



Review

Saving maternal lives in resource-poor settings: Facing reality

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Abstract

Objective: Evaluate safe-motherhood interventions suitable for resource-poor settings that can be implemented with current resources.

Methods: Literature review to identify interventions that require minimal treatment/infrastructure and are not dependent on skilled providers. Simulations were run to assess the potential number of maternal lives that could be saved through intervention implementation according to potential program impact. Regional and country level estimates are provided as examples of settings that would most benefit from proposed interventions.

Results: Three interventions were identified: (i) improve access to contraception; (ii) increase efforts to reduce deaths from unsafe abortion; and (iii) increase access to misoprostol to control postpartum hemorrhage (including for home births). The combined effect of postpartum hemorrhage and unsafe abortion prevention would result in the greatest gains in maternal deaths averted.

Discussion/conclusions: Bold new initiatives are needed to achieve the Millennium Development Goal of reducing maternal mortality by three-quarters. Ninety-nine percent of maternal deaths occur in developing countries and the majority of these women deliver alone, or with a traditional birth attendant. It is time for maternal health program planners to reprioritize interventions in the face of human and financial resource constraints. The three proposed interventions address the largest part of the maternal health burden.

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Keywords: Maternal mortality; Family planning; Postpartum hemorrhage; Abortion; Interventions; Misoprostol

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1. Maternal mortality worldwide

Ninety-nine percent of maternal deaths occur in developing countries and most of these women deliver alone or without a skilled birth attendant (SBA) [1]. More than 500,000 women die from pregnancy and childbirth around the globe annually [2]. For every woman who dies, an estimated 30 women live to suffer severe morbidities including infertility, fistula, and incontinence [1]. In Sub-Saharan Africa (SSA) alone, women are 250 times higher risk of dying during pregnancy or childbirth than their counterparts in industrialized countries [2]. Maternal deaths are highest in the most difficult to access areas (i.e. rural settings)—where women are unable to reach an SBA or appropriate facilities in times of complication during labor or delivery [3]. This burden is compounded by the shear reality that most complications occur at the time of delivery and cannot be predicted beforehand. For example, many pregnancies identified as high risk deliver normally and most life-threatening complications occur in low risk women [4].

The main direct causes of maternal death include postpartum hemorrhage (PPH), sepsis, eclampsia, unsafe abortion, and obstructed labor (Table 1). Using various country datasets, Khan et al. (2006) estimate that hemorrhage is the main cause of maternal mortality in Asia and Africa—accounting for 30% or more of all maternal deaths [5]. Deaths due to eclampsia, unsafe abortion, and obstructed labor combined account for 17.7% and 26.7% of maternal deaths in Africa and Asia, respectively. However, these estimates are likely to be higher as the datasets used do not represent a random sample of the population at risk, but simply availability of data [5]. Misclassification has also been an issue in accurately assessing causes of maternal death [6]. Figures related to abortion, for example, are

probably much higher as social stigma and legal restrictions associated with abortion in many countries means abortion-related deaths may likely go unreported [7].

To date, the primary strategies to reduce MMR by the international community have been to ensure that every woman has ready access to an SBA during delivery and EmOC in case of complications [1]. However, poor settings are often plagued by electricity outages, lack of transportation or viable roadways to reach higher level facilities, absence of potential trainees for professional clinical positions, and professional migration. The devastating shortage in human resources and necessary infrastructure across the developing world makes these interventions impossible to achieve quickly.

2. Skilled attendants

Safe-motherhood service packages to reduce MMR are shown to be highly cost-effective, yet a nurse, midwife, or doctor for every delivery is still a distant goal for those regions with the highest MMRs [8]. The World Health Organization (WHO) estimates that there are 57 countries with a critical deficit of health workers adding up to 2.4 million doctors, midwives and nurses. SSA and South & South East Asia are currently experiencing the greatest deficit [9]. In places such as Africa, where global burden of disease is as high as 24%, only 3% of the world's available providers are living and working in Africa. This is a sharp contrast to the Americas (incl. Canada and the US) which has 10% of the global burden of disease, but has 37% of available health workers [9]. This has dire consequences on maternal health. The lowest MMRs occur in those countries where the highest proportion of deliveries are attended by an SBA and where contraceptive prevalence (CPR) is high (Table 2). In developing coun-

Table 1
Distribution of causes of maternal deaths by region and available priority interventions

	Average percent distribution ⁵			Available priority intervention(s)
	Africa	Asia	Latin America, the Caribbean	
Hemorrhage	33.9	30.8	20.8	AMTSL ^a Uterotonic agents: Oxytocin, Ergometrine, Misoprostol Blood and IV fluids Anti-shock garment Balloon catheter Surgical procedures
Hypertensive disorders	9.1	9.1	25.7	Blood pressure monitoring Antihypertensives Magnesium sulfate Supportive air management
Infections/sepsis	9.7	11.6	7.7	STI treatment Clean delivery Antibiotics Vitamin A supplementation
Unsafe abortion	3.9	5.7	12	Family planning Safe abortion care Post-abortion care
Obstructed labor	4.1	9.4	13.4	Partograph Misoprostol for induction Instrumental delivery Cesarean section
Other direct	7.4	2.1	4.9	
Indirect ^b	32.0	31.4	15.7	

^a AMTSL: active management of third stage of labor (oxytocin; cord traction; uterine massage).

^b Including anemia, HIV/AIDS, and unclassified deaths.

Table 2
Maternal mortality ratio (MMR), percent births attended by a skilled professional, percent rural population, and contraceptive prevalence by region

Region	Maternal mortality ratio (a, b) (deaths per 100,000 live births)	% Births with skilled attendants (b)	% rural (b)	Contraceptive prevalence (%) (b)
World total	402	62	50	54
Developed regions	9	99	25	57
Europe	17	99	28	53
Africa	824	47	61	21
Northern Africa	157	70	48	45
Sub-Saharan Africa	905	53	59	21
Asia	329	58	59	58
Eastern-Asia	53	97	54	81
South-Central Asia	581	39	69	42
South-Eastern Asia	280	69	55	51
Western Asia	127	73	35	29
Latin America/Caribbean	132	83	22	63
Oceania	427	84	29	57

Source: (a) Hill et al. (2007); (b) State of the World's Population (2007).

tries more than half of pregnant women deliver at home without an SBA [10].

