

ORIGINAL RESEARCH ARTICLE

Cost-Effectiveness Analysis of Unsafe Abortion and Alternative First-Trimester Pregnancy Termination Strategies in Nigeria and Ghana

Delphine Hu¹, Daniel Grossman², Carol Levin³, Kelly Blanchard⁴, Richard Adanu⁵, Sue J. Goldie¹

¹Center for Health Decision Science, Department of Health Policy and Management, Harvard School of Public Health, Boston, MA, USA; ²Ibis Reproductive Health, 1330 Broadway, Suite 1100, Oakland, CA 94612, USA; ³Program for Appropriate Technology in Health (PATH), 1455 NW Leary Way, Seattle, WA 98107, USA; ⁴Ibis Reproductive Health, 17 Dunster Street, Suite 201, Cambridge, MA 02138, USA; ⁵Department of Obstetrics and Gynaecology, University of Ghana Medical School, Ghana.

***For Correspondence:** Delphine Hu. *E-mail:* freeflap@gmail.com.

ABSTRACT

To explore the policy implications of increasing access to safe abortion in Nigeria and Ghana, we developed a computer-based decision analytic model which simulates induced abortion and its potential complications in a cohort of women, and comparatively assessed the cost-effectiveness of unsafe abortion and three first-trimester abortion modalities: hospital-based dilatation and curettage, hospital- and clinic-based manual vacuum aspiration (MVA), and medical abortion using misoprostol (MA). Assuming all modalities are equally available, clinic-based MVA is the most cost-effective option in Nigeria. If clinic-based MVA is not available, MA is the next best strategy. Conversely, in Ghana, MA is the most cost-effective strategy, followed by clinic-based MVA if MA is not available. From a real world policy perspective, increasing access to safe abortion in favor over unsafe abortion is the single most important factor in saving lives and societal costs, and is more influential than the actual choice of safe abortion modality (Afr. J. Reprod. Health 2010; 14[2]: 85-103).

RÉSUMÉ

Analyse du rapport coût-efficacité de l'avortement dangereux et les stratégies de l'interruption de grossesse du premier semestre alterne au Nigéria et au Ghana. Afin d'explorer les implications de la politique de l'augmentation d'accès à l'avortement sans danger au Nigéria et au Ghana, nous avons élaboré un modèle analytique de décision à base informatique qui incite l'avortement provoqué et ses complication chez une cohorte de femmes et nous avons évalué de manière comparative le rapport coût-efficacité de l'avortement dangereux et les trois modalités de l'avortement du premier semestre : la dilatation et le curetage à l'hôpital l'aspiration pneumatique manuel (APM) basé à l'hôpital et à la clinique et l'avortement médical à l'aide de misoprostol (AM). Supposons que toutes les modalités soient disponibles, l'AM est l'option la plus coût-efficacité, au Nigéria. Là où l'APM de la clinique n'est pas disponible, l'AM est la prochaine meilleure stratégie. Par contre, au Ghana l'AM est la meilleure stratégie du coût-efficacité, suivie de l'APM qui est basée à la clinique, au cas où l'AM n'est pas disponible. D'une perspective d'une vraie politique mondiale, l'accès croissant à l'avortement sans danger, au lieu de l'avortement dangereux, constitue le seul facteur le plus important pour sauver la vie et les coûts sociétaux et il est plus influent que le vrai choix de la modalité de l'avortement sans danger (Afr. J. Reprod. Health 2010; 14[2]: 85-103).

KEYWORDS: Abortion, sub-Saharan Africa, cost-effective analysis.

INTRODUCTION

Unsafe abortion is a major global public health problem. The World Health Organization (WHO) defines unsafe abortion as a procedure for terminating an unintended pregnancy carried out either by persons lacking the necessary skills or in an environment that does not conform to minimum medical standards, or both¹. In places where abortion is highly restricted by law or access to high quality abortion services is limited, women resort to ending unwanted pregnancies under unsafe, clandestine conditions. Unsafe abortion carries a risk of morbidity and mortality that is several hundred times higher than safe abortion, and accounts for 13% of all maternal deaths and 20% of all disability-adjusted life years (DALYs) lost to maternal conditions worldwide¹.

The problem of unsafe abortion is particularly severe in sub-Saharan Africa where limited uptake of family planning, highly restrictive abortion laws, and poor access to safe abortion services converge to promote concurrently high levels of unintended pregnancies, induced abortion, and unsafe abortion^{1,2,3}. Compared to other regions of the world, sub-Saharan Africa has the highest mortality and complication rates from unsafe abortion and accounts for almost half of all unsafe abortion-attributable deaths globally, although only 24% of all unsafe abortions occur in this region^{1,2}.

Abortion, when performed by a trained health care provider in a safe and legal environment, is one of the safest medical procedures, with mortality rates generally reported to be less than 1 per 100,000⁴. For early pregnancy termination, the WHO recommends: (1) manual or electric vacuum aspiration for up to 12 weeks gestational age; (2) medical abortion with mifepristone plus a prostaglandin for up to 9 weeks gestational age; and (3) dilatation and curettage (D&C) only when vacuum aspiration and medical methods are not available⁴. However, despite these recommendations, D&C continues to be the most widely practiced modality in developing

countries, including those in sub-Saharan Africa, as a result of lack of provider experience and/or inadequate supplies⁴⁻⁷. Compared to D&C, MVA has a superior safety and effectiveness profile and is well-suited to low resource settings since it does not require electricity and can be performed safely by trained, mid-level providers^{8,9}. Similarly, medical abortion employing a regimen of misoprostol can be offered safely at a low cost without significant health infrastructure, medical technology, or a highly trained provider; however, its major drawback is a substantial rate of failure requiring secondary procedures^{8,10,11}. While not widely available, misoprostol is currently registered in eight African countries for the prevention and treatment of postpartum hemorrhage^{11,12} and its "off-label" use for elective abortion has been increasing in this region^{6,11,13}.

Although elective abortion remains highly restricted throughout most of sub-Saharan Africa^{5,14}, modest progress has been made towards reducing legal restrictions in parts of this region. Since 1997, legal indications for abortion have been broadened in eight countries (Benin, Chad, Ethiopia, Guinea, Mali, Niger, Swaziland, and Togo) and, more recently, discussions have been initiated in Nigeria and several other nations with highly restrictive abortion laws around the need for legislative reform^{7,14}. However, despite this progress, women's access to safe abortion services remains extremely limited, even in countries with more indications for legal abortion, as a result of inadequate resources, sociocultural barriers, and lack of political will to provide such services^{7,14}.

To explore the health and economic impact of increasing access to individual modalities of safe abortion in sub-Saharan Africa, we developed a computer-based simulation model of induced abortion and its complications, and conducted a comparative analysis of unsafe abortion and three methods for safe, first-trimester abortion. This model was used previously to assess alternative strategies for elective, first-trimester abortion in Mexico City¹⁵, and here has been contextua-

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

lized to conduct country-specific analyses in Nigeria and Ghana. Although abortion laws are less restrictive in Ghana compared to Nigeria, access to safe abortion services is very limited in both countries. The results were used to quantify the expected health benefits and cost savings associated with policies that facilitate access to safe abortion in these two countries and similar countries in sub-Saharan Africa.

METHODS

ANALYTIC OVERVIEW

Incorporating the best available data, we developed a computer-based decision analytic model of induced abortion and its complications, and conducted a comparative analysis of unsafe abortion and three methods for safe, first-trimester pregnancy. Modalities for safe, elective termination included: (1) dilation and curettage (D&C), (2) manual vacuum aspiration (MVA), (3) clinic-based medical abortion using a regimen of vaginal misoprostol alone. The model was used to conduct country-specific analyses in Nigeria and Ghana. We did not evaluate strategies involving medical abortion with mifepristone since, at the time of our study, mifepristone was neither registered in Nigeria nor broadly available in Ghana^{2,6,11,12,16}. Model outcomes included intermediate outcomes such as failed initial procedure and major complications (defined as hemorrhage, infection, shock, instrumental injury), and long-term aggregate population measures such as average per-woman lifetime costs (\$US 2007) and life expectancy. Strategies were ranked by increasing cost, and incremental cost-effectiveness ratios were calculated. The incremental cost-effectiveness ratio was defined as the additional cost of a specific strategy divided by its additional clinical benefit (e.g., increased life expectancy expressed as years of life gained or saved) compared with the next least expensive strategy. Strategies that were more costly and less effective, or more costly and less cost-effective, compared to the next best strategy, were considered strongly and weakly dominated, respectively. One- and two-way sensitivity analyses were conducted to assess the effect of varying baseline estimates and assumptions on our results. Analyses were conducted from both a health payor and modified societal perspective, and followed the recommendations for economic evaluations made in several published guidelines¹⁷⁻²⁰.

