

Pregnancy Failure and Misoprostol - Time for a Change

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Pregnancy failure in the first trimester is one of the commonest reasons for women to seek emergency medical services. Indeed, curettage for this indication was responsible for up to three quarters of all nighttime emergency gynecologic interventions in one review.¹ The term “pregnancy failure” is, however, not a clinical one but, rather, describes a range of conditions in which an implanted fertilized ovum ceases to develop to the point of viability. Included in the category of early pregnancy failure are spontaneous abortion (both complete, in which all the products of conception have been expelled, and incomplete, in which some products remain), anembryonic gestation (in which no embryo has developed), and missed abortion (occult embryonic or fetal death, in which a pregnancy has ended, but no clear symptoms herald this event).

Arguably, the most common reason for early pregnancy failure is unwanted pregnancy and subsequent induced abortion. When good-quality medical services for elective termination of pregnancy are unavailable, women presenting for care after botched or incomplete procedures are often misclassified as having complications of spontaneous pregnancy loss. Women who have undergone clandestine or illegal procedures may be unwilling to disclose this fact, and so the causes of pregnancy failure (and the reliability of diagnoses) differ in places in which abortion services are available and those in which they are restricted. For example, after passage of New York State’s liberalized abortion law in 1970, recorded rates of spontaneous abortion fell by 20 percent in Brooklyn’s municipal and affiliated hospitals.² The rates of misclassification are likely to

be even higher in places in which abortion is highly stigmatized or illegal. In Romania, recorded rates of spontaneous abortion declined by over 40 percent after the legalization of abortion in 1990.³

The treatment most commonly offered to women with these conditions is surgical emptying of the uterus, with the use of sharp curettage or electric or manual vacuum aspiration, depending on local practice standards. Expectant management (waiting for the process of pregnancy loss to end spontaneously) is also sometimes offered to women with uncomplicated clinical presentations. But waiting is a slower route to resolution of the problem, and some women still will need surgery. Nonetheless, many women are willing to accept these inconveniences to avoid an invasive procedure.

In the past decade, the prostaglandin E1 analogue misoprostol—an available, safe, and relatively inexpensive drug originally approved by the Food and Drug Administration for the prevention of gastric ulcers during long-term use of nonsteroidal anti-inflammatory drugs—has been suggested as an alternative approach to managing early pregnancy failure.⁴ Indeed, misoprostol has been proposed (and in some places widely used) for a variety of other obstetrical or gynecologic indications: induction of labor, preparation of the cervix for surgical procedures, prevention or treatment of postpartum hemorrhage, and pregnancy termination. Although the use of misoprostol for these indications has become increasingly common worldwide, such uses have remained “off label,” and the pharmaceutical industry has largely looked the other way in matters of



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drug development and product registration for these potential uses. As a result, many studies have been limited by small numbers of subjects, as well as by the use of idiosyncratic regimens and nonstandard or vague definitions of cases and outcomes.

In this issue of the *Journal*, Zhang et al. report the results among 652 women with early pregnancy failure who were randomly assigned (in a 3:1 ratio) either to receive misoprostol (one or two 800-µg doses vaginally) or

to undergo vacuum aspiration⁵; women assigned to misoprostol underwent vacuum aspiration if medical therapy was unsuccessful. The results convincingly demonstrate the efficacy, safety, and acceptability of misoprostol to treat pregnancy failure (mostly missed abortion and anembryonic gestations) and show that this treatment may be an option that is preferable to surgery for some women. Indeed, in this series, over 80 percent of women given medical treatment needed no surgical inter-

vention. Overall, the medically and surgically treated groups had similar and highly favorable ratings of their treatments.

The results of this report, together with those of earlier reports,^{6,7,8,9,10,11,12} provide clinicians with information they need to use this medication responsibly for the management of early pregnancy failure. However, some questions remain.

Existing studies demonstrate that the use of misoprostol is more effective than expectant management (nonintervention) for early pregnancy failure, the other main alternative to immediate surgical treatment.^{6,7,8} Missed abortion appears to be slightly less easily and less successfully resolved with the use of misoprostol therapy than is incomplete abortion.^{5,13} This finding suggests that whereas surgery is more of a “one size fits all” proposition for treating early pregnancy failure, medical treatment may not be. In addition, the lowest effective dose of misoprostol for each condition for which it is used is not yet clear, and this dose may turn out to be different for different categories of pregnancy loss.^{5,7} We also do not know whether repeated doses of misoprostol consistently result in greater efficacy than a single dose followed by sufficient time for it to work.⁹

Questions also remain about the route of administration, with almost every imaginable variant having been used. (Oral, vaginal, rectal, buccal, and sublingual use have all been reported.) Some studies suggest that vaginal application of misoprostol increases the success rate and reduces side effects as compared with oral or other routes, whereas the results of other studies indicate that the various routes are equally efficacious and have similar rates of side effects.^{10,11,12} Many studies of vaginal administration have used misoprostol tablets developed and registered for oral use. But the normal procedures of drug registration will make it impossible for a pharmaceutical company to register an oral tablet for vaginal use without considerable additional expenditure on studies and, possibly, reformulation of

A Note from the Guest Editor:

Globally, 585,000 women die each year from complications of pregnancy and childbirth. Efforts to diminish this toll will require attention to hemorrhage, infection, unsafe abortion, eclampsia and obstructed labor, all major causes of maternal mortality. Misoprostol, a prostaglandin analogue that is registered in over 60 countries for treatment and prevention of gastric ulcers caused by prolonged use of anti-inflammatory medications, is becoming very widely used “off-label” for reproductive health indications, including prevention and treatment of postpartum hemorrhage, induced abortion, treatment of incomplete abortion, missed abortion and fetal death in utero, as well as preparation of the cervix for gynecologic surgical procedures. Developing the promise of misoprostol for its reproductive health indications could significantly improve maternal health globally, since the pill is easy to store, inexpensive, stable at a wide range of temperatures and easily administered. These features make it an ideal technology for low-resource settings.

Advances in health care do not always require the invention of new technologies or new drugs. Sometimes, it is possible to make substantial improvements in health care merely by adapting existing technology or changing the way drugs are used. Looking at new ways to use what is already on hand can be more economical and faster than searching to invent new technologies from scratch. Indeed, that is what is happening right now with misoprostol, a drug that has caused great excitement in the maternal health community because of its efficacy in many serious health conditions—and because it is already widely available internationally.

In order to be widely used in official programs, however, the drug needs to have official registration for its use in new circumstances. Lack of such registration is one of the current challenges to the expansion of programs offering this drug. While we work toward and anticipate new products specifically developed for maternal health indications, the dissemination of information can enable more providers and health care systems to use the current marketed drug “off-label.” If national health systems, international and national professional organizations and health experts come together to endorse specific regimens for use of the drug, it is possible that its promise can be more widely realized in a shorter time.

This issue of *PAC in Action* contains several resources that can be useful in considering the use of misoprostol in postabortion care services. We hope that by making more information on this topic available to more health care providers, health systems and women’s health advocates, this issue will help to realize the potential of a new approach to saving women’s lives.

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the tablet. So far, no company has made such an investment, in part because it would be almost impossible for such a product to compete successfully with the inexpensive misoprostol tablets currently available.