Even if efforts to increase the number of SBAs were moving ahead quickly, developing countries face another issue—brain drain, the tendency of trained individuals to migrate to urban areas and more developed nations. The International Federation of Gynecology and Obstetrics and International Confederation of Midwives recommend that there be one skilled provider for every 5000 individuals. However, with current brain drain, the average physician to population ratio is as low as 1 doctor for every 100,000 people in developing countries. In the rural areas, where 80% of populations from the developing world live, this ratio is even lower [11]. Thus, although there are safe-motherhood interventions which have been shown to be highly cost-effective, the doctors, nurses or midwives needed at every delivery to care for them is still a distant goal for those regions with the highest MMRs [8].

3. Emergency obstetric care

Barriers to reducing MMR are further compounded by the reality that even if there were available health workers, there is a significant shortage in facilities and equipment for clinical personnel to provide emergency maternal care. EmOC refers to a set of interventions prescribed for women who are suffering from complications during labor or delivery that require professional assistance. It is divided into two levels of care: Basic EmOC (BEOC) and Comprehensive EmOC (CEOC). BEOC are performed in a health center, but does not require an operation theatre. Interventions include administration of antibiotics, oxytocics, and anticonvulsants, manual removal of placenta or other retained products of pregnancy, and an assisted vaginal delivery. CEOC requires an operation theatre and is often performed in district hospitals. Interventions include BEOC services as well as caesarean section and safe blood transfusion [1].

According to the WHO, United Nations Children's Fund (UNICEF), and United Nations Population Fund (UNFPA), the minimum number of EmOC facilities per population is 4 BEOC and 1 CEOC per 500,000 people [2]. A recent study done by Paxton et al. (2006), examined 39 countries to determine the global availability of EmOC facilities. The study found that CEOC facilities

tend to be available even in the poorest of countries, however BEOC are consistently unavailable in countries with high and moderate MMRs. The authors point out that even though most countries have access to the minimum required CEOC facilities there remains a significant fear about the quality of care being provided at EmOC facilities, whether care is being provided equitably, and how accessible facilities are geographically and financially to healthcare seekers [12].

EmOC requires skilled staff, a reliable transportation system, adequate supply of drugs and functioning equipment (including operation theatres for CEOC), and are thus difficult to scale up in poor settings [13]. The reality is that even if there is the minimum number of CEOC facilities per 500,000 individuals, these centers are rarely fully functioning in the places they are needed most and are typically only built in urban locations, making them completely inaccessible to the poorest of the poor living in rural areas. Therefore we suggest it is imperative to explore alternative strategies to reduce MMR.

4. Methods

We reviewed literature available on public databases including PubMed, Population Information Online, Web of Science, and the Scholarly Journal Archive, using the terms: health worker shortage, developing countries, maternal mortality, causes of maternal death, traditional birth attendants, misoprostol, birth attendant, postpartum hemorrhage, third stage of labor, developing world, community interventions, oxytocics, active management, maternal health interventions, abortion, unintended pregnancies, contraception. We also searched the reference lists from the articles found using these terms. Publication period was not specified and all studies the search engine returned were considered.

In addition, relevant documents from the WHO, UNICEF, and UNFPA were reviewed. We employed Stat Compiler to gather country-specific data from the last available Demographic Health Survey (DHS) for each country. The Population Reference Bureau Data Compiler was also used for further country-specific information. Specific MMR information was gathered from DHS reports, Hill et al. (2005), and the State of the World Population 2007 report.

To determine the three suggested maternal health interventions on which program planners should focus their efforts, we first tabulated the distribution of causes of maternal mortality and the interventions that have been proven to avert those causes (Table 1). We focused on those interventions that could be scaled up without having to increase existing health delivery infrastructure and/or human capacity and require a low level of skilled provider to carry out the intervention.

After deciding on the three interventions that should be prioritized, we used the WHO Mother Baby Package (MBP) to assess the relative effectiveness of the intervention, and Monte Carlo simulations to assess the potential number of maternal lives that could be saved after program implementation. Regional and country level estimates are calculated as examples of settings that would benefit the most. The MBP prescribes a set of 18 basic interventions considered essential for decreasing maternal and neonatal mortality in resource poor settings [14]. The package describes simple, effective interventions

needed before, during, and after delivery for the mother and newborn. It also outlines the maximum impact on averting maternal deaths that individual interventions can have after their implementation.

Using the information provided by the MBP and Fortney's study on the potential impact of family planning services (1987), Monte Carlo simulations were run for each intervention (10,000 trials for each) [14,15]. Simulations were conducted using Crystal Ball 7 software, a stochastic modeling supplement for Excel. We performed multivariate sensitivity analysis on the results of each model to assess contribution to variance given our underlying assumptions. Models were run for SSA, Asia, Niger, Rwanda, Burkina Faso, and Cambodia. The four countries were chosen based on their high MMRs, the proportion of population living in rural regions (>75%), and their low CPRs (<20%). Assumptions used in the models are the number of maternal deaths, proportion of deaths due to a direct cause of maternal death, and range of possible program dissemination into the population and poten-

Table 3
Monte Carlo simulation assumptions

Region/country	Number of maternal deaths (a, b)	Proportion of attributal cause of maternal death (%) (c)	Estimated number of maternal deaths	Program coverage (%)	Estimated impact of intervention (%) (c, d)
Postpartum hemorrhage					
Sub-Saharan Africa	270,500	25	67,625	20–80	55–82
Asia	240,600	25	60,150	20–80	55–82
Niger	12,269	25	3,067	20–80	55–82
Rwanda	5,199	25	1,300	20–80	55–82
Burkina Faso	4,662	25	1,166	20–80	55–82
Cambodia	2,022	25	506	20–80	55–82
Family planning					
Sub-Saharan Africa	270,500	13	35,165	20–80	26–58
Asia	240,600	13	31,278	20–80	26–58
Niger	12,269	13	1,595	20–80	26–58
Rwanda	5,199	13	676	20–80	26–58
Burkina Faso	4,662	13	606	20–80	26–58
Cambodia	2,022	13	263	40–80 (e)	26–58
Safe Abortion					
Sub-Saharan Africa	270,500	13	35,165	20–80	75–95
Asia	240,600	13	31,278	20–80	75–95
Niger	12,269	13	1,595	20–80	75–95
Rwanda	5,199	13	676	20–80	75–95
Burkina Faso	4,662	13	606	20–80	75–95
Cambodia	2,022	13	263	20–80	75–95

Source: (a) Hill et al. (2005); (b) State of the World's Population (2007); (c) Source: WHO Mother Baby Package; (d) Source: Fortney (1987); (e) 40–80% possible program dissemination for family planning services was used as current contraceptive prevalence in Cambodia according to (b) is 19%.

tial program impact. These assumptions were then used to calculate the number of maternal deaths that could be averted with varying degrees of program dissemination (Table 3).