MODEL

We developed a state-transition Markov model

(using TreeAge Pro, version 7.0, TreeAge Software, Inc, Williamstown, MA) that simulates induced abortion and its potential complications, including alternative modalities for elective abortion. The target population is a representative cohort of women (Nigerian or Ghanaian) seeking pregnancy termination. A woman can have a safe or unsafe abortion, following which outcomes include a successful procedure, method failure without complications, a major complication, or death. Method failure without complications is defined as the need for post-procedure surgical uterine re-evacuation as a result of incomplete abortion, prolonged bleeding, or for any other reason. We defined a major complication as shock, instrumental injury, infection (i.e., endometritis, pelvic inflammatory disease, peritonitis, and septicemia), and / or hemorrhage necessitating transfusion. Unsafe abortion can also result in the long-term complication of tubal infertility. We assume all complications incur an additional cost and require treatment at a hospital (either inpatient or outpatient) for further management. All women are subject to age- and sex-specific all-cause mortality rates.

DATA

Parameter estimates are presented in Table 1 and the Supplementary Appendix^{1,2,3,6,10,21,22,24-40}. Clinical data used in the model were from the published and grey literature as well as primary data^{1-3,5,21,24-35}. Direct medical costs associated with unsafe abortion, safe abortion modalities (i.e., clinic-based MVA, hospital-based MVA and D&C), and management of complications (failed procedure, major complications, and secondary infertility) were based on the published literature and primary data or were inferred from published sources, if necessary^{30,36-38}. When applicable, a cost-to-charge ratio of 0.6 was used to determine direct medical costs from charge data¹⁷. In addition to direct medical costs, costs related to missed wage earnings were included for analyses conducted under a modified societal perspective^{5,39,40}. A wide plausible range was established for each parameter by using the highest and lowest values reported in the literature. All costs were expressed in 2007 US dollars. Future costs were discounted at a rate of 3% annually. For further details regarding the Methods, please refer to the Supplementary Appendix.

PRIMARY AND SECONDARY ANALYSES

In the baseline analysis, we first performed a comparative analysis of the cost-effectiveness of unsafe abortion and four options for safe, early pregnancy termination. Strategies for elective abortion included (1) hospital-based D&C, (2) hospital-based MVA, (3) clinic-based MVA, and (4) clinic-based medical abor-

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

Table 1. Model Parameters: Baseline Values and Ranges Used in Sensitivity Analyses*.

Variable	Nigeria	Ghana	References
Clinical Parameters (Risk per 1,000 procedures)			
Dilatation and curettage (D&C)			
Method failure without complications†	24 (18-24)	24 (18-24)	21,24,25
Major complications‡	31 (5-61)	31 (5-61)	25,26
Deaths	0.018 (0.001-0.06)	0.018 (0.001-0.06)	1,22,27
Manual vacuum aspiration (MVA)			
Method failure without complications†	22 (11-38)	22 (11-38)	21,24,28,29
Major complications‡	23 (4-49)	23 (4-49)	25,26
Deaths	0.013 (0.001-0.06)	0.013 (0.001-0.06)	1,22,27
Misoprostol per vaginal route, 800 mcg x up to 2 doses			
Method failure without complications†	200 (70-350)	200 (70-350)	10,30
Major complications‡	7.5 (4.5-41)	7.5 (4.5-41)	10,31
Deaths	0.024 (0.002-0.024)	0.024 (0.002-0.024)	32
Unsafe Abortion			
Method failure without complications†	75 (75-225)	88 (34-225)	2,3,5,33
Major complications‡	146 (146-438)	132 (132-438)	2,3,5,33
Secondary infertility	120 (30-120)	120 (30-120)	34
Deaths	8.2 (7.5-8.8)	12.3 (10-50)	1,35
Direct Medical Costs (2007 US\$)			
D&C (hospital-based)	29.69 (29.69-120.10)	18.75 (12.50-20.83)	5,37
MVA (hospital-based)	33.11 (33.11-120.10)	14.58 (12.50-20.83)	5,37
MVA (clinic-based)	13.36 (6.83-19.59)	12.50 (6.25-12.50)	5,37-39
Misoprostol per vaginal route, 800 mcg x up to 2 doses	16.40 (6.60-66.35)	4.17 (3.33-8.33)	5,30,37,38,**
Unsafe Abortion	19.14 (2.78-27.81)	16.67 (12.50-20.83)	5,**
Treatment of complications			
Method failure without complications†	34.64 (6.83-120.10)	20.83 (16.67-124.99)	5,**
Major complications‡	105.41 (48.04-155.65)	166.66 (83.33-499.97)	5,**
Secondary infertility§	104.16 (83.33-239.57)	104.16 (83.33-239.57)	**
Personal Costs (2007 US\$) 			
Dilatation and curettage ††	3.43 (0.5x-2.0x)	1.32 (0.5x-2.0x)	5,39,40

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

Table 1. Model Parameters: Baseline Values and Ranges Used in Sensitivity Analyses.* (Continued)

Manual vacuum aspiration ††	3.43 (0.5x-2.0x)	1.32 (0.5x-2.0x)	5,39,40
Misoprostol per vaginal route, 800 mcg x up to 2 doses ‡‡	10.29 (0.5x-2.0x)	3.96 (0.5x-2.0x)	5,39,40
Unsafe abortion ††	3.43 (0.5x-2.0x)	1.32 (0.5x-2.0x)	5,39,40
Treatment of complications			
Method failure without complications **	3.43 (0.5x-2.0x)	1.32 (0.5x-2.0x)	5,39,40
Major complications‡‡	10.29 (0.5x-2.0x)	3.96 (0.5x-2.0x)	5,39,40
Infertility §§	13.72 (0.5x-2.0x)	5.28 (0.5x-2.0x)	39,40

* D&C = Dilatation and curettage; MVA=manual vacuum aspiration.

† Defined as incomplete abortion, prolonged bleeding, or excessive patient discomfort that requires surgical re-evacuation of the uterus.

‡ Defined as instrumental injury (i.e., laceration of cervix, perforation of uterus), hemorrhage requiring hospitalization, pelvic infection, sepsis, fever requiring hospitalization, or shock.

§ Assumed 25% of women with infertility seek work-up.

|| Determined by multiplying the average minimum daily wage by the number of days spent away from work.

** Ghanaian estimate based on primary data from Korle Bu Teaching Hospital.

†† Assumed 1 day of missed wage earnings.

‡‡ Assumed 3 days of missed wage earnings.

§§ Assumed 4 days of missed wage earnings.

tion using a regimen of vaginal misoprostol alone. The baseline analysis assumed that each modality for safe abortion was equally available and acceptable to women, and could be implemented to the full coverage of those desiring elective abortion. Although we recognize inequalities in access and preference to each modality exist in Nigeria and Ghana, the purpose of the baseline analysis was to examine the relative cost-effectiveness of individual options for safe abortion in order to help define priority interventions for elective abortion programs in each country. The baseline analysis was conducted under a modified societal perspective which considers the procedural cost of safe and unsafe abortion, cost of abortion-related complications, and costs associa-

ted with missed wage earnings.

In a secondary analysis, we sought to simulate a more realistic set of scenarios where the health and economic outcomes were compared for strategies comprised of mixed abortion modalities (including unsafe abortion) in order to reflect their differential accessibility, preference, and uptake.

FINDINGS

CLINICAL AND ECONOMIC OUTCOMES

For both Nigeria and Ghana, model-projected estimates for modality - specific complications were highest for unsafe

abortion and substantially lower for all safe abortion strategies. (Figure 1, Upper Panels A and B) Per 100,000 procedures, medical abortion with misoprostol resulted in the fewest major complications but had the most uncomplicated method failures. Overall, MVA was associated with the lowest complication rate.

Model-projected direct medical costs associated with each of the strategies are shown in Figure 1, Lower Panels A and B. For all surgical modalities, the majority of costs were attributable to the original procedure itself (range, 74-91%).