Although the study by Zhang et al. was conducted in the United States, the development of nonsurgical treatments for early pregnancy failure may have the most importance outside our country. In resource-constrained environments, high-quality surgical care is not readily available to all. The consequences of unsafe abortion are estimated to account for about 13 percent of all maternal deaths worldwide, almost all of which occur in developing countries.¹⁴ Misoprostol therapy as an alternative to surgery appears to be highly acceptable to women wherever it has been tested,^{5,10} and recent evidence shows clearly that using

misoprostol instead of aspiration in an outpatient setting reduces the cost of services.¹⁵ It is likely that women offered misoprostol can be treated and discharged more promptly than those who undergo surgery.⁵ In addition, treatment with pills does not require the immediate availability of sterilized equipment, operating rooms, or surgically skilled personnel.

Despite its promise, the use of misoprostol for early pregnancy failure in resource-poor countries may face substantial obstacles. Where norms for the delivery of medical services are set by governments, off-label use of medications is frequently not allowed. In other cases, physicians may worry that off-label use of medication will result in sanctions or lack of reimbursement. Governments may also be hesitant to adopt a treatment officially that has not been registered or

approved by their own or any internationally recognized regulatory agency.

For the future, both public and private sectors can work toward increasing the availability of dedicated misoprostol products for women's health indications. For now, clinicians have the opportunity to improve care for women by substituting a nonsurgical treatment for curettage or aspiration procedures, but they must be willing to make this transition in the context of the off-label use of a medication. That said, the report by Zhang et al., along with earlier peer-reviewed literature and wide community backing, provides support for such a transition.

Dr. Winikoff is president of Gynuity Health Projects, an organization that conducts research and other initiatives related to reproductive health techniques independent of support from the pharmaceutical industry.

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Misoprostol for Postabortion Care

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Introduction

Misoprostol is a drug that has great potential for advancing women's health, in part because of its promise as a uterine evacuation technology for postabortion care (PAC). Globally, there is a great need for safe, effective and comprehensive PAC services. Approximately 15% of clinically-recognized pregnancies end spontaneously in the first and second trimester.¹ Additionally, an estimated 20 million abortions are induced unsafely annually.

Women in several different clinical circumstances need PAC services. Some women may suffer from incomplete abortion after either a spontaneous or induced abortion. Clinically, this is diagnosed based on symptoms of bleeding, possible passage of tissue and, frequently, an open cervical os (the opening of the cervix); incomplete abortion is particularly common in countries with no safe abortion services. Others may experience a missed abortion, which

typically does not display any overt symptoms, but can be diagnosed based on lack of fetal cardiac activity or empty, irregular gestational sac. Diagnosis of missed abortion is limited without access to ultrasound, which is often unavailable at low-resource facilities.

Women presenting with incomplete abortion are commonly treated with surgical methods such as dilation and curettage (D&C), electrical vacuum aspiration (EVA) and manual vacuum aspiration (MVA). Misoprostol offers an alternative to surgical treatment. It is simple, noninvasive and may be preferred by women.² It may also be the only treatment option at service delivery points that lack skilled personnel and access to surgical equipment. This advantage of misoprostol is particularly important because it has the potential to increase access to treatment for those who need it most—women who suffer complications from clandestine induced abortions. Women who experience spontaneous

abortions are typically treated through a prenatal care provider or an emergency room, and those who experience complications from abortions carried out in a medical facility are generally treated by the original service providers. In contrast, women who suffer complications of clandestine induced abortions may be the most vulnerable to long-term health impacts of those complications. These women have limited access to, and sometimes limited knowledge of, health services for their problems, including hemorrhage, infection and physical damage to the reproductive system. Long-term morbidity can result from pelvic infection and uterine perforation.¹

Background

Misoprostol is a prostaglandin E1 analogue that is approved for the prevention and treatment of gastric ulcers associated with the use of nonsteroidal anti-inflammatory drugs. Prostaglandins are lipids made up of modified fatty acids. There are about 20 naturally occurring compounds in this class and they act in a manner similar to hormones. An analogue is a synthetic form of prostaglandin.² In addition to its use for treatment of incomplete abortion, misoprostol has been utilized for a range of reproductive health indications that fall into three broad categories: labor, delivery and postpartum, evacuation of the uterus after pregnancy failure, and induced abortion.⁴

The drug causes contractions of the muscles of the uterus, thereby reducing bleeding and evacuating uterine contents. Its ability to safely and effectively evacuate the uterus after pregnancy failure, along with its wide availability and low cost, make it a suitable option in many developing countries. Moreover, as no surgical equipment or training in surgical procedures is involved, misoprostol can be administered at various levels of the health care system and by different types of staff.

Research Findings

A number of studies have assessed the safety and efficacy of misoprostol for treatment of incomplete abortion and determined its acceptability to women and providers alike. The high levels of safety, efficacy and satisfaction expressed by women (over 90% of women on average report being 'satisfied' or 'very satisfied' with the method) have generated sufficient confidence to promote the integration of misoprostol into PAC programs. Continuing research can help to pave the way for expansion and integration of this method into PAC services worldwide.

Initial studies on misoprostol focused on finding an appropriate dose and route for this indication. Later work compared misoprostol to surgical treatment options. Studies comparing 600 versus 1200 micrograms (mcg) oral misoprostol in Thailand and Vietnam revealed no difference in the efficacy of the two regimens.^{5,6} In addition, a study comparing misoprostol to MVA for incomplete abortion in Uganda revealed a high success rate for both oral misoprostol (96.3%) and MVA (91.5%). Acceptability of both methods to clients was also high (94.2% misoprostol and

94.7% MVA) and reflects, in part, the acceptability of misoprostol's most common side effects, including bleeding, pain, chills, fever, nausea, vomiting and diarrhea.

The study in Uganda indicates that an overwhelming majority of women who received 600 mcg oral misoprostol avoided surgical evacuation. The side effects profile was as expected (22% of women who received misoprostol and 10.9% of women who underwent MVA reported one or more side effects) and need for ultrasound to confirm complete evacuation of the uterus was infrequent. The study found that comprehensive training increases provider confidence and hence the efficacy of the method. The authors also concluded that PAC based on misoprostol treatment required minimal technical skill, rendering it an ideal choice for rural health centers with limited facilities.¹

Instructions for Use

In June 2004, a group of professionals with epidemiological, clinical and programmatic expertise participated in a one-day meeting in New York and recommended a standard protocol for misoprostol use based on research experience. "Instructions for Use—Misoprostol for Treatment of Incomplete Abortion and Miscarriage"⁷ provides guidance for clinicians and medical personnel in the form of a shadow product label that includes indications and usage, contraindications, effects and side effects, and dosage and administration of misoprostol for incomplete abortion, miscarriage and induced abortion. The instructions have been disseminated in eight languages electronically (available at http://www.gynuity.org/pub_b.html or http://www.gynuity.org/documents/ifu_abortion_eng.pdf for the English version) as well as through clinical trainings, websites and inclusion in scientific articles.

Misoprostol is indicated for treatment of incomplete abortion and miscarriage for women with uterine size less than or equal to 12 weeks LMP at presentation. Success rates range from 66-100% (closer to the higher figure in recent studies) using the recommended dose for incomplete abortion (single dose of 600 mcg misoprostol orally). For missed abortion, success ranges from 60-93% using the recommended dose (800 mcg misoprostol vaginally). The use of misoprostol for evacuating retained products of conception will not be 100% effective, and therefore some small number of women will still require surgical evacuation; nonetheless, misoprostol has tremendous potential as a treatment for pregnancy failure.⁸

Moving from Research to Practice

Despite the promising results of misoprostol research, integration of misoprostol into PAC programs poses some challenges. Foremost among these is the need to share information so that women will seek and providers will offer the method. Providers need to be convinced of the safety and effectiveness of the method before they are willing to offer it. Furthermore, since few providers have been trained in the use of misoprostol for PAC, expanded training is critical to its introduction. This training should

prepare providers to counsel and treat women who present with incomplete abortion appropriately, as misoprostol is not the right technology for uterine evacuation in all cases. For instance, severe hemorrhage with unstable vital signs would preclude the use of misoprostol; surgical intervention should take place immediately in this and other emergency situations. Staff offering misoprostol should also be able to identify cases of infection and provide or refer for timely surgical intervention.

