PREVENTION OF POSTPARTUM HEMORRHAGE STUDY: WEST JAVA, INDONESIA

By Mohammad Zulkarnain

WORD COUNT 14519
TIME SUBMITTED 11-JAN-2020 04:14PM
PAPER ID 53710893

PREVENTION OF POSTPARTUM HEMORRHAGE STUDY: WEST JAVA, INDONESIA

INTRODUCTION

Background

Reducing maternal mortality in Indonesia—currently estimated to be 340 deaths per 100,000 live births—has been a priority for Indonesia's Ministry of Health (MOH) since 1991. Between 4.5 and 5 million women give birth in Indonesia each year. Only 66% of women in Indonesia and 48% of women in West Java give birth with a skilled provider (Statistics Indonesia and ORC Macro 2003). Approximately 7% of all live births are accompanied by self-reported excessive postpartum bleeding, or postpartum hemorrhage (PPH), and PPH is estimated to cause almost half of the 18,000 maternal deaths in Indonesia each year (Central Bureau of Statistics 1991; Central Bureau of Statistics et al. 1998). The percentage of maternal deaths due to PPH in Indonesia (45%) is much higher than in other parts of the world, such as sub-Saharan and West Africa (25% and 27%, respectively).

PPH can lead to death within 2 hours if it is not managed immediately. Because it is impossible to predict who will get PPH, all women who give birth should have present a skilled provider who can perform active management of the third stage of labor. This involves giving an injection of oxytocin (10 units intramuscularly) immediately after the birth of the baby, using controlled cord traction to facilitate delivery of the placenta, and massaging the uterus to keep it contracted after delivery of the placenta. Giving women oxytocin immediately after childbirth is probably the single most important intervention used to prevent PPH (Goldberg, Greenberg, and Darney 2001). Women given oxytocin lose less blood, decreasing the incidence of PPH and anemia. A woman who receives oxytocin delivers her placenta faster and is less likely to require manual removal of her placenta, a painful procedure that increases the risk of infection. Other uterotonic drugs, such as prostaglandins, are effective in controlling hemorrhage but most have the disadvantages of being more expensive and having increased side effects such as diarrhea, vomiting, and abdominal pain. One notable exception is misoprostol (Cytotec®, Searle AG; Misoprost®, Cipla Inc.), a prostaglandin E_1 analogue that is available in tablet form. Although first developed for treatment of stomach ulcers, misoprostol has become an important drug in obstetric practice due to its ability to make the uterus contract and become firm (Goldberg, Greenberg, and Darney 2001). Its action is similar to oxytocin, but its advantage over oxytocin—which can be given only by injection—is that it is stable at room temperature and can be given orally, vaginally, or rectally. Furthermore, misoprostol is relatively inexpensive and does not require administration by a skilled provider.

Studies have shown that misoprostol is effective and very safe for preventing PPH. El-Refaey et al. (1997) showed that misoprostol given immediately after birth of the baby resulted in significantly lower rates of PPH than when no uterotonic drug was used. This finding has been confirmed by several other studies (as reviewed by Broekhuizen 2000).

Compared to oxytocin, misoprostol is slightly less effective in preventing PPH. A meta-analysis of several studies found that 18% of women would have PPH if no uterotonic drug were given, 3.6% would have PPH if misoprostol were used, and 2.7% would have PPH if oxytocin were used (Prendiville et al. 1988). In hospital settings or when proper storage conditions and safe injection can be guaranteed, oxytocin is preferable to misoprostol for active management of the third stage of labor (Gülmezoglu et al. 2001; Hogerzeil, Walker, and De Goeje 1993). In other circumstances, such

as home birth without a skilled provider, misoprostol should be considered. Prabhakar, Duvekot, and Dattwyl (2001) concluded in their review that when oxytocin is not available, misoprostol use to prevent PPH should be considered a strategy. A recommendation (i.e., good and consistent evidence to support the recommendation), and the U.S. Pharmacopeia Expert Advisory Panel recommended that prevention of PPH be considered an "accepted" indication in the U.S. Drug Information Monograph on misoprostol (Kapczynski 2001).

Misoprostol taken immediately after the birth of the baby is safe but is associated with some minor side effects, such as shivering, nausea, and headache. Shivering typically begins 5 to 10 minutes after taking misoprostol but usually lasts no more than 30 minutes and requires no additional therapy. El Refaey et al. (2000) and Ng et al. (2001) found shivering in 72% and 33%, respectively, of women given misoprostol. However, El Refaey et al. (2000) observed shivering in 3% of women given oxytocin and in 20% of women who were not given a uterotonic drug. Gundogmus et al. (1999) documented that the side effects are dose dependent, and determined that the optimal dose of misoprostol for postpartum use is 600 µg.

The U.S. Agency for International Development (USAID) is seen by the Indonesian Government as a critical partner in providing technical assistance to reduce maternal mortality and morbidity through programs such as JHPIEGO's Maternal and Neonatal Health (MNH) Program. Indonesia MNH Program goals include increasing maternal and neonatal survival by expanding interventions to prevent and manage complications of pregnancy and childbirth and encouraging pregnant women to seek care from skilled providers during pregnancy, childbirth, and the postpartum period.

The MNH/Indonesia Program began work in Indonesia in November 1999 in partnership with the MOH, Ministry for Women's Empowerment (Menneg PP), National Family Planning Coordinating Board (BKKBN), Indonesia Association of Obstetricians and Gynecologists (*Perkumpulan Obstetri dan Ginekologi*, POGI), Indonesian Midwifery Association (IBI), National Clinical Training Network (NCTN), local nongovernmental organizations (NGOs), and donor partners such as the World Health Organization (WHO) and USAID. The MNH/Indonesia Program has supported several initiatives to reduce PPH through promoting the practice of active management of the third stage of labor as part of a national effort to improve basic childbirth skills, as well as to support better community participation through birth preparedness and complication readiness (BP/CR).

In 2001, the MNH/Indonesia Program began collaborating with the MOH through a national steering committee, POGI, and the WHO Collaborating Center for Perinatal, Maternal, and Child Care (WHO CC) in Bandung to conduct the Prevention of Postpartum Hemorrhage Study to investigate the prevention of PPH using misoprostol at home births.

Study Objectives

This study offered an intervention designed to lower the incidence of PPH in rural Indonesia where a large proportion of births are not attended by skilled providers. The purpose of the study was to demonstrate the safety, acceptability, feasibility, and program effectiveness (SAFE) of community-based distribution of misoprostol for prevention of PPH, as addressed by the following questions:

- Can community health workers (*kader*) safely and effectively distribute misoprostol and provide information to women and their social supports on correct timing and use of misoprostol after home births?

- Can women giving birth at home, unaided by skilled providers, accept and correctly take misoprostol immediately after the birth of the baby, based on education provided during the antenatal period?
- How acceptable is misoprostol to women receiving it?
- How effective is misoprostol when controlled by the woman?

METHODS

The study protocol, which called for a non-random experimental design, was approved through the Western Institutional Review Board (WIRB) in the US, on behalf of JHPIEGO as an affiliate of The Johns Hopkins University (JHU) and partner of the MNH Program; the University of Indonesia Institutional Ethical Review Board; and the Indonesian MOH. The study was also reviewed and authorized by POGI.

Timeline

The study review and authorization timeline is shown in **Table 1**. The review process included national-level recognition of the serious problem of PPH by the MOH and the need for appropriate socialization among regional- and district-level health departments and community orientation to support the use of misoprostol.

The implementation of the PPH Study had a 12-month timeline (**Table 2**) and occurred in three phases: materials development and field team training; participant enrollment, distribution of misoprostol, and data collection; and data analysis and dissemination and presentation of results.

PPH Study training modules were developed by MNH/Bandung field staff based on the study protocol and implementation strategy. The orientation and training of the field team was accomplished by the study manager, field epidemiologist, lead field supervisors, three trainer midwives, and two obstetrician physicians. Initially, the eight field supervisors were trained 10–12 September 2002. The field supervisors then assisted with the three training sessions, conducted from 16 September to 5 October 2002, to train the midwives, postpartum interviewers, and community volunteers. The field supervisors, midwives, and postpartum interviewers were given a 3-day orientation and training session. For the community volunteers, the training session was extended to 5 days to allow for additional role play and practice with the counseling material. An integral part of the training for field implementation teams was strengthening their skills in facilitation, counseling, and interpersonal communication.

Table 1. PPH Study Review and Authorization Timeline (January to August 2002)

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug
Administrative Authorization								
National Endorsement								
Governmental Dept. Authorization								
Steering Committee Cooperative Agreement								
Socialization								
Provincial-Level								
District-Level								
Community-Level								

The study findings were presented to the Prevention of PPH National Steering Committee in June 2003. The results were presented during formal project completion meetings including provincial-, district-, and community-level officials in June 2003, and at the national level at the annual POGI conference in July 2003 (**Table 2**).

