

Can midlevel health-care providers administer early medical abortion as safely and effectively as doctors? A randomised controlled equivalence trial in Nepal



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Summary

Background Medical abortion is under-used in developing countries. We assessed whether early first-trimester medical abortion provided by midlevel providers (government-trained, certified nurses and auxiliary nurse midwives) was as safe and effective as that provided by doctors in Nepal.

Methods This multicentre randomised controlled equivalence trial was done in five rural district hospitals in Nepal. Women were eligible for medical abortion if their pregnancy was of less than 9 weeks (63 days) and if they resided less than 90 min journey away from the study clinic. Women were ineligible if they had any contraindication to medical abortion. We used a computer-generated randomisation scheme stratified by study centre with a block size of six. Women were randomly assigned to a doctor or a midlevel provider for oral administration of 200 mg mifepristone followed by 800 µg misoprostol vaginally 2 days later, and followed up 10–14 days later. The primary endpoint was complete abortion without manual vacuum aspiration within 30 days of treatment. The study was not masked. Abortions were recorded as complete, incomplete, or failed (continuing pregnancy). Analyses for primary and secondary endpoints were by intention to treat, supplemented by per-protocol analysis of the primary endpoint. This trial is registered with ClinicalTrials.gov, NCT01186302.

Findings Of 1295 women screened, 535 were randomly assigned to a doctor and 542 to a midlevel provider. 514 and 518, respectively, were included in the analyses of the primary endpoint. Abortions were judged complete in 504 (97.3%) women assigned to midlevel providers and in 494 (96.1%) assigned to physicians. The risk difference for complete abortion was 1.24% (95% CI –0.53 to 3.02), which falls within the predefined equivalence range (–5% to 5%). Five cases (1%) were recorded as failed abortion in the doctor cohort and none in the midlevel provider cohort; the remaining cases were recorded as incomplete abortions. No serious complications were noted.

Interpretation The provision of medical abortion up to 9 weeks' gestation by midlevel providers and doctors was similar in safety and effectiveness. Where permitted by law, appropriately trained midlevel health-care providers can provide safe, low-technology medical abortion services for women independently from doctors.

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Introduction

Each year, 210 million women throughout the world become pregnant and nearly one in five chooses to terminate the pregnancy.¹ About 22 million pregnancies are terminated unsafely, and nearly all (98%) of these unsafe abortions take place in developing countries.² In many countries where abortion is not restricted by law, access to safe abortion is poor because of a shortage of skilled medical staff and surgical facilities. Early first-trimester medical abortion, by administration of an antiprogesterone (mifepristone) followed by a prostaglandin analogue (usually misoprostol), has provided millions of women worldwide with a safe, effective, and acceptable alternative to surgical abortion, which is usually done by manual vacuum aspiration. More than 20 years ago, medical abortion was recognised as likely to have particular application in those low-resource countries where skilled medical and surgical experience were in short supply.³ Most medical abortions do not

require the health-care infrastructure needed for manual vacuum aspiration, although back-up vacuum aspiration is needed for a small percentage of women.

Medical abortion remains under-used and inaccessible for many women in developing countries because almost all national regulations restrict its prescription and supervision to doctors.⁴ However, the safety record of medical abortion makes it amenable to provision by midlevel health-care providers (non-physician health-care workers such as midwives and nurses) in regions where doctors are unavailable. Training of midlevel health-care providers in medical abortion with appropriate referral systems would expand access to safe abortion services and would be consistent with the global trend towards task-shifting in places where doctors are costly and scarce.^{5,6} These providers have the potential to provide accessible, low-cost, and safe abortion services in developing countries in which abortion is not restricted by law. Results from a previous randomised trial⁷ in

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South Africa and Vietnam showed that midlevel providers can perform first-trimester abortions by vacuum aspiration as safely as doctors do. Nonetheless, questions remain about the standard of care and safety of medical abortion provided by midlevel health-care providers.^{4,8}

In Nepal, unsafe abortion is the third largest cause of maternal mortality.⁹ Surgical termination of pregnancy on request up to 12 completed weeks of gestation has been provided by certified doctors at registered government sites since 2004. Midlevel providers (staff nurses) were permitted to do surgical abortions up to 8 weeks' gestation in these sites. Since 2009, medical abortion has been available for pregnancies of less than 9 completed weeks of gestation (≤ 63 days). At the time of the study, the provision of medical abortion services by nurses was limited to government facilities in which a doctor was present; nurses did not provide medical abortion independently from physicians' oversight. The aim of this study was to assess whether early first trimester medical abortion provided by midlevel health-care providers was as safe and effective as that provided by doctors in Nepal.