5. Results

5.1. What will make a difference in resource-poor settings?

Access to an SBA, as achieved in countries such as Sri Lanka, must not be abandoned in any way, and improved access to EmOC is imperative where it is achievable. However, in the intermediate term for the 50 million women who do not have SBAs and are beyond the reach of EmOC, only a few priority interventions (Table 1) are realistic. After reviewing the literature, we found that achievable, cost-effective, scalable strategies to reduce MMR in resource-poor settings include: decreasing the number of unintended pregnancies by increasing access to contraception; confronting the public health implications of unsafe abortion by increasing access to contraception, comprehensive abortion care, safe abortions (SA), and post-abortion care (PAC); as well as controlling PPH by increasing misoprostol availability (including for home births).

If we examine the direct causes of maternal death, we will find that interventions aimed at preventing unwanted pregnancies, unsafe abortion, and PPH share something in common which others do not. They can be implemented outside of the hospital, in the hands of lower-level providers, and even at home. Hypertensive disorders and obstructed labor for example, require highly trained assistance in a facility that has sufficient equipment, including magnesium sulfate solutions for eclampsia, and an operating room for cesarean-sections. Sepsis/infection interventions, including STI treatment and antibiotic administration are also facility-based in today's global medical establishment and are thus difficult to scale up in poor-resource settings.

5.2. Family planning

Two hundred and five million pregnancies occur annually worldwide, 35% of which are unintended and 22% of which end in an induced abortion. Most of these pregnancies (182 million) happen in the developing world. Two-thirds of these pregnancies occur among women who are not using any method of contraception, making FP a significant contributor to maternal health. Contraceptive use decreases the risk of maternal death by decreasing the odds of being pregnant [15]. Fig. 1, a graph assembled using MMR and CPR

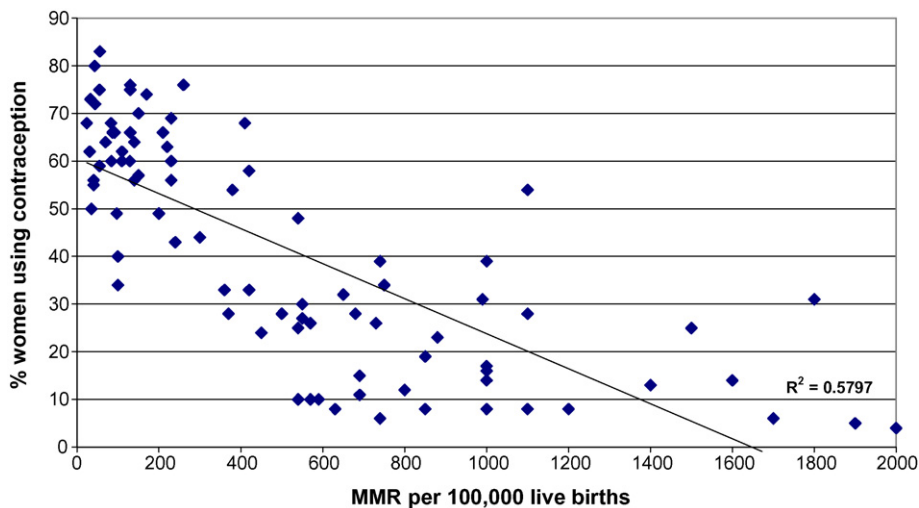


Fig. 1. Maternal mortality and contraceptive prevalence for countries with a DHS in the last 5 years. Source: Demographic and Health Surveys (DHS), country specific data for the last five.

data from the DHS, demonstrates a strong negative correlation.

Today, there are over 100 million married women alone who have an unmet need for contraception. Most of these women live in SSA and South & Southeast Asia [16]. Among those women who become pregnant and elect to have an abortion, they are at risk of severe complications, including death if they do not have access to a skilled provider. It is estimated that 11% of induced abortions in developing countries are done in unsafe conditions. This is over 20 million women who are at risk of dying every year from a completely preventable condition [16]. Yet, by increasing modern contraceptive use, the rate of abortion will decline dramatically. The Center for Population report, entitled *The Role of Family Planning in Preventing Abortion*, acknowledges that there have been countries where use of contraception and abortion rates appear to be rising at the same time. However, authors reiterate that historical examples across the globe demonstrate that this “phenomenon may occur because the desire to have smaller families may be increasing faster than the availability of contraceptive information/services and the consistent use of effective contraceptives” [17].

Contraception also has a differentially positive impact on the MMR because contraceptives are sometimes adopted first by the women over age 35 and under 20. Adolescence, older age, high-parity and short birth intervals are all known risk factors for maternal mortality [18]. It is estimated that the impact of FP on reducing MMR among women below the age of 20, above the age of 39, or among those with a parity of more than 5 ranges from a 25% to 58% [15].

Provision of family planning (FP) is a solution that can be achieved quickly and is sustainable. There are many reasons why women may not choose to use contraceptives. It is important, therefore, to address any fears or preferences that women may have in choosing a method to control their own fertility. Common concerns include possible health and side effects, a woman’s belief that they are not at risk of getting pregnant, and having to negotiate contraceptive use with a partner or her own religious beliefs. However, in communities where several choices are made available, women are more likely to find a method that is appropriate for them. Injectable contraceptives, the method of choice

for many women in rural areas, such as Depo, have now given program planners a way of reaching women with an unmet need for contraception more quickly. Although Depo requires an injection, studies are indicating that low level providers, such as paramedics and community health workers, are able to properly administer Depo injection to women at the community level [19]. Furthermore, studies have shown high acceptability of injectables as it is both a long-term method and can be done privately without negotiation with one’s partner [20].

