

Derivation of parameter estimates

A detailed description of the data sources and reasoning behind the parameter estimates used is given below. Our estimates were based on a range of sources including published reviews, trials, published case reports and longitudinal studies and author opinion.

Parameter estimates related to post-partum haemorrhage and intra-partum death are given in Table A1. Estimates related to puerperal sepsis and other post-partum deaths are given in Table A2.

Table A3 shows the societal parameters used per economic quintile. For each intervention package, we considered what would happen with best guess coverage estimates, and also supplied pessimistic and optimistic estimates. The best guess estimates correspond to probable coverage for each intervention package, whereas the pessimistic and optimistic estimates correspond to the least and best coverage, respectively, that were judged to be plausible. These estimates provide bounds for the potential effect of the intervention packages. An indication of substantial benefit under a pessimistic set of parameters, strongly suggests that the package should be explored further; conversely, an indication of little benefit under an optimistic set of estimates, suggests that there is little justification for exploration of real-world implementation.

The parameter estimates that differ between sub-Saharan Africa as a whole and Malawi are presented in table A4. Since the estimates for sub-Saharan Africa are more uncertain than are those for Malawi, we have not attempted to provide upper and lower bounds for these. Estimation was most difficult for parameters related to the incidence of sepsis and the case fatality of sepsis, and access to antibiotics under each intervention package.

Table A1: Parameter estimates related to post-partum haemorrhage and intra-partum maternal deaths in Malawi. *speculative estimates.

Parameter	Estimate
Probability that a woman will take misoprostol if given outside of a health facility. See note (1)	85%*
Probability that a health facility will have uterotonic drugs available (baseline scenario). See note (2)	79%
Probability that a health facility will have uterotonic drugs available (after the HF strengthening intervention). See note (3)	95% *
Incidence of severe (>1000ml) PPH without uterotonic. See note (4)	3.84%
Incidence of severe (>1000ml) PPH with oxytocin. See note (5)	2.34%
Incidence of severe (>1000ml) PPH with misoprostol. See note (6)	2.96%
Case fatality of severe PPH after delivery in a health facility. See note (7)	2.2%
Case fatality of severe PPH after delivery outside of a health facility. See note (8)	15%
Probability that a woman dies during delivery from causes other than PPH if she gives birth within a health facility. See note (9)	0.06%*
Probability that a woman dies during delivery from causes other than PPH if she gives birth outside of a health facility. See note (10)	0.18%*

1. Sanghvi^{A1}, in a study in Indonesia where misoprostol was distributed in the community, reported that 98% of 1348 pregnant women accepted misoprostol from CHWs. Of the 1348 women, 67% took misoprostol while 32% received an injected uterotonic (given by health provider). Thus almost all women who did not receive a uterotonic from a health provider took the misoprostol provided. Rajbhandari and

colleagues^{A2} report on a study providing misoprostol to over 2100 women in Nepal who delivered at home without a skilled birth attendant. 78% of women reported taking misoprostol. Most of the 22% of women who did not use misoprostol gave the presence of a skilled birth attendant as the reason (presumably due to the availability of oxytocin). Exact figures are not given, but even using a reasonably conservative value for 'most' (60%), the use of misoprostol by women without access to oxytocin comes to around 90%. Of the women that did take misoprostol, 89% took it as recommended while the remainder took it after delivery of both baby and placenta. Thus, in these two studies, the acceptance by local women of misoprostol was very high (>90%). We use an estimate of 85% for this study. This parameter is not considered dependent on economic quintile.

2. Unpublished data from Malawi: from routine monthly data collection from 62 health centres in 3 districts of Malawi studied over 17 months (April 2007 – August 2008) (source, Colbourn T, Malawi Community Paediatric Research Unit). This is consistent with an availability of oxytocin of 75% reported by Leigh et al.^{A3} in a survey of 94 health centres in Malawi in 2005.