Methods

Participants and study design

Women met eligibility criteria if their pregnancy was less than 9 weeks (≤ 63 days) of gestation according to date of last menstrual period and as estimated by bimanual pelvic examination, if they were older than 16 years, resided no more than 90 min journey from the study clinic, and were willing to be randomly assigned to a provider, to return to the clinic 10–14 days after the start of treatment, and to provide written informed consent. A woman was ineligible if she had any contraindication to medical abortion: previous allergic reaction to any of the drugs in the medical abortion regimen; known or suspected ectopic pregnancy or undiagnosed adnexal mass; inherited porphyria; chronic adrenal failure; long-term corticosteroid therapy; haemorrhagic disorder or anticoagulant therapy; or an intrauterine device that could not be removed before administration of mifepristone.

This study was a multicentre, randomised, controlled equivalence trial to assess outcomes of medical abortion services provided by midlevel health-care providers and doctors in settings with low health-care resources. Women seeking termination of early first-trimester pregnancy were randomly assigned to medical abortion managed by doctors or by midlevel health-care providers and followed up for completeness of abortion and any complications. Data were collected between April 15, 2009, and March 17, 2010, in five district hospitals in hilly (Bhaktapur, Baglung, Dhading) and lowland regions (Rupendehi, Chitwan) in Nepal. The feasibility of the study was tested on a sample of 53 women in a pilot phase from Jan 7, to Feb 26, 2009. District hospitals are small government health facilities equipped to provide

emergency obstetric services with less than 25 beds in rural and peri-urban areas. The hospitals had sufficient staff to establish a group of doctors and a group of midlevel health-care providers for implementation of the study. As a surrogate for how providers would manage in an independent setting and to reduce interactions between the two groups, each study site established separate waiting areas and examination rooms for midlevel health-care providers and doctors.

The study was developed, coordinated, and funded by the UNDP/UNFPA/WHO/World Bank Special Programme of Research Development and Research Training in Human Reproduction (HRP) at WHO, Geneva, Switzerland. A coordinating centre was established at the Centre for Research on Environment Health and Population Activities (CREHPA) in Kathmandu, Nepal. Reporting of the trial follows CONSORT reporting guidelines.^{10,11} The study was approved by the Scientific and Ethical Review Group of the Reproductive Health and Research Department (RHR) and the Research Ethics Review Committee of WHO in Geneva, Switzerland, the National Health Research Council (NHRC) of Nepal, and was endorsed by the Department of Health Services, Ministry of Health and Population, Nepal.

Randomisation and masking

We used a computer-generated randomisation scheme stratified by study centre with a block size of six generated at RHR, WHO in Geneva, Switzerland. Sealed opaque envelopes containing the random allocation were consecutively numbered and were opened and assigned sequentially to women by a research assistant once written informed consent had been obtained. The random allocation sequence was generated by use of SAS software (SAS Institute, Cary, NC, USA).

Procedures

Only providers trained in manual vacuum aspiration were eligible for medical abortion training. All 25 eligible providers in the study hospitals participated in the study. Midlevel health-care providers consisted of eight staff nurses (3-year degree) and three auxiliary nurse midwives (18 months of training). The doctors were six obstetricians and gynaecologists, three general practitioners, and five doctors (with a Bachelor of Medicine and Bachelor of Surgery Degree). Participating providers underwent a 3-day training course in medical abortion and were certified by the National Health Training Centre. Table 1 summarises the characteristics of the providers. Female research assistants with backgrounds in nursing, health, and social science were employed to take part in the study. They did screening interviews for study eligibility and for provisional eligibility for medical abortion, implemented randomisation procedures, and collected data at admission, before misoprostol insertion, and at scheduled and unscheduled follow-up visits. They tracked women who

did not attend scheduled visits. Providers reviewed the forms completed by the research assistants and had full responsibility for clinical management of each case; they made the final decision on eligibility for the study and for medical abortion after physical examination, and recorded clinical data on physical examinations, administration of the drug, case management, and abortion outcome.

