Direct Patient Interventions That Can Reduce Maternal Mortality in Developing Countries:

A Systematic Review

Gina Brown, MPAS, PA-C; Lindsay Allen, MPA, PA-C; Anne Torkelson, MPA, PA-C

BACKGROUND AND OBJECTIVES: Maternal mortality is a major concern in developing countries. This study identified and evaluated specific direct patient interventions made in developing countries that could result in a decrease of the maternal mortality rate.

METHODS: A systematic review of articles from Cochrane Library and MEDLINE databases was conducted. Articles chosen for review focused on small, practical, clinical interventions, while large, program, or government policy-based interventions were excluded.

RESULTS: Sixty-eight articles were reviewed, and nine were selected for evaluation. Calcium supplementation during pregnancy had a maternal mortality relative risk of 0.80 (95% CI=0.70–0.91). Women with an interpregnancy interval of 18 to 24 months have a significantly lower risk of complications, while shorter and longer interpregnancy intervals were associated with an increase in maternal adverse outcomes or maternal death (adjusted odds ratio 2.54; 95% CI 1.22-5.38). Active management of the third stage of labor, specifically the use of uterotonic agents, decreased a woman's risk of postpartum hemorrhage, which is the leading cause of maternal mortality in most developing countries.

CONCLUSIONS: The use of calcium supplementation to decrease maternal mortality is beneficial with a Grade A Recommendation. Educating women to space pregnancies according to lowest risk times is given a Grade D Recommendation. Using uterotonics as active management of the third stage of labor is given a Grade B Recommendation. These simple implementations can potentially save many lives, especially in remote areas and areas of low resource.

(Fam Med 2013;45(8):550-7.)

Maternal mortality (MM) refers to maternal deaths that result from pregnancy or childbirth. While not considered a significant risk in developed countries, the risk of a woman dying in her lifetime from a complication of pregnancy or childbirth is about one in six in the poorest parts of the world, as compared to one in 30,000 in Northern Europe.[1] In an effort to reduce maternal mortality, the United Nations (UN), International Monetary Fund, Organization for Economic Co-operation and Development, and the World Bank created the fifth Millennium Development Goal (MDG 5) to reduce maternal mortality by 75% from 1990–2015.[2] Since the initiation of this goal, and its adoption by many countries worldwide, the maternal mortality rate (MMR) (defined as the number of maternal deaths in a given time period per 100,000 women of reproductive age[1]) has declined. The UN reports the worldwide MMR for 2010 as 210, down from 400 in 1990.[3] This decrease can be significantly attributed to extensive programs that increase access to health care, train large numbers of nursing attendants or midwives, and implement prenatal and postnatal health care. Countries such as Bangladesh, China, Bolivia, Indonesia, Nepal, and others have had success in these areas.[4-6] Many developing countries have not succeeded in significantly reducing MMRs, however. (The MMR for Sub-Saharan Africa averages 500.[3]) This is often due to a lack of political stability to initiate country-wide initiatives that require consistent input and evaluation. Interventions that require significant government involvement are likely to fail in countries whose political systems are in chaos.

From Wichita State University, Wichita, KS.

Although unlikely to bring the level of results that a large governmental program can achieve, small, direct changes to patient care can save many lives without the requirement of continuous government oversight. Medical providers can utilize direct clinical interventions and train others to use them, in an effort to reduce maternal mortality even in countries where government programs are floundering.

The purpose of this study is to identify direct patient interventions that have been successful in reducing MMR and that individual providers can practice without needing to depend on the stability of the county's infrastructure. A comparative study of this type is lacking and could help to reduce the MMR in countries that have failed in the past. This systematic review will attempt to address this gap as well as provide an evaluation of which implementations are most effective.

Methods

Search Strategies and Selection Process

Included in this review are articles found from searching the Cochrane Library and MEDLINE databases. The initial search was conducted using the following search terms: maternal mortality, maternal health, and maternal death. After possible appropriate interventions were identified, a second search was conducted. Search terms included third stage of labor, postpartum hemorrhage, nutrition in pregnancy, calcium in pregnancy, uterine massage, active management, and interpregnancy interval. Manual reviews of article bibliographies were also conducted to search for related articles of interest. Limitations used were data from human subjects and English language studies from 2000 to the present.