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

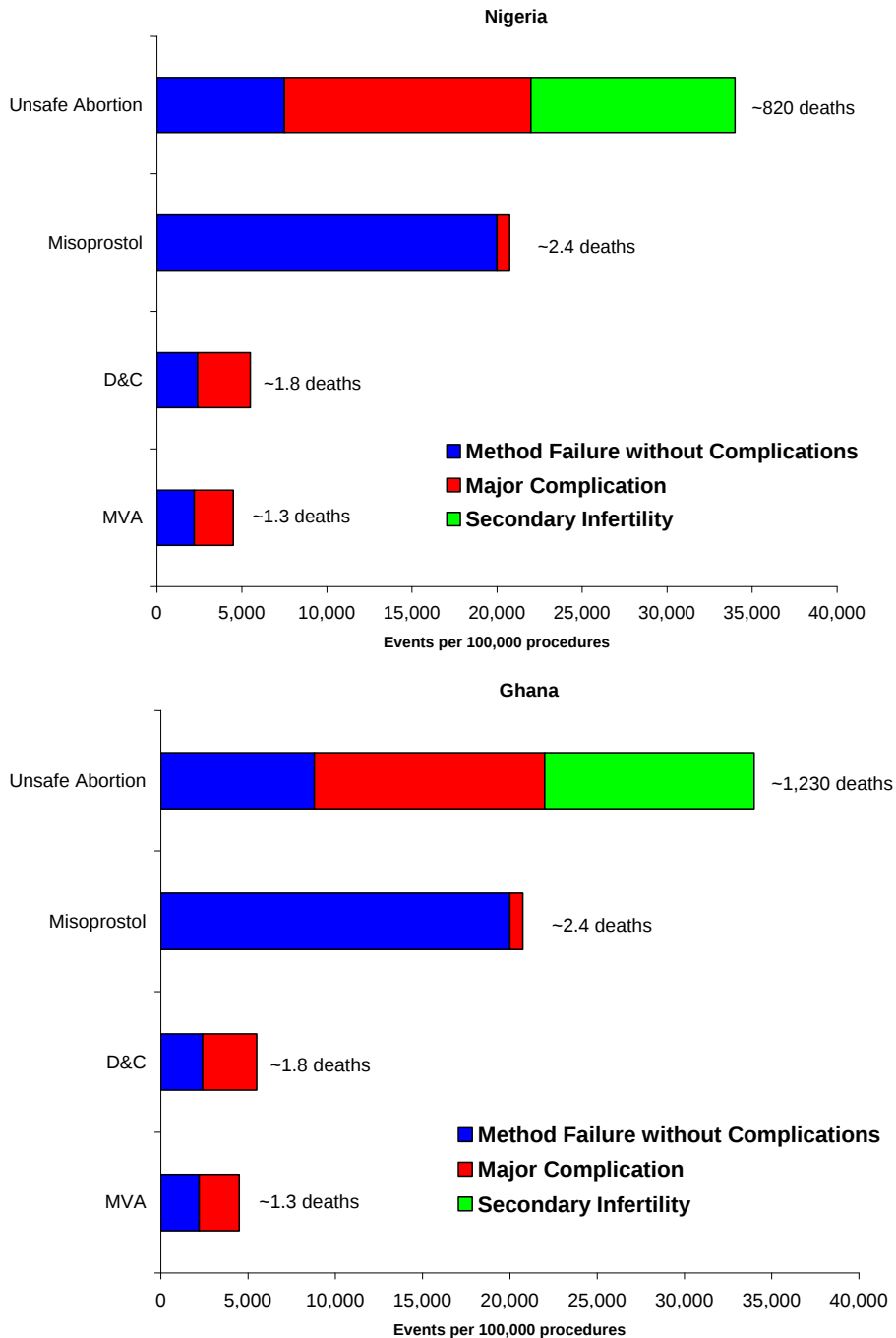


Figure 1a (Upper Panel A and B). Model-projected distribution of complications attributable to abortion. Model generated estimates for complications associated with the three abortion modalities all provided substantial benefits over unsafe abortion. Excluding method failure without complications, both MVA and medical abortion using a regimen of vaginal misoprostol resulted in the fewest serious complications.

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

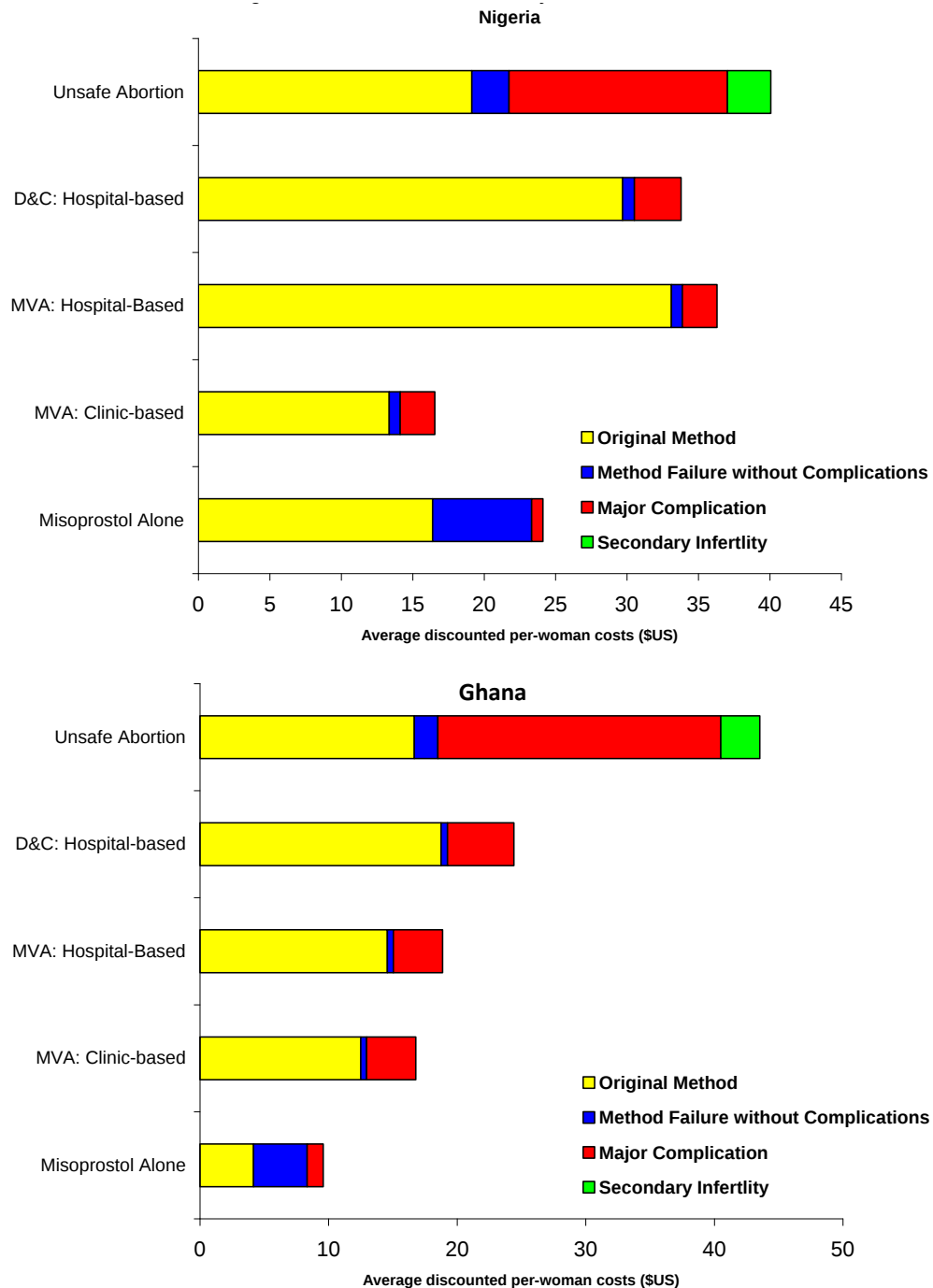


Figure 1b (Lower Panel A and B). Model-projected distribution of costs. For all safe surgical abortion modalities, the majority of costs were attributable to the procedure itself. In contrast, the procedural cost of unsafe abortion accounted for a significantly smaller proportion of the total costs, with nearly two-thirds attributable to the treatment of complications.

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

Costs related to complications ranged from 9% to 26% of total costs for surgical strategies and were substantially higher for medical abortion with misoprostol (31-57% of total costs), largely due to method failure without complications. In contrast to safe abortion, the procedural cost of unsafe abortion accounted for a significantly smaller proportion of the total costs, with more than 50% attributable to the treatment of complications.

COST EFFECTIVENESS

The average per-woman discounted lifetime costs, discounted years of life gained per 1,000 women, and incremental cost-effectiveness ratios associated with our comparative (baseline) analysis of unsafe abortion and alternative safe abortion modalities for Nigeria and Ghana are shown in Table 2. Under a modified societal perspective, all safe abortion modalities were preferable to unsafe abortion, and were associated with substantial life expectancy gains and cost-savings relative to unsafe abortion. In Nigeria, clinic-based MVA was the least costly and most effective option, and therefore dominated the competing strategies. While equally as effective as clinic-based MVA, hospital-based MVA was the most expensive strategy. D&C and medical abortion using vaginal misoprostol provided comparable benefits although the latter was less costly. In contrast, in the Ghana analysis, medical abortion was the most cost-effective option owing to its low procedural cost (In Ghana, the baseline cost of medical abortion was approximately one-third the cost of clinic-based MVA). Clinic-based MVA was more effective than medical abortion but was associated with a cost of \$16 855 per life-year gained. Hospital-based MVA and D&C were more expensive and no more effective than clinic-based MVA, and were therefore strongly dominated.

In addition to conducting the baseline analysis under a modified societal perspective, further analyses were performed using two alternative perspectives, including a health payor and limited health payor perspec-

tive. Under a health payor perspective, which considers the cost to health systems of providing safe abortion (but not unsafe abortion) and care for all abortion-related complications, all safe abortion modalities were less costly and more effective than unsafe abortion in Ghana. In contrast, in the Nigerian analysis, while all safe abortion modalities were more effective than unsafe abortion, only clinic-based MVA was less costly than unsafe abortion under the health payor perspective. This difference in results is primarily due to country-specific variations in the baseline cost of providing alternative safe abortion modalities, particularly in relation to each other and to unsafe abortion.

When the analysis was conducted from a limited health payor perspective, which considers the direct medical costs of only abortion-related complications (not the original procedure), MVA (either clinic- or hospital-based) was the least costly and most effective strategy in both countries. All safe abortion modalities were associated with substantially lower costs compared to unsafe abortion (Table 2).