5.3. Safe abortion and post-abortion care

When speaking of the impact which abortion can have on MMR, it is not abortion which causes a woman to die. It is having one that is unsafe, which puts her at risk of complications such as hemorrhage and sepsis. According to the WHO, the definition of a unsafe abortion is “a procedure for terminating an unintended pregnancy carried out either by person lacking the necessary skills or in an environment that does not conform to minimal medical standards, or both.” It is estimated that around 5 million women are hospitalized every year for PAC [21]. This accounts for the largest proportion of hospital admissions for gynecological services in the developing world [7]. Among those women who have children, it is estimated that 220,000 children lose their mothers [21]. It is believed that worldwide, 67,000 women die from PAC—the equivalent of 13% of total maternal deaths [16]. It is estimated that the impact of SA services on reducing maternal mortality ranges 75–95% [14].

Unsafe abortion is an important cause of maternal death. Developed countries, for example, would not have achieved very low MMRs without access to SA. Furthermore, by preventing unwanted pregnancies, unsafe abortion is easily preventable [11]. Even where abortion is an illegal practice, several steps can be taken to reduce MMRs attributed to it. The first, is to improve access to contraception (as explained above) and PAC (including FP counseling) [22]. The second is to provide SA to the extent allowed by the law.

There are several options for first trimester abortion and PAC. These include both surgical (e.g. manual vacuum aspiration (MVA) and dilation and curettage) and medical methods (e.g. mifepristone

Table 4
Misoprostol for safe abortion (incl. missed abortion) and post-abortion care

Author	Year	Country	n	Study	Results [RR (95% CI)] and conclusions
Post-Abortion care					
Coughlin	2004	UK	131	Effectiveness of 400 µg oral misoprostol for first trimester incomplete miscarriage	Successful treatment was achieved in 77.7% of women Single dose of 400 µg of oral misoprostol was an effective treatment for women presenting with an incomplete miscarriage
Murchison	2004	USA	41	Study of 800 µg misoprostol intravaginal administration for uterine evacuation for missed abortion	Overall success rate was 78%. 'Intravaginal miso is a safe, effective alternative to surgical curettage for the treatment of missed abortion
Blum ^a	2007	–	–	Review of all English language articles published before October of 2007 using misoprostol to treat incomplete abortion and miscarriage in the first trimester	Sufficient evidence exists to support miso as a safe and effective means of non-surgical uterine evacuation Recommendation: 600 µg oral miso to treat incomplete abortion in women during the first trimester.
Gemzell-Danielsson ^b	2007	–	–	Review of published literature on misoprostol to treat missed abortion in first trimester.	800 µg vaginal miso is as effective and safe as traditional surgical treatment 600 µg sublingual miso can also be used for same indication.
Sharma	2007	India	50	Prospective study of 600 µg misoprostol every 3 h for a maximum of 3 doses for women up to 13 weeks gestation for missed abortion.	Success rate was 86% (up to 72 h) Acceptability of the method was 69.7%
Vejborg	2007	Denmark	355	Study of effectiveness of single dose vaginal misoprostol 400 µg to reduce the number of surgical interventions in early pregnancy failure	Single dose misoprostol reduced the number of surgical interventions Success rates of miso treatment varied according to ultrasonographic definitions of pregnancy failure, time of assessment and criteria for success
Safe abortion in the first trimester					
Herabutya	1997	Thailand	84	Compare 200 µg misoprostol vs. placebo in women with a missed abortion	200 µg vaginal misoprostol produced spontaneous expulsion in women with a missed abortion and reduced the need for surgical treatment 83.3% in miso prostol group aborted spontaneously compared to 17.1% in the placebo group ($p < 0.0001$)

Table 4 (Continued)

Author	Year	Country	n	Study	Results [RR (95% CI)] and conclusions
Moreno-Ruiz ^c	2006	–	–	Review published reports of first-trimester medical abortion regimens that do not include mifepristone with at least 100 participants and were published since 1990. Author examines misoprostol alone.	Alone or in combination with methotrexate, misoprostol is an efficacious alternative to mifepristone for the medical termination of pregnancy
Faundes ^d	2007	–	–	Review of publications reporting on misoprostol alone for pregnancy termination within the first 12 weeks of pregnancy. Authors compare vaginal administration of 800 µg of misoprostol repeated up to three times at 6, 12 or 24 h interval to (i) oral administration at the same dose; and (ii) sublingual administration at 3 h intervals.	Vaginal administration of 800 µg repeated up to three times has an 85 to 90% effectiveness in most studies Oral administration is less effective Sublingual administration is as effective Oral and sublingual administration appear to be better accepted than vaginal administration Most studies are limited to first 9 weeks of pregnancy. More research is needed for >9 weeks
Prasad	2008	India	140	Comparison between saline-soaked misoprostol (800 µg) administered vaginally and surgical evacuation in hospital setting.	Single does vaginal misoprostol has comparable success rate as surgical method for termination. Side effects were fewer in miso group and had higher acceptability rate

^a Blum et al. examine twenty-six studies: Chug (1999); Chung (1999); Pang (2001); Gronlund (2002); Ngai (2001); Demetroulis (2001); de Jonge (1995); Pandian (2001); Agostini (2005); Bagratee (2004); Creinin (1997); Davis (2004); Graziosi (2004); Henshaw (1993); Moodliar (2005); Muffley (2002); Zhang (2005); Ngoc (2005); Blanchard (2004); Weeks (2005); Shwekerela (2007); Dao (2007); Bique (2007); Trinder (2006); Rakotovo (2006).

^b Gemzell-Danielsson et al. examine eight additional studies: Kovavisarach (2002); Wood (2002); Heard (2002); Kovavisarach (2005); Ngoc (2004); Tang (2003); Herbutya (1997); Lister (2005).

^c Moreno-Ruiz et al. examine twelve additional studies on misoprostol alone: Carbonell (2003); Singh (2003); Zikopoulos (2002); Jain (2002); Jain (2001); Carbonell (2001); Bugalho (2000); Velazco (2000); Carbonell (1999); Carbonell (1997); Carbonell (1997); Wiebe (2004).

