First dose of misoprostol administration at home or in hospital for medical abortion between 12–22 gestational weeks in Sweden (PRIMA): a multicentre, open-label, randomised controlled trial

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See Comment page 826

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Summary

Background Medical abortion after 12 gestational weeks often requires a stay in hospital. We hypothesised that administering the first misoprostol dose at home could increase day-care procedures as compared with overnight care procedures, shorten inpatient stays, and improve patient satisfaction.

Methods This multicentre, open-label, randomised controlled trial was done at six hospitals in Sweden. Participants were pregnant people aged 18 years and older who were undergoing medical abortion at 85–153 days of pregnancy. Randomisation was done in blocks 1:1 to mifepristone administered in-clinic followed by home administration or hospital administration of the first dose of misoprostol. Allocation was done by opening of opaque allocation envelopes. Due to the nature of the intervention, masking was not feasible. Between 24–48 h after mifepristone 200 mg, the participants administered 800 µg of misoprostol either at home 2 h before admission to hospital or in hospital. The primary outcome was the proportion of day-care procedures (defined as abortion completed in <9 h). The intention-to-treat analysis included all participants randomly assigned to receive the study drug and who had known results for the primary outcome. Individuals who received any treatment were included in the safety analyses. This trial is registered at ClinicalTrials.gov, NTC03600857, and EudraCT, 2018-000964-27.

Findings Between Jan 8, 2019, and Dec 21, 2022, 457 participants were randomly assigned to treatment groups. In the intention-to-treat-population, 220 participants were assigned to the home group and 215 to the hospital group. In the home group, 156 (71%) of 220 participants completed the abortion as day-care patients, compared with 99 (46%) of 215 in the hospital group (difference 24·9%, 95% CI 15·4–34·3; p<0·0001). In total, 97 (22%) of 444 participants in the safety analysis had an adverse event. Seven (2%) of 444 participants aborted after mifepristone only. Two (1%) of 220 in the home group aborted after the first dose of misoprostol, before hospital admission.

Interpretation Home administration of misoprostol significantly increases the proportion of day-care procedures in medical abortion after 12 gestational weeks, offering a safe and effective alternative to in-clinic protocols.

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Introduction

In countries where abortion is legal, the proportion of medical abortions compared with surgical abortions is increasing, expanding access for those seeking induced abortion.[1] This trend has so far been most noticeable in abortions before 12 gestational weeks. Self-managed medical abortions have played a crucial role in enhancing accessibility and have empowered pregnant people in various contexts. The COVID-19 pandemic has further amplified this trend, with provision of telemedical abortion allowing even more people to be in control of their abortion descisions.[2–5] However, although abortions before 12 gestational weeks have become more self-managed, abortions after 12 gestational weeks continue to be predominantly in-hospital procedures, often requiring overnight stays due to a prolonged abortion process (>9 h). These factors hinder clinics without admission privileges from providing medical abortions at these gestational lengths.

With the combined treatment of mifepristone and misoprostol, the duration from the first misoprostol dose to fetal abortion has decreased. Previous studies[6–13] indicate that 60–85% of medical abortions after 12 gestational weeks were completed within 8–12 h, with a median induction time of approximately 6 h and a mean of 2–3 misoprostol doses required for fetal abortion. These findings suggest that most abortions after 12 gestational weeks could be managed as day-care

Research in context

Evidence before this study

After 12 weeks of pregnancy, commencement of medical abortion treatment with the first dose of misoprostol at home before admitting patients to an inpatient unit for continuation might reduce inpatient stay duration. We conducted an extensive search on PubMed for relevant reviews and trials published in English from database inception to June 1, 2023, using the keywords "second trimester medical induced abortion", "termination of pregnancy", "day-care", and "home administration". The search identified no randomised controlled studies with day care as the primary outcome for medical abortion with mifepristone and misoprostol after 12 gestational weeks. We found one prospective uncontrolled observational trial evaluating the safety, acceptability, and feasibility of a day-care protocol for second trimester medical abortion. A pooled analysis assessing the feasibility of day-care included data from six clinical studies not specifically focusing on day-care as an objective. A small randomised controlled trial also studied the efficacy of starting the abortion process at home in second trimester medical pregnancy termination. In this study only misoprostol, not mifepristone, was administered.

Added value of this study

To our knowledge, this trial is the first to comprehensively report on the efficacy, safety, and acceptability of initiating abortions after 12 weeks of pregnancy at home with day-care as the primary outcome. Our findings demonstrate the feasibility of increasing the number of people who undergo day-care abortions by administering the first dose of misoprostol at home before admitting them to hospital. Furthermore, our results highlight the high patient satisfaction rate, high safety, and the low risk of complications and expulsion before admission.