Our inclusion criteria involved looking at systematic reviews, randomized controlled trials, and cohort studies that presented practical, clinical interventions. Exclusion criteria included articles with low levels of evidence, such as case studies and studies that had poor follow-up. Also excluded were articles that referred to infrastructure changes instead of a specific clinical intervention, as well as interventions that would require specialized or complex training. Sixty-eight studies were selected for detailed review. Nine of the 68 met all our criteria and were chosen for analysis.

Classification of Evidence and Grade of Recommendation

The nine studies chosen for analysis were categorized according to their level of evidence using the Oxford Center for Evidence-based Medicine (CEBM) Levels of Evidence.[7] Data, outcomes, levels of evidence, and methodological strengths and weaknesses were considered to present graded recommendations based on the Oxford CEBM Grade of Recommendation scale.[7]

Results

There were three patient interventions identified that are potentially effective in reducing maternal mortality. These include calcium supplementation, spacing pregnancies to appropriate intervals, and the practice of prophylactic uterotonics during the third stage of labor. The summary of these articles is presented in Table 1.

Calcium Supplementation

Two studies were evaluated for calcium supplementation—a meta-analysis by Imdad et al[8] and a systematic review by Hofmeyr et al.[9] When combining these two studies, a total of 23 randomized control trials were reviewed. Both studies showed that calcium supplementation reduced maternal mortality and maternal morbidity, especially in high-risk populations such as teenagers, patients that had had preeclampsia during a previous pregnancy, and populations with low baseline dietary calcium intake. The Imdad et al study showed calcium supplementation during pregnancy resulted in significant reduction in maternal mortality as compared to the control group, with a relative risk (RR) of 0.80 (95% CI=0.70-0.91),[8] while the Hofmeyr et al study showed that maternal death or serious morbidity was reduced by 20% for women taking calcium supplementation (RR 0.80; 95% CI=0.65 to 0.97).[9]

Interpregnancy Intervals

The effect of interpregnancy interval on maternal mortality appears to be inconclusive in current literature. A retrospective cross-sectional study that involved 456,889 women from 18 different countries in Latin America and the Caribbean compared three interpregnancy intervals (<6 months, 6–59 months, and >59 months) for adverse maternal outcomes. With the interpregnancy interval defined as the time between a woman's last delivery and the beginning of the next pregnancy, women with short pregnancy intervals (<6 months) had an increased risk of pregnancy-related death (odds ratio of 2.54, 95% CI=1.22–2.38).[10] A later study involving 14,930 women in Brazil did not report consistent findings, however, and no association between interpregnancy interval and maternal mortality was identified.[11] This does not nullify the previous study, however, and further discussion can be found below.

Active Management of Third Stage of Labor

Prophylactic uterotonics is the main medical practice in active management. We identified five studies that evaluated the effects of prophylactic uterotonics or active management versus therapeutic uterotonics or expectant management.

A retrospective study (level 2b) done in Ghana by Geelhoed et al[12] reported that postpartum hemorrhage (PPH) occurred in 17.4% of the expectant management group and 13.7% in the active management group. The maternal mortality caused by PPH remained the same, but the incidence of PPH was decreased.[12]

Table 1: Summary of Literature Examining Interventions for Reducing Maternal Mortality