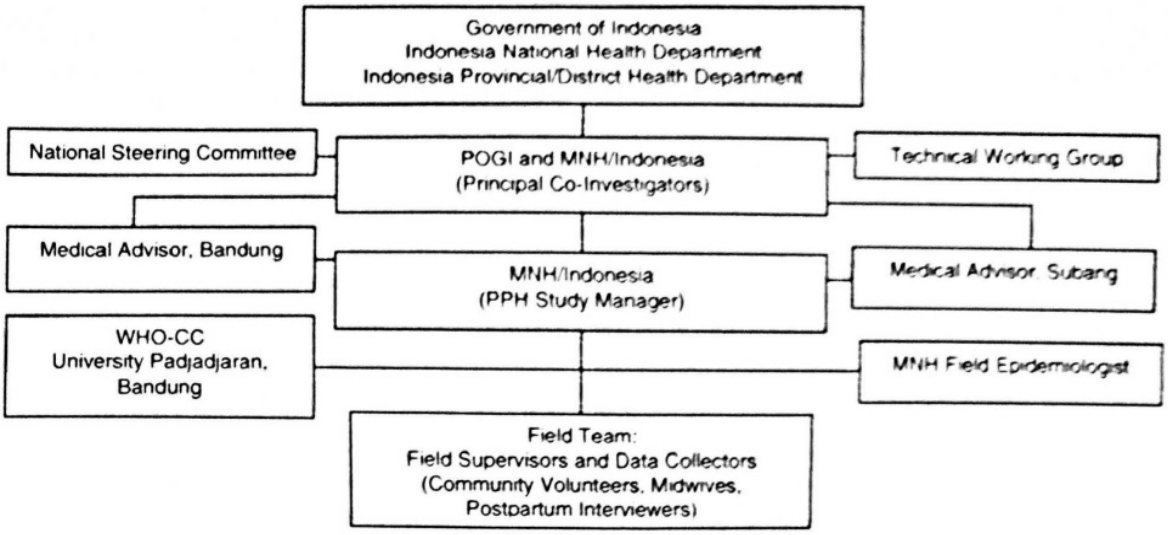
Table 2. PPH Study Implementation Timeline (August 2002 to July 2003)

	2002					2003						
	Aug	**Sep**	**Oct**	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**
Phase I												
Materials development and field team training												
Phase II												
Participant recruitment/ enrollment												
Distribution of misoprostol and safety monitoring												
Data collection												
Phase III												
Data quality control, analysis, and summary												
Dissemination of results to stakeholders												
Presentation of results at all levels												

Organizational Structure

One of the strengths of the organizational structure of the study was the establishment of strong linkages between the MOH, POGI, and MNH/Indonesia through the establishment of a National Steering Committee and a Technical Working Group (**Figure 1**). These organizational relationships facilitated national and regional support to ensure successful project implementation.

Figure 1. PPH Study Organizational Structure



Study Areas

The study was implemented through the MNH/Indonesia Program in the province of West Java. Based on the Indonesian 2000 census report, West Java has a population of 42 million, which is equivalent to the population of California, Oregon, and Washington states combined. Data from the annual health profile indicated that there were 5,772 midwives practicing in West Java, confirming that there is a low ratio of midwives to pregnant women.

Bandung District was chosen as the intervention area and Subang District was chosen as the comparison area. Villages in these two areas were reported to be comparable with respect to level of use of skilled providers during childbirth and availability of a hospital for emergency treatment of complications within reasonable reach (1- to 2-hour travel time) for the majority of women in the district. The villages also met low-resource criteria (Central Bureau of Statistics et al. 1998). Each of the two study areas has an existing network of community volunteers (*kader*) who work as peer-educators in association with public community health centers (*Puskesmas*). The population in each study area selected met the sample size requirement for the study design, which called for a 2:1 ratio of intervention area women to comparison area women to ensure sufficient power to detect the difference in perceived excessive bleeding.

Identification and Recruitment of Participants

Identification through Household Census

Before initiation of the PPH Study, a census was completed in both study areas. The Central Bureau of Statistics (*Badan Pusat Statistik* [BPS]) in Bandung District completed the household survey to identify all women in the two study areas who were pregnant in August 2002. The census was completed by screening teams that included men and women who worked with BPS to create the original maps for the year 2000 national census.

A total of 180 BPS screeners were responsible for visiting 57,900 households in the two districts during a 4-week survey period. Screeners were expected to visit 15 households per day, on average. To complete the screening phase in 25 working days, each screener was responsible for an area of

approximately 300–375 households. Screeners were paid *Rupiah* (Rp) 4,000 (about $0.50 USD) per household and reimbursed for transportation costs after questionnaire submission.

BPS screeners visited each house within their assigned areas. Upon arriving in the neighborhood, the screener introduced her/himself to the neighborhood community volunteer. The volunteer facilitated the introduction of the screener to families in the neighborhood, showed the Provincial/District Health Department (*Dinas Kesehatan* [*DinKes*]) letter of permission, and explained the purpose of the household census. The screener then spoke to the head of household, or any adult if the head of household was not present, and requested the names of all women in the household between the ages of 15 and 49 years. The screener spoke with each of these women in person to ask if they were currently pregnant. The screener's instructions were to continue to re-visit the houses in her/his assigned area until s/he had spoken with each woman personally.

Screeners used a standard protocol and special consent form for enquiry about pregnancy, including asking "have you missed two menstrual periods?" A followup question was phrased in a way to allow women who were not sure about the date of their last menstrual period to answer in the affirmative ("Is there a possibility that you may be pregnant?"). Pregnancy status was confirmed (by a midwife, if necessary) during the study enrollment in October, 4–6 weeks later.

All women, not just women who were planning a home birth, were placed on the list and coded for pregnancy status. Each household that was visited by a BPS screener received a POGI-MNH/Indonesia orange and white sticker with a unique identification number (geocode). At the time of study enrollment, women who were misidentified as pregnant or who were no longer pregnant were recorded in the field supervisor logbook and reported to the MNH/Bandung office.

Recruitment

Participant recruitment occurred during the 4-week period from 10 October to 5 November 2002. Eligible women were recruited to participate in the study when they visited the community health center or antenatal care clinic (comprehensive services post, *Posyandu*), or during a home visit by a community volunteer. Pregnant women who agreed to participate in the study and completed the informed consent process were enrolled in the study.

An oral consent process, which does not require a signature from the survey participant, was used for the study because of the low education level of community members, with only 20% of ever-married women having 4 years or more schooling (Central Bureau of Statistics et al. 1998). The consent form was read to each woman, and oral consent was requested and documented for those who agreed to participate in the study.

The consent process was conducted in the language (e.g., *Bahasa* Sunda, Java, or Indonesia) that was appropriate for the participant. The consent forms and questionnaires were created in English, translated into *Bahasa* Indonesia, pre-tested, approved by the WIRB, and translated back into English to ensure accuracy of translations. A *Bahasa* Sunda dictionary of appropriate substitute words was provided to data collectors for use with *Bahasa* Indonesia questionnaires so that a standardized definition was used for each word. The consent process involved describing the purpose of the study, measures taken to ensure confidentiality, and the details of what the visits and interviews involved. The women were given assurance that declining to participate in the study, or withdrawing from the study at any time, would in no way jeopardize the services they would receive.

All women received counseling about prevention of PPH and were told that emergency medical care for any complication of pregnancy or birth would be provided free of cost at the nearest specified health center or referral hospital. The cost of care and materials was reimbursed under a contractual agreement with the midwives, health centers, and district hospitals, and transportation costs were prepaid through health centers (see **Appendix A** for clarification). Women were given the names and telephone numbers of the midwives, doctors, and obstetricians in their district who formed a health safety network for the study, and maps showing the location of the nearest health center and district hospital. The potential side effects were discussed during the counseling, and women were encouraged to drink warm sweet tea or use a blanket if they felt chilled. If more than normal bleeding occurred after taking misoprostol or if side effects persisted, participants were reminded to seek care with the nearest skilled provider or at the nearest health center.

Comparison Area

Two sub-districts in Subang District (population 60,000), Cipeundeuy and Pabuaran, served as the comparison area. Eleven villages served by two public health clinics were included in the comparison area (**Table 3**).

Participants in the Subang comparison area received counseling on prevention of PPH and agreed to participate in one interview by a trained postpartum interviewer within 4 weeks after giving birth. The participants were advised to seek care should they experience any complication during pregnancy or birth, but they were not offered misoprostol and had no additional risk from participating in the study.

Table 3. PPH Study Areas by District and Village

District	Sub-District	*Puskesmas*	Villages Served
Bandung (intervention area; population 135,500)	Bale Endah	Bale Endah	Bale Endah, Andir
		Rancamanyar	Rancamanyar, Malakasari, Bojongmalaka
		Jelekong	Jelekong, Manggahang
Subang (comparison area; population 60,000)	Cipeundeuy	Cipeundeuy	Cipeundeuy, Cimayasari, Wantilan, Lengkong, Jalupang, Banggalamulya, Sawangan
	Pabuaran	Pringkasap	Pringkasap, Karanghegar, Kosar, Caracas

Intervention Area

Seven villages in Bandung District (population 135,500), served by three public health clinics, formed the intervention area (**Table 3**).

Participants agreed to take part in three interviews (initial visit, visit during third trimester, and visit within 4 weeks after birth). The home visits consisted of counseling that included the purpose of the study, the correct timing and use of misoprostol to prevent PPH, the risks of taking misoprostol before birth of the baby, and common side effects of misoprostol. The counseling also included details of what to do in case a side effect or complication occurred, and where and from whom to seek care. A flip-book visual aid and dual language script was used for the counseling session. This information was shared in the local language, as appropriate. Women were encouraged to have a family member or other support person listen to the counseling session. Approximately 75% of the women had their spouse, mother, mother-in-law, and/or other support person present during the counseling session.

After the counseling session, women and household members were asked to describe in their own words what misoprostol was used for (*tablet PAS bayi* ["tablet that avoids bleeding immediately"]), the safe use of misoprostol, and the risks associated with misuse of misoprostol, as a means of verifying their understanding. To ensure the safety of study participants, counseling was repeated until participants could correctly restate the information provided. At the conclusion of the second counseling visit during the third trimester of pregnancy, women who agreed to accept misoprostol were given the package containing three 200-µg misoprostol tablets. The tablets were packaged in a heat-sealed plastic bag, together with pictorial and written safety instructions. Women who chose to give birth with a midwife (*bidan*) at home could take misoprostol, but these women were counseled that the midwife could administer oxytocin if she chose to, thereby overriding the research protocol.