Implications of all the available evidence

Implementing at-home initiation of medical abortion after 12 weeks represents a substantial step towards transferring these procedures from hospitals to self-management and outpatient units. This study supports previous observational studies that this approach is both safe and acceptable. To improve global access to abortions after 12 gestational weeks, we must streamline existing medical protocols, simplifying treatment and empowering women to make autonomous decisions. Mortality rates due to unsafe abortions are highest in low-resource settings, and people undergoing medical abortions after 12 gestational weeks present a particularly vulnerable group. At-home initiation and day-care treatment could be pivotal in addressing this issue and facilitating improved access to safe and effective abortion care.

procedures (ie, <9 h).[6–13] By allowing home administration of the first misoprostol dose, the inpatient time could be further shortened, increasing the number of people that can be treated as day-care patients, if safety and acceptability can be maintained. The feasibility of home administration of the first dose of misoprostol to increase the rate of day-care abortions has been the topic of previous non-randomised research and our aim is to more rigorously quantify it.[14]

Day-care treatment for abortions after 12 weeks offers numerous advantages such as potential expansion of abortion care to primary and secondary health-care units, and service provision in areas where such care is currently unavailable due to lack of trained staff or in-house hospital beds. Additionally, day-care treatment could make valuable resources available at tertiary care levels, promoting task sharing between midwives and physicians and reducing cost. Being solely treated in a day-care unit could mean no need to transfer to another department at night and possibly being cared for by the same staff during the whole treatment. Moreover, this method could potentially reduce economic losses for the person due to less time away from work and possibly shorter travel distance to the day-care unit. Administering the first dose of misoprostol at home would also allow extended contact with the immediate family—a preference expressed by patients in earlier studies.[11,15,16]

In this randomised controlled trial, we aimed to investigate whether at-home administration of the first misoprostol dose (ie, home priming) would result in a higher proportion of people undergoing a medical abortion beyond 12 gestational weeks as day-care patients while ensuring safety and acceptability.

Methods

Study design

The Priming at Home Trial (PRIMA) was a multicentre, open-label, randomised controlled trial, initially conducted at one university hospital and two large public hospitals in Stockholm, Sweden, and one university hospital in Gothenburg, Sweden. 2 years after trial start, the number of study sites was increased to include a further two university hospitals in Malmö and Örebro, Sweden, to increase recruitment. No other change was made to the protocol. The trial adhered to the CONSORT guidelines and the Declaration of Helsinki.

Ethics approval was obtained by the regional Swedish Ethical Review Authority in Stockholm, 2017/2312-31/2 (Dec 20, 2017) and the amendment (Dnr 2021-00404) was approved on Feb 24, 2021. The study protocol can be found at https://medrxiv.org/cgi/content/short/2024.08.08.24311688v1. This trial is registered at ClinicalTrials.gov, NTC03600857, and EudraCT, 2018-000964-27.

Participants

People who sought induced abortion care at the abortion clinic of the respective study site were asked to participate if they fulfilled the inclusion criteria and had no exclusion criteria.

Inclusion criteria were singleton pregnancies dated from 12 gestational weeks and 1 day (85 days) to 21 gestational weeks and 6 days (135 days), which is the legal limit in Sweden for fetuses with non-lethal conditions. After 18 gestational weeks and 0 days permission for any abortion must be granted by the Board of Health and Welfare.[17] People who were seeking abortion; had permission for fetal, social, or maternal indications, if required; who were aged 18 years and older; and who were willing to participate in the study were screened for eligibility.

Individuals were excluded if they were unable to communicate in Swedish or English. People with a non-viable pregnancy (confirmed by ultrasonography) or with a fetus with a malformation that was judged as having a potential effect on the time to abortion were excluded. People with a contraindication to the use of mifepristone or misoprostol (eg, adrenal pathology or known allergy to the medication) or with a pre-existing health condition for whom the procedure of a medical abortion would have compromised their condition were also excluded. All participants were given oral and written information about the study, had the opportunity to ask questions, and signed written informed consent before random assignment. In addition, participants received information according to the Swedish guidelines on the risk of abortion occurring before reaching hospital.

Sex and gender data were not collected.

Randomisation and masking

The randomisation procedure was done by an independent research nurse at the clinical trial centre, who was not otherwise involved in the trial. Randomisation was concealed 1:1 with computer-generated blocks of 4–12. Opaque numbered envelopes containing the randomisation allocation were created by a masked member of the research team, who had no further involvement in the study. After informed consent was obtained from the participant, the study nurse, midwife, or physician working at the abortion clinic opened the envelopes in consecutive order. Masking of the participant was not deemed feasible due to the characteristics of the intervention. The allocation groups were unmasked for data entrants. While performing the statistical analysis, the groups were masked to the researcher.

Procedures

Designated study coordinators and physicians at each site performed a physical examination including documentation of vital signs, BMI, haemoglobin, blood group, Rhesus typing, vaginal examination (to test for bacterial vaginosis and chlamydia and gonorrhoeal infection), and ultrasonography to establish gestational age at recruitment.

Eligible individuals who fulfilled the inclusion criteria without exclusion criteria were randomly assigned to either the home group or the hospital group.