3. Estimate based on unpublished Malawi data (source, Colbourn T, Malawi Community Paediatric Research Unit).

4. From Carroli et al.^{A4} systematic review. Carroli^{A4} reported an incidence of 3.84% of severe PPH among 4999 women for expectant management of labour. We note that this estimate is not region-specific, and hence may represent an under-estimate of the incidence of severe PPH with expectant management in sub-Saharan Africa.

5. From Hofmeyr and Gülmezoglu^{A5}. They report that prophylactic administration of oxytocin has a relative risk of 0.61 compared to no uterotonic. We have applied this relative risk to the 3.84% incidence of severe post-partum haemorrhage (see (4)) to obtain an estimate of 2.34% for the incidence of severe post-partum haemorrhage after oxytocin.

6. From Hofmeyr and Gülmezoglu^{A5}. They report wide heterogeneity in the measured efficacy of misoprostol compared with a placebo for the prevention of post-partum haemorrhage although all studies show some effect in the reduction of bleeding. For different doses of misoprostol, Hofmeyr and Gülmezoglu^{A5} report that the relative risk compared to a placebo was 0.77 for 600µg dose and 0.54 for the

400µg dose. Using the relative risk of 0.77, we estimate an incidence of severe post-partum haemorrhage of 2.96% after taking misoprostol. This is consistent with oxytocin being more clinically effective than misoprostol.

7. Etuk and Asuquo^{A6} report a case fatality of 2.2% from severe post-partum haemorrhage over a 6 year period at a Nigerian teaching hospital.

8. Reliable data for the case fatality of post-partum haemorrhage for women who give birth outside of a health facility do not exist. Some women will have access to emergency care within a health facility despite giving birth elsewhere, while some will not. We use our estimates of incidence and case fatality within health facilities (2,4,5 above) and estimates of Maternal Mortality Ratio (MMR) and health facility use in Malawi to calculate a plausible estimate for the case fatality of PPH for women who give birth outside of a health facility. Khan and colleagues^{A7} report that in Africa haemorrhage is the cause of 34% of maternal deaths. While this percentage relates to all maternal haemorrhage deaths and not just PPH, given that PPH accounts for the large majority of haemorrhage deaths^{A8} and that deaths from PPH are likely to be a greater contribution to total deaths in sub-Saharan Africa alone, we use the Khan estimate as is here. The MMR in Malawi was estimated at 984 per 100,000 in the 2004 (Demographic and Health Survey) DHS^{A9} and at 807 per 100,000 in the Malawi Multiple Indicator Cluster Survey^{A10} in period 2000 – 2006. Thus, out of 100,000 women there will be about 274 deaths from haemorrhage according to the Khan^{A7} estimates and using the lower estimate of MMR of 807. The MDHS04^{A9} reported that 57% of all births took place within a health facility. Assuming that uterotonics are available on average about 79% of the time (from (2)), we assume a total incidence rate of severe haemorrhage of 2.7% in health facilities ($0.79 \times 2.34\% + 0.21 \times 3.84\% = 2.7\%$). With a case fatality of 2.2%, we thus calculate that 34 ($0.027 \times 0.022 \times 0.57 \times 100,000 = 34$) of the 274 deaths per 100,000 women are for women who gave birth in a health facility. Thus the remaining 240 maternal deaths occurred in women who gave birth outside of a health facility. Assuming an incidence of 3.84% of severe haemorrhage for the 43% of women giving birth outside of a health facility, we estimate that $0.43 \times 100,000 \times 0.0384 = 1651$ women giving birth outside of a health facility suffered a severe haemorrhage. Thus, if 240 of these 1651 die, this gives a case fatality estimate of 15% for women who experience severe post-partum haemorrhage having given birth outside of a health facility. This is a very rough estimate but we believe it is plausible.