Author and Year	Design and Level of Evidence	Details of Design Techniques	Statistical Outcomes	Conclusion Highlights
Patient Intervention: Calcium Supplementation				
Imdad et al[8] (2011)	Meta-analysis (level 1a)	• 10 RCTs, all in developing countries • Calcium supplementation 0.5 g/day–2.0 g/day or placebo • Supplementation started at 20–32 weeks gestation and given through delivery	• Maternal mortality 20% risk reduction (95% CI=0.70-0.91) • Pre-eclampsia 59% risk reduction (95% CI=0.24-0.69) • Eclampia 32% risk reduction (95% CI= 0.48-0.97) • Gestational HTN 45% risk reduction	• Greater benefit seen in women with a higher pre-pregnancy risk; 82% risk reduction in high-risk women, 49% risk reduction in low-risk women
Hofmeyr et al[9] (2010)	Systematic review (level 1a)	• 13 RCTs, n=15,730, low–high risk women, underdeveloped and developed countries • Calcium supplementation of at least 1.0 g/day started at or prior to 34 weeks gestation	• Maternal death or serious morbidity 20% risk reduction (95% CI=0.65-0.97)	• Greatest risk reduction was seen in women with high risk for pre-eclampsia and low baseline calcium level
Patient Intervention: Interpregnancy Interval				
Conde-Agudelo and Belizan[10] (2000)	Retrospective cross sectional study (level 2a)	• 456,889 parous women delivering singleton infants in Latin America and Caribbean hospitals from 1985–1997 Interpregnancy intervals: • <6 months—2.8% of women • 18–23 months—77.7% of women • >59 months—19.5% of women	• <6 months interpregnancy interval has significantly greater risk of maternal death (adjusted odds ratio 2.54; 95% CI= 1.22–5.38) • >59 months pregnancy interval 1.8 times more likely to develop preeclampsia and eclampsia than women with 18–23 months pregnancy interval	• Relationship between maternal mortality and interpregnancy interval of <6 months • No relationship between the interpregnancy interval and the risk of postpartum hemorrhage or gestational diabetes
Cecatti et al[11] (2008)	Cross-sectional study (level 2b)	• 14,930 parous women delivering singleton infants in a hospital in Brazil from 1986–2000 Interpregnancy intervals: a wide variety of intervals were evaluated, with significant findings in the following groups: • <6 months—7% of women • >59 months—20.9 % of women	• <6 months interval had a greater risk of low birth weight (adjusted odds ratio 1.74; 95% CI=1.18–2.55) and preterm birth (1.56; 95% CI=1.01–2.46) • Longer intervals (>59 months) associated with lower risk of delivery by C-section (0.69; 95% CI=0.56–0.82) and increased risk of PROM (1.57; 95% CI= 1.20–2.06) and low birth weight (1.46; 95% CI=1.03–2.06)	• Short interval associated with increased risk of poor perinatal outcomes but not maternal outcomes • Long interval associated with increased risk of PROM was the only adverse maternal outcome identified

(continued on next page)

Table 1: Continued

Author and Year	Design and Level of Evidence	Details of Design Techniques	Statistical Outcome	Conclusion Highlights
Patient Intervention: Active Management of Third Stage of Labor				
Geelhoed[12] (2002)	Retrospective study (level 2b)	• 8,928 women who delivered vaginally in a rural hospital in Berekum, Ghana, from Jan 1, 1992 to Jan 1, 1999 • Active management group used 10 units of oxytocin IM after delivery, early cord clamping, and controlled cord traction	Active Management (n=3840) • 13.7% postpartum hemorrhage Expectant Management (n=5088) • 17.4% postpartum hemorrhage	• Maternal mortality due to PPH remained the same after implementation of active management, but the incidence of PPH were decreased
Begley[13] (2010)	Systematic review (level 1a)	• Seven studies included • n=8,247 women expecting to give birth vaginally with varied bleeding risk • Studies compared active, expectant, and mixed management • Active management included uterotonic administration, cord clamping, and cord traction • Expectant management does not use any components of active management • Mixed management uses one or two components of active management • Four of the seven studies compared active to expectant management. • Study did not specifically look at maternal mortality	Active Versus Expectant Management of all women (included four studies) • Significant reduction in average of severe PPH >1,000mL up to 24 hrs postpartum (RR 0.34; 95% CI=0.14-0.87) • Significant reduction in maternal hemoglobin < 9g/dL at 24 to 48 hrs (RR 0.05; 95% CI=0.30-0.83) • Significant reduction in primary blood loss >500 mL, (RR 0.34, 95% CI=0.27–0.44) • Significant reduction in mean maternal blood loss, (95% CI= -95.96 to -61.64) • Reduction in need for maternal blood transfusion (RR 0.35, 95% CI=0.22–0.55) • Reduction in need for therapeutic uterotonics, (RR 0.19, 95% CI=0.15-0.24) • Other neonate outcomes and non-life-threatening outcomes were found but are not applicable to maternal mortality	• Clinically important findings that could potentially reduce maternal mortality were found with the use of active management, specifically the reduction of severe PPH and need for blood transfusions and therapeutic uterotonics.
Hofmeyr[14] (2008)	Systematic review (level 1a)	• Over 40,000 participants • 46 RCTs • Compared: -misoprostol to placebo -misoprostol to other uterotonics -misoprostol doses	Maternal death • 11 deaths identified, eight received ≥ 600µg misoprostol Outcomes • Women taking 600 micrograms (RR 0.77, 95% CI=0.59–1.00) or 400 micrograms (RR 0.63, 95% CI=0.44-0.91) of misoprostol had less blood loss than placebo • Women receiving misoprostol either prophylactically or as treatment had more adverse events (diarrhea, abdominal pain, etc) than women receiving placebo or other uterotonic, but severe morbidity was similar between groups (16 of 10,281 on prophylactic misoprostol versus 16 of 10,292 on other prophylactic uterotonics)	• Women given ≥ 600 µg misoprostol had more pyrexia than women with 400–500 µg, but no increased benefit for reducing blood loss by using the higher dose • Misoprostol is effective in reducing blood loss, but the lowest effective dose should be used to avoid side effects • 200 µg dose has uterotonic effects