After random assignment, all participants took 200 mg of mifepristone orally at the outpatient clinic attached to the hospital site, according to Swedish legal requirements. The participant received the date and time when they should return to the inpatient unit to continue the treatment. All participants were told to return earlier in the case of heavy bleeding or severe pain. Between 24–48 h after taking mifepristone, the participants in the home treatment group administered the first dose of misoprostol (800 µg) deep vaginally at home, together with pain medication, and returned to the hospital 2 h later to receive the remaining treatment in hospital.[18] The participants in the hospital group self-administered the first dose of misoprostol deep vaginally upon arrival at hospital. After admission, the participants followed the same protocol for medical abortion after 12 gestational weeks, with repeated doses of misoprostol (two tablets at 400 µg each) sublingually every 3 h until fetal abortion.

Pain medication with non-steroidal anti-inflammatory drugs (known as NSAIDs) and paracetamol were administered every 8 h, starting together with the initial dose of misoprostol. When required, opioids or other analgesic options such as transcutaneous electrical nerve stimulation or paracervical blockade were offered. Pain was assessed during the abortion using a visual analogue scale (0–100 mm).

If the abortion was still ongoing after the first day, a repeated dose of mifepristone was given in the evening and a new round of misoprostol treatment was initiated the next morning.[7,19,20] After the second day with misoprostol, if abortion was still ongoing, individual treatment with options such as balloon or osmotic dilatation or amniotomy with intravenous oxytocin were initiated. The surgical option with dilatation and evacuation was only suggested after all other treatments had failed.

After fetal and placental abortion, the participants were observed in hospital for a minimum of 1 h to monitor vital signs and vaginal bleeding. Reasons for any stay beyond clinical routine were documented. Before discharge, the participants assessed maximal pain during the abortion, satisfaction with the treatment, and side-effects experienced via a questionnaire.

A follow-up by a designated study coordinator or investigator was done within 2–4 weeks after the abortion. The follow-up assessment was conducted by telephone or email and asked questions regarding any extra visits or complications after discharge, use of contraception, and satisfaction with the abortion treatment.

Outcomes

The primary outcome was the proportion of participants completing the medical abortion treatment as day-care patients. Day care was defined as any stay up to 9 h from time of admission to discharge from the inpatient unit. The primary outcome was assessed at discharge. Abortions were also classified as either complete (no additional treatment needed for fetal or placental abortion) or incomplete (vacuum aspiration performed due to retained placental tissue). The final outcome of the medical abortion was assessed at the follow-up.

Other secondary outcome measures included the difference in time spent in hospital in hours between groups, the difference in the induction to abortion interval (defined as the minutes from the first dose of misoprostol at home or at the hospital until fetal abortion), the completed abortion rate at 24 h, and the number of doses of misoprostol used.

The difference between the groups in satisfaction of the abortion procedure was measured on a scale from 1 to 5 (1 meaning very unsatisfied and 5 meaning very satisfied). Acceptability of the allocated treatment was measured with the question: if you were to choose, where would you prefer to take the first dose of misoprostol, with the options of home or hospital. Acceptability was also measured as the proportion of participants who needed to be admitted to hospital before the planned admission and for what reasons. Pain on predetermined timepoints, measured on a visual analogue scale, was compared between the groups.

In the safety assessment, any differences in the number of complications, surgical interventions, adverse events, and serious adverse events were noted. Serious adverse events included bleeding requiring blood transfusion, prolonged hospital stay, or surgical interventions other than vacuum aspiration. Another outcome was fetal abortion before admission to hospital.

Statistical analysis

Evidence from previous studies on proportions of medical abortion day-care procedures compared with overnight hospitals stays after 12 gestational weeks, or total duration of stay in-clinic, is sparse, which made power calculation difficult. We estimated that a difference of 10% in the primary outcome between the intervention and control group was clinically relevant, regardless of the proportion of individuals who received day care in the control group. We selected a power of 90% and a sample size of 784 (392 in each group) to demonstrate an increase in the primary outcome measure from 70% in the hospital group to 80% in the home group using a two-sided test with an α of 0·05. To compensate for loss to follow-up, the sample size was increased to 896.

All data were uploaded to the protected web-based REDCap available through the Karolinska Institute. The data were cleaned and variables created according to the study protocol and data analysis plan. The data were then exported for statistical analysis using SAS 9.4.

The intention-to-treat population was defined as all participants randomly assigned, except those who withdrew consent before abortion and those who did not have an abortion. The per-protocol population was defined as all participants in the intention-to-treat analysis except for those who crossed over to the other treatment group, and seven participants who were found in retrospect to not fulfil inclusion criteria but still were included. We performed the analysis of the primary outcome on the intention-to-treat population and on the