9 and 10. We have estimated the probability that a woman dies during delivery from causes other than PPH if she gives birth within a health care facility based on figures for obstructed labour and hypertensive disorders. Khan and colleagues^{A7} estimate that in Africa, 4·1% of maternal deaths are due to obstructed labour and 9·1% to hypertensive disorders. If Malawi has an MMR of 807 then 107 women will die of one of these two causes out of every 100,000 who give birth. Thus the estimated risk of a woman dying from other causes, regardless of her place of birth, is $107/100,000 = 0\cdot107\%$. Assuming that it is three times as likely for a woman to die if she gives birth outside of a health facility and that 57% of women give birth in a health facility, we have estimated the likelihood of death from non-PPH causes during childbirth in a health care facility to be 0·06% and that of death from non-PPH causes during childbirth outside of a health facility to be 0·18%. The numbers of maternal deaths from PPH and sepsis following delivery calculated using the model are not particularly sensitive to these values, and so while these estimates are based partly on educated guesswork, we believe that they are of the right order of magnitude and fit for purpose.

Table A2 – Parameter estimates related to sepsis and other post-partum maternal deaths in Malawi. All estimates are speculative.

Parameter	Estimate
Incidence of puerperal sepsis after delivery within a health facility. See point (1)	1.5%
Incidence of puerperal sepsis after delivery outside a health facility. See point (1)	3.0%
Case fatality of sepsis if antibiotics are taken. See point (2)	2.1%
Case fatality of sepsis if no antibiotics are taken. See point (2)	17%
Probability of dying of causes other than PPH or obstetric causes between delivery and time for onset of puerperal sepsis if delivery took place outside of a health facility. See point (3)	0.02%
Probability of dying of causes other than PPH or obstetric causes between delivery and time for onset of puerperal sepsis if delivery took place in a health facility. See point (3)	0.01%

1. Dolea and Stein in the WHO report on the burden of maternal sepsis^{A11} note that comparison of different studies reporting on maternal sepsis is difficult due to the different definitions of maternal sepsis that abound. Another problem in estimating incidence and case fatality of sepsis is that "most post-partum infections take place after hospital discharge"^{A11}, so that where there is no postnatal follow-up, cases can go unreported. To account for the problem of different definitions of maternal sepsis, we use incidence and case fatality rates from the same study. AbouZahr^{A12} gives estimates of both for sub-Saharan Africa and we use this study as the basis of our parameter estimation. AbouZahr^{A12} reported an incidence of puerperal sepsis of 2.37% and Dolea and Stein^{A11} assume that mothers are twice as likely to develop a puerperal infection after vaginal delivery outside of a health facility than after delivery within one. Given the low rates of caesarean section in sub-Saharan Africa, we use their assumption here to estimate the incidence of sepsis after delivery after birth in a

health facility and outside of a health facility. Gwatkin^{A13} et al. report that in sub-Saharan Africa 44.8% of women give birth in either a public or a private health care facility. Thus if s is the incidence of puerperal sepsis after delivery in a hospital, then we estimate s using the equation: $s \times 0.448 + 2s \times 0.552 = 0.0237$ giving an estimate of 1.5% for the incidence of puerperal sepsis in sub-Saharan Africa after a woman has given birth in a health facility, and 3.0% if she has given birth in the community.

2. AbouZahr^{A12} reported a case fatality rate of 11% for sepsis following delivery in sub-Saharan Africa. In a study of historical changes in maternal death rates in the United Kingdom, Tew^{A14} reports that the death rate from puerperal sepsis fell by a factor of 10 between 1936 (before antibiotics were available) and 1950 (when effective antibiotics were generally available). Antibiotics, while the major reason for this dramatic reduction, were not the only improvements during these 14 years, and so we arbitrarily assume that the case fatality for sepsis without antibiotics is 8 times that with antibiotics. We further assume that in sub-Saharan Africa as a whole about 40% of women with sepsis will obtain antibiotics. In this case, if b is case fatality of sepsis in sub-Saharan Africa with antibiotics, then we estimate it using the equation: $0.4 \times b + 0.6 \times 8b = 0.11$, giving a case fatality for sepsis with antibiotics of 2.1% and without antibiotics of 17%. These are very rough estimates but we believe that they are plausible.