Availability and training in ultrasound technology is another important consideration in the use of misoprostol for PAC. Ultrasound can be used to confirm complete evacuation of the uterus, but over-reliance on the technology and misinterpretation of results by poorly trained personnel can cause unnecessary surgical intervention. Not all providers need be trained to use ultrasound, but referral centers and relevant medical and technical personnel will need to understand its uses and limitations.

A third challenge is dealing with follow-up. A follow-up visit is recommended, but women who are “cured” and feel well often do not want to take the time to return to the clinic. The follow-up visit offers an additional opportunity for contraceptive counseling, a final assessment of the women’s treatment status and increased access to other reproductive health services. Therefore, women need to understand, and providers need to stress, the benefits of a return visit.

While the three challenges mentioned above are more clinical in nature, it is also critical to convince program planners of the value of misoprostol for PAC programs. Existing PAC programs, strengthened through community and service provider partnerships, have offered a critical platform for the introduction of misoprostol. For instance, much of the work with misoprostol in West Africa was facilitated by a large amount of PAC work already underway in the region.

In settings where there are no PAC programs, meetings with local experts, Ministry of Health officials and key providers from the region provide an important forum to promote the use of misoprostol. From a programmatic perspective, national and regional meetings provide opportune moments to disseminate research findings and influence national guidelines and policies related to PAC. These interactions could lead to partnerships with providers in peri-urban and rural areas where access to PAC is often limited. Involvement of local authorities in the research process similarly facilitates the long-term integration and scale-up of new methods.

Future Research

In order to promote and optimize the use of misoprostol for PAC further research is needed. Cost-benefit analyses that compare misoprostol to surgical methods can increase policy-makers’ enthusiasm about introducing the technology. In addition, newer—and potentially less expensive—regimens are under investigation using sublingual (under the tongue) and buccal (in the cheek) routes of administration. Additional questions about acceptable bleeding levels and duration and risk of infection among certain groups of women can also be addressed through further research.

Drug Registration

One of the greatest challenges to widespread use of misoprostol for PAC—and therefore the development of sustainable service delivery models—is the regulatory status and availability of the drug. Misoprostol is currently registered and available in over 80 countries, but in almost all cases it is marketed only for its gastrointestinal indications. As misoprostol is not registered for use in PAC, its integration into PAC programs is often hindered by MOH reticence and lack of any formal marketing of the product. Under the best circumstances, programs would have access to a product registered and marketed for PAC indications with availability through normal commercial and subsidized channels. It is impossible to create a misoprostol program without a product; therefore ensuring the availability of the product will necessarily be one of the first steps in implementing the program.

In places with no registered product for PAC, interested groups can engage in advocacy and information dissemination. Innovative ways for hospitals to acquire drug supplies can also assist in pilot program development. Small companies willing to take risks may move forward the task of registering misoprostol for PAC, especially if assisted by public-private partnerships.

Conclusions

Realistically, safe and effective services are needed to prevent complications of abortion, not just to treat them. The provision of PAC therefore does not replace adequate access to safe abortion services. For women who do require PAC, misoprostol should not replace access to safe surgical treatment, since surgical treatment will sometimes be necessary because of the woman’s condition or as back-up. Instead, comprehensive PAC programs will enhance the quality of services offered to women by providing them with a range of treatment options and the most appropriate care.

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Postabortion Family Planning: A Vital Element for Reducing Maternal Morbidity and Mortality

Diane Bushley

This issue of *PAC in Action* focuses on the potential of using misoprostol for uterine evacuation in PAC services. Misoprostol is an option for achieving one of the five Essential Elements of PAC—treatment of incomplete and unsafe abortion. However, regardless of the technology used for uterine evacuation in PAC services, these services should include all of the Essential Elements, including postabortion family planning (PAFP). Postabortion family planning plays a vital role in reducing maternal morbidity and mortality due to abortion complications, which is ultimately the goal of all PAC programming. This article highlights the importance of PAFP and best practices in PAFP, and offers a description of how PAFP is integrated into the misoprostol treatment protocol for PAC services.

The Impact of Postabortion Family Planning

The benefits of PAFP are numerous—for women's health, families and country health systems. Postabortion family planning can prevent unintended pregnancies that can lead to repeat abortions, over time reducing the need for PAC services. A study conducted by Ipas in Zimbabwe showed that provision of PAFP resulted in reduced incidences of both unplanned pregnancy (15% at the intervention site vs. 34% at the control site) and repeat abortion (2.5% vs. 5.3%, respectively) up to 12 months after PAC services (Johnson et al. 2002). The difference in unplanned pregnancies between the control and intervention sites was statistically significant, while the difference in repeat abortions was not. This finding is supported by the wealth of evidence showing the inverse relationship between family planning access and abortion—abortion rates are typically lowest where access to and use of family planning are highest (Gillespie 2004).

A more recent study has also demonstrated compelling health reasons for

spacing the next pregnancy after an abortion. This is particularly important for women who want to become pregnant again as soon as possible, which may be the case in the event of spontaneous abortion. Research by Conde-Agudelo et al. (2005) indicates that delaying conception for at least five months through use of PAFP improves maternal and neonatal outcomes in the subsequent pregnancy.

Regardless of whether it is used to prevent unintended pregnancy or space a subsequent planned pregnancy, PAFP, like all FP, can ultimately reduce maternal mortality. Data from 15 countries in West Africa reveal that maternal mortality rates were lowest in countries where contraceptive prevalence was highest (IPPF 2006). According to the Alan Guttmacher Institute, addressing the current unmet need for contraception (201 million women globally) would avert 52 million pregnancies each year, preventing 142,000 pregnancy-related deaths, including those caused by unsafe abortion.

Best Practices in Postabortion Family Planning Service Delivery

Postabortion family planning is clearly critical to the success of both PAC and Safe Motherhood initiatives and to ensuring that PAC clients have the knowledge and resources they need to avoid future unintended pregnancies or space a subsequent desired pregnancy. Over the past decade, various research projects and PAC program experience have yielded some important best practices in PAFP provision. Because clinical studies show that fertility may return as early as 11 days postabortion, PAFP services should be provided as close to the time of PAC services as possible, either at the PAC service delivery point or via referral to an accessible FP facility.

Several studies have also indicated that contraceptive acceptance among PAC clients is highest when FP services are

offered at the PAC service delivery point. An operations research study conducted by Solo et al. (1999) compared three models for PAFP provision, and showed that women who receive contraceptive services directly from their PAC provider on the gynecological ward (Model 1) were more likely to accept contraception than those who received those services from a FP provider on the gynecological ward (Model 2) or through referral to the FP clinic (Model 3).

Despite these documented best practices, there are still many barriers to PAFP. In many countries, sociocultural norms dictate that women need their male partners' approval to use FP. Providers sometimes support this practice, despite the fact that national policies often explicitly state partners' approval of FP use is not required.