Clinical procedures for medical abortion followed the Nepalese medical abortion protocol and no changes were made in the procedures for the purposes of the study. Ultrasonography is not part of the Nepalese protocol for medical abortion but machines were available and used at the providers' discretion; such use was recorded for the study. Oral antibiotics were not routinely prescribed, and pregnancy tests were not done. Use of pregnancy tests and ultrasound is not routine for medical abortions in Nepal. Testing and treatment for sexually transmitted infections followed national syndromic protocols. All women were offered 400 mg ibuprofen for pain relief. Assigned providers gave counselling, and undertook vaginal and cervical inspection and abdominal and pelvic bimanual examination to establish duration of gestation.

The regimen consisted of one 200 mg tablet of mifepristone and four 200 µg tablets of misoprostol packaged in a single blister pack (Medabon, Sun Pharmaceutical Industries Ltd, Mumbai, India). The assigned provider gave the woman the mifepristone tablet orally on day 1 and administered the misoprostol tablets vaginally on day 3. After misoprostol insertion, the woman was monitored in hospital for 3 h; her assigned provider examined her bimanually to assess the status of the abortion before she left the hospital. 10–14 days after the administration of mifepristone, the woman returned for a follow-up visit to the same assigned provider for a clinical assessment of the outcome of the abortion. Additional follow-up visits were scheduled with the assigned provider if needed, and women were encouraged to return at any time for unscheduled visits.

The primary endpoint was complete abortion without manual vacuum aspiration within 30 days of treatment. Incomplete abortion was defined as products of conception remaining in the uterus with continued bleeding, bulky uterus, and open cervix at examination, possibly necessitating surgical evacuation at the discretion of the provider or at the woman's request. Failed abortion (continuing pregnancy) was recorded when clinical examination indicated continuing symptoms of pregnancy and manual vacuum aspiration was needed to terminate the pregnancy.

The secondary endpoint measured case-management decisions by recording case-management discussions and referrals between providers to assess the extent to which each group provided medical abortion services independently. Serious adverse events (haemorrhage necessitating blood transfusion, conditions necessitating hospitalisation) were recorded. The completeness of the abortion and any complications were identified by an

interview with the woman and by clinical examination. Women were also asked whether they had visited any non-study hospital, clinic, or provider during the study.

Data management was organised locally by data entry personnel at CREHPA and at RHR, WHO in Geneva. Research assistants sent case record forms weekly to CREHPA and retained copies in their clinics. Data were entered at CREHPA by use of the OpenClinica clinical trial software, checked for accuracy, and corrected after consultation of clinical records and research assistants. Data were reviewed monthly by the Study Coordinator at WHO with further checking and review of clinic records as necessary.

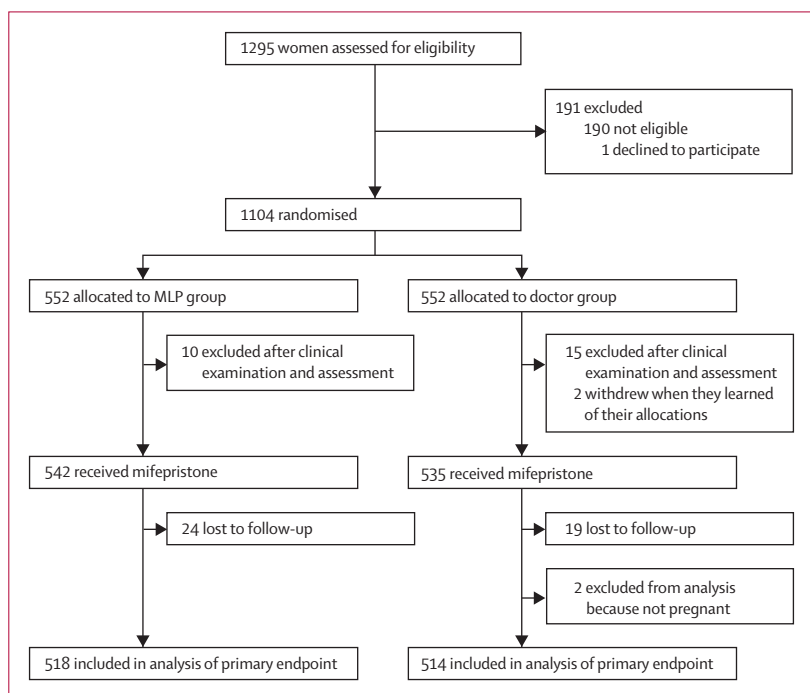


Figure 1: Trial profile

MLP=midlevel health-care providers.