Socialization and Community Orientation

The study socialization and community orientation consisted of a series of public meetings in communities in each of the study areas, although the study did not use extensive advertising or promotion. The socialization strategy targeted expectant families and was primarily designed to offer a community forum to clarify the nature of the short-term study. These forums were based on the existing MNH BP/CR model that encourages birth preparedness at the individual level, enabling families to take responsibility for protecting their own health. The meetings included informal community leaders (Head of District [*Bupati*], Head of Sub-District [*Kapala Camat*], and Head of Village [*Kapala Desa*]), religious leaders, health professionals, traditional birth attendants (TBAs), and other community members, and provided an introduction to the study as well as the study leadership team and trained community volunteers. Discussions highlighted that the intervention offered a broader range of choices about preparations for childbirth. Through community contacts, midwife coordinators and village midwives (*bidan di desa*) were encouraged to share information about the initiation of the PPH Study. **Figure 2** illustrates the review and dissemination of the study's socialization messages.

Data Collector Characteristics

The data collectors, including community volunteers, midwives, and postpartum interviewers, were recruited from the study areas and selected by the WHO-CC, Bandung, in collaboration with MNH/Indonesia. Selection criteria included educational background, work experience, and previous training. Community volunteers and postpartum interviewers were interviewed, screened for their communication skills, and given a 2-minute acuity evaluation. During the data collector recruitment, emphasis was placed on selecting highly-motivated community volunteers who were committed to serving in their own neighborhoods. Community volunteers were asked a question about why they were motivated to assist with the PPH Study. Their most common response was "to gain experience working with pregnant women and knowledge about the risk of pregnancy and childbirth" (20/52 volunteers interviewed). More than 20% (11/52) of the community volunteers mentioned that they felt it was their responsibility to the community to participate in the PPH Study. One volunteer said, "I want to help because the project concerned somebody else's life and I am interested in encouraging the *bidan*." Only one community volunteer mentioned an interest in gaining extra income from the small payment for submitting questionnaires. The characteristics of the selected data collectors are shown in **Table 4**.

Figure 2. PPH Study Socialization Infrastructure to Promote Community Awareness

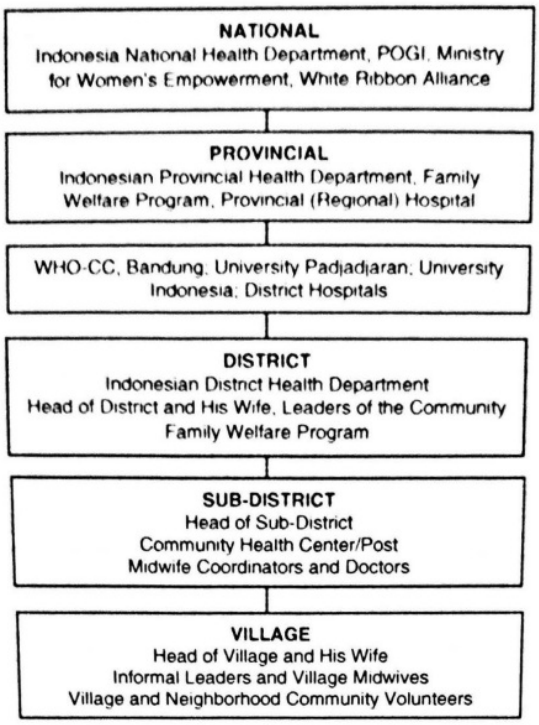
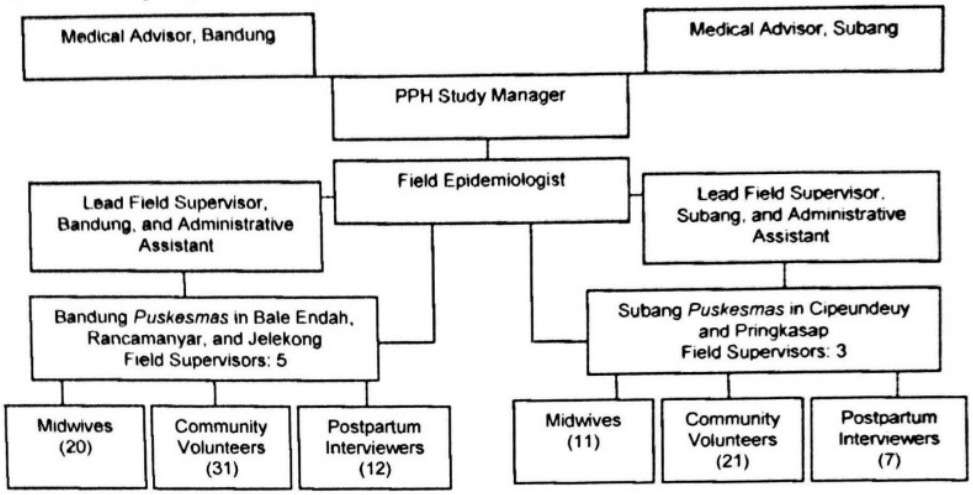


Table 4. Characteristics of Data Collectors

Characteristic	Community Volunteers	Postpartum Interviewers	Midwives
Average age (range)	40 years (24–65)	37 years (23–54)	34 years (25–62)
Ethnicity	86% Sundanese	77% Sundanese	76% Sundanese
Gender	96% women (50/52)	90% women (17/19)	100% women (31/31)
Average number of children (range)	3 (1–8)	3 (1–8)	2 (1–5)
Educational level	48% junior high graduates, 24% high school graduates	82% high school graduates, 16% college graduates	100% nursing academy graduates
Occupation	81% housewives	63% housewives	70% health center midwives, 30% village midwives
Years of work experience (range)	12 years (1–28 years)	9 years (1–21 years)	11 years (5–41 years)
Active in comprehensive services post/Family Welfare Program	92%	88%	0%

Figure 3 illustrates the distribution of the field team by study area. The study was specifically designed to be implemented using existing healthcare infrastructure and community resources, including the existing network of community volunteers. The figure differentiates the service delivery component (white boxes) from the research component (gray boxes).

Figure 3. PPH Study Supervision System: Service Delivery and Research Components



Data Collection

The study outcome measures included:

- Number of pregnant women in the intervention area who agreed to receive information and misoprostol, measured by the number of participants who accepted counseling and misoprostol.
- Number of pregnant women who actually took misoprostol immediately after birth, measured by participants reporting use of misoprostol after childbirth and tabulation of reasons for use and non-use of misoprostol.
- Number of participants who perceived excessive postpartum blood loss among women who used misoprostol compared to those who did not use misoprostol, measured by participants' responses to postpartum interview questioning about whether they experienced more than normal bleeding after birth.

Quantitative Component

Standardized survey questionnaires were used to gather information from study participants who were interviewed. Four main questionnaires were used:

- The recruitment ("*Kader* First Visit") questionnaire collected data on sociodemographic characteristics, obstetric history, and level of knowledge about PPH and misoprostol. The questionnaire also asked the woman to identify a support person who would be with her when she gave birth, and that person was included in the counseling session.
- The third trimester ("8th Month Visit") questionnaire, used only in the intervention area, was primarily a job aid the community volunteer used to determine whether the woman had already received her third trimester counseling session and the misoprostol. If not, the questionnaire guided the community volunteer through the survey process.

- The postpartum interview questionnaire for the Bandung intervention area was used to collect information on the woman's understanding of the counseling given to her about PPH and about misoprostol; information about any complications the woman experienced during birth, including perceived blood loss; if and when she used the misoprostol; and if she would recommend it to others. The postpartum interview questionnaire for the Subang comparison area collected information about complications the woman experienced during birth, including perceived blood loss.
- The midwife delivery questionnaire was a self-administered questionnaire completed by midwives attending births in the two study areas. The questionnaire collected similar information to that collected in the postpartum interview in the intervention area, focusing on use of the misoprostol and symptoms or complications experienced by the woman during birth and the immediate postpartum period, including an estimate of the amount of blood loss (measured in a kidney bowl). It also covered the midwife's willingness to recommend use of misoprostol for other women.

During the recruitment month, community volunteers visited all houses of the women on their assigned list. If a women had not been recruited, the volunteer conducted the consent process and completed the recruitment visit questionnaire. After the interview, the community volunteer recorded the unique identifying number (geocode) on the woman's PPH Study ID card and coversheet of the questionnaire, including the date, data collector's name, participant's name, address, head of household's name, study area, sub-location (neighborhood), and house number.

If the woman had not yet started her 8th month of pregnancy, the community volunteer checked the woman's antenatal care card for the estimated due date. The community volunteer counseled the woman on prevention of PPH and told her that she would visit again later in the pregnancy, but did not give the misoprostol at this visit. If the woman had started her 8th month of pregnancy, the volunteer asked the participant if she had already been offered and accepted misoprostol:

- If the participant had not been offered misoprostol, the community volunteer began completing the third trimester visit questionnaire, invited the support person, if present, to join in the counseling session, and offered counseling about prevention of PPH and the safe storage and use of misoprostol. The volunteer recorded whether or not the woman accepted the misoprostol.
- If the participant had been offered misoprostol but declined to accept it at the first visit, the community volunteer asked the woman if she had changed her mind and if she was now interested in receiving the misoprostol. If the participant did not wish to accept the misoprostol, the community volunteer stopped the interview. If the participant did wish to accept the misoprostol at that time, the community volunteer began the questionnaire and offered counseling and the misoprostol. The community volunteer recorded that the participant accepted the misoprostol during the second visit.
- If the participant had accepted misoprostol previously, the community volunteer stopped the interview and did not provide additional counseling or record information. The community volunteer reported the case to the field supervisor, who then reconciled the participant records.

