would be transferred to an in-patient clinical setting. The

logistics for where, when and how to transfer, as well as the relationship between the outpatient and inpatient facilities, would depend on the setting and need to be established in advance. Transfer would also need to be available for any serious complications or interventions requiring additional equipment or a higher-level clinician.

3.7. What type of providers would be needed to provide necessary care?

To assess clinician requirements, we listed the various components of abortion care including clinical assessment, counseling/education, dispensing of abortion medications, providing pain medications, monitoring abortion progress and conducting needed interventions, and noted the level of provider for each at our included study sites (Table 4). In several of these settings, physicians provided the care at most steps as required by their health system guidelines. However, Vietnam and Tunisia provide evidence that the majority of the care can be safely and successfully provided by midlevel clinicians such as nurses and midwives. If a referral and transfer system is in place for urgent care, the day-service model could benefit from task-sharing, allowing the majority of clinical monitoring as well as the administration of the abortion medicines, pain medication and antiemetics to be managed by nurses/midwives.

4. Discussion

Evidence from these pooled data supports the feasibility of providing second-trimester medical abortion as a 1-day service, especially for individuals at ≤18 weeks' gestation. Clinical guidelines should be developed to facilitate the establishment of day-service models in a variety of settings. Such guidelines, including from international health and large service delivery organizations, could include dosing regimens, pain management strategies, task shifting recommendations and standards for when to intervene, for example, avoiding unnecessary surgical interventions in order to complete the abortion process within the outpatient time frame. In resource-constrained settings, second-trimester abortions occupy valuable beds in inpatient settings and increase costs associated with hospital care. A day service could be based within, or adjacent to, a hospital or could be more remote with ready access to a hospital as needed. While serious complications are rare [16,17], recognition and referral for further management are important, necessitating standards for transfer and strong linkages with higher-level facilities for emergency care and to assist individuals whose abortion is still in process beyond the operating hours of the service.

The practicality of our proposed model is strengthened by some examples of service delivery changes. For instance, self-administration of mifepristone at home was successfully introduced for second-trimester abortion management in public sector clinics in South Africa [18]. More so, a 1-day model is currently in use in the United Kingdom for medical abortion care at 13–21 weeks' gestation [16]. A summary of cases showed that three quarters (723/999, 72.4%) had a successful abortion as a day client. While this success rate is higher than our 10-h rate (62.2%), the median gestational age of their population was lower than ours (15 vs. 17 weeks), with a much higher proportion presenting at 13–16 weeks (75% vs. 39%). In addition, we could not ascertain how many hours they allowed for a day-service process. Finally, allowing some nonphysician providers, such as nurses and midwives, to oversee much of second-trimester care is supported by the World Health Organization [19] and is currently the norm in a number of Scandinavian countries [14].

While we have data to support the safety and efficacy of an outpatient model, acceptability has not been documented. Studies of medical abortion in the first trimester have shown that most clients opt to have their abortions at home versus staying in a clinic setting [20–23]. In addition, research comparing second-trimester mifepristone–misoprostol medical abortions to misoprostol-alone procedures has shown a penchant for completing the abortion process more quickly [12,13]. However, favoring quicker expulsion does not necessarily translate to a preference for outpatient services, and we do not have evidence regarding acceptability of same-day discharge in the second trimester. Following one study in South Africa, hospital staff reported that many clients preferred to stay overnight in order to better rest and recover and avoid taking public transportation at night (personal communication, Dr. Deborah Constant, University of Cape Town, 2017). However, these reports were not collected systematically; in addition, this feedback comes from one clinic location in one setting. Research regarding acceptability is clearly needed, and a model that allows for client choice in timing of discharge should be explored to maximize quality of care.

While we believe that the data demonstrate the potential of a day service for second-trimester medical abortion, our analysis has some weaknesses. All of the studies were conducted by the same organization (ours), so there is the possibility of unintentional bias in how the protocols were developed and implemented. As well, we only included experiences with a combined mifepristone–misoprostol regimen. We do not know if a day procedure would work (or if it would be feasible) with a misoprostol-alone regimen given that the time to completion is longer [12,13]. We were also not able to explore the impact of a longer interval between mifepristone and misoprostol, which might lead to a shorter time to expulsion [24]. More research in this area would be beneficial. Finally, a pooled data analysis is less robust than a true meta-analysis; however, we believe that a pooled data approach is appropriate to address the proposed service delivery model raised in this paper. Future research should document the effectiveness of integrating this model of care in health systems globally and demonstrate its potential as a way to expand access to second-trimester abortions outside of tertiary-level services, where, for now, the large part of later abortions takes place. Evaluation should include measures of uptake and success, as well as an assessment of impact on availability of services. Qualitative research to document individual experiences would also fill an evidence gap in the literature and guide improvements in quality of care of second-trimester abortion care.

In many parts of the world, access to safe abortion in the second trimester remains limited or unavailable [25]. When services exist, second-trimester medical abortion management varies widely according to applicable laws, public policies, facility and provider practices, and skill or preferences that may not routinely reflect best evidence or client-centered care [2]. This paper presents clinical evidence regarding safety and efficacy; we realize that additional efforts may be needed at

Table 4
Level of provider at each stage of the abortion process in each of the six studies included in the pooled analysis

Study	Country	Conducted clinical assessment to determine eligibility	Provided counseling/education	Dispensed mife	Dispensed miso	Dispensed pain meds	Monitored throughout MA process	Conducted interventions
Ngoc 2011	Vietnam	Midwife or doctor	Midwife	Midwife	Midwife	Midwife	Midwife	Doctor
Abas 2016	Vietnam	Midwife or doctor	Midwife	Midwife	Midwife	Midwife	Midwife	Doctor
Dabash 2015	Tunisia	Mostly midwife	Mostly midwife	Midwife	Midwife or doctor	Doctor	Midwife or doctor	Doctor
Louie 2017	Armenia	Doctor	Doctor	Doctor	Nurse	Nurse	Nurse	Doctor
Platais (in review)	Uzbekistan	Doctor	Doctor	Doctor	Nurse or doctor	Nurse or doctor	Nurse or doctor	Doctor
Platais (in review)	Ukraine	Doctor	Doctor	Nurse or doctor	Nurse or doctor	Nurse or doctor	Nurse or doctor	Doctor

the local level to address legal and structural barriers to care. It is time to think creatively and practically about how to improve access to these services. Streamlining services and expanding the available workforce could increase access to safe second-trimester abortion care.

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