	MLP (n=11)	Doctors (n=14)	Total (n=25)
Age (years)			
Mean (SD)	41.9 (6.8)	42.4 (11.0)	42.2 (9.2)
Median (IQR)	44.0 (36.0–46.0)	45.5 (30.0–52.0)	44.0 (34.0–50.0)
Range	30.0–50.0	27.0–56.0	27.0–56.0
Sex			
Female	11 (100%)	3 (21%)	14 (56%)
Male	0 (0%)	11 (79%)	11 (44%)
Years of professional medical practice			
Mean (SD)	21.8 (7.3)	14.1 (10.8)	17.5 (10.0)
Median (IQR)	25.0 (16.0–27.0)	15.0 (2.5–20.0)	18.0 (10.0–26.0)
Range	9.0–30.0	2.0–34.0	2.0–34.0

MLP=midlevel health-care providers. IQR=interquartile range.

Table 1: Background characteristics of providers

	MLP (n=542)	Doctors (n=535)	Total (n=1077)
Age (years)			
Mean (SD)	28.1 (6.0)	28.0 (5.8)	28.0 (5.9)
≤19	32 (6%)	28 (5%)	60 (6%)
20–29	296 (55%)	310 (58%)	606 (56%)
30–39	186 (34%)	170 (32%)	356 (33%)
≥40	28 (5%)	27 (5%)	55 (5%)
Marital status			
Married or cohabiting	530 (98%)	528 (99%)	1058 (98%)
Separated, divorced, widowed	3 (<1%)	1 (<1%)	4 (<1%)
Single	9 (2%)	6 (1%)	15 (1%)
Education			
Never attended or not completed primary school	169 (31%)	154 (29%)	323 (30%)
Primary school	103 (19%)	86 (16%)	189 (18%)
Lower secondary school	75 (14%)	70 (13%)	145 (13%)
Secondary school	114 (21%)	138 (26%)	252 (23%)
Higher than secondary school	81 (15%)	87 (16%)	168 (16%)
Height (cm)			
Mean (SD)	151.5 (5.4)	151.8 (5.3)	151.6 (5.4)
Weight (kg)			
Mean (SD)	48.8 (8.0)	49.5 (8.4)	49.2 (8.2)
Livebirths			
Mean (SD)	2.3 (1.1)	2.2 (1.1)	2.3 (1.1)
No data	51 (9%)	47 (9%)	98 (9%)
0	2 (<1%)	4 (<1%)	6 (<1%)
1–2	323 (60%)	322 (60%)	645 (60%)
3–8	166 (30%)	162 (30%)	328 (30%)
Previous induced surgical abortions			
Mean (SD)	0.2 (0.7)	0.3 (0.7)	0.2 (0.7)
No data	51 (9%)	47 (9%)	98 (9%)
0	365 (67%)	342 (64%)	707 (66%)
1	87 (16%)	108 (20%)	195 (18%)
2–5	39 (7%)	38 (7%)	77 (7%)

MLP=midlevel health-care providers.

Table 2: Characteristics of women undergoing early medical abortion by type of provider

Statistical analysis

This equivalence trial was designed to assess the similarity between two types of providers of medical abortion with a potential cluster effect on the primary endpoint among service providers. The margin of equivalence, Δ, was 5% and the range –5% to 5% was predefined as an acceptable range of completion rates between the two types of providers. The margin was based on clinically and statistically important differences as well as ethical criteria, cost, and feasibility.^{12,13}

The sample size of 1086 women was calculated to be sufficient (with a two-sided 95% CI and 80% power) to establish equivalence.¹⁴ The sample size calculation allowed for 10% loss to follow-up and for a potential cluster effect among service providers with an estimated intraclass correlation coefficient of 0.001 from a previous study.⁷ The cluster effect could occur because some service providers might provide better

medical abortion services than others due to individual variations in, for example, years of medical practice or individual aptitude.