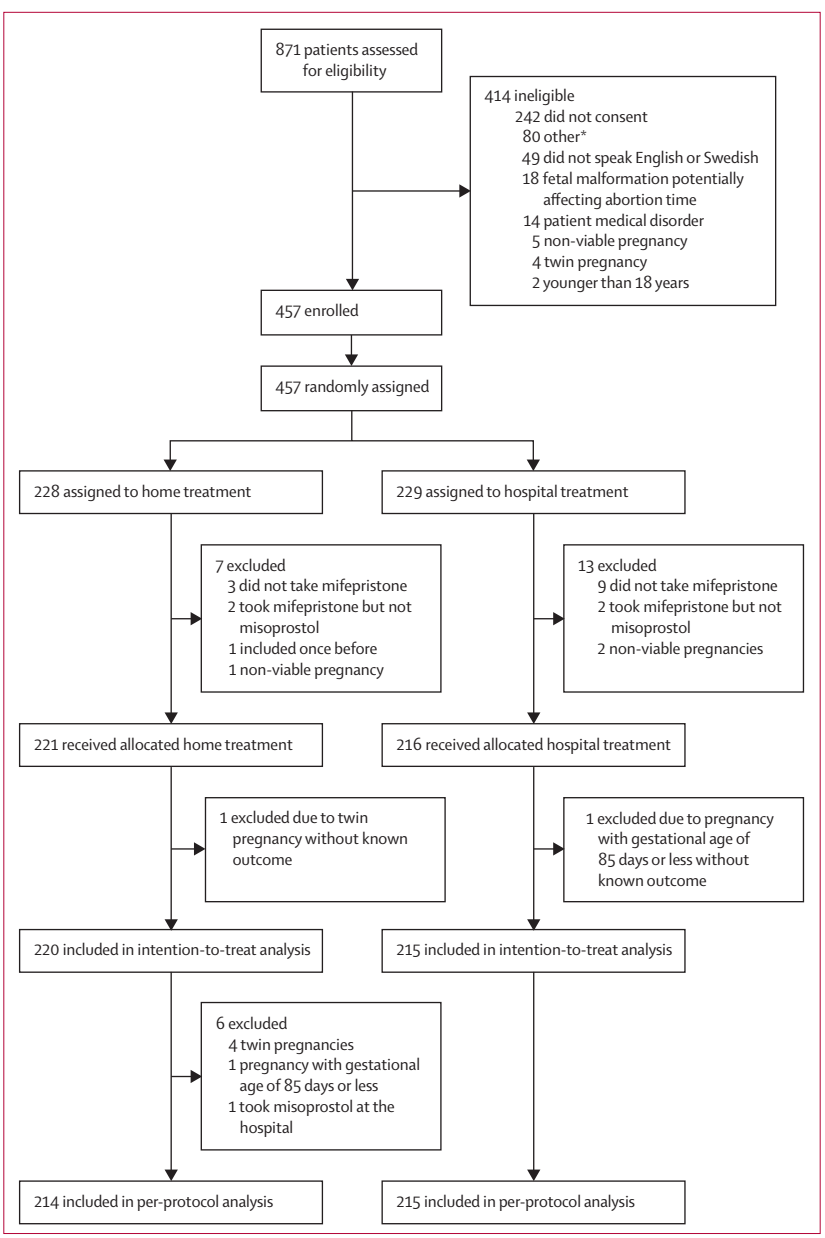

Figure 1: **Trial profile**
*Other included long distance to hospital, not a resident in Sweden, and family logistics.

per-protocol population as a complementary analysis to check the robustness of the result regarding protocol violators. All other analyses were done on the intention-to-treat population.

Background characteristics are presented as mean and range for continuous variables since the majority of the variables were non-normally distributed. Dichotomous data are presented as count and percentage. Primary and secondary outcomes are presented as differences in group means (95% CI) for continuous variables and as differences in group percentages (95% CI) for dichotomous variables. CIs were based on *t* tests for continuous variables and score statistic for dichotomous variables.[21] For comparison between groups we used Fisher's exact test for dichotomous variables, Mantel-Haenszel χ^2 linear-by-linear test for ordered categorical variables, and independent *t* test for continuous variables. All tests are two-sided with α levels of 0·05, meaning that a p value less than 0·05 was considered statistically significant. Secondary outcomes included information on safety of the intervention and are presented descriptively. Background characteristics that might have affected the primary outcome were analysed post hoc with relative risk (RR) including 95% CI and p value. Statistical analyses were performed using SAS 9.4.

All sites were monitored by an independent monitor during the study period. The monitoring plan included monitoring at each site at trial initiation and once more for sites that had more than 20 participants.

	Home group (n=220)	Hospital group (n=215)
Participant age (years)	31·5 (6·0)	31·2 (6·1)
BMI (kg/m²)*	21·1 (4·6)	24·9 (4·4)
Site		
Danderyd Hospital, Stockholm, Sweden	42 (19%)	40 (19%)
Karolinska University Hospital, Stockholm, Sweden	45 (21%)	46 (21%)
Stockholm South General Hospital, Stockholm, Sweden	53 (24%)	56 (26%)
Sahlgrenska University Hospital, Gothenburg, Sweden	67 (31%)	59 (27%)
Skåne University Hospital, Malmö, Sweden	10 (5%)	9 (4%)
Örebro University Hospital, Örebro, Sweden	3 (1%)	5 (2%)
Abortion indication		
Fetal	76 (35%)	64 (30%)
Social	137 (62%)	141 (66%)
Unknown	7 (3%)	10 (5%)
Previous births	100 (46%)	103 (48%)
One previous birth	62 (28%)	54 (25%)
Two or more previous births	58 (26%)	58 (30%)
0 previous vaginal births	121 (55%)	109 (51%)
1 previous vaginal birth	51 (23%)	55 (26%)
2 previous vaginal births	48 (22%)	51 (24%)
Previous induced abortions†		
0 previous induced abortions	122 (56%)	108 (51%)
1 previous induced abortion	57 (26%)	55 (26%)
2 or more previous induced abortions	40 (18%)	51 (24%)
Gestational days by ultrasound at time of mifepristone‡	107·2 (17·8)	107·3 (17·2)

Data are n (%) or mean (SD). *n=210 for the home group and 208 for the hospital group due to missing data. †n=219 for the home group and 214 for the hospital group due to missing data. ‡n=219 for the home group and 215 for the hospital group due to missing data.