(continued on next page)

Table 1: Continued

Author and Year	Design and Level of Evidence	Details of Design Techniques	Statistical Outcome	Conclusion Highlights
Cotter[15] (2001)	Intervention review (level 1a)	• RCTs or quasi-RCTs, including women planning to have a vaginal delivery, oxytocin was given prophylactically in third stage of labor Compared: • Oxytocin versus no uterotonics (n=>3,000) • Oxytocin versus ergot alkaloids (n=>2,800) • Oxytocin plus ergometrine versus ergot alkaloids (n= >2,800)	Oxytocin versus no uterotonics • Benefits specifically related to indictors of blood loss such as PPH >500mL (RR 0.50; 95% CI=0.43-0.59) or >1000mL (RR 0.61; 95% CI=0.44-0.87) and the need for therapeutic oxytocics (RR 0.50; 95% CI= 0.39-0.64) Oxytocin versus ergot alkaloids • No statistically significant difference between the two oxytocics • Association of fewer manual placenta removals (RR 0.57; 95% CI=0.41-0.79) Oxytocin plus ergometrine versus alkaloid • Little evidence of synergistic effect using oxytocin plus ergometrine other than slight reduction in the rate of blood loss >500mL (RR 0.44; 95% CI=0.20-0.94)	• Neonatal outcomes were evaluated as well • Due to wide CI, no analysis was done on the relationship with manual removal of the placenta or the need for a blood transfusion
Patted[16] (2009)	Randomized control trials (level 1b)	• n=1,602 women from four districts in Karnataka, India • n=812 intervention group • n=808 placebo group • Intervention group=single dose of 600 micrograms of misoprostol orally, administered after delivery and within 5 minutes of umbilical cord clamping and cutting • Placebo group=no misoprostol • Symptoms were categorized as absent, mild to moderate, or severe • Perinatal, clinical, and demographic characteristics similar in both groups	Misoprostol Group • 47% reduction of PPH (*P*<.0001) • Significant increase shivering and fever at 2 hrs postpartum (severe in 2.5%; *P*<.0001) • 4.6% shivering at 24 hrs (*P*<.001) and increased rate of fever (*P*<.03) at 24 hrs • 28% reported at least one side effect • Four (0.5%) women required transfer to higher level of care • One woman required manual removal of placenta Placebo Group • 12% had acute hemorrhage • 1.4% reported shivering at 24 hrs • 37% reported at least one side effect • 12 (1.5%; *P*<.05) women required transfer to higher level of care • Three women required manual removal of placenta	• No significant difference in nausea, vomiting, or diarrhea between two groups at 2 hrs postpartum • 24 hrs postpartum all shivering was reduced in both groups • No statistically significant differences between rates of infection • One death occurred but was non-hemorrhage related

Begley et al[13] analyzed data from seven studies and compared a variety of third stage management options. Four of the seven studies looked at active management (cord traction with early cord clamping and prophylactic uterotonic) versus expectant management in women with varied bleeding risks and found a statistically significant decrease in severe primary PPH of >1,000 mL up to 24 hours postpartum (average risk ratio (RR) 0.34; 95% CI= 0.14–0.87; T^2 0.38; Chi^2 *P*=0.08; I^2 60%). A decrease in the number of women with a hemoglobin less than 9 g/dL at 24 to 72 hours was also statistically significant (average RR 0.50; 95% CI=0.30–0.83). Other significant findings that could potentially relate to maternal mortality included a reduction in primary blood loss, a decreased need for both maternal blood transfusions and therapeutic uterotonics. (See Table 1) These studies did not report specifically on maternal mortality, however.[13]