Postabortion Family Planning Provision in the Misoprostol Treatment Protocol

Per the treatment protocol used in Gynuity's research on misoprostol and PAC in Burkina Faso, Ghana, Tanzania and Uganda, PAC clients typically visit the facility twice. At the first visit, they receive treatment counseling and information about misoprostol, including side effects and efficacy. After administration of misoprostol, they are observed for a few minutes, discharged at the discretion of the provider, and scheduled for a follow-up visit seven days later. If uterine evacuation is not complete at the follow-up visit, clients can choose to have a surgical intervention or return in another seven days for a check-up, by which time evacuation will usually be complete.

Although PAC clients who are treated with misoprostol may spend less time overall at the facility than clients treated with MVA or D&C, they are offered FP counseling and contraception or referral for these services in accordance with the standard practice at the facility. The two-visit protocol also provides an

additional opportunity for FP counseling and provision. Clients can begin using most contraceptives (oral contraceptives, condoms, contraceptive jellies and foams, the cervical cap, diaphragms, injectables and implants) immediately after the first visit to the facility, but should wait until uterine evacuation is complete before having an IUD inserted.

Programmatic Updates

General Programmatic Information

Planned Parenthood Federation of America-International® and los Centros Médicos de Orientación y Planificación Familiar (Medical Centers for Counseling and Family Planning or CEMOPLAF), one of Ecuador's largest private providers of reproductive health services, will initiate a PAC program in July 2006. CEMOPLAF currently runs 29 health facilities throughout Ecuador offering contraceptive services, community health care, maternity and obstetric care, STI/HIV prevention, adolescent reproductive health programs, hospital care and an integrated program in reproductive health. Given the growing body of evidence that misoprostol alone is safe and effective for treatment of incomplete abortion, PAC services will include the use of both MVA and misoprostol-only protocols for treatment of incomplete and unsafe abortion. In year one, a group of providers selected from two CEMOPLAF centers will be trained in the provision of PAC services. These providers will form a CEMOPLAF training team, which will subsequently train providers in two more health centers during the first year. CEMOPLAF's goal over the next six years is to integrate PAC services into their menu of services—using both misoprostol and MVA—at all 29 sites. For more information, please contact **Heather Sayette** at heather.sayette@ppfa.org

Equipment

In 2005, Ipas published *Planning for a Sustainable Supply of Manual Vacuum Aspiration Instruments: A Guide for Program Managers* (by Marian Abernathy) as a tool to help program managers plan for sustainability of MVA instruments for

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Soto J, Billings DL, Obunga CA, Ominde A, Makumi M. Creating linkages between incomplete abortion treatment and family planning services in Kenya. *Studies in Family Planning* 1999;30(1):17-27.

Winikoff B, Sullivan M. Assessing the role of family planning in reducing maternal mortality. *Studies in Family Planning* 1997;18:128-143.

postabortion care and abortion care services. First published in English and now available in French and Spanish, it is one of the first tools to offer guidance for programmatic personnel in developing a sustainable supply of MVA instruments.

The Guide was developed based on Ipas' and other agencies' efforts to develop sustainable supplies; discussions with in-country personnel from a variety of organizations; and input from a group of training, service delivery and logistics and procurement experts—many of them from the PAC Consortium. Since each country is unique, the Guide does not provide a standard methodology that will work in every situation. Instead, it helps program planners (1) frame thinking on the process of developing sustainable supplies of MVA instruments; (2) identify major system features (of the supply chain or logistics system such as financing or budget management and regulatory environment) that should be taken into account; and (3) clarify the types of inputs involved. Additionally, the Guide includes six case studies that illustrate possible approaches to achieving sustainable supplies.

To date, Ipas has incorporated elements of the Guide into its training and service delivery programs. Additionally, Pathfinder International's Peru Program used the Guide to conduct an assessment of their recently completed PAC program in 50 public-sector facilities nationwide, and is striving to develop a sustainability plan.

Ipas is interested in learning about other applications of the Guide. Please send suggestions or other

feedback to training@ipas.org. Single hard copies can be obtained free of charge for those in developing countries; free, downloadable electronic versions are also available on the web:

English: http://www.ipas.org/publications/en/PLANMVA_E05_en.pdf

French: http://www.ipas.org/publications/fr/PLANMVA_F05_fr.pdf

Spanish: http://www.ipas.org/publications/es/PLANMVA_S05_es.pdf

Research and Evaluation

In collaboration with TAHSEEN, a USAID-funded population project, and the Egyptian Ministry of Health and Population, the Population Council's Frontiers in Reproductive Health Program (FRONTIERS) is conducting operations research in six public Egyptian hospitals to test the feasibility, acceptability and effectiveness of two models of integrating family planning (FP) with postabortion services.

Model I involves providing FP counseling to postabortion patients on the Ob/Gyn ward and referring them to a separate FP clinic while Model II involves provision of FP methods on the ward. The two models were implemented in tandem. To date, assessment of Model 1 is complete and assessment of Model 2 is underway.

Final study results, which are expected in September 2006, will help the MOHP develop a policy for linking FP to curative services for postabortion patients. For more information, please contact **Hala Youssef** at houssef@pccairo.org

FRONTIERS and EngenderHealth's ACQUIRE project are carrying out an operations research project to examine the feasibility of providing PAC in

decentralized settings (health centers and dispensaries) in rural Tanzania. Research in Senegal has shown that, while it is feasible to provide integrated postabortion care (PAC) in lower-level facilities such as health posts, deficiencies in quality of care and logistical problems still impede full access to services.¹ This current project will document the process of introducing PAC services and determine the acceptability, impact and cost of the services, with particular focus on the effectiveness of referral networks established as part of the PAC process. Additionally, the project will address some of the problems identified through the Senegalese experience, including (1) improving audio and visual privacy and confidentiality by creating a separate room for MVA procedures in all facilities, (2) reducing delayed access to services by sensitizing all staff and, where possible, ensuring that more than one provider can perform MVA services at each facility through on-the-job training and (3) improving infection prevention through enhanced training and job aids. For more information, please contact **Monica Wanjiru** at mwanjiru@pcnairobi.org

Resources

The following documents from the Hesperian Foundation are now available on the web. For more information contact **Hesperian** at lisa@hesperian.org or (888) 729-1796.

Hesperian Foundation. 2006. Women's Health Exchange Issue #12. Berkeley, CA: Hesperian Foundation.

Hesperian's new Women's Health Exchange issue on postabortion care includes a training guide for exploring the barriers that health care providers face (from access to resources to attitudes) in providing lifesaving care for women suffering complications from an incomplete miscarriage or abortion; information about manual vacuum aspiration (MVA); stories of midwives who are learning to provide MVA and other emergency care and the benefits of training community health workers in these skills; and resources for finding out more about the causes of unsafe abortion and

how to provide effective postabortion care, including postabortion FP. Access the online version at our new website: www.hesperian.org

Klein, Susan, Suellen Miller and Fiona Thomson. 2005. *A Book for Midwives: Care for Pregnancy, Birth, and Women's Health*. Berkeley: Hesperian Foundation.