To assess the equivalence between midlevel health-care providers and doctors, the risk difference between the two provider types together with their 95% CI was derived by use of a generalised estimating equation (GEE) model with treatment as the fixed effect and service provider as a random effect as implemented in the PROC GENMOD procedure of SAS version 9.2 (SAS Institute, Cary, NC, USA). The CI gives an interval estimate of the true population difference Δ. If the CI of the risk difference between the two groups falls within the predetermined margin of equivalence (–5% to 5%), the two types of providers can be considered equivalent. In addition, covariate-adjusted analyses were done on six prespecified baseline characteristics of participants (centre, age, duration of gestation, parity, number of previous induced abortions, and body-mass index). The number and percentage of women with each side-effect from the medical abortion were calculated and compared by use of a χ² test. The analyses for the primary and secondary endpoints were on an intention-to-treat basis, supplemented by per-protocol analysis of the primary endpoint.

This trial is registered with ClinicalTrials.gov, NCT01186302.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study. The corresponding author had the final responsibility for the decision to submit for publication.

Results

Of 1295 women screened for eligibility, 190 were ineligible for medical, geographical, or follow-up scheduling reasons, and one woman declined to take part in the study (figure 1). 1104 women were randomised. After clinical examination, in the midlevel health-care providers' group ten women were excluded: in eight, the duration of gestation was longer than 9 weeks; one had signs of ectopic or adnexal mass; and one was diagnosed with cervical polyps. In the doctors' group 15 women were excluded: in 12, the duration of gestation was longer than 9 weeks; one had signs of ectopic or adnexal mass; one was not pregnant; and one had a miscarriage before receiving any drugs. Additionally, two women withdrew from the study before physical examination when they were told of their group allocation.

Loss to follow-up of women receiving treatment was 24 of 542 (4%) in the midlevel health-care providers' group and 19 of 535 (4%) in the doctors' group. Women lost to follow-up were, on average, less educated than those

followed up. Two women in the doctors' group were excluded from the analysis because at follow-up they were shown not to have been pregnant: one was a long-time user of a 3-monthly injectable contraceptive, and the other one had had a manual vacuum aspiration 37 days before.

Participating doctors had, on average, fewer years of professional medical practice than midlevel health-care providers and a higher proportion were men (table 1). Baseline characteristics of women included in the analysis were similar by type of provider (table 2). On average, women were 28 years old and married with two children. More than 25% had had an induced abortion previously and about 30% had never attended school or had not completed primary school. Overall mean duration of gestation was 6.6 weeks as reported by the date of the last menstrual period and 6.8 weeks by clinical examination and did not differ by type of provider (table 3). In women reporting the date of their last menstrual period (84%), there was a high level of congruence between duration of gestation based on that date and that based on clinical examination. No important difference was noted between the two types of provider (data not shown). Doctors were more likely to use ultrasonography (23 cases) than were midlevel health-care providers (two cases).

The clinical outcomes of medical abortion from intention-to-treat and per-protocol analyses were similar by type of provider (table 4). For women with a recorded outcome, the overall intention-to-treat complete abortion rate was 96.7%, the incomplete abortion rate 2.8%, and continuing pregnancy rate 0.5% at 30 days from start of treatment. The risk difference for complete abortion rates between midlevel providers and doctors was 1.24% (95% CI -0.53 to 3.02), and the estimated 95% CI was well within the equivalence range for both intention-to-treat and per-protocol analyses (table 4, figure 2). Therefore, equivalence between midlevel health-care workers and doctors can be established for the primary endpoint. For the covariate-adjusted analyses, the GEE model did not converge when all six covariates were entered simultaneously. With a stepwise approach, only woman's age and duration of gestation produced converging GEE models for both the intention-to-treat and per-protocol populations (table 4, figure 2). The webappendix shows the rate of complete abortion by gestational age (see webappendix p 1).

All 34 incomplete and continuing pregnancies were terminated by manual vacuum aspiration by the assigned provider. No serious adverse events were recorded. Women reported typical side-effects such as nausea, vomiting, diarrhoea, abdominal pain, chills, and fever with no difference by type of provider (data not shown). 12 cases with midlevel health-care providers and 13 cases with physicians were discussed with another provider or referred (data not shown). Midlevel health-care providers reported discussing less than 2% of cases with doctors and referred less than 1% of cases to a doctor, a pattern similar to that of doctors.