A systematic review (level 1a) by Hofmeyr et al[14] included over 40,000 participants in 46 randomized controlled trials where the uterotonic, misoprostol, was compared to either placebo or another uterotonic. Twenty of these studies utilized active management, 20 did not describe third-stage management, and others utilized other approaches such as expectant management or caesarean section. In regards to blood loss (>1,000 ml), the misoprostol groups of 600 micrograms (RR: 0.77; 95% CI:=0.59–1.00) and 400 micrograms (RR: 0.63; 95% CI=0.44–0.91) had less blood loss than the placebo group. The studies that compared misoprostol to placebo involved 7,156 women. Although this review did look at maternal mortality, the number of deaths were so few that no significant result could be reported.[14]

An intervention review by Cotter et al[15] included 14 trials. The comparison of oxytocin to no uterotonics included over 3,000 women and revealed clear benefits to women who received prophylactic oxytocin as part of routine management of the third stage of labor. Benefits specifically relate to indicators of blood loss such as PPH greater than 500 mL (RR 0.50; 95% CI=0.43–0.59) or greater than 1,000 mL (RR 0.61; 95% CI=0.44-0.87) and the need for therapeutic oxytocics (RR 0.50; 95% CI=0.39–0.64).[15]

A study by Patted et al[16] was a randomized control trial (level 1b) of 1,602 participants; 812 were randomized into the group receiving 600 µg of oral misoprostol, the remaining 808 received placebo. Twelve percent of women in the placebo group had an acute PPH, whereas only 4.7% of the misoprostol group had an acute hemorrhage. This 47% reduction in the misoprostol group was significant at the *P*<.0001 level. The only death that occurred in the study was non-hemorrhage related.[16]

Discussion

As the purpose of the study was to identify direct patient interventions that providers with limited training could implement with or without a stable infrastructure in place, it is not surprising that large studies of small interventions in developing countries that result in high levels of evidence and a strong recommendation are limited. Calcium supplementation, however, was supported by two level one studies and had a direct result in decreasing mortality as well as morbidity, allowing for a Grade A recommendation for this intervention. The most benefit was observed in women with low baseline calcium levels and at the highest risk of developing preeclampsia.[9] Gestational hypertension, preeclampsia, and eclampsia pose a significant risk to women, especially women in developing countries where emergency medical care may not be available. Implementation of calcium supplements for women in populations with poor nutrition or low calcium intake effectively reduces these events, as well as mortality. The dose of supplemental calcium used in these studies ranged from 0.5–2.0 grams per day and was started at a wide range of gestational ages but always at 34 weeks gestation or earlier.[8,9] An internationally accepted dose has not been defined and further research to determine a recommended dose is needed. Nonetheless, these studies indicate that calcium supplementation may be an effective yet inexpensive intervention that does not require complex training or a stable infrastructure.

The intervention of an interpregnancy interval over 6 months cannot be given a strong recommendation, however. This is due to the inconsistent findings of the two studies analyzed. The latter study by Cecatti et al[11] did not support the relationship between maternal mortality and interpregnancy interval of <6 months found by the first study by Conde-Agudelo and Belizan.[10] The findings of the latter study are not as strong, however, as all data came from one tertiary hospital in Brazil and may not represent Brazil or underdeveloped countries as a whole. Of note is that the MMR in the Brazilian study was 33.7 per 100,000 live births, much lower than the national average. (MMR in 1995 in Brazil was 96 per 100,000 live births.[17]) The Brazilian study (14,930 participants) was also much smaller than the study that collected data from 18 countries in Latin America and the Caribbean (456,889 participants).

The inconsistencies of the two studies that considered a direct relationship between interpregnancy interval and maternal mortality will only allow for a Grade D recommendation; however, the design of the Conde-Agudelo and Belizan study included multiple different hospitals in multiple different countries[10] and is more applicable to the population intended for this review. Conde-Agudelo and Belizan found that shorter interpregnancy intervals are associated with higher rates of third-trimester bleeding, premature rupture of membranes, puerperal endometritis, anemia, and maternal death. Longer interpregnancy intervals were associated with an increased risk of preeclampsia and eclampsia and gestational diabetes.[10] Women may benefit from choosing to have their interpregnancy interval spaced between 18 and 23 months, or at least longer than six months, when their risk of complications is lower. Incorporating education about birth spacing into the clinical setting is simple, inexpensive, and does not require a stable infrastructure or complicated training.