Misoprostol packets that were reported lost or damaged were not replaced by the community volunteer. The participant was told to contact the midwife coordinator at the community health center for replacement packets of misoprostol, which allowed strict control of misoprostol distribution.

Participants were asked about use of misoprostol at the postpartum interview. If the participant volunteered that she took the misoprostol before birth, the postpartum interviewer was told to immediately contact the field supervisor to complete a participant followup interview. A separate questionnaire on misuse of misoprostol was prepared as part of the PPH Study safety monitoring. Although there were no cases of misuse of misoprostol, this questionnaire would have been completed if any participant had mistakenly taken misoprostol while still pregnant (**Appendix B**). A separate questionnaire was created for use in the event of an adverse event (ruptured uterus or maternal death).

Qualitative Component

Focus group discussions (FGDs) and in-depth interviews (IDIs) were used to elicit further opinions about the acceptability of misoprostol. The objectives of the qualitative component were to:

- Provide information on perception, attitude, and behavior on various issues related to pregnancy and the use of misoprostol in the intervention area;
- Collect information on the distribution process and the acceptability and effectiveness of misoprostol, which are influenced by various factors in the community; and
- Provide programmatic recommendations about potential scale-up and replication within a district-wide program to prevent PPH.

Qualitative data collection was completed by an experienced, trained qualitative research team from the WHO-CC, Bandung, in collaboration with MNH/Indonesia. A total of 90 participants (85 women and five men: 20 women who had recently given birth and 70 community members, including midwives, TBAs, and community volunteers) from the Bale Endah intervention area participated, and qualitative data were gathered from verbatim transcripts from eight FGDs and 35 IDIs. FGDs were used to collect general information from community members and healthcare providers, and IDIs were used to collect more detailed information from selected community members.

The FGDs consisted of four groups of women who had recently given birth, two groups of midwives, and two groups of community volunteers:

- Two groups of women who had recently given birth and who used misoprostol: one group of women who had a skilled provider at the birth and one group who did not have a skilled provider present;
- Two groups of women who had recently given birth who did not use misoprostol: one group of women who had a skilled provider at the birth and one group who did not have a skilled provider present;
- Two groups of midwives: one group of midwives who attended the PPH Study training session and one group of private midwives who did not attend the training session; and
- Two groups of community volunteers: one group of MNH-trained volunteers who had participated in the 5-day training and one group of non-MNH volunteers who did not attend the training session.

Table 5. Methods of Qualitative Data Collection

Group	Focus Group Discussions	In-Depth Interviews
Women who used misoprostol	2	7
Women who did not use misoprostol	2	–
Midwives	2	7
Community volunteers	2	7
TBAs	–	7
Support person	–	7
Total	**8**	**35**

The FGD facilitator guidelines included essential questions about the study grouped within five topics and three themes. Transcripts were organized and coded using an alphanumeric coding system for the theme and relevant topic (e.g., Theme A, Topic 2, or Theme B, Topic 1):

- Theme A: PPH Study information and counseling. For example, What do respondents say and think about misoprostol and PPH counseling? What do they say about the connection between misoprostol and PPH? What do they think of the community meetings or other sources of information they had? What do community volunteers and midwives think about the effectiveness of the counseling and community information meetings?
- Theme B: distribution of misoprostol. For example, How do women get misoprostol? What do they think about the way they received it through the community volunteer network? What are the best ways to distribute misoprostol to all pregnant women, including the women who don't use the services of midwives or doctors? Where is misoprostol available for sale, and is it accessible to women (cost, location)?
- Theme C: decision-making about use of misoprostol. For example, What reasons do women have for taking or not taking misoprostol? What did they discuss with other people after finding out about misoprostol? How did that influence them? What do women hear about experiences of others who use misoprostol, and perceptions about who uses misoprostol? How did using misoprostol influence decisions about childbirth planning (such as with whom and where to give birth)? What are the partnerships or cooperation between midwives, community volunteers, and TBAs? How did using misoprostol influence care-seeking, referral, and care practices during pregnancy, childbirth, and postpartum?
- Topic 1: perceived benefits/advantages
- Topic 2: perceived barriers/disadvantages
- Topic 3: how barriers were overcome (problem solving)
- Topic 4: cues or triggers to decisions or action (social, economic, and physical reasons)
- Topic 5: recommendations for improvements/how to replicate successes

Study and Safety Monitoring

The PPH Study supervision system served to ensure that consent procedures, counseling, and distribution of misoprostol were conducted according to a standard protocol. Data collection and submission of the completed questionnaires were monitored, including tracking the performance of each community volunteer with regard to questionnaire accuracy and timeliness. The field supervision structure of the PPH Study included a field epidemiologist, two field supervisors, and eight community health center-level field supervisors divided between the two study areas (**Figures**

4 and 5). The field team supervisors were responsible for reporting on safety indicators, including quick identification of any woman who may have taken misoprostol before the baby was born. Safety protocols for the PPH Study included a detailed written protocol for reporting of adverse events (maternal death or ruptured uterus) to the University of Indonesia Institutional Ethical Review Board and the WIRB within 10 days of becoming known to the study team. For details related to protocols for detection and reporting of adverse events, verbal autopsy reports, and reporting misuse of misoprostol, see **Appendix B**.

Figure 4. PPH Study Implementation Infrastructure, Bandung District Intervention Area (boxes shaded in gray are villages)

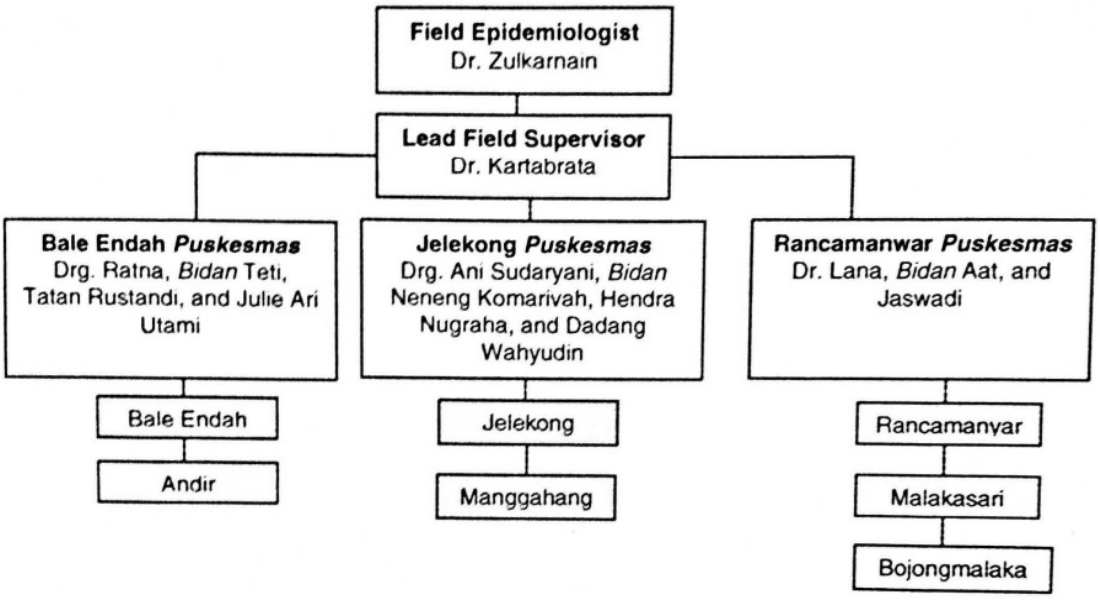
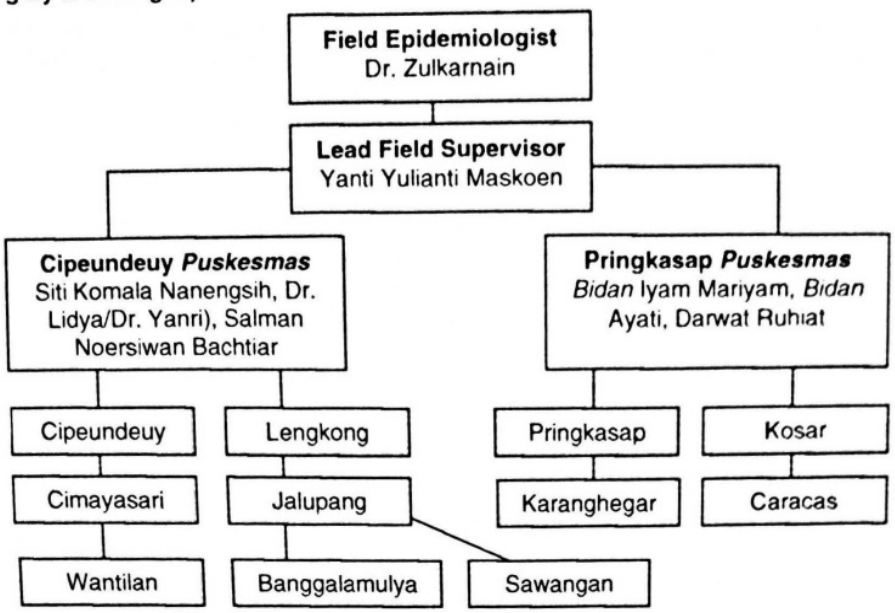


Figure 5. PPH Study Implementation Infrastructure, Subang District Comparison Area (boxes shaded in gray are villages)



Data Entry and Data Analysis

Completed questionnaires were submitted to field supervisors based in health centers or auxiliary field offices who reviewed the questionnaires for completeness and accuracy before submission to the lead field supervisor at the MNH/Bandung field office. When the questionnaires arrived at MNH/Bandung, they were reviewed again for completeness, recorded in a logbook, and sent to data operators for data entry.