Table 1: **Baseline characteristics of the intention-to-treat population**

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Jan 8, 2019, and Dec 21, 2022, 871 people were screened for eligibility. Of these individuals, 457 were randomly assigned, and 20 were subsequently excluded. Of 437 participants, 221 (51%) were assigned to home treatment and 216 (49%) to the hospital group (figure 1). Two pregnancies (one twin pregnancy in the home group and one pregnancy with a gestational age below 85 days in the hospital group) had no known outcome and were therefore excluded, resulting in 435 participants included in the intention-to-treat analysis. In the safety analysis all assigned participants were included except for those who did not take mifepristone and one participant who was included twice. The study was stopped prematurely, as advised by the Data and Safety Monitoring Board, at 51% of the planned sample size due to slow recruitment. However, with 435 participants, a power of 90% and a reference proportion of 45%, a minimum detectable difference of 16% in the

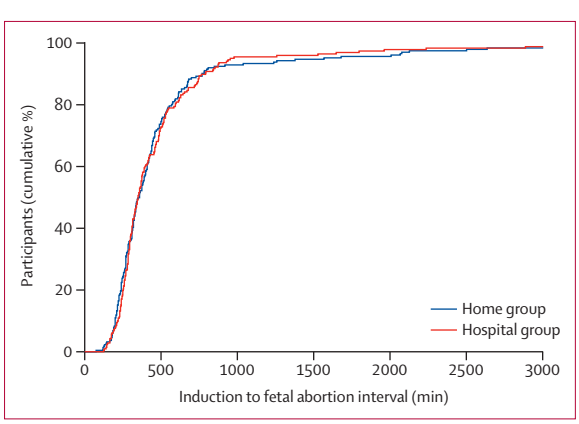

Figure 2: **Cumulative percentage of participants' induction to abortion time, by group**

experimental group would yield a significant result with an α of 5%.

Five participants aborted before admission and had no documented arrival or discharge times. Two participants in the home group aborted after mifepristone and misoprostol and three in the hospital group aborted after mifepristone only. They were all included in the intention-to-treat and per-protocol analyses for the primary outcome.

Six participants were excluded from the per-protocol analysis. One participant was randomly assigned to the home treatment group but started to bleed at home before taking misoprostol and therefore attended hospital early and administered misoprostol after arrival in hospital. Five participants were initially incorrectly included: four twin pregnancies and one with a gestational age outside the study protocol. In the per-protocol analysis, the home treatment group consisted of 214 (50%) participants and the hospital group 215 (50%) participants.

Baseline characteristics were similar between the groups (table 1). The participants had a mean age of 31·3 (SD 6·0) years at baseline with 203 (47%) of 435 being nulliparous, and 203 (47%) of 433 having had a previous induced abortion. The mean gestational age was 107·2 days (SD 17·5) at the time of mifepristone administration. In total, 278 (64%) of the 435 participants had an abortion due to social indication (ie, reasons that are not fetal or medical), 140 (32%) due to fetal anomalies, and 17 (4%) had unknown reasons. Participants were recruited at Sahlgrenska University Hospital, Gothenburg (126 [29%]); Stockholm South General Hospital, Stockholm (109 [25%]); Karolinska University Hospital, Stockholm (91 [21%]); Danderyd Hospital,