Studies showing significant findings between active management with the use of uterotonics and a reduction in maternal mortality are lacking, but several studies report significant correlations between active management/uterotonics and a reduction in postpartum hemorrhage. Four of the five studies appropriate for this review are level one studies, and the fifth is level two. Extrapolating that reducing PPH will also reduce maternal mortality results in a Grade B recommendation for active management and prophylactic uterotonics. Postpartum hemorrhage is the leading cause of maternal mortality in most developing countries and in September 2012, the World Health Organization (WHO) published new recommendations for the prevention of PPH. Prophylactic uterotonics in the third stage of labor is the main intervention recommended in WHO's new guidelines; controlled cord traction is only recommended if a skilled birth attendant is performing the procedure, early cord clamping is no longer recommended, and sustained uterine massage is not recommended if oxytocin is administered.[18,20] Of the many complications that occur in the third stage of labor, postpartum hemorrhage is among the most common and is often fatal. There are numerous maternal morbidities that accompany PPH, including anemia, increased hospital stays, and difficulty establishing breast-feeding. Transfusion of blood carries significant risks outside of developed countries, and decreasing the need for blood transfusions is very beneficial. Administration of uterotonics in the third stage of labor has become standard of care, with several uterotonics that are proven to be effective in managing PPH.[19,21] The uterotonic of choice, according to the new WHO recommendations, is oxytocin (10 IU, IV/IM), but misoprostol is also considered effective.[18,20] This is consistent with the studies in this review; some studies utilized oxytocin, others included ergometrine or a mixture of oxytocin and ergometrine, others used misoprostol, and one included ergot alkaloids. All studies showed a benefit in reducing PPH compared to placebo or no uterotonic, but side effects and contraindications of uterotonics varied.[12-16] One study that did not meet all requirements for our review compared 400µg oral misoprostol to 10 IU of oxytocin IM. No significant difference was found between the groups on average blood loss and pre- and post-hemoglobin levels.[19,21] The option to use misoprostol instead of oxytocin is important to this review as the aim was to identify interventions that could be implemented without a stable infrastructure or complex training. Oxytocin is not thermostable, it must be properly stored to ensure its efficacy, and special training is also needed for proper administration. Misoprostol is thermostable and will not degrade in hot tropical climates; it is administered orally (or vaginally or rectally) and does not require special training.[19,21] A study by Patted et al[16] found that oral misoprostol reduced the incidence of PPH by almost 50% in communities with inadequate resources, where a physician was not attending the delivery. This makes misoprostol an important alternative to oxytocin in areas where electricity is unreliable or where a trained birth attendant is unavailable. Optimal dosing of misoprostol remains confusing, however. One study found that 600 µg of misoprostol was safe for mothers and neonates,[16] and another found that 600 µg did not differ significantly from 400–500 µg doses.[14] WHO recommendations acknowledge that "there is no evidence to show that a 600 µg dose of misoprostol provides greater efficacy over a 400 µg dose".[18,20] Further studies to determine the most effective dose with the fewest side effects are needed.

Study Limitations

The number of studies that specifically correlated interventions with maternal mortality were few. This resulted in recommendations from extrapolations, except in the case of calcium supplementation. We reviewed data on other interventions such as reducing sepsis and infection, use of non-pneumatic anti-shock garments, supplemental iron to treat anemia in the intrapartum and postpartum period, and uterine massage to treat PPH. However, the level of evidence would not allow us to make a graded recommendation; therefore such studies were excluded from this review.

Limiting interventions to those that did not require a stable infrastructure or significant training, as well as finding studies that were carried out in developing countries, limited the number of studies for review but also made the selected studies more applicable to our purpose.

Table 2: Graded Recommendations for Clinical Interventions to Reduce Maternal Mortality

Intervention	Grade of Recommendation
Calcium supplementation	Grade A
Moderate interpregnancy interval	Grade D
Prophylactic uterotonic in third stage of labor	Grade B

Conclusions

Three interventions that met our requirements were identified (see Table 2). Calcium supplementation to reduce gestational hypertension and related disorders, including maternal mortality, is beneficial with a Grade A Recommendation. Educating women to space pregnancies according to lowest risk times (between 18–23 months) is given a Grade D Recommendation. Using uterotonics as the main component in active management of the third stage of labor is given a Grade B Recommendation because the studies showed a reduction in PPH but not maternal mortality specifically. Oxytocin is the uterotonic of choice due to fewer side effects, but misoprostol is an acceptable alternative in areas lacking trained birth attendants or reliable cold storage. These simple implementations can potentially save many lives, especially in remote areas and areas of low resource, where the most help is needed to reduce maternal mortality.