^d Faundes et al. examine eight additional studies which analyze misoprostol alone for first trimester induced abortion: Carbonell (1998); Jain (1999); Bugalho (1996); Blanchard (2005); von Hertzen (2007); Ngai (2000); Salakos (2005); Carbonell (2003).

and misoprostol combination as well as misoprostol alone). Among options available, women living in low-resource settings would benefit most from regimens of misoprostol alone, backed by MVA if needed, or MVA, as they usually require fewer subsidies. Moreover, both technologies can be used to successfully manage incomplete abortions. They are safe, effective, cheap, can be performed without general anesthesia, and usually preempt the need for overnight stay, saving hospital and individual costs [23].

Table 4 is a list of studies and their results/recommendations on using misoprostol alone for both elected and missed abortions as well as PAC. Evidence indicates that misoprostol-alone is a safe and effective means to induce abortion or treat abortion complications [24–33]. Furthermore, researchers have found that misoprostol is as effective and as acceptable to women as MVA, and thus well-suited for low-resource settings [34–36]. Overall, misoprostol has the potential to help significantly reduce the number deaths related to unsafe abortion.

Table 5
Options to prevent/treat postpartum hemorrhage

Place of delivery	Type of assistance	Options
Comprehensive obstetric care facility	Highly skilled	AMTSL Uterotonics Oxytocin Ergometrin Misoprosol Fluid replacement Blood transfusion Surgery
Basic obstetric care, i.e. primary health care facility	Skilled	AMTSL Uterine massage ^a Cord traction ^a Uterotonics Oxytocin: IV ^b , Uniject ^{b,c} Ergometrin ^{b,c} Misoprostol Fluid replacement ^b Antishock garment ^d Hydrostatic condom balloon catheter ^{a,d}
Household level	Skilled	AMTSL Uterine massage ^a Cord traction ^a Uterotonics Oxytocin: Uniject ^{a,c} Misoprostol
	Traditional birth attendant	HBLSS Uterine massage ^a Uterotonics Misoprostol
	None	HBLSS Uterotonics Misoprostol

HBLSS: home-based live saving skills.

^a Requires special skills and training.

^b Requires injection, skills and training.

^c Requires electricity and special storage.

^d Under study, requires high resources.

5.4. Postpartum hemorrhage

PPH is the leading cause of maternal mortality worldwide. An estimated 14 million women experience pregnancy-related hemorrhage each year. It is clinically defined as blood loss greater than or equal to 500 mL. Eighty percent of PPH cases are due to uterine atony, whereby the uterus fails to contract after the baby delivers. Other causes of PPH include retention of the placenta or pieces of the placenta, lacerations or tears of the cervix, vagina, or perineum, and uterine rupture. Unfortunately ninety percent of women do not present

with risk factors, making PPH prevention extremely important especially in low-resource settings, where access to care is scarce or non-existent [1,37]. It is estimated that the impact of PPH management on reducing MMR, ranges from 55% to 82% [14].

Options to prevent or treat PPH depend largely on place of delivery setting and resources (Table 5). We focused on what is feasible, affordable, and sustainable in home deliveries with limited resources and minimally trained delivery attendants. The most commonly recommended methods of managing PPH include active management of the third stage of labor

Table 6
Misoprostol and the prevention of postpartum hemorrhage

Author	Year	Country	n	Study	Results [RR (95% CI)] and conclusions
Bhullar	2004	USA	848	RCT comparing Buccal 200 µg misoprostol tablet or placebo at time of cord clamping	Miso vs. placebo for blood loss >500 mL: RR0.65 (0.33–1.29) Buccal miso at cord clamping is not more effective than placebo in reducing PPH
Langenbach ^a	2005	–	30017	Meta-analysis of 22 RCTs of misoprostol vs. placebo or misoprostol vs. other uterotonics	Miso vs. Placebo for blood loss >500 mL and >1000 mL: RR0.85 (0.63, 1.14) Miso vs. Oxytocics for blood loss >500 mL: RR1.4 (1.22, 1.56)) Miso vs. Oxytocics for blood loss >1000 mL: RR1.25 (0.94, 0.17) Miso is not an inferior drug; Conventional uterotonic drugs should not be used in settings where they are entirely unsuitable
Prata	2006	Egypt	2532	Pre-/Post- study comparing current AMTSL practices with oxytocin vs. with misoprostol 600 µg oral	Miso vs. current practices for blood loss ≥500 mL: RR0.30 (0.16, 0.56) Where oxytocin and/or ergometrine are not consistently used during AMTSL, misoprostol should be considered for inclusion in AMTSL
Zachariah	2006	India	2023	RCT comparing 2 mg intravenous ergometrine, 10 U IM oxytocin, and 400 µg misoprostol	No significant difference between three groups, $p=0.623$ for blood loss >500 mL, $p=0.146$ for blood loss >1000 mL, $p=0.234$ for the need of additional oxytocics Oral misoprostol is as effective as conventional oxytocin agents in preventing PPH and can be recommended for low-resource settings
Alfirevic ^b	2007	–	22749	Systematic Review of 7 RCTs of misoprostol 600 µg oral or sublingual vs. injectible uterotonics	Miso vs. Placebo in community settings: RR0.59 (0.41, 0.84); in hospital settings: RR1.34 (1.23, 1.74) Miso vs. Injectible Oxytocin: RR1.34 (1.16, 1.55) Conc: Use misoprostol when conventional injectible uterotonics are not available
Baskett	2007	Canada	622	Double-blind RCT comparing 400 µg oral misoprostol with 5 unites of intravenous oxytocin	No difference between two groups, $p=0.98$ The routine use of 400 µg of oral misoprostol was no less effective than 5 U of intravenous oxytocin in reducing blood loss after delivery for blood loss of >1000 mL
Enakpene	2007	Nigeria	864	RCT comparing oral misoprostol 400 µg with 500 µg IM methylergometrine.	Miso vs. Ergometrine for blood loss >500 mL: RR0.14 (p -value < 0.0001) Oral miso was more effective in reducing blood loss during third stage of labor than ergometrine

^a Study examines fifteen studies: Amant (1999); Bamigboye (1998); Bamigboye (1998); Benchimol (2001); Bugalho (2001); Caliskan (2003); Caliskan (2002); Cook (1999); El-Refaei (2000); Gerstenfeld (2001); Gulmezoglu (2001); Hofmeyr (2001); Hofmeyr (1998); Karkanis (2002); Kundodyiwa (2001); Lam (2004); Ng (2001); Oboro (2003); Ray (2001); Surbeck (1999); Vilmala (2004); Walley (2000).