Electronic and hardcopy data were stored under lock and key. Personal identifiers were entered into the data file during the course of the study and then stripped from the questionnaires and the electronic data file at the completion of the study. The study manager, field epidemiologist, lead field supervisors, data operators, and those involved in the provision of technical assistance from the Baltimore and Jakarta offices had access to the data throughout the study to allow for consultation on data quality and data cleaning, but without identification of study participants. None of the information collected in the questionnaires was of a sensitive nature.

Two trained data operators entered data from the questionnaires using SPSS Data Entry Station software. Data cleaning for all questionnaires was the responsibility of the lead field supervisors who worked closely with field supervisors and data operators at the MNH/Bandung field office. Results were checked for consistency and summarized using routine frequency and cross tabulation techniques with SPSS statistical software. The quality of the data was checked through dual entry of a 10% random sample of participant questionnaires to confirm or correct data values. Questionnaires with inconsistent or missing data were rechecked in the field for completion by the *kader* or postpartum interviewer. Approximately 9% of the questionnaires were found to have missing data and were sent back to the field for correction. Typically, one question was left incomplete in the eight-page questionnaire. The most common errors were related to either the 20-digit participant identification number (geocode) or the serial number of the misoprostol packet, and were resolved by re-checking the participant identification number or misoprostol log sheets.

The PPH Study protocol called for intent-to-treat–based comparisons when information about preventing PPH or side effects related to use of misoprostol was summarized. The research team summarized quantitative results of the PPH Study primarily using frequency and cross-tabulation in SPSS statistical software. In-depth analyses were completed using logistic regression multivariate models with STATA statistical software to allow for the use of adjustment factors representing differences in parity, education level, socioeconomic status, and history of antepartum hemorrhage between the two groups of study participants.

The qualitative interview transcript analysis and summarization was completed by the trained qualitative research team from the WHO-CC, Bandung, in collaboration with MNH/Indonesia. Verbatim transcripts from the FGDs and IDIs were summarized using word and phrase searches in MS Excel and NUD*IST software based on thematic guidelines. The verbatim transcripts were also translated into English for review by the PPH Study team.

FINDINGS

Characteristics of Study Participants

Of the 3,111 women who were initially identified as pregnant, a total of 1,855 pregnant women agreed to participate in the study (**Table 6**). Based on the language spoken most often at home, the study participants were primarily Sundanese (91% in Bandung and 95% in Subang). A few participants were Javanese or Batak. A total of 44 women were lost to followup (31), experienced a loss of pregnancy after enrollment (10), or died (3), leaving a total of 1,811 women as active participants in the study. The maternal deaths, which were unrelated to the use of misoprostol, were reported to the University of Indonesia Institutional Ethical Review Board and the WIRB within 10 days by the study manager, in accordance with IRB regulations. One death was due to dengue shock syndrome, one was due to multiple organ failure related to eclampsia, and one was due to congestive heart failure related to pre-existing heart disease. These three cases received a full review, including completion of a verbal autopsy report by the PPH Study ob/gyn medical advisors.

All study participants had similar socioeconomic backgrounds. Subang women tended to be younger and were more likely to be first-time mothers, although the difference in age was small (average age 27.0 years in Bandung compared to 26.4 years in Subang; see **Table 7**). Women in Bandung were more likely to have higher education level and socioeconomic status (e.g., own a TV or motorcycle), although a few participants from both areas owned cars.

Table 6. Summary of PPH Study Participant Followup

Participant Followup	Bandung	Subang
Number of women identified as pregnant in census survey	2,367	744
Women who gave birth before enrollment or were otherwise unavailable	1,007	249
Number of women enrolled in study	1,360	495
Participant followup:		
Women lost to followup (moved to different area)	27	4
Spontaneous miscarriage/loss of pregnancy after enrollment	9	1
Reported maternal deaths	2	1
Number of active participants	1,322	489

Table 7. Characteristics of Study Participants

Participant Characteristic	Bandung (N = 1.322)	Subang (N = 489)
Age	27.0 years	26.4 years
Education:		
Literate	1,223 (92.5%)	418 (85.5%)
Junior high or beyond	773 (58.5%)	181 (37.0%)
Parity:		
First-time mother	427 (32.3%)	199 (40.7%)
One or more children	895 67.7%)	290 (59.3%)
Five or more children	54 (4.1%)	5 (1.0%)
Obstetric history:		
Previous cesarean section	43 (3.3%)	3 (0.6%)
Previous birth where postpartum bleeding was perceived to be more than normal	76/895 (8.5%)	20/469 (4.3%)

Of the active participants in the intervention area, 1,291 women accepted the misoprostol. Thirty-eight of these women had cesarean sections and 182 were given oxytocin instead of misoprostol by their midwives, leaving 1,071 participants who were still eligible to use misoprostol. Of these women, 72 chose not to use misoprostol, leaving 999 women who accepted and used misoprostol.

The details of attendance at birth, as determined by the postpartum interview, are summarized in **Table 8**. Of interest is that the number of women in the Bandung intervention area who had a skilled provider at birth (54.5%) was significantly lower than the number of women in the Subang comparison area (76.0%). The lower number in Bandung is probably a result of the Subang area health department's economic incentive to encourage midwives and TBAs to work together during a birth, rather than a result of the Bandung women's decision against using a skilled provider because they had access to misoprostol to prevent PPH (see also **Table 12**).

Table 8. Birth Attendants among PPH Study Participants

	Bandung	Subang
Total number of births among active participants	1,322	489
Birth attended by skilled provider:	721 (54.5%)	372 (76.0%)
Doctor	137 (10.4%)	53 (10.8%)
Midwife	584 (44.2%)	319 (65.2%)
Birth attended by TBA	580 (43.9%)	117 (23.9%)
Birth attended by family member or other untrained assistant	21 (1.5%)	0 (0.0%)

Assessment of Safety

Findings of this study showed that the counseling and distribution of misoprostol are safe. Following one-on-one counseling sessions, women were successful in taking misoprostol in a self-directed manner without the supervision of a skilled healthcare provider. **Table 9** summarizes safety data related to the use of misoprostol. Few women taking misoprostol reported nausea, abdominal cramps, vomiting, or diarrhea, which are commonly caused by oxytocin. Shivering was a common side effect with misoprostol (**Table 9**); however, it is also common in normal childbirth, even

among women who do not receive a uterotonic drug. The side effects were usually noticed 5–10 minutes after ingestion of misoprostol and lasted about 15–30 minutes.

Logistic regression analysis was used with adjustment for inter-group differences. Study results indicate that women in the intervention area were 25% less likely to perceive excessive bleeding (as measured by the number of cloths used during the first 24 hours after the birth; odds ratio [OR] = 0.75, 95% confidence interval [CI] 0.55–1.03, p = 0.094). Women in the intervention area were 30% less likely to need an emergency referral for any birth complication (OR 0.69, 95% CI 0.49–0.98, p = 0.035) and 45% less likely to need an emergency referral for PPH (OR = 0.55, 95% CI 0.24–1.23, p = 0.144) compared to women from the comparison area. The overall number of emergency referrals due to birth complications was less than 10% (1%; 1,811), with only 47 emergency referrals suspected to be due to PPH (**Table 10**).

Table 9. Safety Monitoring Related to the Use of Misoprostol

	Bandung Intervention Area (N = 999)*	Subang Comparison Area (N = 489)
Percentage of participants who perceived excessive postpartum blood loss	117 (11.7%)	66 (13.5%)
Level of minor side effects:		
Shivering after childbirth	442 (44.2%)	48 (9.8%)
Fever after childbirth	352 (35.2%)	28 (5.7%)
Percentage who had emergency referral for PPH	22 (2.2%)	19 (3.9%)

* Number includes only women who accepted and used misoprostol.

Table 10. Emergency Referrals among All Study Participants

Emergency Referral	Bandung Intervention Area (N = 1,322)*	Subang Comparison Area (N = 489)
Referrals due to all birth complications, including suspected PPH	114 (8.6%)	62 (12.7%)
Referrals due to suspected PPH	28 (2.1%)	19 (3.9%)

* Number includes all women in intervention area.

Interviews with the midwives showed that the midwives believed that study participants took misoprostol at the correct time, felt safer having the misoprostol at home, and were well prepared to cope with the anticipated minor discomforts or potential side effects after use of misoprostol.

Comments on the Safe Use of Misoprostol

"They feel safer because there won't be bleeding. The aim is good. If [the misoprostol] is in the health center, it is fine as long as it is under the control of the midwife." Bidan N.T.

"For the first [woman], the shivering was not too long…one experienced [shivering] for 2 hours, but some didn't experience shivering in my practice." Bidan N.

Assessment of Acceptability

Misoprostol was accepted by the study participants, and most women gained approval for use of misoprostol from their husbands and family members after the community volunteers visits. Most participants reported that they would recommend misoprostol to a friend, use it for their next birth, or pay for it if it was available (**Table 11**).