Among the safe abortion modalities, strategies were similar in terms of life expectancy but had substantial differences with regard to their comparative economic costs. Figure 2 (Nigeria and Ghana respectively) presents the societal cost savings associated with two strategies, clinic-based MVA and medical abortion with vaginal misoprostol, relative to a baseline strategy of unsafe abortion (blue columns, Figure 2), and relative to the current, most prevalent practice in sub-Saharan Africa, D&C (green columns, Figure 2). In Nigeria, provision of medical abortion with misoprostol in the place of unsafe abortion would save over \$1,000,000 per 100,000 procedures (Figure 2). The provision of clinic-based MVA over unsafe abortion would save even more (over \$2,500,000 per 100,000 procedures). Similarly, in Ghana, a transition from unsafe abortion to clinic-based MVA or medical abortion with misoprostol would be associated with a cost-savings exceeding \$2,700,000 and \$3,150,000

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

Table 2. Health and economic outcomes of three modalities in Nigeria and Ghana to terminate first-trimester pregnancy^a

Strategy	Lifetime costs ^c , 2007 US\$ <i>Modified Societal Perspective</i>	Lifetime costs ^c , 2007 US\$ <i>Health Payor Perspective</i>	Lifetime costs ^c , 2007 US\$ <i>Limited Payor Perspective</i>	Years of life gained per 1,000 ^d	ICER, \$ per YLS <i>Modified Societal Perspective</i>	ICER, \$ per YLS <i>Health Payor Perspective</i>
Nigeria						
Unsafe abortion	45.64	20.92	20.92	-	-	-
MVA: Clinic-based	20.29	16.55	3.19	183.1	e	e
Misoprostol per vaginal route ^b	35.17	24.12	7.72	182.9	dominated ^g	dominated ^g
D&C: Hospital-based	37.62	33.79	4.10	183.0	dominated ^g	dominated ^g
MVA: Hospital-based	40.04	36.30	3.19	183.1	dominated ^g	dominated ^g
Ghana						
Unsafe abortion	45.65	26.87	26.87	-----	---	---
Misoprostol per vaginal route ^b	13.84	9.59	5.42	290.8	f	f
MVA: Clinic-based	18.23	16.79	4.29	291.0	16,855	27,654
MVA: Hospital-based	20.31	18.87	4.29	291.0	dominated ^g	dominated ^g
D&C: Hospital-based	25.89	24.42	5.67	290.9	dominated ^g	dominated ^g

a y= years; YLS= years of life saved; ICER = incremental cost-effectiveness ratio; MVA= manual vacuum aspiration.

b Misoprostol per vaginal route assumes 800 mcg, up to 2 doses.

c Average per-woman discounted (3%) lifetime costs (2007 US\$); limited payor perspective includes cost of complications only; health payor perspective includes cost of safe abortion modalities and complications; a modified societal perspective includes patient time costs and cost of abortion modalities (safe and unsafe) and complications.

d Average discounted (3%) years of life gained per 1000 women, relative to unsafe abortion.

e Clinic-based MVA is more effective and less costly than all other strategies.

f Medical abortion using misoprostol is the most cost-effective strategy.

g This strategy is more expensive and less effective than MVA and is therefore strongly dominated.

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

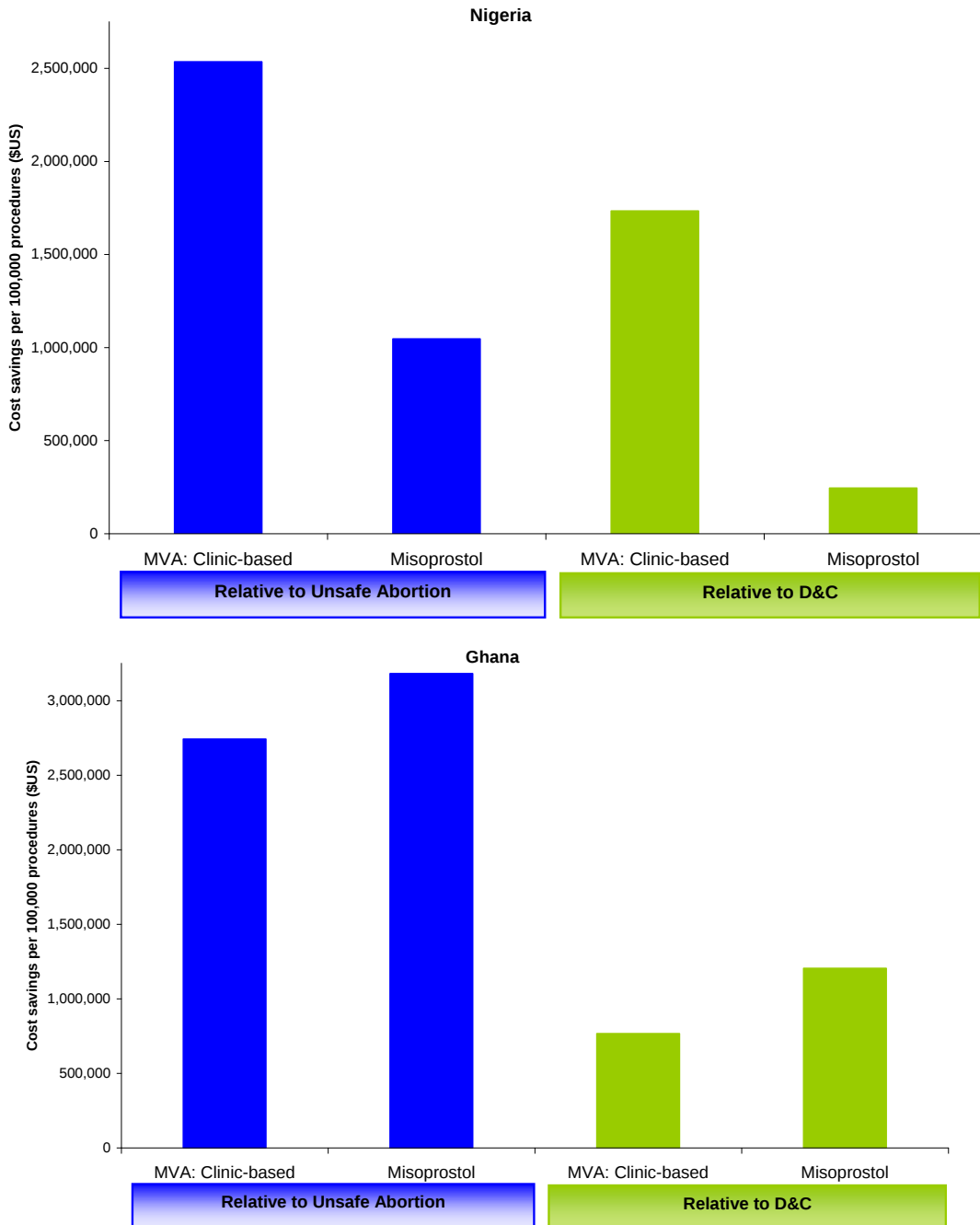


Figure 2. Cost savings of clinic-based MVA and medical abortion using misoprostol relative to unsafe abortion and safe abortion with D&C (Modified Societal Perspective). Relative to a baseline strategy of unsafe abortion, a strategy of 100% clinic-based MVA or 100% medical abortion with vaginal misoprostol alone would save between \$1 and \$3 million in Nigeria and Ghana. Relative to most commonly practiced first-trimester abortion method of D&C, shifting to clinic-based MVA would save \$0.75 and \$1.75 million per 100,000 procedures in Ghana and Nigeria, respectively.

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

per 100,000 procedures, respectively (Figure 2). In addition, in both countries, substantial cost-savings ranging from \$200,000 to \$1,700,000 per 100,000 procedures could be realized with a change in clinical practice from D&C to clinic-based MVA or medical abortion with misoprostol.

SENSITIVITY ANALYSES

In one-way sensitivity analyses, the primary results of the Nigerian analysis were robust to changes in the plausible range of values of all parameters with clinic-based MVA remaining the most effective and least costly option. However, the rank order of medical abortion with misoprostol relative to the remaining strategies was sensitive to changes in the complication rate (i.e., uncomplicated method failure or major complications) associated with medical abortion using misoprostol, the cost of managing an uncomplicated method failure, and the cost of providing medical abortion.

In the Ghana analysis, the relative cost-effectiveness of clinic-based MVA compared to medical abortion using misoprostol (e.g., rank order or magnitude of incremental cost-effectiveness ratio) was sensitive to changes in complication rate (i.e., mortality, major complications, or uncomplicated method failure) associated with either modality, the cost of treating an uncomplicated procedural failure, and the cost of providing clinic-based MVA or medical abortion. Beyond the threshold values of 3.3% (basecase, 0.75%) for medical abortion-associated major complication rate, \$8.11 (basecase, \$12.50) for clinic-based MVA, and \$45.50 (basecase, \$20.83) for treatment of uncomplicated method failure, clinic-based MVA became equally, or more cost-effective, than medical abortion using misoprostol.