^b Study examines three additional studies than Langanbach: Derman (2006); Hoj (2005); Walraven (2005).

(AMTSL), which involves the administration of a prophylactic uterotonic, delivery of the placenta with controlled cord traction, and uterine massage after delivery of the placenta. AMTSL reduces the length of the third stage of labor and boosts uterine contractions, decreasing the risk of PPH [38]. However, it requires a skilled attendant, a viable supply of uterotonics, and items needed for injection administration. Furthermore, once PPH is established, the treatment of PPH – through administration of a uterotonic – becomes extremely important [38].

Oxytocin is the uterotonic drug of choice for AMTSL, and should be made available whenever a skilled attendant is present and appropriate storage conditions exist [39]. Ergometrine, also used for AMTSL, is less stable in field conditions than oxytocin, and has increased risk of serious side effects in hypertensive women [40]. Both drugs need to be administered parentally. Therefore, without a skilled attendant present to make the injection, ergometrine and oxytocin cannot be chosen for PPH management in home births in developing countries where most deliveries occur. Alternative methods like nipple stimulation and oral ergometrine have shown no advantage over injectable uterotonics [41,42].

Misoprostol has long been recognized as a safe and efficacious drug for controlling PPH. It can be used by itself or as a part of AMTSL, in place of oxytocin or ergometrine whenever an SBA is not available and appropriate storage conditions do not exist [43]. Its low cost, ease of administration (rectal, oral, sublingual) and stability in tropical climates make it an ideal solution for home births [44]. Table 6 reviews studies examining the use of misoprostol in the prevention of PPH in community and hospital settings. Despite the relative superiority of conventional injectable uterotonics, to date nobody has rejected misoprostol as an appropriate drug where injectable uterotonics are not available or cannot be administered [43,45–52]. Furthermore, systematic reviews of randomized controlled trials found decreased need for additional uterotonics when comparing misoprostol to placebo, and recommend misoprostol to be used in developing countries [45,51,52]. Results from a recent study, for example, comparing misoprostol with a placebo in home births found that misoprostol was associated with a 50% reduction in PPH in a resource-poor setting [53]. One of the most recent review studies even concludes that

Table 7

Estimated potential number of maternal deaths averted by intervention according to region and country

Region	Mean	Range [min–max]
Postpartum hemorrhage		
Sub-Saharan Africa	23,225	7443–44427
Asia	20,630	7179–39441
Niger	1,052	372–2056
Rwanda	448	160–829
Burkina Faso	400	142–769
Cambodia	174	61–342
Safe abortion		
Sub-Saharan Africa	14,903	5663–28395
Asia	13,286	4891–24495
Niger	677	254–1213
Rwanda	287	107–535
Burkina Faso	259	91–466
Cambodia	111	41–208
Family planning		
Sub-Saharan Africa	7,408	2213–16411
Asia	6,547	1947–14199
Niger	336	97–746
Rwanda	142	42–307
Burkina Faso	128	37–280
Cambodia	63	27–126
Postpartum hemorrhage, family planning, and safe abortion		
Sub-Saharan Africa	45,577	23401–75424
Asia	40,456	18598–68415
Niger	2,063	958–3247
Rwanda	876	429–1380
Burkina Faso	784	396–1239
Cambodia	386	265–582
Postpartum hemorrhage and family planning		
Sub-Saharan Africa	30,485	12691–56362
Asia	27,158	11543–48331
Niger	1,388	592–2474
Rwanda	587	223–1023
Burkina Faso	529	223–929
Cambodia	259	157–414

misoprostol should not be branded an inferior drug for the prevention of PPH [51].

5.5. Potential maternal deaths averted

According to our simulations, we found that implementing FP, SA and PAC, as well as PPH management services in low-resource settings will have a significant impact on reducing MMR. Table 7 shows the number of maternal lives that can be saved by providing our three suggested priority interventions to women in

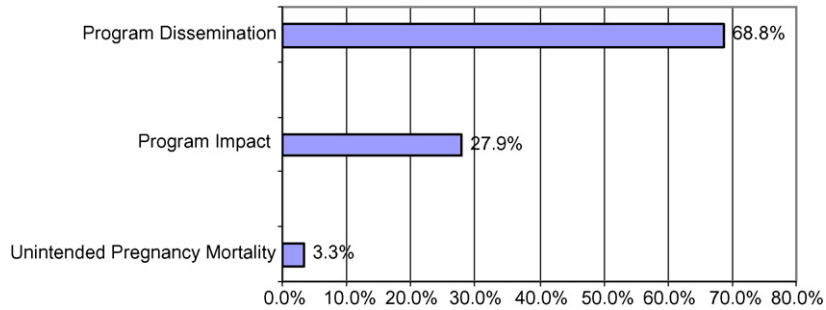


Fig. 2. Sensitivity analysis: Sub-Saharan Africa Model Maternal Deaths Averted due to Family Planning Services.

SSA, Asia, and four low-resource countries—Niger, Rwanda, Burkina Faso, and Cambodia. The table also depicts the number of lives that could be saved a combination of the interventions were implemented. Specifically, we examined the result of combining (i) FP and PPH management services; and (ii) all three interventions. We refer to program dissemination to estimate the potential coverage of the interventions.

Implementing PPH programs, including those which will reach women who are delivering at home and/or without an SBA, will avert the greatest number of maternal deaths. In SSA, where maternal mortality is the highest in the world, regional gains in maternal lives saved will be the greatest. At the country level, our examples demonstrate that Niger will benefit the most in terms of potential maternal death averted due to PPH. This is in comparison to countries with lower MMR, such as Cambodia, where gains will be smaller.