Table 11. Acceptability of Misoprostol to Prevent PPH

	Baseline
Women who gained approval for use of misoprostol from husband and family members	1,000/1,001 (99.8%)
Women who would recommend misoprostol to a friend	870/909 (95.7%)
Women willing to use misoprostol again at their next birth	868/909 (95.5%)
Women who would purchase misoprostol if available	847/909 (93.1%)

Comment on the Acceptability of Misoprostol

"They seemed to accept it. The women are grateful because they are afraid of bleeding. But with this *tablet PAS bayi* program, they become more at ease. She was bleeding when she delivered her first baby, but the second one, she participated in this program, got the medicine, and there was no bleeding." TBA D.

Assessment of Feasibility

The feasibility of this intervention depended on identifying a means of distributing misoprostol to all pregnant women, including those who planned to give birth at home. Specific questions related to the feasibility of continuing the intervention and potential expansion to a national program to prevent PPH were addressed by qualitative survey among participants.

Based on summary information from IDIs, the majority of people interviewed felt that the best way to ensure that every pregnant woman has an opportunity to receive information about prevention of PPH, including those who do not plan to use skilled providers, is to allow trained community volunteers to work cooperatively with skilled midwives within their respective communities. Midwives are trusted healthcare providers, and the FGDs and IDIs showed that the midwives supported the training of community volunteers and worked cooperatively with community volunteers. Most community volunteers indicated they felt valued and would continue to volunteer in the future.

Another aspect of feasibility relates to the availability of misoprostol in the community. Misoprostol was found to be readily available and in stock at local pharmacies, as well as peripheral health centers. The cost of misoprostol for private purchase ranged between Rp 5,000 and 10,000 ($0.55 to $1.10 USD), making it comparable in cost to oxytocin. What makes misoprostol less expensive is that it can be taken orally; therefore, there is no cost for a syringe and needle, and no fee for the skilled provider as there would be with injection of oxytocin or other injectable uterotonic drug. Another important measure of feasibility relates to community members' willingness to pay for misoprostol. Of the 84% of women in the intervention area who reported willingness to pay for misoprostol, 60% reported that they would pay at least Rp 5,000.

PPH study results provide positive evidence that pregnant women are likely to continue to seek childbirth care at the midwife's house and are not inclined to home birth just because they have a drug that can prevent PPH (Table 12).

Table 12. Location of Childbirth among PPH Study Participants in Bandung Intervention Area[a]

Location of Childbirth	Previous Childbirth	Current Childbirth during Study
Participant's home	475 (54.8%)	408 (47.1%)
Midwife's home	244 (28.2%)	328 (37.9%)
TBA's home	67 (7.7%)	47 (5.4%)
Healthcare facility	77 (8.9%)	81 (9.4%)
Other[b]	3 (0.3%)	2 (0.2%)

[a] N = 866. Women who gave birth to their first child were excluded.
[b] Includes births that occurred in a car.

Assessment of Effectiveness

This study focused on the safe use and programmatic effectiveness of the distribution of misoprostol among pregnant women who planned to have home births. The purpose of this study was not to demonstrate the clinical effectiveness of misoprostol or compare it to other methods of preventing PPH, as this has already been well documented (as reviewed by Brookhuizen 2000). However, results described in the section on safety assessment show that women in the intervention area were less likely to require referral for PPH or any other birth complication, demonstrating the effectiveness of misoprostol. This finding was confirmed during interviews with midwives, the majority of whom reported that they believed that misoprostol was effective in preventing PPH and was an effective alternative if oxytocin was not available.

The distribution by community volunteers proved to be effective. The community volunteers are respected members of the neighborhood and were effective in gaining pregnant women's approval to participate in the study as well as in encouraging women to accept and use misoprostol.

Comment on the Effectiveness of Misoprostol

"The drug is beneficial ... no diarrhea, no vomiting, just the shivering." Bidan E

LESSONS LEARNED

An important lesson learned during the PPH Study in Indonesia was that the active participation of the National Steering Committee was important not only for the success of the study but also for the rapid acceptance of the study findings. The National Steering Committee included Indonesian government officials at the national, provincial, district, and sub-district levels, leaders within the health professions, and our Indonesian collaborating and implementing partners. The National Steering Committee leadership, including the Director of the [illegible], immediately confirmed their commitment to roll out the interventions as a national [illegible] of PPH program in Indonesia after presentation of the study findings. The active participation of the National Steering Committee was important for the success of the study because national leadership facilitated [illegible].

- Rapid acceptance of the study findings,
- Commitment to include a national PPH program in the national health planning agenda and budget, and
- District-level planning for implementation of a PPH pilot program using the existing healthcare service infrastructure.

The importance of having a program coordinator based in community health centers should be highlighted. It was important to have a responsible person to keep a running count of misoprostol packets issued to community volunteers, because safety and potential misuse of misoprostol was a primary concern of the Indonesian MOH and other stakeholders. The health center coordinator must be very conscientious about completing logbooks for the release of misoprostol and keeping close count of the number of misoprostol packets in locked cabinets. Volunteers must be accountable for each misoprostol packet distributed, and unused packets should be re-collected, to avoid the uncontrolled sharing of misoprostol with individuals who may not have had the benefit of safety information or counseling.

A competency-based training workshop is necessary to adequately prepare healthcare providers and community volunteers to use the counseling information and learn about the safe use and potential side effects of misoprostol. Monthly updates and review of the safe use of misoprostol should be integrated into periodic routine meetings with community volunteers as a way to continually re-train. Biweekly contacts between community volunteers and health center coordinators would provide an appropriate level of supervision to complete counseling and distribution of misoprostol once initial orientation, training, and practice sessions are complete. In summary, preparation for the community-based intervention should include:

- Holding program coordinators based in community health centers responsible for safe distribution of misoprostol,
- Conducting a competency-based training workshop to adequately prepare health providers and community volunteers to successfully use the counseling information, and
- Ensuring biweekly contacts between community volunteers and health center coordinators to provide an appropriate level of supervision.

RECOMMENDATIONS

The Study team recommends that a step-wise approach be used to scale up and roll out the prevention of PPH intervention, beginning in the current study areas by fully integrating the intervention within the existing service delivery system. In addition, new areas should be identified for initiating the PPH intervention as a means of scaling up within the province of West Java.

In planning the scale-up of the PPH intervention, policies regarding distribution of misoprostol by community volunteers will need to be addressed, as will how districts will finance this intervention. There is also a need to clearly designate the network of MOH staff and skilled providers who will ensure sound training and supervision of the national prevention of PPH program.

Issues being considered by the PPH National Steering Committee are the policies related to how misoprostol will be distributed by trained community volunteers, how to make the medicine available at low cost, and how to refine the requirements for supervision and reporting that will be incorporated at community health centers to make the national prevention of PPH program safe

and effective in Indonesia. The MOH will facilitate the importation and packaging of the misoprostol and is currently investigating how to authorize the importation of misoprostol for a program in Bandung District. Pharmacists need to be educated that misoprostol should not be given to women without a valid prescription and appropriate counseling about PPH prevention and the safe use of misoprostol. Drug regulatory bodies should also continue to regulate and re-educate the pharmaceutical sales industry.

It is recommended that the cost of misoprostol be subsidized to the extent possible or, alternatively, that the government negotiate a lower public sector price. Before rolling out the intervention to the entire nation, it would be prudent to review the lessons learned from this study. An incremental scale-up approach could be used in a few community health centers within several districts in West Java. After the PPH counseling flip-books, training materials, and supervision protocols have been successfully implemented in West Java, the materials can be adapted to meet the service delivery needs in other provinces.

In summary:

- A step-wise approach should be used to scale up and roll out the prevention of PPH intervention;
- In planning the scale-up of the PPH intervention, policies regarding distribution of misoprostol by community volunteers will need to be addressed; and
- Before rolling out the intervention to the entire nation, the lessons learned from this study should be used to improve service roll-out in Indonesia.

CONCLUSION

The Indonesia MOH successfully partnered with POGI and the MNH/Indonesia Program to implement the Prevention of PPH Study in West Java. Study results showed that trained and supervised personnel can successfully provide PPH prevention counseling and information and then safely distribute misoprostol to pregnant women. The study also found that women can understand the information provided, act on it appropriately, and safely take misoprostol at the correct time. A large proportion of users reported that they would be willing to use misoprostol in their next pregnancies, pay for it themselves, and recommend it to friends. Women in the intervention area were less likely to perceive excessive bleeding or need an emergency referral for PPH or any other complication compared to women in the comparison area. Overall, the combination of the use of active management of the third stage of labor using oxytocin provided by the midwife and the use of misoprostol by the woman if a midwife is not available at home birth has great potential for expanding prevention of PPH in Indonesia.

IMPLICATIONS FOR FUTURE PROGRAMMING

Recognizing that PPH is a major cause of maternal mortality in Indonesia, and that this intervention safely prevents PPH, the PPH Study National Steering Committee and the MOH decided to disseminated the study results widely. The MOH agreed to incorporate the community-based use of misoprostol into their existing PPH prevention program, and in June 2003, the MOH directed that this PPH prevention strategy be expanded rapidly and incorporated into the national health program.

The MOH hopes to continue the PPH prevention program in selected communities within several provinces, including West Java, Banten, Lampung, and South Sumatra. The MNH/Indonesia

Program hopes to provide technical assistance in developing national and regional trainers for community volunteers, reviewing guidelines for adaptation of counseling and informational materials, and developing and implementing appropriate supervision, performance improvement, and monitoring systems with a view to gradually transferring the complete implementation effort to regional and district health authorities within a 3-year technology transfer timeline.