ALTERNATIVE ASSUMPTIONS ABOUT THE TOTAL ABORTION RATE

Data from national surveys indicate an increasing desire among African women, including those living in Nigeria and Ghana, to

delay their first birth and/or limit family size⁴⁴⁻⁴⁶. Unless the uptake of family planning can keep pace with these demands, it is likely the incidence of unsafe abortion and the total abortion rate (defined as the average number of abortions a woman can be expected to have over a lifetime) will increase over the coming years⁵.

The total abortion rate is currently unknown for Nigeria, Ghana, or sub-Saharan Africa. In the baseline analysis, we conservatively assumed a total abortion rate of 1.0 abortion per life-time. In a secondary sensitivity analysis, we explored the health and economic implications of total abortion rates that were greater than 1. Figure 3 presents the years of life gained per 100,000 procedures and cost savings per 100,000 procedures, compared to unsafe abortion, for several alternative assumptions where the total abortion rate ranges from 1.0 to 2.0. For the strategies of clinic-based MVA and medical abortion with misoprostol, the years of life gained and cost savings increased in proportion to the rise in total abortion rate. However, the total abortion rate did not influence the relative cost-effectiveness of alternative safe abortion modalities (data not shown). In Nigeria, clinic-based MVA remained the most effective and least costly option over the plausible range of values for this variable, whereas, in Ghana, medical abortion using misoprostol remained the least costly and most cost-effective strategy.

REAL WORLD IMPLICATIONS

In contrast to the baseline analysis which assumed each modality of safe abortion was equally available, in reality, access to the individual safe abortion modalities is highly variable and contingent on a number of factors including cost, convenience, acceptability and availability⁴⁷. For example, in Nigeria, only 60% of all elective abortions are estimated to occur in public or private health facilities, mostly with D&C⁶. To reflect this situation, a more realistic set of scenarios were simulated for both countries in which combi-

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

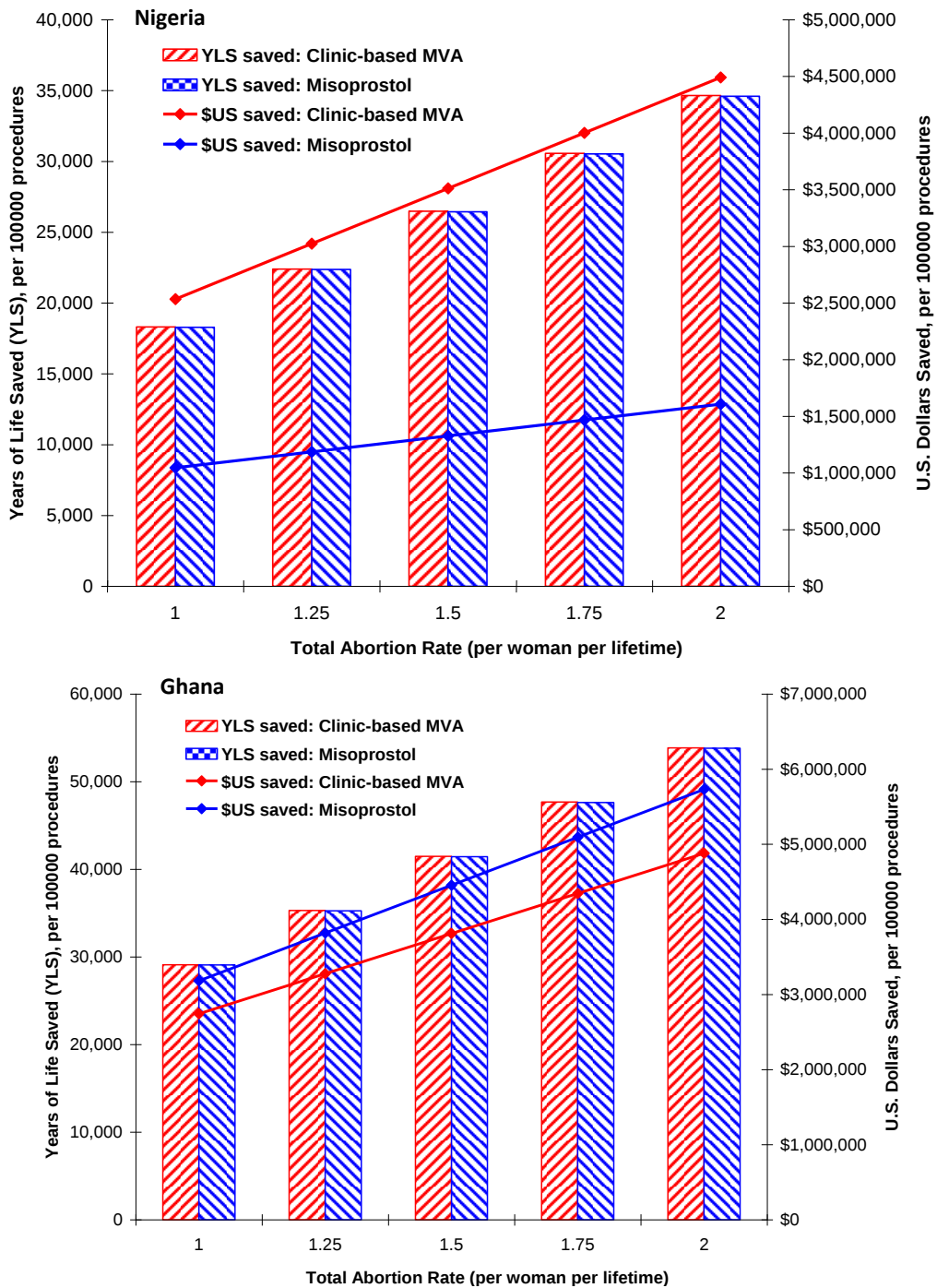


Figure 3. Alternative assumptions for the average number of abortions per lifetime: health and economic outcomes. As the total abortion rate rises, the years of life gained (red and blue columns) and cost savings (red and blue lines) increase proportionally for the strategies clinic-based MVA (red) and medical abortion with misoprostol (blue) (Modified Societal Perspective).

nations of abortion modalities were used, reflecting their differential accessibility, preference, and uptake. (Figure 4)

Figure 4 presents the years of life gained per 100,000 procedures and cost savings per 100,000 procedures for several scenarios, in comparison with unsafe abortion, and illustrates several important points. First, transitioning from unsafe to safe abortion, regardless of modality, is the most influential factor on saving both lives and societal costs. For example, provision of safe abortion for 60% of women that would otherwise get an unsafe abortion has a large impact on years of life saved (~11,000 years life saved per 100,000 procedures in Nigeria and ~ 17,500 years life saved per 100,000 procedures in Ghana). Furthermore, if access to medical abortion provides a feasible and acceptable option, such that all women are assured access to safe abortion, years of life gained per 100,000 procedures are more than 18,300 and 29,000 in Nigeria and Ghana, respectively, compared with unsafe abortion. In contrast, a transition in practice pattern from one where 50% of women that would otherwise receive D&C to clinic-based MVA, without changing the percentage that pursue unsafe abortion, provides very small incremental health benefits (~3 years life saved per 100,000 procedures) although does save substantial costs.

DISCUSSION

Our results underscore the importance of enhancing access to safe abortion in Nigeria, Ghana, and similar countries in sub-Saharan Africa, and illustrate three fundamental principles for safe abortion policy and service planning. First and foremost, irrespective of modality, the provision of safe abortion in place of unsafe abortion is the single most important factor in improving health and economic outcomes associated with elective pregnancy termination. Second, clinic-based MVA is the most cost-effective surgical option for safe, first-trimester abortion and,

wherever possible, transitioning from D&C to clinic-based MVA will result in lower costs, and reduce complications and deaths. Third, medical abortion should be promoted as a nonsurgical option for elective abortion. In contexts where women face barriers to accessing surgical abortion facilities and would otherwise pursue unsafe abortion, the option of medical abortion will save lives and reduce both societal and health care costs.

Our findings generally agree with the current WHO guidelines which recommend vacuum aspiration and medical abortion as the preferred methods for safe, first-trimester abortion⁴. In both countries, clinic-based MVA and medical abortion were the two most cost-effective methods for early elective pregnancy termination over a wide range of plausible assumptions. However, the relative rank order of these two strategies differed for Nigeria and Ghana, owing to country-specific and sector-specific variations in the baseline cost of service provision (Baseline cost estimates for safe abortion provision were from the public sector in the Ghanaian analysis whereas Nigerian cost estimates reflect the mean of a mix of facilities from the private and public domain). In Nigeria, clinic-based MVA was the most effective and least costly method, given it is available, accessible and acceptable to women seeking first-trimester elective abortion. If clinic-based MVA is not accessible, we found medical abortion using the vaginal misoprostol regimen to be the next best strategy. Conversely, in Ghana, medical abortion with misoprostol was found to be the most cost-effective method, with clinic-based MVA as the next best alternative, if medical abortion is not accessible. It should be noted that the WHO does not specifically recommend misoprostol-only regimens for first-trimester abortion⁴; nevertheless, several randomized, controlled studies conducted in developing countries have demonstrated this drug's safety, efficacy, and acceptability in early pregnancy termination^{48,49}.