This manual, which was awarded "American College of Nurse-Midwives Notable Book 2006," has proved a vital resource for midwives around the world. Combining clear language, medical accuracy and a focus on simple, low-cost treatments, the new edition is reorganized and revised to better support care during labor and management of obstetric emergencies. The book also includes new chapters on postabortion care and manual vacuum aspiration. www.hesperian.org

The following PAC resources are now available in Arabic on the Population Council's website. Contact **Laura Raney** at lraney@pcdc.org for more information:

Improving the counseling and medical care of postabortion patients in Egypt <http://www.popcouncil.org/pdfs/arabic/ImprovingCounselingPacEgypt.pdf>

Counseling the husbands of postabortion patients in Egypt: Effects on husband involvement, patient recovery, and contraceptive use: <http://www.popcouncil.org/pdfs/arabic/CounselingHusbandPAC.pdf>

Scaling-up improved postabortion care in Egypt: Introduction to university and Ministry of Health and Population hospitals: <http://www.popcouncil.org/pdfs/arabic/ScalingUpPac.pdf>

Postabortion case load study in Egyptian public-sector hospitals <http://www.popcouncil.org/pdfs/arabic/PACStudyEgPSHosp.pdf>

¹ EngenderHealth. 2003. Taking postabortion care services where they are needed: An operations research project testing PAC expansion in rural Senegal. FRONTIERS Final Report. Washington, DC: Population Council. http://www.popcouncil.org/pdfs/frontiers/FR_FinalReports/Senegal_PAC.pdf

Working Group Updates

Communications Task Force

Co-Chairs: **David Nelson**, IntraHealth, dnelson@intrahealth.org and **Laura Raney**, Population Council, LRaney@pcdc.org

Communications Task Force (TF) members provided positive feedback on the new colors and layout of the November 2005 newsletter. They also agreed to promote wider newsletter distribution through their own organizations and other contacts. PAC Consortium members are encouraged to submit suggestions for list serves through which the newsletter could be distributed to David Nelson. TF members also expressed a need for a Portuguese translation of the newsletter, and will pursue this possibility.

Another major topic of conversation was the need to update and revamp the PAC Consortium website. Meeting participants agreed to have a conference call to discuss the need for additional categories, new links and a redesign of the homepage in order to ensure that the website meets its mandate—to serve as a clearinghouse for information. Once the website has been updated, participants discussed the possibility of increasing awareness about the website by creating a CD-ROM for distribution at Global Health and other conferences. Lastly, the group discussed encouraging more active use of the list serve as a resource for communication on Consortium-related issues between the semi-annual meetings. List serve members are encouraged to submit news items from their respective organizations to the co-chairs between issues of *PAC in Action* for distribution via the list serve or the website.

Essential Elements Task Force

Co-Chairs: **Inés Escandón**, EngenderHealth/ACQUIRE Project, iescandon@engenderhealth.org and **Kiyomi Tsuyuki**, former CATALYST/Population Fellow, ktsuyuki@gmail.com

Essential Elements Task Force members have made several changes to the monitoring and evaluation (M&E) framework for the Essential Elements of PAC, including adding indicators and results for the community and service provider partnerships element and further defining the indicator for stigma. The current working draft of the framework will be added to the PAC Consortium website; however, the TF suggests revision of the M&E framework in early 2007 to (1) add indicators that demonstrate the impact of community mobilization on PAC; (2) expand indicators on referral and counter-referral; (3) include qualitative indicators; and (4) incorporate indicators for special populations (e.g., youth and displaced persons). Now that the USAID PAC Strategy is widely distributed, the TF also plans to include the USAID PAC indicators in the framework. Finally, TF members identified the need to obtain feedback from the field on indicators to inform the development of additional M&E guidance and tools.

The group discussed how to increase communication among TF members beyond the meetings twice a year, and suggested including one or two indicators from the M&E framework in each PAC newsletter and asking readers to provide feedback on their experiences measuring these indicators. They also proposed gathering information through the Implementing Best Practice (IBP) Initiative's Electronic Communications System (ECS), and will conduct a small pilot test to determine the extent to which this approach may be effective.

PAC Technologies Task Force

Co-Chairs: **Nancy Harris**, John Snow International, nharris@jsi.com and **Sheila Raghavan**, Gynuity Health Projects, sraghavan@gynuity.org

The topic of the PAC Consortium plenary was misoprostol, so discussion in the PAC Technologies Task Force focused on other technologies, primarily MVA. TF members discussed the need to develop assessment reports of key PAC countries to better track progress over time and to identify barriers to scaling up and sustaining PAC. Reports would include recent information on PAC, including MVA supply and the status/availability of misoprostol. TF members suggested countries with active PAC programs for initial reports, including Bangladesh, Bolivia, India, Kenya, Malawi, Nepal, Nigeria, Peru, Russia, Senegal, Tanzania, Uganda, Zambia and Zimbabwe. Next steps include finalization of a country list, development of assessment report formats and collection of information by designated Consortium partners in each country.

Issues raised by TF members for further discussion included: (1) availability of MVA through public, private and commercial channels and how to achieve sustainable supply systems; (2) quality of equipment; (3) transparency in pricing at the country level; and (4) availability of single-, double-valve and MVA Plus aspirators. TF members agreed that PAC Consortium agencies should be advocates for sustainable supplies. Finally, TF members identified a need to attract more groups (nongovernmental organizations and other agencies such as universities and faith-based organizations) and USAID-funded country projects to participate on this TF. Interested organizations are encouraged to contact the TF co-chairs.

PAC and Safe Motherhood Task Force

Co-Chairs: **Koki Agarwal**, JHPIEGO, kagarwal@jhpiego.net and **Elizabeth Westley**, Family Care International (FCI), ewestley@fcimail.org

Koki Agarwal and Elizabeth Westley, co-chairs of the group, provided some history of the PAC and Safe Motherhood Task Force. The group agreed that, although there is not a strong current "agenda" for the group, it is nevertheless important to continue to provide a forum for the discussion of PAC and Safe Motherhood issues, especially given how closely entwined these issues often are at the service delivery level. This group therefore agreed to continue to meet and discuss relevant issues semiannually, with the possibility of undertaking new tasks between meetings if the need should arise. Co-chairs are seeking more active participation from individuals who are committed to PAC and Safe Motherhood. Please contact either of them for further information.

Youth-Friendly PAC Working Group

Chair: **Gwyn Hainsworth**, Pathfinder International, ghainsworth@pathfind.org

The Youth-Friendly PAC Working Group met prior to the PAC Consortium meeting. Members worked on finalizing the draft of the technical guidance on youth-friendly PAC. The guidance uses the Essential Elements of PAC as a framework and is geared toward program managers and service providers. It will be distributed over the PAC Consortium list serve for final comments and will be formally presented for approval during the next Consortium meeting.

A summary of the draft guidance was also presented during the APHA conference. For more information on adolescents and PAC, please see the PAC Consortium website at www.pac-consortium.org

An Adolescent and PAC Resource List is available at <http://www.pac-consortium.org/Pages/resources.html>

Revitalization of the Francophone Regional Postabortion Care Initiative

Maureen Corbett, IntraHealth International, Holley Stewart, Population Reference Bureau and Amadou Hassane Sylla, CEFOREP

Revitalizing the Francophone Regional PAC Initiative was the subject of a meeting among USAID cooperating agency and donor partners held in Dakar, Senegal, March 1-2, 2006. The Initiative was launched in March 2002 with a regional conference, also in Dakar, attended by delegations from 12 countries as well as donors and CAs. Since that time, several countries have established and/or expanded the availability, acceptability, quality and use of postabortion services, although much remains to be done to address unsafe and incomplete abortion, which is a major cause of maternal morbidity and mortality in the region.