	MLP (n=542)	Doctors (n=535)	Total (n=1077)
Number of women reporting LMP	456 (84%)	450 (84%)	906 (84%)
Duration of gestation from LMP (weeks)			
Mean (SD)	6.6 (1.1)	6.6 (1.1)	6.6 (1.1)
Median (IQR)	6.4 (5.9-7.4)	6.4 (5.7-7.4)	6.4 (5.7-7.4)
Range	4.0-9.1	4.3-9.0	4.0-9.1
Number of women clinically examined	542 (100%)	535 (100%)	1077 (100%)
Duration of gestation by clinical examination (weeks)			
Mean (SD)	6.9 (1.0)	6.6 (1.0)	6.8 (1.0)
Median (IQR)	7.0 (6.0-8.0)	6.0 (6.0-8.0)	6.0 (6.0-8.0)
Range	5.0-9.0	5.0-9.0	5.0-9.0
Ultrasonography used to assess duration of gestation	2 (0.4%)	23 (4.3%)	25 (2.3%)

MLP=midlevel health-care providers. LMP=date of last menstrual period. IQR=interquartile range.

Table 3: Assessment of duration of gestation by provider

	MLP	Doctors	Risk difference for the primary endpoint* (95% CI)	Risk difference for the primary endpoint-adjusted analysis† (95% CI)
ITT analysis				
Number of women	518	514
Complete abortion	504 (97.3%)	494 (96.1%)	1.24% (-0.53% to 3.02%)	1.49% (-0.17% to 3.14%)
Incomplete abortion	14 (2.7%)	15 (2.9%)
Continuing pregnancy	0	5 (1.0%)
PP analysis				
Number of women	504	472
Complete abortion	490 (97.2%)	455 (96.4%)	0.89% (-1.11% to 2.88%)	1.12% (-0.70% to 2.93%)
Incomplete abortion	14 (2.8%)	12 (2.5%)
Continuing pregnancy	0	5 (1.1%)

MLP=midlevel health-care providers. ITT=intention to treat. PP=per protocol. *Estimated from a generalised estimating equation model with treatment as the fixed effect and service provider as a random effect. †Adjusted for woman's age and duration of gestation.

Table 4: Outcomes of medical abortion by type of provider

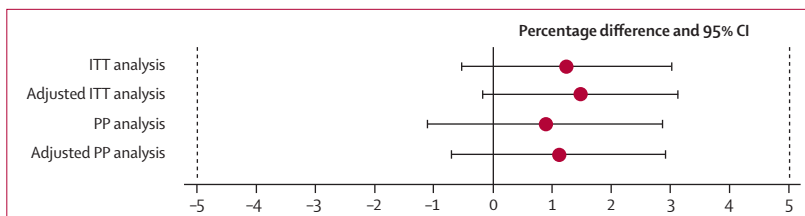


Figure 2: Percentage difference and 95% CI of complete abortion by midlevel health-care providers compared with doctors

ITT=intention to treat. PP=per protocol.

Discussion

This randomised controlled equivalence trial assessed clinical outcomes, safety, and case management of early medical abortion provided by nurses and auxiliary nurse midwives compared with doctors. These findings provide evidence that midlevel providers with previous training in abortion care can, after additional training in medical abortion, independently administer medical abortion

See Online for webappendix

Panel: Research in context**Systematic review**

When developing the study protocol, we searched PubMed and Popline for relevant articles with the keywords “abortion”, “medical abortion”, “nurse-midwives”, “midwife”, “mid-level provider”, “nurse practitioner”, “non-physician clinician”, and “physician assistant”. Given the paucity of research in this area, we reviewed all studies and reports about midlevel providers of medical abortion and manual vacuum aspiration in developed and developing countries.

Interpretation

Findings from our study showed that midlevel providers of medical abortion can administer medical abortion as safely as doctors in a low-resource setting in which ultrasonography and pregnancy tests are rarely used. These results build on one previous randomised controlled trial of midlevel providers and manual vacuum aspiration that showed equivalence in safety between midlevel providers and doctors in developing countries. Several observational studies lend support to the competency of midlevel health-care providers as providers of medical abortion. Taken together, these studies show that appropriately trained and government certified midlevel providers of both medical abortion and manual vacuum aspiration can provide safe and effective abortion services independently from physicians.

safely and effectively in a low-resource setting where pregnancy tests, antibiotics, and ultrasonography are available but rarely used. These equivalence results are robust irrespective of the analysis population.