In terms of cost-effectiveness, the WHO recommends a value of three-times the national gross domestic product per capita or

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

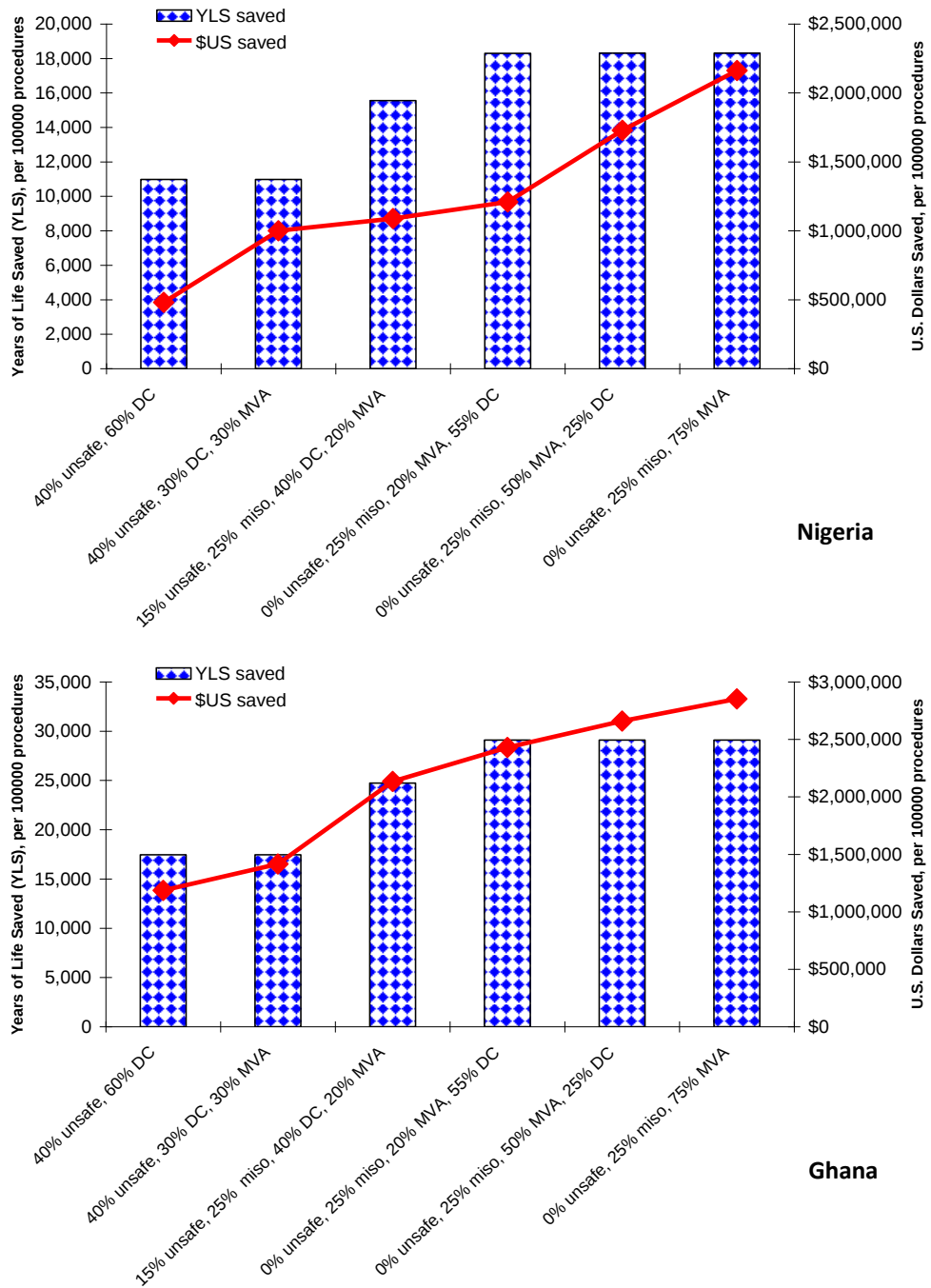


Figure 4. Alternative mixed strategies for first-trimester abortion: health and economic outcomes. The years of life gained (blue striped columns) and cost savings (red line) improve as access to safe abortion increases and unsafe abortion is minimized (going from left to right columns). Regardless of modality mix, the years of life and costs saved from reducing unsafe abortion far outweigh all differences between strategies. Cost savings increase as the modality mix transitions towards enhanced access to clinic-based MVA.

less as a measure by which to judge the cost-effectiveness of health interventions²⁰. Given that all safe abortion modalities were associated with substantial cost-savings relative to a baseline strategy of unsafe abortion under the modified societal perspective, provision of safe abortion services may well be considered among the most cost-effective health interventions in Nigeria, Ghana, or any other country where unsafe abortion is prevalent. Our previous comparative analysis of first-trimester abortion modalities in Mexico City reached the same conclusion¹⁵. The Mexico City study also found the cost-savings associated with shifting from unsafe to safe abortion to be roughly 10x higher in Mexico compared to Nigeria or Ghana¹⁵. However, this reduced cost-savings in Nigeria and Ghana compared to Mexico is not entirely surprising for several reasons. First, the national gross domestic product per capita is 7.4x and 10x higher in Mexico than in Nigeria and Ghana, respectively⁵⁰. Second, the cost of treating major complications is roughly 7-12x higher in Mexico compared to Nigeria and Ghana whereas the cost of surgical safe abortion modalities is only 4-6x higher in Mexico. This cost differential is a principle factor in the higher cost-savings with shifting from safe abortion to unsafe abortion in Mexico compared to Nigeria and Ghana. Reasons for the much lower cost of treating major abortion-related complications in Nigeria and Ghana may include lower personnel costs or reduced use of technology. Third, the majority of women in Nigeria (and likely Ghana) who experience complications secondary to induced abortion do not seek medical care⁵¹. According to the Guttmacher Institute, experts believe approximately 60% of women with severe abortion-related complications do not receive treatment⁵¹. Subsequently, since these complications go untreated, they do not contribute to the overall lifetime cost of unsafe abortion. Finally, induced abortion (both safe and unsafe) may be safer in Nigeria (and likely Ghana) now compared to the past. This is suggested by the substantial reduction in the estimated proportion

of women with hospital-requiring complications secondary to induced abortion⁵.

Overall, our results were most influenced by variables related to the cost and performance of medical abortion using misoprostol (e.g., procedural cost, cost of treating an uncomplicated method failure, major complication rate, and uncomplicated method failure rate). Changes in these variables led to alterations in the rank order of alternative strategies, particularly in the comparative cost-effectiveness of clinic-based MVA and medical abortion using misoprostol. Misoprostol is generally more expensive in Africa than in Western Europe and many parts of Asia, and the price of misoprostol may be rising in this region as providers and drug outlets in the private sector react to the increase in demand for this drug¹¹. For example, in Kampala, Uganda, misoprostol is available in pharmacies for \$1.50 per tablet (200 mcg)⁵², whereas in the U.S. the cost of misoprostol is less than \$1 per 200 mcg tablet⁵³. Our review of the evidence suggests that the drug is three to four times more expensive in Nigeria compared to Ghana. If misoprostol becomes more widely accepted and utilized for medical abortion and other indications in sub-Saharan Africa, the large scale purchase of this drug may result in substantial price reductions, especially if competition develops among different manufacturers of the medicine. In addition to improving access to low-cost misoprostol, it is critical that mifepristone also be registered in more African countries so that women can have access to the most effective medical abortion regimen.

Indirect evidence from national surveys suggests the number of unsafe abortions in Nigeria and Ghana may be increasing^{5,45,46}. Researchers hypothesize this is due in part to a growing desire among African women to prevent premarital births and limit family size, and further suggest this trend may persist, or even accelerate, with the continuing economic growth and urbanization of this region⁴⁴. Given that up to 30% and 40% of all maternal deaths are attributable to unsafe abortion in Ghana and Nigeria, respectively, it is unli-

kely Millennium Development Goal 5 of reducing the maternal mortality ratio by three - quarters will be achieved without confronting the issue of unsafe abortion^{5,11}.

There are several approaches to reducing the impact of unsafe abortion, including increased uptake of modern contraception, legalization of elective abortion, provision of safe abortion services, improvement of provider skills, and provision of quality postabortion care⁸.

Use of safe, effective contraception reduces the need for unsafe abortion by preventing unintended and unwanted pregnancies, the root cause of unsafe abortion. In countries where national contraceptive programs have been implemented, abortion rates have fallen with the increased use of modern contraception⁸. This approach is particularly relevant to Nigeria and Ghana where extremely low contraceptive uptake and high unmet need for contraception intersect to create high levels of unwanted pregnancy and unsafe abortion. However, while increased use of family planning services can substantially reduce the incidence of unintended pregnancies, it cannot entirely eliminate the need for abortion⁸. Even the most effective contraceptive methods can fail and result in unwanted pregnancy. Moreover, in Africa, women face substantial sociocultural barriers (e.g., lack of knowledge, fear of contraception, objections from partner or family members) to accessing effective contraception and it will take time to change societal attitudes about family planning^{6,11}. Therefore, there will continue to be a requirement for safe abortion services in Nigeria, Ghana and similar parts of sub-Saharan Africa.