The Secretariat of the Initiative, the regional African institution *Centre de Formation et de Recherche en Santé de la Réproduction* (CEFOREP) hosted the March 2006 meeting, bringing together representatives from Senegal's Ministry of Health, UNFPA, USAID, WHO and UNICEF, as well as

representatives from cooperating agencies and projects, including Africa's Health in 2010, IntraHealth, Population Council/Frontiers, Policy Dialogue Information Project (PDI), Extending Service Delivery Project (ESD), MSH/Senegal, AWARE RH and Ipas.



Participants at the 2002 Francophone PAC conference in Dakar.



Country teams developed action plans for PAC at the 2002 conference. Here participants review the plan for Côte D'Ivoire.

Discussions during this two-day meeting focused on four priority areas for revitalizing country-level PAC activities and programs: (1) emergency obstetric care; (2) postabortion FP and repositioning FP to prevent unwanted pregnancies; (3) community mobilization and involvement; and (4) mid- and community-level providers. The group reviewed the status of country-level action plans; identified practices that had contributed to progress and factors that had created obstacles; and brainstormed how these obstacles could be overcome through adaptation of better practices.

The meeting also provided a venue for introducing the Implementing Best Practices (IBP) Initiative, which is led by a consortium of 23 organizations, including WHO, USAID and UNFPA and promotes documentation, dissemination and implementation of best practices in reproductive health. Concrete discussions and planning took place to see how the IBP Consortium could assist in the follow-up of the Francophone Regional PAC Initiative.

A report from the meeting will be available in June. To obtain a copy of this report or for more information about the Francophone Regional PAC Initiative, please contact **Amadou Hassane Sylla**, CEFOREP, ahsylla@sentoo.sn

Improving Access to and Quality of PAC Services in Kenya through Revolving Loan Funds

Joyce Kinaro, Planned Parenthood Federation of America-International Africa Regional Office

Complications of abortion are one of the major causes of maternal mortality in Africa, and Planned Parenthood Federation of America-International's (PPFA-I) strategy for reducing maternal mortality in the region includes improving the quality of PAC services. In Cameroon, Kenya, Nigeria and Sudan, PPFA-I has offered PAC training for public- and private-sector doctors and mid-level providers, supported practitioner networks and provided MVA kits.

The situation in Kenya parallels that of other countries in the region. The "National Assessment of the Magnitude and Consequences of Unsafe Abortion in Kenya," conducted in 2004 by the Kenya Medical Association, the Ministry of Health, the Kenya Chapter of the Federation of Women Lawyers and Ipas, indicated that about 300,000 abortions are performed each year. Among these, an estimated 20,000 women and girls with complications of abortion are hospitalized and 2,600 women die from these complications.



Since 1996, PPFA-I has partnered with the Kisumu Medical Educational Trust (KMET) to improve the overall health and well-being of women in rural Kenya by ensuring access to reproductive health services. The KMET project has combated high maternal and morbidity rates by training private practitioners and mid-level providers in rural areas in Western Kenya in comprehensive reproductive health techniques, including contraceptive distribution and the provision of PAC services and by providing them with the necessary MVA equipment and supplies.

The 96 medical doctors and 25 mid-level providers who have received PAC training, including MVA for treatment of incomplete and unsafe abortion, from KMET have formed a PAC Providers' Network. Through a revolving loan fund project implemented in 2004, network members are able to borrow

up to 300,000 Kenyan shillings (US \$4,000) to renovate their private clinics, which helps them expand the RH services they offer. To date, approximately one quarter of the network members have benefited from this fund.

Jackson Mworia is a Kenya Enrolled Community Health Nurse who operates a small private clinic in a rural community in Meru District in Eastern Kenya. He participated in a PPFA-I-sponsored PAC training in May 2004, and is a member of the PAC Providers' Network. In June 2005, he received a loan of 250,000 Kenyan Shillings (US \$3,378), which he used to renovate his clinic, purchase a stock of essential drugs and improve infection control.

Given the additional space provided by the renovation, the clinic can now serve more clients. An increase from 10 to 50 clients per day between June and November 2004 helped Mr. Mworia make his monthly loan payments. Before becoming a PAC Network provider, Mr. Mworia referred most of his PAC clients elsewhere. However, since the training, the number of PAC clients has gradually increased from an average of four clients per month in June 2004 to 20 in May 2005.

Mr. Mworia noted that the Revolving Loan Fund has enabled him to meet basic requirements and to improve overall quality of care.

"...I was straining a lot [financially] in ensuring infection control, which was a government requirement to renew my clinic license..."

Once he repays his current loan, Mr. Mworia hopes to obtain another loan to expand the clinic to include an operating theater. Through the KMET provider network, PPFA-I is building the capacity of private PAC providers in remote communities in Africa, enabling individuals in poor underserved communities to access quality reproductive health services such as postabortion care.

For more information, please contact **Joyce Kinaro** at joyce.kinaro@ppfa.or.ke

Calendar

May 30-June 2, 2006

33rd Annual Global Health Council (GHC) Conference, "Excellence, Innovation and Influence: Pathways to Results." Washington, D.C., Omni Shoreham Hotel.

May 30, 2006 (1-6 p.m.)

PAC Consortium Meeting at the Global Health Council Conference, "Postabortion Family Planning: Rights, Realities and Recommendations." Washington D.C., Omni Shoreham Hotel.



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Annotated Bibliography on Misoprostol for Treatment of Incomplete Abortion and Miscarriage

1. Agostini A, Ronda I, Capelle M, Romain F, Bretelle F, Blanc B. Influence of clinical and ultrasound factors on the efficacy of misoprostol in first trimester pregnancy failure. *Fertility and Sterility* 2005;84(4):1030-1032.

This prospective observational study enrolled 276 women with early pregnancy failure. All women received 800 mcg misoprostol intravaginally followed by clinical and ultrasound examination 24 hours later. The overall success rate was 65.2% (180/276). A multivariate analysis demonstrated that success rate was inversely proportional to parity: 70.9% for nulliparous women (73/103), 73.7% for primiparous women (45/61), 56.6% for women with para 2 (30/53), and 54.2% for women with para >2 (32/59) (P=.03).

2. Bagratee JS, Khullar V, Regan L, Moodley J, Kagoro H. A randomized controlled trial comparing medical and expectant management of first trimester miscarriage. *Human Reproduction* 2004;19(2):266-271.

104 women with pregnancy failures were randomized to receive either 600 mcg misoprostol or placebo vaginally. Repeat doses were offered if evacuation was not complete the following day. At Day 7, women who had not experienced complete evacuation of uterine contents were given a surgical evacuation. The overall success rate in the misoprostol arm was 88.5% compared with 44.2% in the placebo arm. There was no significant difference in success rates between the two arms among women experiencing an incomplete abortion (100% vs 85.7%). However, women experiencing a missed abortion had a much higher success rate with misoprostol (87%) as compared to placebo (29%).

3. Blanchard K, Taneepanichskul S, Kiriwat O, Sirimai K, Svirirojana N, Mavimbela N, Winikoff B. Two regimens of misoprostol for treatment of incomplete abortion. *Obstetrics and Gynecology* 2004;103:860-865.

This randomized trial enrolled 169 women with diagnosed incomplete abortion. Women received either a single or repeated dose of 600 mcg of misoprostol taken orally. Follow-up was conducted two weeks following misoprostol administration. There was no difference in efficacy between the two treatments: 66% of women in the single dose arm and 70% of women in the repeat dose arm experienced complete expulsion without the need for surgical intervention.