The intervention impact and potential for coverage of SA services has the possibility of averting the greatest number of maternal deaths in countries with high MMR, such as Niger. Preventing unsafe abortions and providing PAC services will, however, save an even

greater number of maternal lives. Similarly discussed above, countries with lower MMR, such as Cambodia, will benefit but gains will not be as large.

The majority of gains from family planning program coverage will be in countries with the lowest CPRs. In our regional examples, SSA demonstrates the largest gain in potential maternal lives saved. This is the same in our country-level examples, where Nigeria, with a CPR of 4% and 17% in rural and urban areas, respectively, has the potential to benefit the most from family planning interventions. Cambodia, on the other hand, with a CPR of 19% and 21% in rural and urban areas respectively, will again see smaller gains.

Combining interventions is important in maximizing the number of maternal lives that can be averted. In places where safe abortion services are not legally possible, governments should focus their resources on PPH, FP, and PAC. In SSA and Asia, implementing both interventions would save around 30,485 and 27,158 maternal lives, respectively. However, implementing all three suggested services (i.e. including safe abortion and PAC) would prevent about 45,577 and 40,456 maternal deaths in SSA and Asia, respectively.

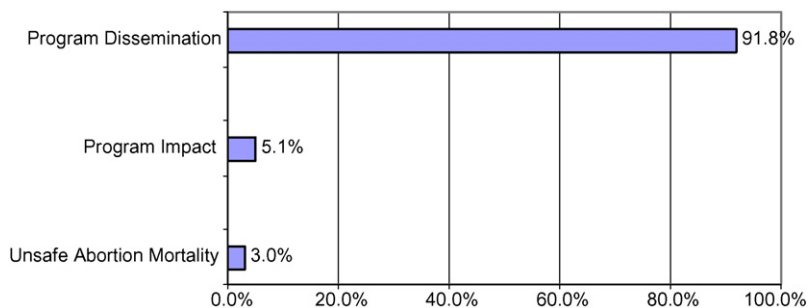


Fig. 3. Sensitivity analysis: Sub-Saharan Africa Model. Maternal Deaths Averted due to Safe Abortion Services.

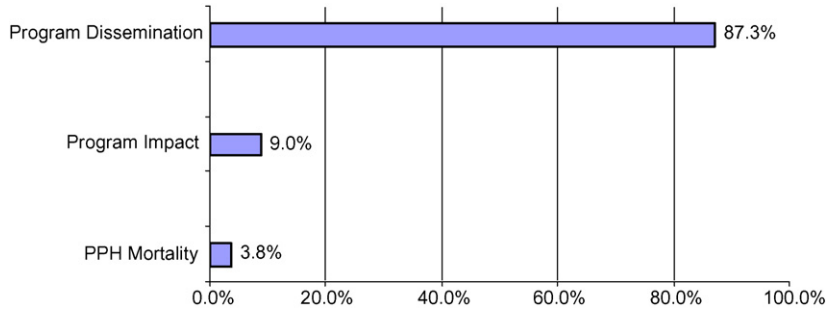


Fig. 4. Sensitivity analysis: Sub-Saharan Africa Model. Maternal Deaths Averted due to Postpartum Hemorrhage Management.

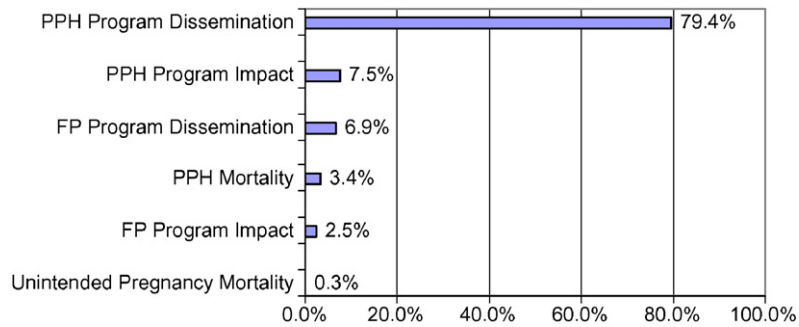


Fig. 5. Sensitivity analysis: Sub-Saharan Africa Model. Maternal Deaths Averted due to Postpartum Hemorrhage and Family Planning Services.

As with the implementation of individual interventions, those regions with higher MMRs will experience a much higher reduction in maternal mortality than those with lower MMRs.

Sensitivity analyses of models which combined the interventions demonstrated that PPH management is the largest contributor to the variance in maternal lives saved. In all settings, the variance was mostly

due to changes in the PPH management program dissemination. When combining FP and PPH interventions, program coverage of PPH services contributed to 61–79% of the variance. When combining all three interventions, FP, SA/PAC, and PPH services, PPH program coverage contributed to 47–59% of the variance.

Results from the sensitivity analysis for the individual interventions suggested demonstrate that for

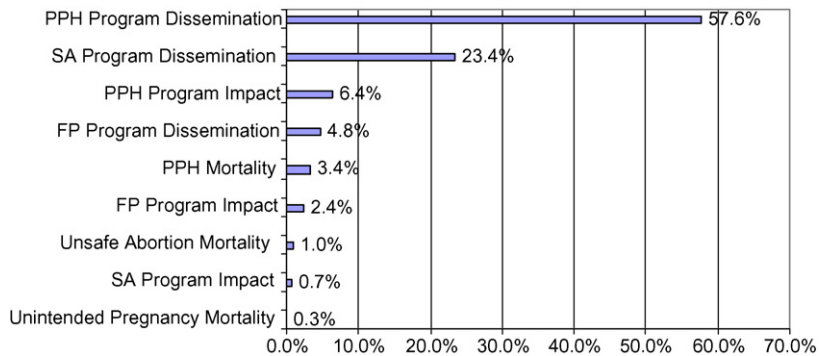


Fig. 6. Sensitivity analysis: Sub-Saharan Africa Model. Maternal Deaths Averted due to Safe Abortion, Family Planning and Postpartum Hemorrhage Management Services.

each program, the major contributor to variance was the extent of program coverage. Figs. 2–6 show the contribution to variance in deaths averted for each simulation run for SSA. In all models which tested only FP services, program coverage contributed to 69–71% of the variance (with the exception of Cambodia, where program coverage contributed to 44% and intervention impact contributed to 49% of the variance). For SA/PAC models, program coverage contributed to 91–93% of the variance. For PPH management models, program coverage contributed to 87–89% of the variance.