In preparation for this effort, JHPIEGO will develop tools and guidelines for implementing a community-based distribution system of misoprostol for prevention of PPH. These materials will be translated into English and packaged for possible use in the Asia and Near East Region, and will include distributor/counselor and supervisor selection criteria, training modules, and monitoring recommendations. Such materials can be used both to assist in implementation and to advocate for support of the intervention by national- and local-level stakeholders.

The MNH Program received support from the Near East Bureau of USAID to sponsor a PPH Initiative to continue activities in Indonesia and organize a regional PPH conference. The MNH Program, in collaboration with the Ministry of Public Health of the Royal Thai Government and the Chulalongkorn University, held a 3-day meeting in Bangkok, Thailand. The January 2004 meeting included leaders from MOHs, clinicians, health professionals, and international development partners with the purposes of:

- Reviewing the evidence supporting strategies for prevention of PPH in settings where skilled providers may or may not be available,
- Examining best practices for implementing large-scale programs for preventing and treating PPH, and
- Developing action plans to prevent and treat PPH using evidence-based approaches and best practices.

This regional meeting brought together leading experts, program managers, and safe motherhood professionals from Asia, Near and Far East, and Western Pacific regions. The meeting drew attention to what providers can do to reduce the occurrence of PPH and provided opportunities to hear about state-of-the-art interventions, explore innovative approaches, discuss challenges in bringing such care to vulnerable populations, participate in skills enhancement sessions, debate program approaches, and plan for concerted actions (Pfitzer and Sanghvi 2004).

GUIDANCE FOR INTRODUCTION IN OTHER COUNTRIES

This intervention is suitable for countries or regions where a large proportion of births are not attended by skilled providers and where there is an existing network of community workers or volunteers who are willing to visit all pregnant women. Countries interested in implementing this intervention should:

- Obtain a commitment at the national-level to scale up, if introduction of intervention is successful in a small area;
- Invest sufficiently in training and supervision;
- Monitor progress; and
- Use the available training and counseling materials, program implementation guides, evaluation tools, and posters to facilitate implementation.

APPENDIX A

SUPPLEMENTAL CLARIFICATION OF EMERGENCY MEDICAL CARE

ESSENTIAL POINTS TO CLARIFY

1. The PPH Study protocol requires that emergency medical care be provided through the **existing public health service delivery system** for pregnant women who experience birth complications. The key to the sustainability of any future Indonesian National Prevention of PPH Program will be the use of the existing health clinic/doctor/midwife/community volunteer health delivery system. This point is essential, because the POGI-MNH Prevention of PPH demonstration project is authorized by a decree by the Head of the Indonesian National Health Department (*Kepala Departemen Kesehatan* [*DepKes*]), Dr. Azrul, that calls for the roll out of an Indonesian National PPH Program.

2. Emergency medical care costs will be reimbursed by the MNH/Indonesia Program based on the existing tariffs established by the public health service delivery system, including reimbursement for:

- transportation to obtain medical treatment at five study area community health centers or two study area referral hospitals (*Rumah Sakit Hasan Sadikin* [RSHS] in Bandung or *Rumah Sakit Umum* [RSU] in Subang);
- medication (e.g., oxytocin), medical supplies (e.g., dextrose, Ringer's lactate solution), or equipment and supplies (e.g., syringes, infusion set); and
- standard tariff for service delivery by skilled providers.

However, fees will not be reimbursed for private hospitals, private physicians, or traditional birth attendants.

SINGLE ISSUE TO NEGOTIATE

For several months, the MNH Program financial staff have been negotiating with the two district hospitals and five community health centers within the PPH study areas, each of which has either a signed contract or an MNH Program Letter of Intent to complete a contract at this time. The single issue that needs to be negotiated and resolved is the fee for the village midwife (or the midwife at the community health center) who may offer emergency medical care to stabilize a study participant during her "off duty" hours when the community health center is closed. The MNH Program has agreed to make an exception to reimburse private midwives to strengthen the "emergency care safety net" for study participants who may experience birth complications and require immediate emergency care and stabilization before referral.

The study team decided that the highest possible reimbursement for a single emergency care visit with a private midwife cannot exceed four times the standard government rate (Rp. 5,000 [community health center] to 15,000 [referral hospital]). The MNH Program cannot be responsible for the entire private midwife delivery fee, because their fees far exceed the standard government tariffs. Private midwives are, however, authorized to request that the client pay the remainder of their fee.

APPENDIX A

SUPPLEMENTAL CLARIFICATION OF EMERGENCY MEDICAL CARE

ESSENTIAL POINTS TO CLARIFY

1. The PPH Study protocol requires that emergency medical care be provided through the **existing public health service delivery system** for pregnant women who experience birth complications. The key to the sustainability of any future Indonesian National Prevention of PPH Program will be the use of the existing health clinic/doctor/midwife/community volunteer health delivery system. This point is essential, because the POGI-MNH Prevention of PPH demonstration project is authorized by a decree by the Head of the Indonesian National Health Department (*Kepala Departemen Kesehatan* [*DepKes*]), Dr. Azrul, that calls for the roll out of an Indonesian National PPH Program.

2. Emergency medical care costs will be reimbursed by the MNH/Indonesia Program based on the existing tariffs established by the public health service delivery system, including reimbursement for:

- transportation to obtain medical treatment at five study area community health centers or two study area referral hospitals (*Rumah Sakit Hasan Sadikin* [RSHS] in Bandung or *Rumah Sakit Umum* [RSU] in Subang);
- medication (e.g., oxytocin), medical supplies (e.g., dextrose, Ringer's lactate solution), or equipment and supplies (e.g., syringes, infusion set); and
- standard tariff for service delivery by skilled providers.

However, fees will not be reimbursed for private hospitals, private physicians, or traditional birth attendants.

SINGLE ISSUE TO NEGOTIATE

For several months, the MNH Program financial staff have been negotiating with the two district hospitals and five community health centers within the PPH study areas, each of which has either a signed contract or an MNH Program Letter of Intent to complete a contract at this time. The single issue that needs to be negotiated and resolved is the fee for the village midwife (or the midwife at the community health center) who may offer emergency medical care to stabilize a study participant during her "off duty" hours when the community health center is closed. The MNH Program has agreed to make an exception to reimburse private midwives to strengthen the "emergency care safety net" for study participants who may experience birth complications and require immediate emergency care and stabilization before referral.

The study team decided that the highest possible reimbursement for a single emergency care visit with a private midwife cannot exceed four times the standard government rate (Rp. 5,000 [community health center] to 15,000 [referral hospital]). The MNH Program cannot be responsible for the entire private midwife delivery fee, because their fees far exceed the standard government tariffs. Private midwives are, however, authorized to request that the client pay the remainder of their fee.

APPENDIX A

SUPPLEMENTAL CLARIFICATION OF EMERGENCY MEDICAL CARE

ESSENTIAL POINTS TO CLARIFY

1. The PPH Study protocol requires that emergency medical care be provided through the **existing public health service delivery system** for pregnant women who experience birth complications. The key to the sustainability of any future Indonesian National Prevention of PPH Program will be the use of the existing health clinic/doctor/midwife/community volunteer health delivery system. This point is essential, because the POGI-MNH Prevention of PPH demonstration project is authorized by a decree by the Head of the Indonesian National Health Department (*Kepala Departemen Kesehatan* [*DepKes*]), Dr. Azrul, that calls for the roll out of an Indonesian National PPH Program.

2. Emergency medical care costs will be reimbursed by the MNH/Indonesia Program based on the existing tariffs established by the public health service delivery system, including reimbursement for:

- transportation to obtain medical treatment at five study area community health centers or two study area referral hospitals (*Rumah Sakit Hasan Sadikin* [RSHS] in Bandung or *Rumah Sakit Umum* [RSU] in Subang);
- medication (e.g., oxytocin), medical supplies (e.g., dextrose, Ringer's lactate solution), or equipment and supplies (e.g., syringes, infusion set); and
- standard tariff for service delivery by skilled providers.

However, fees will not be reimbursed for private hospitals, private physicians, or traditional birth attendants.

SINGLE ISSUE TO NEGOTIATE

For several months, the MNH Program financial staff have been negotiating with the two district hospitals and five community health centers within the PPH study areas, each of which has either a signed contract or an MNH Program Letter of Intent to complete a contract at this time. The single issue that needs to be negotiated and resolved is the fee for the village midwife (or the midwife at the community health center) who may offer emergency medical care to stabilize a study participant during her "off duty" hours when the community health center is closed. The MNH Program has agreed to make an exception to reimburse private midwives to strengthen the "emergency care safety net" for study participants who may experience birth complications and require immediate emergency care and stabilization before referral.

The study team decided that the highest possible reimbursement for a single emergency care visit with a private midwife cannot exceed four times the standard government rate (Rp. 5,000 [community health center] to 15,000 [referral hospital]). The MNH Program cannot be responsible for the entire private midwife delivery fee, because their fees far exceed the standard government tariffs. Private midwives are, however, authorized to request that the client pay the remainder of their fee.

The MNH Program has fulfilled the ethical obligation to provide a strong "emergency care safety net" for all study participants, including the women recruited from the control communities in Subang. The MNH Program made an exception to the policy of not reimbursing midwives for private medical care by offering them:

- Advanced training in prevention of PPH,
- Incentive payments for assisting with enrollment of eligible women,
- Full reimbursement of all costs associated with the replacement value of drugs/medical supplies used for emergency care for participants,
- Reimbursement of transportation costs if the midwife accompanies the participant to the hospital (community health center midwife coordinators receive advanced payment from the MNH Program to cover costs), and
- Payment of up to four times the standard government tariff for a simple emergency care visit.