Midlevel health-care providers have been trained in medical abortion in several countries but assessments have been limited to those of in-house training. The role of these care providers in the introduction of medical abortion has been examined in India,¹⁵ Vietnam,¹⁶ Nepal,⁸ and the USA.^{17,18} Two papers reviewed the evidence on midlevel health-care providers of abortion but did not specifically address safety or acceptability by doctors and these providers (panel).^{4,19}

The overall complete abortion rate of 96.7% was comparable with rates in other studies that used the same regimen (93.5% to 97.7%).^{20–22} Previous studies of medical abortion in Nepal showed completion rates of 91.3%²³ with oral administration of 400 µg misoprostol and 96%²⁴ with vaginal administration of 800 µg misoprostol. In gestations of up to 63 days' amenorrhoea, the rate of continuation of pregnancies with the regimen used here was less than 1%,²⁵ in line with our results. The numbers of incomplete abortions for both types of providers were similar, 14 cases for midlevel health-care providers and 15 cases for doctors, with no difference in propensity to evacuate cases of incomplete abortion that might have become complete over time.

Despite its availability, ultrasonography was rarely used by any provider to assess duration of gestation or completeness of the abortion at follow-up. This study supports guidelines that emphasise the safety of medical abortion without the routine use of ultrasonography before or after abortion.²⁶ The study was designed to maximise the generalisability of the findings for the public

sector in Nepal and other developing countries. It was conducted in public-sector district hospitals and all 25 full-time public-sector providers received the same government-certified training in medical abortion. The clinical procedures for medical abortion did not deviate from the national protocol. The sociodemographic characteristics of women included in our study were very similar to those of a national sample of women seeking induced abortion in Nepal done in 2006.²⁷

Some issues might affect the external validity and applicability of the findings. In this study, midlevel health-care providers had more years of professional experience than did the doctors. In ad-hoc multivariate analyses, years of professional experience did not have any effect on equivalence results (data not shown). Although the socioeconomic and demographic characteristics of study participants are typical of women seeking abortions throughout Nepal, they might not be representative of women living in underserved rural areas of this country. District hospitals are also not representative of the small health facilities located in remote areas of Nepal, which are staffed exclusively by midlevel health-care providers.

A limitation of the findings is that the study was part of the first wave of medical abortion training in Nepal, and the initial training curriculum has since been revised. Future medical abortion outcomes might differ as the national protocol is adapted to follow women's needs and new regimens. A further limitation of the study is that although separate waiting and examination rooms for the two groups were set up for the duration of the study, both types of providers worked in the same hospital and in the same environment. Although this controlled environment optimised comparison, it might have led to a convergence of outcomes that would not have happened if the women had been assigned to providers at different clinics.

The Nepalese medical abortion protocol at the time of the study was rather burdensome with three clinic visits and physical examinations. Testing home use or omitting the follow-up visit are important topics for future research of medical abortion in Nepal. However, 96.3% of women reported that they would prefer having a medical abortion at the clinic and 3.7% at home, which suggests that visits to the clinic were acceptable for these women.

In conclusion, nurses and auxiliary nurse midwives could have an important role in making life-saving abortion methods accessible to women living in remote areas of developing countries, as long as timely back-up manual vacuum aspiration is accessible if providers themselves are not trained in this technique. In areas with shortages of physicians, decentralisation of medical abortion services to include government-certified midlevel health-care providers who work independently from doctors would greatly increase women's access to safe abortion services. Appropriately trained providers can administer safe, low-technology medical abortion services for women who might otherwise turn to unsafe abortion, exposing themselves to the risks of disabilities and death.

Contributors

IKW developed the protocol and study design, directed the study and the data analysis, and was the lead author of the report. DW was the statistician for the study and participated in the study design, data analysis, data interpretation, and writing of the report. NTMH was the study coordinator and participated in data collection, management, and analysis, and writing of the report. KT was the principal investigator and was responsible for the overall supervision of the trial and participated in the implementation of study, data analysis, and the writing of the report. AT was responsible for the coordination and implementation of the study in Nepal and participated in the data management, data analysis, and the writing of the report. IS participated in the development of the protocol, data analysis, and the writing of the report. DTB and OM participated in the development of the protocol and the writing of the report. All authors had access to the data, commented on subsequent drafts, and approved the final submitted version.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