4. Chung TK, Cheung LP, Leung TY, Haines CJ, Chang AM. Misoprostol in the management of spontaneous abortion. *British Journal of Obstetrics and Gynaecology* 1995;102(10):832-5.

This prospective, observational study enrolled 252 women with diagnosed incomplete abortion. All women were first treated with expectant management. Two weeks after the initial diagnosis, women who were found to still have significant retained products of conception were given 400 mcg oral misoprostol every 4 hours for a total of 3 doses. They were reassessed the following morning for complete evacuation. 141 women had retained products at the two week follow-up and were treated with misoprostol. Of those women, 88 (62%) did not require surgical intervention.

5. Chung TK, Lee DT, Cheung LP, Haines CJ, Chang AM. Spontaneous abortion: a randomized, controlled trial comparing surgical evacuation with conservative management using misoprostol. *Fertility and Sterility* 1999;71(6):1054-9.

635 women were enrolled in this randomized trial comparing the efficacy of misoprostol for treatment of incomplete abortion to that of surgical evacuation. Women in the misoprostol arm received 400 mcg of oral misoprostol every 4 hours up to a total dose of 1200 mcg. Evaluation of success was made the following morning. Of the 321 women who received misoprostol, 159 (50%) expelled the products of conception and did not require surgical intervention.

6. Creinin MD, Moyer R, Guido R. Misoprostol for medical evacuation of early pregnancy failure. *Obstetrics and Gynecology* 1997;89:768-772.

Twenty women were randomized to receive 400 mcg oral misoprostol or 800 mcg vaginal misoprostol for treatment of early pregnancy failure. The dose was repeated in 24 hours if a gestational sac was still present. After an additional 24 hours, women failing to expel the products of conception were given a surgical evacuation. 12 women received oral misoprostol and 8 women received vaginal misoprostol. Successful expulsion occurred in 3 of 12 women (25%) in the oral group and 7 of 8 women (88%) in the vaginal group.

7. Davis AR, Robilotto CM, Westhoff CL, Forman S, Zhang J; National Institute of Child Health Human Development (NICHD) Management of Early Pregnancy Failure Trial. Bleeding patterns after vaginal misoprostol for treatment of early pregnancy failure. *Human Reproduction* 2004;19 (7):1655-8.

77 women diagnosed with early pregnancy failure were enrolled in this prospective cohort study and randomized to receive either 800 mcg of dry or moistened (2 ml saline) vaginal misoprostol. Self-reported bleeding and sanitary product usage were recorded in a daily diary over a 2-week period. Hemoglobin was assessed at enrollment and 2 weeks later. Women reported bleeding or spotting every day for the 14 days observed. Sanitary pad usage was highly variable (mean 30.5, range 2-125 pads over the 2-week period) and not related to changes in hemoglobin. Self-assessed heavy bleeding days were few (median 3) and usually occurred immediately after treatment. Complete expulsion without dilation and curettage (D&C) occurred in 85% of women. The mean decrease in hemoglobin was 0.5 g/dl (SD 1.2)

8. Demetroulis C, Saridogan E, Kunde D, Naftalin AA. A prospective randomized control trial comparing medical and surgical treatment for early pregnancy failure. *Human Reproduction* 2001;16(2):365-9.

This prospective study randomized 80 patients to surgical evacuation or medical management with 800 mcg of vaginal misoprostol for early pregnancy failure. This study included women with both incomplete and missed abortions. Follow-up was conducted 10 days following treatment administration. The failure rate in the misoprostol group was 7% among women with incomplete abortion and 23% among women with missed abortion. None of the patients assigned to the surgical arm required repeat evacuation. All patients with successful treatments in the misoprostol group expressed satisfaction with the treatment as compared to only 58% of women in the surgical group.

9. Graziosi GCM, Mol BW, Ankum WM, Bruinse HW. Management of early pregnancy loss. *International Journal of Gynecology and Obstetrics* 2004;86:337-346.

A meta-analysis was conducted of 13 randomized clinical trials that reported a comparison of misoprostol and curettage, misoprostol and expectant management, or expectant management and curettage for early pregnancy loss. Combined data in women with missed abortion managed expectantly or treated with misoprostol showed complete evacuation rates of 28% (49/173; range 14-47%) and 81% (242/298; range 60-83%) respectively. In women with incomplete abortion, these rates were 94% (31/33; range 80-100%) and 99% (75/76; range 99-100%) respectively. Both expectant management and misoprostol treatment reduce the need for curettage for early pregnancy loss, but for women with missed abortion misoprostol seems to be much more effective than expectant management.

10. Gronlund L, Gronlund AL, Clevin L, Anderson B, Palmgren N, Lidegaard A. Spontaneous abortion: Expectant management, medical treatment or surgical evacuation. *Acta Obstet Gynecol Scand* 2002;Aug 81(8):781-2.

This study compared treatment of spontaneous abortion by expectant management, 400 mcg vaginal misoprostol, and surgical evacuation. 78 women were enrolled. After treatment, women were reevaluated at days 8 and 14. Successful evacuation of the uterus was achieved in 14/17 (82%) women in the expectant management group, in 28/31 (90%) of women treated with misoprostol and in 29/30 (97%) of women receiving surgical evacuation.

11. Henshaw RC, Cooper K, El-Refaey H, Smith NC, Templeton AA. Medical management of miscarriage: non-surgical uterine evacuation of incomplete and inevitable spontaneous abortion. *British Medical Journal* 1993;306:894-5.

This open study evaluated the outcome of 44 women treated with sulprostone or 400 mcg oral misoprostol for incomplete or inevitable abortion. The authors combined the data from the two groups due to a lack of differences in the outcomes in the two groups. Treatment failed in 2 of the 43 evaluated patients with the remaining 41 women achieving complete uterine evacuation after 12-18 hours.

12. Herabutya Y, O-Prasertsawat P. Misoprostol in the management of missed abortion. *International Journal of Gynecology and Obstetrics* 1997;56:263-6.

This study compared the efficacy of vaginal misoprostol (200 mcg) compared to placebo for use prior to dilation and curettage for treatment of missed abortion. 84 women were randomized to receive the treatment one day prior to scheduled surgery. 83.3% of the women in the misoprostol group

spontaneously expelled the products of conception prior to the surgery. This was significantly higher than the 17.14% who expelled in the placebo group.

13. de Jonge ET, Makin JD, Manefeldt E, De Wet GH, Pattinson RC. Randomised clinical trial of medical evacuation and surgical curettage for incomplete miscarriage. *British Medical Journal* 1995;311(7006):662.

This trial enrolled 50 women who presented with incomplete miscarriage. Women were randomized to either medical management consisting of a single dose of 400 mcg oral misoprostol or surgical curettage. The outcome was assessed 12 hours after misoprostol administration. After 12 hours, only 3 (13%) of the women in the misoprostol group had achieved complete evacuation of the uterus.

14. Moodliar S, Bagrattee JS, Moodley J. Medical vs. surgical evacuation of first-trimester spontaneous abortion. *International Journal of Gynecology and Obstetrics* 2005;91:21-26.

94 women diagnosed with incomplete abortion were randomized to receive 600 mcg misoprostol intravaginally or surgical curettage. The overall success rate of medical management was 91.5%; 1/3 of women (15 of 47) had complete abortions after only 1 dose of misoprostol and 8.5% required evacuation of retained products of conception after 1 week because of treatment failure. The success rate in the surgical arm was 100%. Women in the medical arm experienced a longer duration of bleeding and a greater need for analgesia. More women who received medical treatment would recommend it or choose it in the future than in the surgical arm.