	Home group	Hospital group	Difference between group means (95% CI)	p value
Primary outcome				
Treated as day-care patient (<9 h)	156/220 (71%)	99/215 (46%)	24·9 (15·4 to 34·3)	<0·0001
Secondary outcomes				
Hours in clinic from admission to discharge	219; 10·3 (10·8)	211; 13·1 (12·5)	−2·8 (−5·0 to −0·6)	0·014
Induction to fetal abortion interval (min)	218; 494·1 (511·0)	211; 493·1 (553·5)	1·0 (−100·1 to 102·0)	0·98
Induction to placental abortion interval (min)	218; 525 (517)	211; 533 (563)	7·9 (−110·5 to 94·7)	0·88
Time between fetal and placental abortion (min)	219; 30·5 (46·7)	212; 39·7 (59·7)	−9·2 (−19·4 to 1·0)	0·077
Number of doses of misoprostol used*	218; 2·92 (1·71)	211; 2·93 (1·79)	−0·0 (−0·3 to 0·3)	0·92
1	19/220 (9%)	13/215 (6%)	..	..
2	88/220 (40%)	97/215 (46%)	..	..
3	67/220 (31%)	51/215 (24%)	..	..
4	22/220 (10%)	29/215 (14%)	..	..
5	11/220 (5%)	13/215 (6%)	..	..
6	2/220 (1%)	1/215 (1%)	..	..
7	1/220 (1%)	2/215 (1%)	..	..
≥8	8/220 (4%)	5/215 (2%)	..	..
Number of tablets of misoprostol used	218; 7·97 (3·83)	211; 8·02 (4·02)	−0·1 (−0·8 to 0·7)	0·89
Completed abortion rate at 24 h	198/219 (90%)	191/212 (90%)	−0·3% (−6·4 to 5·7)	1·00
Surgical interventions performed for retained placenta or bleeding at time of abortion	14/219 (6%)	18/212 (9%)	−2·1% (−7·5 to 3·3)	0·52
Pain on visual analogue scale at admission (mm)	193; 28·4 (26·0)	175; 5·83 (13·19)	22·5 (18·4 to 26·7)	<0·0001
Pain on visual analogue scale at abortion (mm)	164; 39·7 (35·1)	150; 39·0 (33·9)	0·6 (−7·0 to 8·3)	0·87
Satisfaction with abortion treatment	..	..	..	0·078
1 (very disappointed)	0/200	1/188 (1%)	..	..
2	0/200	3/188 (2%)	..	..
3	4/200 (2%)	4/188 (2%)	..	..
4	25/200 (13%)	28/188 (15%)	..	..
5 (very satisfied)	171/200 (86%)	152/188 (81%)	..	..
Preference of first misoprostol administration	..	..	..	<0·0001
Home	155/200 (78%)	96/188 (51%)	26·4% (16·7 to 36·1)	..
Hospital	45/200 (23%)	92/188 (49%)	−26·4% (−36·1 to −16·7)	..
Hospital admission before planned time of arrival	..	..	..	0·64
No	130/166 (78%)	130/172 (76%)	2·7% (−6·8 to 12·3)	..
Yes	36/166 (22%)	42/172 (24%)	−2·7% (−12·3 to 6·8)	..

Data are n/N (%) or n; mean (SD). *The loading dose equals four tablets of misoprostol (800 µg), and the following doses equal two tablets per dose.

Table 2: **Primary and secondary outcomes for the intention-to-treat population**

Stockholm (n=82 [19%]); Skåne University Hospital, Malmö (19 [4%]); and Örebro University Hospital, Örebro (8 [2%]). At screening 24 (6%) individuals were diagnosed with a genital infection.

For the primary outcome by intention-to-treat analysis, 156 (71%) of 220 participants in the home group completed the abortion treatment as day-care procedures, compared with 99 (46%) of 215 in the hospital group (difference 24·9%, 95% CI 15·4–34·3; p<0·0001). The corresponding proportions in the per-protocol population were 151 (71%) of 214 in the home group and 99 (46%) of 215 in the hospital group (difference 24·5%, 95% CI 15·0–34·0; p<0·0001).

Mean time spent in hospital was 10·3 h (SD 10·8) in the home treatment group and 13·1 h (SD 12·5) in the control group (–2·78, 95% CI –5·00 to –0·56; p=0·014).

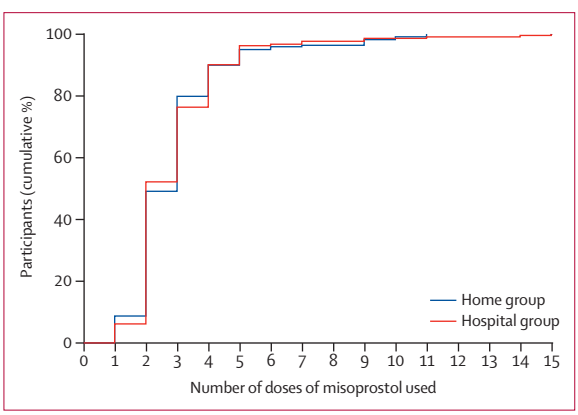

Figure 3: **Cumulative percentage of the number of misoprostol doses used per participant, by group**

See Online for appendix

	Home group (n=224)	Hospital group (n=220)
Number of adverse events	60	62
Number of participants who had an adverse event*	47 (21%)	50 (23%)
Bleeding >500 mL during the abortion and the inpatient stay	15 (7%)	16 (7%)
Bleeding after discharge from clinic	13 (6%)	14 (6%)
Allergic reaction	1 (<1%)	0
Infection after discharge from clinic	8 (4%)	12 (6%)
Fetal abortion before admission after mifepristone only	2 (1%)	5 (2%)
Fetal abortion before admission after mifepristone and first dose of misoprostol	2 (1%)	0
Retained placenta after discharge	12 (5%)	6 (3%)
Other adverse event	7 (3%)	9 (4%)

Data are n (%) unless otherwise specified. *12 adverse events were also assessed as serious adverse events, six in each group.