3. In our opinion, a reasonable estimate for the probability of that a woman dies of causes other than PPH or obstetric causes between delivery and time for onset of puerperal sepsis is 0.01% if delivery took place in a health facility and 0.02% if delivery took place outside of a health facility. The numbers of maternal deaths from PPH and sepsis following delivery calculated using the model are not particularly sensitive to these values, and so while these estimates are based on educated guesswork, we believe that they are of the right order of magnitude and fit for purpose.

Table A3 – Demographic parameters and estimates for the extent of coverage that could be reached in Malawi. Data are number, percentage or estimated percentage [pessimistic guess-optimistic guess]. *speculative estimates

Package 1: Health-facility strengthening

Package 2: Health-facility strengthening, and improved drug distribution via antenatal-care appointments and community health workers.

Package 3: Health-facility strengthening, and improved drug distribution via antenatal-care appointments, community health workers, and female volunteers in villages.

Parameter	Economic Quintile				
	1 (poorest)	2	3	4	5 (richest)
Total number of women going into labour each year. See point (1)	110,000	127,500	128,500	110,000	90,000
Baseline: proportion of women giving birth in a health facility. See point (1)	47%	47%	52%	64%	85%
Baseline: probability that a woman with sepsis obtains antibiotics. See point (2)	20%*	30%*	40%*	60%*	85%*
All packages of interventions: proportion of women giving birth in a health facility. See point (3)	49%* [47,51]	49%* [47,51]	54%* [52,57]	66%* [64,70]	88%* [85,93]
Package 1: probability that a woman with sepsis obtains antibiotics. See point (4)	25%* [22,30]	35%* [32,42]	45%* [42,52]	70%* [65,75]	90%* [85,95]
Package 2: coverage of misoprostol distribution. See point (1)	81% [68,86]	83% [69,87]	83% [69,87]	86% [72,91]	87% [73,92]
Package 2: probability that a woman with sepsis obtains antibiotics. See point (5)	40%* [30,50]	58%* [50,65]	70%* [60,80]	80%* [70,85]	95%* [90,95]
Package 3: coverage of misoprostol distribution. See point (6)	92%* [90,98]	95%* [92,98]	96%* [92,98]	98%* [96,99]	100%* [97,100]
Package 3: probability that a woman with sepsis obtains antibiotics. See point (7)	70%* [35,85]	75%* [45,85]	80%* [55,90]	90%* [80,95]	99%* [95,98]

1. Estimates marked with (1) were obtained from the 2004 Malawi Demographic and Health Survey^{A9}. For an estimate of the total number of deliveries in Malawi in one year, we used the total number of births in 2006 given in the Malawi country profile of the UNICEF Countdown to 2015 report^{A15}. This total number, 566,000, was divided into economic quintiles according the ratios provided by births per economic quintile within the sample used in MDHS04^{A9}. Since we are using the model to investigate potential impact and not to provide precise forecasts, we equate the number of live

births with the number of deliveries. The survey additionally provided figures on delivery within health facilities and attendance of at least one antenatal care appointment per economic quintile. For the second package of interventions (health facility strengthening and ante-natal care and community health work drug provision), we assume that 90% of antenatal care workers will have misoprostol in stock once a national programme focuses on this strategy, and apply this to antenatal care attendance (defined as at least one antenatal care appointment) per quintile for our estimates. For our pessimistic scenario we assume that only 75% of antenatal care workers will have misoprostol available and in the optimistic case assume that 95% percent of antenatal care workers will have it available.