ACKNOWLEDGMENTS: Content was reported in poster form only at the 2012 American Academy of Physician Assistants annual conference in Toronto.

CORRESPONDING AUTHOR: Address correspondence to Ms Brown, 4005 E. Lewis, Wichita, KS 67218. 316-978-5683. Fax: 316-978-3669. gina.brown@wichita.edu.

References

1. Ronsmans C, Graham WJ. Maternal mortality: who, when, where, and why. Lancet 2006;368(9553):1189-200.
2. Hogan MC, Foreman KJ, Naghavi M, et al. Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millennium Development Goal 5. Lancet 2010;375:1609-23.
3. Millennium Development Goals Indicators. The Millennium Development Goals Report 2012. http://mdgs.un.org/unsd/mdg/Host.aspx?Content=Data/Trends.htm. Accessed August 7, 2012.

4. Koblinksy M, Anwar I, Mridha MK, Chowdhury ME, Botlero R. Reducing maternal mortality and improving maternal health: Bangladesh and MDG-5. J Health Popul Nutr 2008;26(3):280-94.

5. Chowdhury ME, Ahmed A, Kalim N, Koblinsky M. Causes of maternal mortality decline in Matlab, Bangladesh. J Health Popul Nutr 2009;27(2):108-23.

6. WHO, UNICEF, UNFPA, and the World Bank. Trends in maternal mortality: 1990–2008 estimates developed by WHO, UNICEF, UNFPA, and The World Bank. Geneva: World Health Organization, 2010.

7. Centre for Evidence-based Medicine. Oxford Centre for Evidence-based Medicine—Level of evidence. March 2009. www.cebm.net/index.aspx?o=1025. Accessed December 3, 2012.

8. Imdad A, Jabeen A, Bhutta ZA. Role of calcium supplementation during pregnancy in reducing risk of developing gestational hypertensive disorders: a meta-analysis of studies from developing countries. BMC Public Health 2011;11.

9. Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Sys Rev 2010;8:CD001059.

10. Conde-Agudelo A, Belizan JM. Maternal morbidity and mortality associated with interpregnancy interval: cross-sectional study. BMJ 2000;321:1255.

11. Cecatti J, Correa-Silva E, Milanez H, Morais S, Souza J. The association between inter-pregnancy interval and maternal and neonatal outcomes in Brazil. Matern Child Health J 2008;12:275-81.

12. Geelhoed D, Visser L, Agordzo P, Asare K, Schagen van Leeuwen J, Van Roosmalen J. Active versus expectant management of the third stage of labor in rural Ghana. Acta Obstet Gynecol Scand 2002;81:172-3.

13. Begley CM, Gyte GML, Murphhy DJ, Devane D, McDonald SJ, McGuire W. Active versus expectant management for women in the third stage of labour. Cochrane Database of Systematic Reviews 2010;7:CD007412.

14. Hofmeyr G, Gulmezoglu A, Novikova N, Linder V, Ferreira S, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. Bulletin-World Health Organization 2008;87:666-77.

15. Cotter AM, Ness A, Tolosa JE. Prophylactic oxytocin for the third stage of labour. Cochrane Database of Systematic Reviews 2001;4:CD001808.

16. Patted SS, Goudar SS, Naik VA, et al. Side effects of oral misoprostol for the prevention of postpartum hemorrhage: results of a community-based randomized controlled trial in rural India. J Matern Fetal Neonatal Med 2009;22(1):24-8.

17. WHO Global Health Observatory Data Repository. Maternal mortality ratio (per 100,000 live births). http://apps.who.int/gho/data/?vid=240#. Accessed November 20, 2012.

18. WHO recommendations for the prevention and treatment of postpartum haemorrhage. http://apps.who.int/iris/bitstream/10665/75411/1/9789241548502_eng.pdf. Accessed February 3, 2013.

19. Afolabi EO, Kuti O, Orji EO, Ogunniyi AO. Oral misoprostol versus intramuscular oxytocin in the active management of the third stage of labour. Singapore Med J 2010;51(3):207.