Table 3: **Adverse events, as self-reported by the participant and as assessed by the investigator**

There was no detectable difference between the groups regarding the induction to fetal abortion interval (figure 2), completed abortion rate at 24 h, or mean number of doses of misoprostol used until abortion (table 2; figure 3). RR was estimated for the effect of parity, gestational length, BMI, and maternal age on the primary outcome. Both a previous vaginal birth (RR 1·60, 1·36 to 1·89; p<0·0001) and a gestational age less than 126 days (RR 2·31, 1·49 to 3·58; p=0·0002) were associated with completing the abortion within the range of day care. There was no detectable association with BMI (RR 0·90, 0·70 to 1·15 for BMI ≥30 *vs* <30 km/m²; p=0·38) or maternal age (RR 1·27, 0·98 to 1·64 age <25 years *vs* ≥25 years; p=0·070).

The level of satisfaction was similar between the groups: 171 (86%) of 200 in the home group and 152 (81%) of 188 in the hospital group were very satisfied with their allocated treatment. More participants in the home group preferred their allocated administration compared with the hospital group (155 [78%] of 200 *vs* 92 [49%] of 188; difference 26·4, 95% CI 16·7–36·1; p<0·0001; table 2).

The mean pain score on the visual analogue scale at fetal abortion did not differ between the groups (39·7, SD 35·1 in the home group *vs* 39·0, SD 33·9 in the hospital group; difference 0·646, 95% CI –7·035 to 8·327; p=0·87). Nor did the number of times the participants required extra pain relief medication differ, with the majority requesting 0–2 times (154 [70%] of 219 in the home group *vs* 144 (68%) of 211 in the hospital group; difference 2·1, 95% CI –7·1 to 11·3; p=0·72). There was no difference between the groups in the proportion of participants who were admitted earlier than the planned hospital arrival time: 36 (22%) of 166 in the home group and 42 (24%) of 172 in the hospital group were admitted before the planned time (–2·7, 95% CI –12·3 to 6·8; p=0·64; table 2). There were no unexpected side-effects related to mifepristone or misoprostol (appendix p 1).

The types and number of adverse events did not differ between the groups; in the home group 47 (21%) of 224 individuals in the safety population had an adverse event from the time of mifepristone administration until follow-up, compared with 50 (23%) of 220 in the hospital group. Heavy vaginal bleeding (defined as ≥500 mL) during the hospital stay or after discharge was the most common adverse event (table 3). There was no difference in the proportion of individuals requiring surgical evacuation at the time of abortion.

In total, six (3%) of 224 participants in the home-treatment group and six (3%) of 220 in the hospital group had a serious adverse event (table 3, appendix p 1). Seven (2%) participants of the 444 individuals in the total safety population aborted before hospital admission, having only taken mifepristone (two in the home treatment group and five in the hospital group). Two (1%) participants in the home group aborted on the first dose of misoprostol before admission to hospital. All of these abortions occurred 24–48 h after

administrating mifepristone. For the two participants in the home group that aborted after misoprostol but before hospital admission, fetal abortion happened on their way to hospital (1 h 15 min and 2 h after misoprostol). Of those who aborted after mifepristone but before misoprostol there were two serious adverse events. None of the individuals who had fetal abortions after misoprostol but before hospital admission had a serious adverse event.

Discussion

This multicentre, randomised controlled trial provides clear evidence that administration of the first misoprostol dose at home increases the proportion of people who have a medical abortion after 12 weeks' gestation as day-care patients, compared with overnight care, without compromising safety and with greater acceptability compared with the current hospital-administration routine. The benefits were particularly evident for participants who had previously had children and those with a gestational age of up to 18 weeks. Although current guidelines limit self-management to 12 weeks' gestation, the results of this study mean that people can be allowed greater autonomy at later gestations also. A day-care procedure, in contrast to in-hospital care, means that access to abortion beyond 12 weeks can be expanded to outpatient clinics, possibly reducing waiting time, and resources can be saved both for the individual and health-care system.

Our results robustly support findings from earlier non-randomised studies on home administration of the first misoprostol dose for abortions after 12 gestational weeks. In a 2019 review,[15] pooled data from six clinical studies reported that abortion occurred within 8 h for 47% of people with pregnancies at 13–18 weeks. The authors proposed that implementing a day-care time limit of 10 h, with an additional 2 h of treatment before admission, could potentially work for 85% of cases in an outpatient unit.[15] In accordance with this conclusion, an observational study[11] administering the first misoprostol dose at home, followed by repeated doses at the day-care unit, resulted in nearly 90% of people being managed as day-care patients, with a median time to abortion of 7·2 h. However, this study did not define a time limit for day care.[11] In the present study, with a strict day-care definition set at less than 9 h, 71% of participants were successfully treated as day-care patients.