2. We note that this parameter represents the combined probability that a woman will recognise the signs of infection, seek and then obtain antibiotics either from a health facility or elsewhere. There are no data specifically available on access to antibiotics for women with signs of postnatal infection. Houweling et al.^{A16} described median levels of health care use across 45 developing countries (over half outside sub-Saharan Africa) among the poorest and richest wealth quintiles. For delivery care, the median level was 47% with the poorest and richest quintiles receiving 23% and 85% respectively. Delivery care had the largest quintile differences compared with antenatal care, immunization, and treatment of acute respiratory infections (ARI) or diarrhoea in children. For ARI treatment the figures were 46%, with 32% and 62% in the poorest and richest quintiles. Treatment of ARI was self-reported so use of antibiotics cannot be assumed, and hence the figures represent the best case scenario. We have therefore set our best guess estimate for women in the poorest quintile obtaining an antibiotic after birth at 20%, and have adjusted the values for the other quintiles accordingly, taking into account that the quintile differences for delivery care are the most pronounced.

3. All packages of interventions considered involve a policy of health facility strengthening, especially focusing on drug supply and management and quality of care. To estimate the potential impact of such strengthening we used the percentage increase in skilled birth attendance between 1992 and 2004 and then doubled it. Zere et al.^{A17} report that delivery attendance by skilled medical personnel in Malawi increased from 55% in 1992 to 56% in 2004, giving a relative increase of 2% ($1.02 \times 55\% = 56\%$). Thus we increased the use by 4% from our baseline estimates (e.g. for quintile 1, $1.04 \times 46.8\% = 49\%$). For our pessimistic estimates we assumed no increase from baseline and for the optimistic case a relative increase of 10% (capped

at 100% use). If these estimates seem overly pessimistic, it is worth noting that the latest UN statistics (<http://mdgs.un.org/unsd/mdg/Data.aspx>) show a reduction in attendance by trained medical personnel in Malawi to 54% in 2006.

4. The strengthening of drug supply and quality of care in health facilities is unlikely to increase dramatically the use of antibiotics in the poorest quintile women, as non-attendance is often determined by lack of geographical access to facilities, inability to afford drug fees and cultural confinement during the early postnatal period.

5. The probability that a woman with a puerperal infection obtains antibiotics from a community health worker will depend upon the recognition of symptoms and signs of sepsis by families, the knowledge that community workers can provide antibiotics, the coverage and availability of community workers, the rate of attrition of community workers from their posts through sickness, death or resignation, the maintenance of drug resupply to these workers, and the probability that drugs for maternity cases are not used for other purposes. In Malawi the outreach workers (health surveillance assistants) each cover 1,000-2,000 population, or 4 - 10 villages^{A18}. Our estimates are based on an assumption that this method of drug distribution could increase coverage by up to 60% over intervention package one for the poorest quintile households.

6. We assume that coverage will be higher than in the case of package two. Provision through maternity boxes held by volunteers will depend upon access to the volunteer and the likelihood that the box has been supplied or resupplied under a new government supply programme. Given that only 15-20 women will deliver in most villages (in one year), the likelihood of contact between the volunteer and the pregnant mother will be high. Our estimates for coverage are driven mainly by anticipated problems in maintaining supply, even if volunteers can replenish stocks through visits to health centres as part of a new national programme to implement this strategy. The additional impact of volunteer supply of prophylactic misoprostol over and above community worker or antenatal care clinic supply is not considered to be large given the high rates of attendance at antenatal clinics. Note also that Rajbhandari et al.^{A2} report that out of the 3072 women in their study, 2957 (96%) received misoprostol from local women's volunteers in rural Nepal during their pregnancy. Thus our estimates of coverage by package three of over 90% in Malawi seem plausible. Note that the likelihood of a woman taking misoprostol appropriately if given it is a separate parameter (see estimate (1) in Table A1).

7. The same assumptions apply as in point 6. However the supply of antibiotics to mothers with signs of infection by village volunteers is likely to be substantially higher than by community health workers given their proximity and accessibility.

Table A4 – Demographic parameters and estimates for the extent of intervention coverage that could be reached in sub-Saharan Africa. Data are number or percentage. *speculative estimates.