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References

- Singh S, Wulf D, Hussain R, Bankole A, Sedgh G. Abortion worldwide: a decade of uneven progress. New York: Guttmacher Institute, 2009.
- WHO. Unsafe abortion: global and regional estimates of the incidence of unsafe abortion and associated mortality in 2008. 6th edn. Geneva: World Health Organization, 2011 (in press).
- Rodger MW, Baird DT. Induction of therapeutic abortion in early pregnancy with mifepristone in combination with prostaglandin pessary. *Lancet* 1987; **330**: 1415–18.
- Yarnall J, Swica Y, Winikoff B. Non-physician clinicians can safely provide first trimester medical abortion. *Reprod Health Matters* 2009; **17**: 61–69.
- McPake B, Mensah K. Task shifting in health care in resource-poor countries. *Lancet* 2008; **372**: 870–71.
- WHO. Task shifting: global recommendations and guidelines. Geneva: World Health Organization, 2007.
- Warriner IK, Meirik O, Hoffman M, et al. Rates of complication in first-trimester manual vacuum aspiration abortion done by doctors and mid-level providers in South Africa and Vietnam: a randomised controlled equivalence trial. *Lancet* 2006; **368**: 1965–72.
- Tamang A, Tamang J. Availability and acceptability of medical abortion in Nepal: health care providers' perspectives. *Reprod Health Matters* 2005; **13**: 110–19.
- Pradhan A, Suvedi BK, Barnett S, et al. Nepal maternal mortality and morbidity study, 2008/2009. Kathmandu, Nepal: Family Health Division, Department of Health Services, Government of Nepal, 2010.
- Moher D, Hopewell S, Schulz KF, et al, for the CONSORT Group. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trial. *BMJ* 2010; **340**: c869.
- Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; **340**: c332.
- von Hertzen H, Piaggio G, My Huong NT, et al, for the WHO Research Group on Postovulatory Methods of Fertility Regulation. Efficacy of two intervals and two routes of administration of misoprostol for termination of early pregnancy: a randomised controlled equivalence trial. *Lancet* 2007; **369**: 1938–46.
- Wiens BL. Choosing an equivalence limit for noninferiority or equivalence studies. *Control Clin Trials* 2002; **23**: 2–14.
- Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ, for the CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *JAMA* 2006; **295**: 1172–74.
- Iyengar SD. Introducing medical abortion within the primary health system: comparison with other health interventions and commodities. *Reprod Health Matters* 2005; **13**: 13–19.
- Ganatra B, Bygdeman M, Thuy PB, Vinh NG, Loi VM. From research to reality: the challenges of introducing medical abortion into service delivery in Vietnam. *Reprod Health Matters* 2004; **12** (24 suppl): 105–13.
- Samora JB, Leslie N. The role of advanced practice clinicians in the availability of abortion services in the United States. *J Obstet Gynecol Neonatal Nurs* 2007; **36**: 471–76.
- Joffe C, Yanow S. Advanced practice clinicians as abortion providers: current developments in the United States. *Reprod Health Matters* 2004; **12** (24 suppl): 198–206.
- Berer M. Provision of abortion by mid-level providers: international policy, practice and perspectives. *Bull World Health Organ* 2009; **87**: 58–63.
- Ashok PW, Templeton A, Wagaarachchi PT, Flett GM. Factors affecting the outcome of early medical abortion: a review of 4132 consecutive cases. *BJOG* 2002; **109**: 1281–89.
- Tang OS, Chan CC, Ng EH, Lee SW, Ho PC. A prospective, randomized, placebo-controlled trial on the use of mifepristone with sublingual or vaginal misoprostol for medical abortions of less than 9 weeks gestation. *Human Reprod* 2003; **18**: 2315–18.
- von Hertzen H, Honkanen H, Piaggio G, et al. WHO multinational study of three misoprostol regimens after mifepristone for early medical abortion. I: Efficacy. *BJOG* 2003; **110**: 808–18.
- Karki C, Pokharel H, Kushwaha A, Manandhar D, Bracken H, Winikoff B. Acceptability and feasibility of medical abortion in Nepal. *Int J Gynaecol Obstet* 2009; **106**: 39–42.
- Medical Abortion Task Force. Medical abortion in six pilot districts of Nepal: implementation results (January–June 2009). Nepal: FHD/DoHS/Ministry of Health and Population, 2009.
- Baird DT. Medical abortion in the first trimester. *Best Pract Res Clin Obstet Gynaecol* 2002; **16**: 221–36.
- WHO. Safe abortion: technical and policy guidance for health systems. Geneva: World Health Organization, 2003.
- FHD/Ipas/CREHPA. Summary Report: Nepal Comprehensive Abortion Care (CAC) National Facility-based Abortion Study 2006. Kathmandu, Nepal: FHD/Ipas/CREHPA, 2006.