Furthermore, the results of this study reaffirm the safety of medical abortion after 12 gestational weeks, with no differences in adverse events observed between the study groups. Consistent with previous studies, we found that 1% of the participants required a blood transfusion due to heavy bleeding, and that 5% were treated for an infection related to the abortion, with 1% requiring intravenous antibiotics. These findings align with previous reviews which support the generalisability of the results.[7,15,20]

A concern regarding medical abortion is the potential risk of fetal abortion and bleeding before admission. This study found that more participants aborted following mifepristone and, among those who received the combined treatment and the first dose at home, two (1%) of 220 individuals had fetal abortion after misoprostol but before admission. This rate adds only marginally to the very small and well-known risk associated with the procedure.[11,15,20] Previous pooled analyses of data from six clinical studies on medical abortion after 12 gestational weeks reported a 1% abortion rate within 2 h after misoprostol initiation, but whether these abortions occurred before hospital admission was not specified.[15] Pregnant people should be adequately counselled about this very small but present risk.

Research on the acceptability of home administration of misoprostol for medical abortion after 12 gestational weeks is insufficient. In a prospective study of 230 people, a high satisfaction rate of 97% was reported for the abortion process when the abortion was conducted in an outpatient ward.[11] Our study also found high treatment satisfaction, with no difference between the groups. Participants who self-administered the first dose of misoprostol at home showed a significantly higher preference for their allocation compared with those starting misoprostol in hospital. This difference might be due to having to spend less time in hospital and the increased autonomy of self-management. A retrospective analysis of telemedicine services for abortion after 13 weeks suggested that medical abortion through telemedicine services might be a safe option until 15 weeks' gestation in settings where there is easy access to formal health systems. The need for treatment from formal health systems increased after 15 gestational weeks. Home priming might be an option past 15 weeks' gestation to introduce some level of self-management while maintaining safety and efficacy.[14]

Later gestational time increases the intensity and duration of pain during induced abortion, with around 70–80% of individuals requiring analgesia.[22,23] In this study, pain scores were similar between groups. The participants expressed satisfaction with their pain medication and reported the pain treatment as a positive experience. Previous research shows that people having abortions after 12 gestational weeks rate the pain experience as acceptable, despite reporting intense pain.[7,11,15,22] Further research is needed to optimise self-administered pain treatment for outpatient procedures.

To our knowledge, this is the first randomised controlled trial specifically studying home administration of misoprostol with day care as a specific outcome for medical abortions after 12 gestational weeks. The strength of this study lies in its large sample size, including people from six clinics and four different cities, who were seeking abortion due to both fetal and social indications. Additionally, high acceptability was established within this large sample.

A main limitation of the study is its premature termination. As advised by the Data and Safety Monitoring Board, the trial was terminated prematurely due to slow recruitment. Despite implementing various measures to expedite recruitment, such as adding new sites, it was observed that participants seldom declined participation due to the intervention itself, but rather due to feeling overwhelmed by the overall situation of needing an abortion after 12 gestational weeks. Despite the premature termination of the study, we were able to demonstrate statistically and clinically significant results regarding the primary outcome, which was possible because we had, based on earlier observational studies conducted, underestimated the magnitude of the difference between the two treatment options.

Since the COVID-19 pandemic, the demand for increasing access to induced abortion through telemedicine options has become more evident. Telemedicine for support in self-managed abortion after 12 gestational weeks has been previously described as acceptable.[25] The choice of taking the initial dose at home could benefit people who choose to have their first consultation via telemedicine. Mifepristone and the first dose of misoprostol could then be sent to the patient to be taken at home before admission. Future studies could further explore the telemedicine option for abortion beyond 12 gestational weeks.

This study demonstrates that home administration of the first misoprostol dose increases the proportion of people having a medical abortion after 12 weeks' gestation as a day-care treatment, with maintained safety and acceptability. The findings highlight the potential for developing day-care protocols with support from tertiary care levels, thereby expanding access, reducing waiting times, and saving time and costs, while increasing self-management and expanding choice. Home administration represents one measure that could enhance autonomy in abortion after 12 weeks' gestation, while also expanding access in regions with low admission possibilities.

Contributors

KG-D conceived the study and designed the study together with JRy, HH, and HK-K. KG-D obtained regular approvals and had overall responsibility for the study conduct. JRy, HH, HK-K, KG-D, JRo, KB, KZ, and PT recruited patients and collected the data, JRy, HH, HK-K, and KG-D analysed the data. All authors included enrolled participants into the study, had full access to all the study data, reviewed and edited the manuscript, and approved the final version of the manuscript. All authors accepted the responsibility to submit the paper for publication.

Declaration of interests

KG-D reports honoraria for ad hoc lectures or participation on advisory boards from Bayer, Organon/MSD, Gedeon Richter, Mithra, Natural Cycles, MedinCell, Ferring, Norgene, Exelgyn, Exeltis, Cirqle, RemovAid, and Obseva. HK-K reports honoraria for lectures, participation in courses, or acting as principal investigator in trials from AbbVie, Actavis, Bayer, Gedeon Richter Exeltis, Nordic Pharma, Natural Cycles, Mithra, Teva, Merck, Organon, Ferring, Consilient Health, Evolan, Natural Cycles, Pharmiva, Dynamic Code, Ellen, Estercare, Pharmiva, Gedea, Gesynta, Essity, Preglife, and Takeda. All other authors declare no competing interests.

Data sharing

All data that support the results of this study will be made available upon reasonable request to the corresponding author.

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