Similarly, liberalization of abortion laws has been associated with reductions in abortion and hospitalization rates in several developing countries⁸. Albeit necessary, this approach alone is insufficient without ensuring safe abortion services are available, accessible, and acceptable to women⁸. This has been demonstrated in Ghana where elective abortion has been legal for over thirty years but access to safe abortion is impeded due

to a combination of factors, including lack of awareness of the legality of abortion (by providers and patients), stigma, inadequate supplies, shortages of competent providers, and economic barriers^{7,8}.

In addition to cost-effectiveness, MVA and medical abortion with misoprostol have additional features which are particularly well - suited to resource-poor settings and could facilitate access to safe abortion in low and middle income countries. For example, in contrast to D&C, MVA has low health system requirements, and can be performed in a variety of clinical settings (e.g., health center, private clinic, hospital outpatient or inpatient clinic) and by different types of health providers (e.g., physician, midwife, nurse practitioner)⁸. In fact, a recent randomized equivalence trial in South Africa and Vietnam demonstrated that MVA performed by mid-level providers are as safe and efficacious as those conducted by physicians⁹. A transition in current practice from D&C to MVA and improvement of provider skills could conceivably increase the availability of safe abortion services and simultaneously improve health and outcomes in Nigeria and Ghana. Moreover, the WHO Technical Working Group identifies MVA as an essential service at the first-referral level⁵⁴. This procedure is highly versatile and can be used for a number of clinical indications including first- and second-trimester abortion, menstrual regulation, treatment of incomplete abortion, and endometrial biopsy.

Provision of medical abortion using misoprostol could further enhance access to safe abortion by offering a more private, nonsurgical option for women seeking to terminate pregnancy. Additionally, this drug is easy to store (does not require refrigeration), potentially inexpensive, and holds promise for self-administration at home^{8,55}. In countries where access to surgical abortion services is limited or sociocultural barriers prevent women from openly seeking abortion services, the availability of medical abortion could make the difference between obtaining a safe and unsafe abortion⁴⁷. Model-based stu-

dies suggest a 33% reduction in unsafe abortion-related maternal deaths can be expected in Africa from a 40% shift to misoprostol-induced abortion from unsafe abortion⁴⁷.

Our study has several limitations which merit discussion. First, due to the largely illegal status of abortion in Nigeria, Ghana, and sub-Saharan Africa, reliable clinical data relating to elective abortion (safe and unsafe) are extremely limited. Instead, we relied on: (1) estimates from large, prospective studies, or national or regional databases which tend to reflect outcomes from a range of clinical settings; and (2) surgical abortion data from U.S. the 1970's (a period shortly after abortion laws were relaxed throughout the U.S.) which more closely reflects safety and efficacy profile of surgical abortion in current public health facilities in Nigeria and Ghana. We also applied wide plausible ranges for our estimates in sensitivity analyses. Second, Nigeria-, Ghana- and region-specific data for the cost of safe and unsafe abortion procedures and their complications are scarce. For the baseline cost of unsafe abortion, hospital-based surgical modalities (i.e., D&C, MVA), and complications, we capitalized on the availability of cost estimates from a 2002-2003 survey of 33 hospitals from the private and public sector across eight states in Nigeria⁵. The baseline cost of medical abortion with misoprostol and clinic-based MVA was inferred from published studies^{30,38}. For Ghana, the baseline cost of safe abortion modalities were from Korle Bu Teaching Hospital, a public sector facility, and these estimates are much lower than what would be found in the private sector. Furthermore, many of these cost estimates were user fees and required conversion using a cost-to-charge ratio. While there may be considerable variation in these costs within Nigeria and Ghana and particularly between urban and rural settings as well as between private and public sectors, our cost estimates are consistent with the general trend reported in other developing countries for the various abortion modalities^{7,56,57}. In addition, we used wide plausible ranges for our estimates in sensi-

tivity analyses and found our primary results to be robust. Third, we did not consider less serious types of abortion-related morbidity which might have been treated in a non-hospital clinical setting. Inclusion of these risks might improve the economic attractiveness of medical abortion, although their overall impact on our results is unclear since many women with postabortion complications do not seek care⁵. Fourth, we did not consider the broader societal costs associated with a maternal death, albeit their inclusion would only make our findings stronger. A maternal death has an irrefutable impact on the health and economic well-being of her children and household. However, monetary estimates of this impact are currently unavailable and should be a priority for future research. Finally, we did not evaluate alternative medical abortion regimens comprised of a combination of misoprostol and mifepristone, which is more effective but also more costly than misoprostol alone¹. Currently, mifepristone is unavailable in Nigeria and the cost associated with its use in the country is unknown¹⁶.

This analysis demonstrates the provision of safe abortion in Nigeria, Ghana and other similar countries will reduce complications, decrease mortality, and save money compared to unsafe abortion. The most effective and cost-effective surgical modality for safe, first trimester abortion is clinic-based manual vacuum aspiration. Offering medical abortion to women as an alternative to surgical abortion, especially for those who would otherwise choose an unsafe abortion because surgical abortion is either not accessible or not acceptable to them, will provide additional health and economic gains. In Nigeria and Ghana, a four-pronged approach that includes reducing legal restrictions on abortion to the fullest extent possible, shifting from a practice of D&C to MVA, increasing the availability of MVA in a broad range of non-hospital clinical settings, and enhancing access to medical abortion, will have the best chance to minimize abortion-related morbidity and mortality, and will be cost-saving to health systems and to society.

ACKNOWLEDGEMENTS

We gratefully acknowledge the generous support from the John D. and Catherine T. MacArthur Foundation, grant #07-89007-00GSS.

REFERENCES

1. World Health Organization (WHO). Unsafe abortion: global and regional estimates of incidence of unsafe abortion and associated mortality in 2003. Geneva: WHO, 2007.
2. Singh S. Hospital admissions resulting from unsafe abortion: estimates from 13 developing countries. *Lancet* 2006; 368(9550):1887-92.
3. Sedgh G, Henshaw S, Singh S, Ahman E, Shah IH. Induced abortion: estimated rates and trends worldwide. *Lancet* 2007; 370(9595):1338-45.
4. World Health Organization (WHO). *Safe abortion: technical and policy guidance for health systems*. Geneva: WHO, 2003.
5. Henshaw SK, Adewole I, Singh S, Bankole A, Oye-Adeniran B, Hussain R. Severity and cost of unsafe abortion complications treated in Nigerian hospitals. *Intl. Fam. Plann. Perspect* 2008; 34 (1):40-50.
6. Bankole A, Oye-Adeniran BA, Singh S, Adewole IF, Wulf D, Sedgh G, Hussain R. Unwanted Pregnancies and Abortion in Nigeria: Causes and Consequences. New York: AGI, 2006. <http://www.guttmacher.org/pubs/2006/08/08/Nigeria-UP-IA.pdf> Accessed on 08 September, 2008.
7. Singh S, Wulf D, Husaain R, Bankole A, Sedgh G. *Abortion Worldwide: A Decade of Uneven Progress*. New York: AGI, 2009.
8. Grimes DA, Benson J, Singh S, Romero M, Ganatra B, Okonofua FE, Shah IH. Unsafe abortion: the preventable pandemic. *Lancet* 2006; 368 (9550): 1908-19.
9. Warriner IK, Meirik O, Hoffman M, Morroni C, Harries J, My Huong NT, Vy ND, Seuc AH. Rates of complication in first-trimester manual vacuum aspiration abortion done by doctors and mid-level providers in South Africa and Vietnam: a randomised controlled equivalence trial. *Lancet* 2006; 368(9550):1965-72.
10. Faúndes A, Fiala C, Tang OS, Velasco A. Misoprostol for the termination of pregnancy up to 12 completed weeks of pregnancy. *Intl. J. Gynaecol. Obstet.* 2007; 99(Supplement 2):S172-7.
11. Ipas. *Misoprostol and medical abortion in Africa*. Chapel Hill: Ipas, 2009. http://www.ipas.org/Publications/asset_upload_file683_4512.pdf
12. Fernandez MM, Coeytaux F, de León RG, Harrison DL. Assessing the global availability of misoprostol. *Int J Gynaecol Obstet.* 2009;105(2):180-6.
13. Bankole A, Sedgh G, Oye-Adeniran BA, Adewole IF, Hussain R, Singh S. Abortion-seeking behaviour among Nigerian women. *J Biosoc Sci* 2008; 40(2):247-68.
14. Hessini L, Brookman-Amisshah E, Crane BB. Global policy change and women's access to safe abortion: the impact of the World Health Organization's guidance in Africa. *Afr. J. Reprod. Health* 2006; 10(3): 14-27.
15. Hu D, Grossman D, Levin C, Blanchard K, Goldie SJ. Cost-effectiveness analysis of alternative first-trimester pregnancy termination strategies in Mexico City. *BJOG* 2009; 116(6):768-79.
16. Ipas. *Medical abortion- Implications for Africa*. Chapel Hill: Ipas, 2003. http://www.ipas.org/Publications/asset_upload_file562_2534.pdf Accessed on 08 September 2008.
17. Gold MR, Siegel JE, Russell LB, Weinstein MC (Eds). *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press, 1996.
18. Cost-effectiveness analysis. In: Jamison DT, Breman JG, Measham AR (Eds). *Priorities in Health*. Washington, DC: The World Bank, 2006. pp. 39-59.
19. Drummond M, McGuire A (Eds). *Methods for the Economic Evaluation of Health Care Programmes*. New York: Oxford University Press, 2005.
20. Baltussen R, Adams T, Tan Torres T, Hutubessy R (Eds). *Making Choices in Health: WHO Guide to Cost-Effectiveness Analysis*. Geneva: WHO, 2003.
21. Tietze C, Levit S. Legal abortions: early medical complications. An interim report of the Joint Program for the Study of Abortion. *Fam Plann Perspect* 1971; 3(4):6-14.
22. Institute of Medicine. *Legalized abortion and the public health; report of a study by a committee of the Institute of Medicine*. Washington, D.C.: Natl. Acad. Sci, 1975.
23. Henshaw S. Induced abortion: a world review, 1990. *Int J. Fam. Plann. Perspect.* 1990; 16(2):59-65.
24. Edelman DA, Brenner WE, Berger GS. The effectiveness and complications of abortion by dilatation and vacuum aspiration versus dilatation and rigid metal curettage. *Am. J. Obstet. Gynecol.* 1974; 119(4):473-80.
25. Tietze C. *Induced Abortion: 1979*. New York: Population Council, c1979.
26. Tietze C, Lewit S. Joint Program for the Study of Abortion (JPSA): Early Medical Complications of Legal Abortion. *Stud. Fam. Plann.* 1972; 3(6):97-265.
27. Koonin LM, Smith JC, Ramick M. Abortion surveillance-United States, 1990, *Morbidity and Mortality Weekly Report. CDC Surveillance Summaries* 1993; 42(6):29-57.
28. Goldberg AB, Dean G, Kang MS, Youssof S, Darney PD. Manual versus electric vacuum aspiration for early first-trimester abortion: a controlled study of complication rates. *Obstet. Gynecol.* 2004; 103(1): 101-7.
29. Lafe LE. The menstrual regulation procedure, *Stud. Fam. Plann.* 1977; 8(10):253-6.
30. Levin C, Grossman D, Berdichevsky K, Diaz C, Aracena B, Garcia SG, Goodyear L. Exploring the costs and economic consequences of unsafe abor-