6. Discussion/conclusion

Since the 1987 Safe Motherhood Conference in Nairobi little progress has been made in reducing maternal mortality ratio (MMR). The primary strategy to date has been to promote delivery with a skilled attendant and the provision of emergency obstetric care (EmOC) [1]. However, progress is largely stalled and in parts of Africa the ratio of women to trained professionals is falling [54]. It is imperative to explore alternative strategies if the Millennium Development Goal (MDG) of reducing MMR by three-quarters between 1990 and 2015 is to be met. This paper examines the evidence on available interventions aimed at decreasing MMR, and reassesses what is feasible with existing resources in poor settings. We identify interventions with the greatest potential to reduce MMR on a large scale. Faced with human and financial resource constraints, it is time for maternal health program planners to select those interventions that are both quickly achievable and sustainable.

By 2015, there will be 350 million more women of reproductive age in the developing world than there are today. If we extrapolate the limited progress made since 1990 (the baseline for calculating the MDG), then not only will this MDG go unfulfilled but it could be that in absolute numbers, more women will have died from pregnancy, abortion, and child birth than in any similar interval in human history.

From available priority interventions, only a few are realistic for the 50 million women who deliver without a skilled birth attendant and the millions who deliver at home, away from emergency obstetric care. As the developing world faces significant human and

financial resource shortages, program planners and policymakers must reassess and reprioritize maternal health interventions to include access to contraception, SA and PAC as well as PPH prevention. These key interventions will address a large part of the maternal health burden.

This paper has some limitations which need to be acknowledged. As is the case for any modeling studies, our results were dependent on the assumptions we used. Ours were based mostly on the MBP spreadsheet as well as Hill et al.'s estimate for maternal mortality (2007). We assumed intervention effectiveness to have the same range throughout each region. However, successful implementation of the proposed interventions will depend on the cultural and religious beliefs of each population. Furthermore, the efficacy of the interventions assumes the same level of standard and certain level of quality to produce the results we report. In addition, individual countries represented here fit a particular model of having high MMR, low CPR, as well as low percentage of SBA during delivery. Countries with similar levels in MMR, CPR, and SBA are more likely to show similar gains in comparison to countries with better levels which are more likely to show smaller gains in maternal deaths averted.

Family planning can potentially make a significant impact on MMR for many reasons including the high numbers of unintended pregnancy and unmet need for contraception, the low cost of modern contraceptive methods, and the lack in need for highly skilled professionals to explain and administer most forms of FP (including condoms, oral contraceptive pills, and Depo injection). For poor communities that cannot afford the full cost of modern contraceptives, some degree of subsidy is needed. Fortunately, social marketing and community-based distribution of contraceptives at subsidy prices can be used in resource-poor settings to meet community needs [55].

Providing access to SA and PAC will also significantly reduce MMRs experienced by developing countries. Not all countries will be able to provide SA services. In such situations, SA should be allowed to the extent of the law. PAC, however, should be made available regardless, due to the severe consequences that are likely to follow should the incomplete abortion go untreated. The misoprostol regimen is simple and straight forward and studies have successfully shown that PAC can even be delegated to community-

level providers. The potential for lower level providers to help women with elected abortion and PAC is promising given the current human resources crisis in resource-poor settings.

Misoprostol is an important method for PPH prevention among women who live in low-resource settings. At present, assistance by a traditional birth attendant (TBA), a family member, or delivering alone are the only options for millions of pregnant women especially in Asia and Africa [56]. Misoprostol changes this equation. Currently there is some disillusionment about training TBAs, but the fault in prior efforts may not have been so much that TBAs cannot be trained, but that without adequate referral systems current training would not significantly reduce MMR. Even illiterate TBAs are able to incorporate their knowledge into practice and provide basic maternal care and they have done that in relation to misoprostol use [57–61].

There is evidence for the safe use of misoprostol at the community level. Walraven et al. (2005) demonstrated in a randomized, controlled trial in the Gambia, that misoprostol in the hands of TBAs was safe and effective at home births. Their study, which empowered TBAs to administer 600 mcg of misoprostol orally to women after delivery for the prevention of PPH, demonstrated lower blood loss among those women receiving misoprostol in comparison to placebo [60]. Prata et al. (2005) also showed that TBAs can successfully diagnose PPH using a local garment to measure blood loss after delivery 58 [59] and administer rectally 1000 mcg misoprostol when 500 mL of blood loss was reached (2 kanga) for the treatment of PPH [61]. Furthermore, studies done in Indonesia, Nepal, and Afghanistan showed that self-administration of a prophylactic dose of misoprostol, distributed during pregnancy by trained community healthcare workers is a viable option that can produce promising results [62]. Thus, in order to significantly reduce MMR, at a policy level it will be essential that community level providers and women themselves, where appropriate, have access to misoprostol.

Overall, the combined effect of saving mothers from dying from PPH and UA would result in the greatest gains in the decline in MMR. However, of the three suggested interventions, FP and confronting unsafe abortion are probably the most contentious. Yet, examples of Bangladesh, Tunisia and Iran are a testament that policy makers and the public health community

can together find a prudent way to confront these problems [63–65]. The evidence suggests a variety of service delivery modes and financing mechanisms that combine public and private partnerships to successfully implement the proposed interventions. These include social marketing; social franchising; accreditation; contracting; vouchers systems; and output-based assistance.

Immediate action is needed. The three interventions most likely to significantly reduce MMR all depend more on the attitudes and policies set by governments, international agencies, and donors than on the willingness of those living in resource-poor areas to help themselves. Ministries of Health must still be committed to upgrading district health facilities, and employ every effort to increase access to EmOC as part of basic medical care. However, they must also recognize that until there are enough higher level providers in rural areas, it is crucial that they focus on training non-physicians and medical technicians to provide EmOC, including caesarian sections. Accomplishments in Mozambique, Malawi, and what was once Zaire are evidence that this is safe and efficacious [66–69].

In order to achieve these practical goals, women's access to reproductive health services must be viewed as a universal and unequivocal human right. Without this fundamental recognition, few genuine advances in women's health will ever be accomplished.

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