APPENDIX B

SAFETY MONITORING GUIDELINE

The PPH Study supervision system and safety monitoring guideline ensured that distribution of misoprostol and follow-up of study participants were conducted according to a standard protocol. The safety protocols for the study were designed to serve two purposes:

- Report adverse events—death or ruptured uterus—to the WIRB and University of Indonesia ethical board within 10 days of becoming known to the study team.
- Monitor trends of safety indications, including:
  - Emergency referral due to birth complications,
  - Reports of misuse of misoprostol, and
  - Reports of loss or re-distribution of misoprostol.

REPORTING OF ADVERSE EVENTS

Adverse events—ruptured uterus or maternal death—were reported using a standard safety protocol. If the woman died during the study period, the death was detected through reports from the community health center midwife to the field supervisor. In the intervention area, a death could have been detected during the 6th month visit or at the time of the postpartum interview visit. Study deaths were investigated by the postpartum interviewers and an ob/gyn medical advisor or other physician. A series of documents, hospital records, and family visits were used to complete the verbal autopsy questionnaire. The safety monitoring guideline required that two ob/gyn physicians review the verbal autopsy information and medical records to determine the cause of death (direct obstetric cause or other) and whether the death was related to use of misoprostol. In the event that the two physicians reached conflicting conclusions, a third ob/gyn would have been called to assist with the final decision. If the death was determined to be related to misoprostol use, discussions would begin about whether to stop the study or change the study protocol and safety monitoring guideline. The results of these discussions would be recorded on the WIRB adverse event form and sent to the WIRB [illegible] Baltimore Office), University of Indonesia ethical board, and the Indonesian MOH within the required 10-day period.

A case of ruptured uterus would be detected during the postpartum interview or through a report from the district hospital. The postpartum interview form, along with the special form to document cases of misoprostol administration, would have been sent to the ob/gyn medical advisors for review. The medical advisors would determine whether the ruptured uterus was related to use of misoprostol. Again, in the event that the two physicians reached conflicting conclusions, a third ob/gyn would make the final decision. If the case of ruptured uterus was related to misoprostol use, discussions would have begun about whether to stop the study or change the study protocol or field procedures. These discussions would have begun with the principal investigators, in-country study managers, and [illegible] Baltimore staff. The results of the discussions would have been recorded on the WIRB adverse event form and sent to the WIRB [illegible] Baltimore Office), University of Indonesia ethical board, and the Indonesian MOH within the required 10-day period.

Timeline for Reporting Maternal Death

The day any study staff becomes aware of a maternal death will be counted as Day 1, even if the death occurred earlier. On Day 1 or 2, the maternal death must be reported to the local field

supervisor. The lead field supervisor must immediately contact either the field epidemiologist and/or the study manager, who will notify the medical advisors and principal investigators. By Day 3, the medical advisor, lead field supervisor, or postpartum interviewer must complete a verbal autopsy with the woman's family. By Day 4, the two medical advisors should have copies of the completed verbal autopsy forms, and turn in to the principal investigators the results of their review by Day 5. If needed, discussions regarding decisions about changes to the study protocol or field procedures will occur in the next 1 to 2 days. The [HDTEGO, Baltimore-based principal investigator is responsible for submitting the "[EB "[0 Day SAE Report Form" by Day 10. The appropriate government officials should also be notified at this time, along with the University of Indonesia ethical board.

Timeline for Reporting Ruptured Uterus

The day the study staff, either a postpartum interviewer or medical advisors, becomes aware of a case of ruptured uterus will be counted as Day 1. On Day 1 or 2, the case must be reported to the staff member's direct supervisor, the study manager or field epidemiologist, the medical advisors, and principal investigators. By Day 3, a postpartum interview must be completed. By Day 4, the two medical advisors should have copies of the completed postpartum interview form and misoprostol misuse forms, as appropriate, and turn in to the principal investigators the results of their review by Day 5. If needed, discussions regarding decisions about changes to the study will occur in the next 1 to 2 days. The [HDTEGO, Baltimore-based principal investigator is responsible for submitting the "[EB "[0 Day SAE Report Form," by Day 10. The appropriate government officials should also be notified at this time, along with the University of Indonesia ethical board.

MONITORING SAFETY INDICATORS

Misuse of misoprostol (e.g., taking misoprostol before the baby was born) was an important safety endpoint for the study and was the key parameter to be routinely reporting on data gathered from the field. Taking misoprostol before the birth of the last baby (e.g., the second twin), even if there was no adverse outcome, was reported to MCH, Indonesia and [HDTEGO, Baltimore. There was one report of a study participant who took misoprostol after the birth of the first twin, but before the second twin was born. Follow-up of this case indicated that misoprostol had no harmful effect, however the second fetus was traumatized and documented to be dead before labor began.

Whether the participant took misoprostol before the birth of her baby was determined using the standardized postpartum interview questionnaire. In the case of misuse, the study team would have investigated whether the misuse resulted from a lack of knowledge about how to use misoprostol correctly or from intentional misuse. The study team would have further investigated whether intentional misuse occurred of the woman's own volition, if she was influenced by someone else (husband, mother-in-law, traditional birth attendant, etc.), whether the woman misunderstood the positive factors about the safe use of misoprostol. The study team would have investigated if the woman experienced any unexpected adverse effects that resulted in such care.

Monitoring and reporting on the safety endpoints, including the potential misuse of misoprostol, was an ongoing activity throughout the [PPH Study team and was not a "[EB requirement. The study managers were responsible each month for reporting the percentage of women who used misoprostol before their baby was born, and also the difficulties they were having and their learning environment, as well as the percentages who correctly and successfully used misoprostol to treat the misoprostol. These data were compiled into a database for systematic and site-by-site analysis and reporting purposes. The questionnaire included all study participants who also had a

[illegible]

REFERENCES

Broekhuizen FF. 2000. Misoprostol, its use in obstetrics and gynecology. *Current Problems in Obstetrics, Gynecology, and Fertility* 23: 183–224.

Carpenter JP. 2001. *Misoprostol for Prevention of Postpartum Hemorrhage: An Evidence-Based Review by the U.S. Pharmacopeia.* United States Pharmacopeia: Rockville, MD.

Central Bureau of Statistics (CBS) [Indonesia]. 1991. *Household Health Survey (Survei Kesehatan Rumah Tangga), 1991.* Badan Pusat Statistik, Departemen Kesehatan (BPS–Ministry of Health): Jakarta, Indonesia.

Central Bureau of Statistics (CBS) [Indonesia] et al. 1996. *Indonesia Demographic and Health Survey 1995.* CBS and Macro International: Calverton, MD.

Central Bureau of Statistics (CBS) [Indonesia] et al. 1998. *Indonesia Demographic and Health Survey 1997.* CBS and Macro International: Calverton, MD.

Central Bureau of Statistics (CBS) [Indonesia]. 2002. *District-Level Household Summary Estimate Report, Bandung and Subang District.* Badan Pusat Statistik, Departemen Kesehatan (BPS–Ministry of Health): Jakarta, Indonesia.

El-Refaey H et al. 1997. Use of misoprostol in prevention of postpartum hemorrhage. *Br J Obstet Gynaecol* 104: 336–339.

El-Refaey H et al. 2000. The misoprostol third stage of labor study: A randomised controlled comparison trial between orally administered misoprostol and standard management. *Br J Obstet Gynaecol* 107: 1104-1110.

Goldberg AB, BM Greenberg, and PD Darney. 2001. Misoprostol and pregnancy. *N Engl J Med* 344: 38–46.

Gülmezoglu AM et al. 2001. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. *Lancet* 358: 689–695.

Hogerzeil HV, GJ Walker, and MJ de Goeje. 1993. *Stability of Injectable Oxytocics in Tropical Climates.* World Health Organization: Geneva.

Lumbiganon P et al. 1999. Misoprostol dose related shivering and pyrexia in third stage of labour. WHO collaborative trial of misoprostol in management of third stage of labour. *Br J Obstet Gynaecol* 106: 304–308.

Ng PS et al. 2001. A multicentre randomized controlled trial of oral misoprostol and i.m. syntometrine in the management of the third stage of labour. *Hum Reprod* 16: 31–35.

Pfitzer A and H Sanghvi (eds). 2004. *Preventing Postpartum Hemorrhage: From Research to Practice.* JHPIEGO/MNH Program: Baltimore, MD.

Prendiville WJ et al. 1988. The Bristol third stage trial: Active versus physiologic management of third stage of labour. *BMJ* 297: 1295–1300.

Rogers J et al. 1998. Active versus expectant management of third stage of labour: The Hinchingbrooke randomized controlled trial. *Lancet* 351: 693–699.

Statistics Indonesia (Badan Pusat Statistik) or ORC Macro. 2003. *Indonesia Demographic and Health Survey 2002–2003*. BPS and ORC Macro: Calverton, MD.

PREVENTION OF POSTPARTUM HEMORRHAGE STUDY: WEST JAVA, INDONESIA

ORIGINALITY REPORT

5%

SIMILARITY INDEX

PRIMARY SOURCES

1	www.lp-idaho.org Internet	190 words — 1%
2	reprolineplus.org Internet	156 words — 1%
3	www.jhpiego.org Internet	86 words — 1%
4	www.mnh.jhpiego.org Internet	79 words — 1%
5	krishikosh.egranth.ac.in Internet	71 words — < 1%
6	www.cllc.org.uk Internet	48 words — < 1%
7	aina.org Internet	45 words — < 1%
8	ar.scribd.com Internet	45 words — < 1%
9	pt.scribd.com Internet	27 words — < 1%

EXCLUDE QUOTES ON EXCLUDE MATCHES < 1%

EXCLUDE BIBLIOGRAPHY ON