Cost-effectiveness of safe abortion strategies in Nigeria and Ghana

- tion in Mexico City before legalisation. *Reprod Health Matters* 2009;17 (33):120-32
31. Shannon C, Brothers LP, Philip NM, Winikoff B. Infection after medical abortion: a review of the literature. *Contraception* 2004; 70(3):183-90.
32. Grimes DA. Risks of mifepristone abortion in context. *Contraception* 2005; 71:161. Reeves MF, Creinin MD. Mortality in Perspective: Mifepristone-Misoprostol Medical Abortion [op-ed]. *Johns Hopkins Adv. Stud. Med.* 2006; 6(10): 428-430. http://www.jhasim.com/files/articlefiles/pdf/ASIM%20Master_6_10pOp-Ed.pdf. Accessed 30 July 2008.
33. Ahiadeke C. Incidence of Induced Abortion in Southern Ghana. *Intl. Fam. Plann. Perspect.* 2001; 27(2): 96-101.
34. Ahman E, Dolea C, Shah I. *The global burden of unsafe abortion in the year 2000*. Geneva: WHO, 2006. <http://www.who.int/healthinfo/statistics/bod-abortions.pdf>. Accessed on August 4, 2008.
35. Henaku RO, Horiuchi S, Mori A. Review of Unsafe/Induced Abortion in Ghana. *Bull. St. Luke's Coll. Nurs.* 2007; 33: 93-102.
36. Aboagye PK, Gebreselassie H, Asare GQ, Mitchell EMH, Addy J. *An assessment of the readiness to offer contraceptives and comprehensive abortion care in the greater Accra, Eastern and Ashanti regions of Ghana*. Chapel Hill: Ipas, 2007.
37. Henshaw SK, Singh S, Oye-Adeniran BA, Adewole IF, Iwere N, Cuca YP. The incidence of induced abortion in Nigeria. *Intl. Fam. Plann. Perspect.* 1998; 24(4):156-64.
38. Johnson BR, Benson J, Bradley J, Rábago Ordoñez A. Costs and resource utilization for the treatment of incomplete abortion in Kenya and Mexico. *Soc. Sci. Med.* 1993; 36(11):1443-53.
39. U.S. Department of State. *Nigeria. Country Reports on Human Rights Practices-2007*. Washington, D.C.: U.S. Department of State, 2008. Available at: <http://www.state.gov/g/drl/rls/hrrpt/2007/100498.htm>. Accessed on 01 December 2009.
40. U.S. Department of State. *Ghana. Country Reports on Human Rights Practices-2007*. Washington, D.C.: U.S. Department of State, 2008. Available at: <http://www.state.gov/g/drl/rls/hrrpt/2007/100484.htm>. Accessed on 01 December 2009.
41. Carbonell JL, Varela L, Velazco A, Cabezas E, Fernández C, Sánchez C. Oral methotrexate and vaginal misoprostol for early abortion. *Contraception* 1998; 57(2):83-8.
42. Billings DL. Misoprostol alone for early medical abortion in a Latin American clinic setting. *Reprod Health Matters* 2004; 12(24 Suppl): 57-64.
43. Creinin M, Blumenthal P. Mortality associated with mifepristone - misoprostol medical abortion. *Medscape Gen. Med.* 2006;8(2):26.
44. Lule E, Signh S, Chowdury SA. *Fertility regulation behaviors and their costs: contraception and unintended pregnancies in Africa*. Washington, D.C.: World Bank, 2007.
45. Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF Macro. *Ghana Demographic and Health Survey 2008*. Accra: GSS, GHS, and ICF Macro, 2009. <http://www.measuredhs.com/pubs/pdf/FR221/FR221.pdf>. Accessed on 01 December 2009.
46. National Population Commission (NPC) [Nigeria] and ICF Macro. *Nigeria Demographic and Health Survey 2008*. Abuja: National Population Commission and ICF Macro, 2009. Available at: <http://www.measuredhs.com/pubs/pdf/FR222/FR222.pdf>. Accessed on 01 December 2009.
47. Harper CC, Blanchard K, Grossman D, Henderson JT, Darney PD. Reducing maternal mortality due to elective abortion: Potential impact of misoprostol in low-resource settings. *Int J Gynaecol Obstet* 2007; 98(1):66-9.
48. Prasad S, Kumar A, Divya A. Early termination of pregnancy by single-dose 800 mcg misoprostol compared with surgical evacuation. *Fertil Steril* 2009;(1):28-31. Epub 2008 Mar 4.
49. von Hertzen H, Piaggio G, Huong NT, Arustamyan K, Cabezas E, Gomez M, Khomassuridze A, Shah R, Mittal S, Nair R, Erdenetungalag R, Huong TM, Vy ND, Phuong NT, Tuyet HT, Peregoudov A. Efficacy of two intervals and two routes of administration of misoprostol for termination of early pregnancy: a randomised controlled equivalence trial. *Lancet* 2007 ;369(9577):1938-46.
50. Population Reference Bureau (PRB). *PRB 2009 World Population Data Sheet*. Washington, D.C.: PRB, 2009.
51. The Alan Guttmacher Institute. *Sharing Responsibilities: Women, Society, and Abortion Worldwide*. New York: AGI, 1999.
52. Weeks A, Alia G, Blum J, Winikoff B, Ekwari P, Durocher J, Mirembe F. A randomized trial of misoprostol compared with manual vacuum aspiration for incomplete abortion. *Obstet Gynecol* 2005; 106(3): 540-547.
53. Jain JK, Mishell DR Jr. A comparison of intravaginal misoprostol with prostaglandin E2 for termination of second-trimester pregnancy. *N. Engl. J. Med.* 1994; 331(5): 290-3.
54. World Health Organization (WHO). *Essential Elements of Obstetric Care at First Referral Level*. Geneva: WHO, 1991.
55. Clark WH, Gold M, Grossman D, Winikoff B. Can mifepristone medical abortion be simplified? A review of the evidence and questions for future research. *Contraception* 2007; 75(4):245-50.
56. Ipas. *Medical abortion: making a difference in rural India and around the globe*. Chapel Hill: Ipas, 2008. [http://www.ipas.org/Library/News/News_Items/Medical_abortion_making_a_difference_in_rural_India_around_the_globe.aspx] Accessed 18 July 2008.
57. Program for Appropriate Technology in Health (PATH). *Examining the cost of providing medical abortion in Vietnam*. Seattle: PATH, 2006. [http://www.path.org/files/CP_vietnam_med_abt_cost_study_rpt.pdf] Accessed July 19, 2008.