15. Muffley PE, Stitely ML, Gherman RB. Early intrauterine pregnancy failure: a randomized trial of medical versus surgical treatment. *American Journal of Obstetrics and Gynecology* 2002;187(2):321-5; discussion 325-6.

50 women were randomized to either surgical or medical treatment of early pregnancy failure. The medical regimen consisted of 800 mcg vaginal misoprostol which could be repeated at 24 and 48 hours if significant products of conception remained in the uterus. The outcome was measured 72 hours after misoprostol administration. 15/25 women in the medical group (60%) had successful uterine evacuation and did not require curettage.

16. Ngai SW, Chan YM, Tang OS, Ho PC. Vaginal misoprostol as medical treatment for first trimester spontaneous miscarriage. *Human Reproduction* 2001;16(7):1493-6.

This randomized trial enrolled 60 women with pregnancy failure. Women in the medical arm received 400 mcg of vaginal misoprostol on days 1, 3, and 5. The control group was treated with expectant management only. Final outcome was assessed on day 15. 83% of women in the misoprostol group avoided surgical evacuation as compared to 48% in the control group.

17. Ngoc NTN, Blum J, Durocher J, Quan TTV, Winikoff B. Medical management of incomplete abortion using 600 versus 1200 mcg of misoprostol. *Contraception* 2005;72(6):438-42.

This randomized trial enrolled 300 women presenting with a diagnosed incomplete abortion. Women received either a single (600 mcg) or repeated (600 mcg) oral dose of misoprostol. Final assessment of success was made at Day 10. There were no significant differences in the success rates in the two treatment arms. Misoprostol effectively evacuated the uterus for nearly all women (94.6%).

18. Ngoc NTN, Blum J, Westheimer E, Quan TTV, Winikoff B. Medical termination of missed abortion using misoprostol in Vietnam. *International Journal of Gynecology and Obstetrics* 2004;87 (2):138-42.

200 women with a missed abortion confirmed by ultrasonography were randomized to receive 800 mcg misoprostol either orally or vaginally. All women returned for follow-up care two days later. Efficacy was high in both groups and not statistically significantly different (oral=89.0%, vaginal=92.9%).

19. Pandian Z, Ashok P, Templeton A. The treatment of incomplete miscarriage with oral misoprostol. *British Journal of Obstetrics and Gynecology* 2001;108(2):213-4.

This is a retrospective study of 112 women who received medical management of incomplete miscarriage. The regimen consisted of 600 mcg oral misoprostol followed by two 400 mcg doses every two hours. Complete uterine evacuation was achieved in 95 (85%) women, with a small number of women receiving a repeated misoprostol regimen.

20. Pang MW, Lee TS, Chung TK. Incomplete miscarriage: a randomized controlled trial comparing oral with vaginal misoprostol for medical evacuation. *Human Reproduction* 2001;16(11): 2283-7.

201 women were randomized to oral or vaginal misoprostol for treatment of incomplete miscarriage. 800 mcg of misoprostol was given either orally or vaginally and repeated 4 hours later if products of conception had not been passed. Final outcome was assessed the following day. The success rate was similar in both groups: 61.1% in the vaginal group and 64.4% in the oral group. The incidence of diarrhea was slightly elevated in the oral group.

21. Tang OS, Lau WN, Ng EH, Lee SW, Ho PC. A prospective randomized study to compare the use of repeated doses of vaginal and sublingual misoprostol in the management of first trimester silent miscarriages. *Human Reproduction* 2003;18: 176-181.

This randomized controlled trial of vaginal versus sublingual misoprostol (600 mcg) enrolled 80 women with silent miscarriage. The dose was repeated every three hours for a maximum of three doses. The success rate in both groups was 87.5%. Final determination of success was obtained at days 7 and 43.

22. Tang OS, Ong CY, Tse KY, Ng EH, Lee SW, Ho PC. A randomized trial to compare the use of sublingual misoprostol with or without an additional 1 week course for the management of first trimester silent miscarriage. *Human Reproduction* 2006; 21(1):189-92.

180 women with silent miscarriage (<13 weeks) given 600 mcg sublingual misoprostol every three hours for a maximum of three doses were randomized to receive (i) no extended course of misoprostol or (ii) an extended course of 400 mcg sublingual misoprostol daily for 1 week. The success rates for complete miscarriage were similar in both groups: group 1 was 92.2% (95% CI: 86.1- 97.5%) and group 2 was 93.3% (95% CI: 84.6 - 96.8%). An additional 1 week course of sublingual misoprostol did not improve the success rate or shorten the duration of vaginal bleeding. Instead, it increased the incidence of diarrhea (P < 0.01). Other side-effects were similar in the two treatment groups.

23. Weeks A, Alia G, Blum J, Ekwaru P, Durocher J, Winikoff B, Mirembe F. A randomised trial of oral misoprostol versus manual vacuum aspiration for the treatment of incomplete abortion in Kampala, Uganda. *Obstetrics and Gynecology* 2005;106(3):540-7.

330 women with a clinically diagnosed incomplete abortion were randomized to receive either manual vacuum aspiration or 600 mcg misoprostol orally to complete their abortions. Follow-up was conducted on Day 14. Misoprostol successfully completed the abortion in 96.3% of the evaluable cases. However, it is important to note that nearly 30% of women in both arms were lost to follow-up.

24. Wood SL, Brain PH. Medical management of missed abortion: a randomized clinical trial. *Obstetrics and Gynecology* 2002;99:563-566.

50 women with missed abortion were randomized to receive up to two 800 mcg doses of vaginal misoprostol or placebo. Outcome was assessed one week after misoprostol administration. 80% of women in the misoprostol group and 16% of women in the placebo group had successful expulsion of the pregnancy products and did not require surgical intervention.

25. You JHS, Chung TKH. Expectant, medical or surgical treatment for spontaneous abortion in first trimester of pregnancy: a cost analysis. *Human Reproduction* 2005; 20(10):2873-2878.

An analysis designed to simulate the clinical outcome and health care resource utilization of surgical evacuation, misoprostol and expectant care for women presenting with uncomplicated spontaneous abortion in the first trimester of pregnancy was undertaken using clinical inputs from the scientific literature and cost analyses from the perspective of a public health care provider in Hong Kong. The results showed that misoprostol was the least costly alternative per patient (US\$1,000), followed by expectant care (\$1,172) and surgical evacuation (\$2,007).

26. Zhang J, Gilles JM, Barnhart K, Creinin MD, Westhoff C, Frederick MM; National Institute of Child Health Human Development (NICHD) Management of Early Pregnancy Failure Trial. A comparison of medical management with misoprostol and surgical management for early pregnancy failure. *New England Journal of Medicine* 2005; 353(8):761-769.

652 women with a diagnosed first-trimester pregnancy failure were randomized to receive 800 mcg of misoprostol vaginally or to undergo vacuum aspiration (standard of care) in a 3:1 ratio. The misoprostol group received treatment on day 1, a second dose on day 3 if expulsion was incomplete, and vacuum aspiration on day 8 if expulsion was still incomplete. Of the women who completed the trial according to the protocol, 84% (95% CI: 81 - 87%) treated with misoprostol and 97% (95% CI: 94 - 100%) treated with vacuum aspiration had a complete abortion by day 8.