Package 1: Health-facility strengthening

Package 2: Health-facility strengthening, and improved drug distribution via antenatal-care appointments and community health workers.

Package 3: Health-facility strengthening, and improved drug distribution via antenatal-care appointments, community health workers, and female volunteers in villages.

Best Guess for Sub- Saharan Africa	Economic Quintile				
	1 (poorest)	2	3	4	5 (richest)
Total number of women going into labour each year. See point (1)	6,892,000	6,474,000	6,056,000	5,325,000	3,968,000
Probability that a health facility will have uterotonic drugs available (baseline scenario). See point (2)	50%*	50%*	50%*	50%*	50%*
Probability that a health facility will have uterotonic drugs available (in all intervention packages). See point (2)	85%*	85%*	85%*	85%*	85%*
Baseline: proportion of women giving birth in a health facility. See point (3)	25%	33%	42%	57%	79%
Baseline: probability that a woman with sepsis obtains antibiotics. See point (4)	10%*	20%*	30%*	60%*	85%*
All packages of interventions: proportion of women giving birth in a health facility. See point (5)	29%*	38%*	48%*	65%*	90%*
Package 1: probability that a woman with sepsis obtains antibiotics. See point (4)	20%*	30%*	35%*	70%*	90%*
Package 2: coverage of misoprostol distribution. See point (6)	58%	63%	69%	77%	84%
Package 2: probability that a woman with sepsis obtains antibiotics. See point (4)	25%*	45%*	60%*	80%*	95%*
Package 3: coverage of misoprostol distribution. See point (4)	75%*	80%*	80%*	85%*	90%*
Package 3: probability that a woman with sepsis obtains antibiotics. See point (4)	50%*	60%*	70%*	85%*	95%*

1. We obtained the annual number of births in sub-Saharan Africa from the UNICEF website (<http://www.unicef.org/statistics>). We divided this total number of births between quintiles according to the ratios of fertility rates per quintile for sub-Saharan Africa as provided in Gwatkin^{A13}. Since we are using the model to investigate potential impact and not to provide precise forecasts, we equate the number of live births with the number of deliveries.

2. The MDG Gap Task Force Report 2008 (http://www.un.org/esa/policy/mdggap/mdg8report_engw.pdf) showed that the average public sector availability for essential drugs in sub-Saharan Africa was only 38%. Assuming that oxytocin might be stocked in preference to other drugs we have arbitrarily assumed 50% availability. Under health facility strengthening, we assume that this might increase to 85%.

3. The proportion of women giving birth in a health facility (either public or private) was taken from Gwatkin^{A13} for sub-Saharan Africa per economic quintile.

4. Malawi has been one of the higher achieving countries in sub-Saharan Africa based on indicators of primary care coverage and child survival indicators^{A19}. It also has a stable government, a relatively small and accessible population and recent improvements in child mortality rate decline. We have therefore set our best guess estimates for sub-Saharan Africa well below those for Malawi.

5. The 2007 report by the UK Department for International Development progress towards MDG5^{A20} reported an increase in the proportion of deliveries attended by skilled health care personnel in sub-Saharan Africa from 42% in 1990 to 45% in 2005, representing a 7% increase over 15 years ($1.07 \times 42\% = 45\%$). Thus, erring on the generous side, we assume a relative increase in use of 14% in the presence of health facility strengthening. The latest UN report on MDG indicators (<http://mdgs.un.org/unsd/mdg/Resources/Static/Data/Stat%20Annex.pdf>) reports an increase in the proportion of deliveries attended by skilled health personnel from 42% in 1990 to 47% in 2006, representing a relative increase of 11%. Thus a 14% increase is a reasonable best guess estimate.

6. The proportion of women receiving at least one antenatal care appointment per economic quintile was taken from Gwatkin^{A13}. As for the Malawi estimates above, we

estimated that 90% of antenatal care workers would have misoprostol in stock under this intervention.

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