Cost-effectiveness of maternal and newborn health interventions

and packages in 59 low- and middle-income countries

MERCK for Mothers

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Introduction

Maternal health has long been a stated priority in a variety of global goals and strategies: the Millennium Development Goals[1], the Sustainable Development Goals[2], FP2020[3], and the Global Strategy for Women's Children's and Adolescents' Health[4]. However, many of the goals have not actually been achieved, specifically those around reducing the number of maternal deaths – the deaths of women during pregnancy, childbirth and up to 42 days post-partum. While the approximately 295,000 maternal deaths in 2017 represented a notable decline from the 2000 death toll of 451,000, the 45% decrease fell far short of the MDG5 goal of reducing maternal mortality by three quarters from 1990.[5] The United Nations (UN) estimated that only 9 countries, out of the 95 being monitored, had reached their individual maternal mortality reduction goals[6] by 2015. Since then, it is estimated that only 9 more countries have achieved their individual goals, although this is uncertain given the lack of an updated 1990 estimate from 2015[7].

This report attempts to add novel presentations of cost efficiency and impact to the discourse on maternal and child health. It situates this discourse within the context of limited budgets and finite resources; a reality for the vast majority of countries which struggle to end preventable maternal deaths. While similar costing exercises have been conducted, the findings and funding demands have placed the achievement of strong maternal health beyond the reach of many low- and middle-income countries[8]. Moreover, there remains an unclear understanding of how the indirect costs, opportunity costs, and outcomes, between various Maternal and Newborn Health (MNH) packages of services compare, including Family Planning (FP) and Reproductive Health (RH). This article seeks to bridge that knowledge gap, providing a direct head-to-head comparison between multiple MNH interventions and packages, while also focusing on a subset of countries with the heaviest burden and highest investment need.

Highlights

Individual interventions are not typically offered in isolation. Health services typically deliver interventions, as packages which are delivered either at a single visit, such as antenatal care, or at single time point, such as childbirth. As outlined in the table below, for the purposes of this study, those interventions which are typically offered together were grouped together into packages. The packages were designed prior to seeing the results of the individual interventions, with the exceptions of Package 2B, 8, and 9, which were designed to maximize cost-effectiveness. Package inclusions are outlined Table 1 below:

Table 1: Interventions and Packages

		Package 1: Periconceptual	Package 2: Antenatal Care	Package 2B: Revised ANC	Package 3: Routine Delivery Care - No Emergency Care	Package 4: BEmONC	Package 5: CEmONC	Package 6: Everything except FP	Package 7: Everything including FP	Package 8: BEmONC + FP	Package 9: BEmONC + RH
Periconceptual	Safe abortion services	x						x	x		x
	Post abortion case management (no scale up of safe abortions)										
	Post abortion case management (with Scale-up of safe abortion)	x						x	x		x
	Ectopic pregnancy case management	x						x	x		
	Blanket iron supplementation/fortification	x						x	x		
Antenatal Care	Antenatal care (at least 1 visit)										
	Antenatal care (at least 4 visits)		x	x				x	x		
	TT - Tetanus toxoid vaccination		x	x				x	x		
	IPTp - Intermittent preventive treatment of malaria during pregnancy		x	x				x	x		
	Syphilis detection and treatment		x	x				x	x		
	Calcium supplementation		x					x	x		
	Iron supplementation in pregnancy		x	x				x	x		
	Multiple micronutrient supplementation in pregnancy		x	x				x	x		
	Balanced energy supplementation		x	x				x	x		
	Hypertensive disorder case management		x	x				x	x		
	Diabetes case management		x					x	x		
	Malaria case management		x					x	x		
	MgSO4 management of pre-eclampsia		x	x				x	x		
Delivery Care	Health facility delivery				x	x	x	x	x	x	x
	Clean birth environment				x	x	x	x	x	x	x
	Immediate drying and additional stimulation				x	x	x	x	x	x	x
	Thermal protection				x	x	x	x	x	x	x
	Clean cord care				x	x	x	x	x	x	x
	Uterotonics				x	x	x	x	x	x	x
	Controlled cord traction/removal of placenta				x	x	x	x	x	x	x
	Parenteral administration of anti-convulsants					x	x	x	x	x	x
	Antibiotics for preterm or prolonged PROM					x	x	x	x	x	x
	Parenteral administration of antibiotics					x	x	x	x	x	x
	Assisted vaginal delivery					x	x	x	x	x	x
	Neonatal resuscitation					x	x	x	x	x	x
	Removal of retained products of conception					x	x	x	x	x	x
	Induction of labor for pregnancies lasting 41+ weeks					x	x	x	x	x	x
	Antenatal corticosteroids for preterm labor					x	x	x	x	x	x
	C-section						x	x	x	x	x
	Blood transfusion						x	x	x	x	x

Family Planning	FP - Pills								x	x	x
	FP - Condoms								x	x	x
	FP - Injectables								x	x	x
	FP - Implants								x	x	x
	FP - IUD								x	x	x
	FP - Female Sterilization								x	x	x
	FP - Male Sterilization								x	x	x
	FP Former Traditional Method Users								x	x	x

The key findings of this report are based on a foundational understanding that there is no magic bullet to reducing maternal mortality. A genuine commitment to MNH demands a healthcare system which has the capacity to respond to MNH needs across the spectrum, at all stages. To know where and how to best strengthen MNH health systems in low and middle income countries requires an understanding of where limited budgets can generate the greatest impact. The analysis undertaken shows that the strongest investments in maternal and newborn health within Low- and Middle-Income countries are in the following areas.

1. *Basic Emergency Obstetric and Newborn Care* (BEmONC)

Providing $61.50 worth of benefits for every $1 dollar spent by governments and beneficiaries, the package of interventions with the third highest BCR is BEmONC. This would require an additional $2.2bn per year in investments, and would lead to an expected additional 93,000 avoided maternal deaths, 0.87m avoided newborn deaths and 0.81m avoided stillbirths.

2. Safe & Inclusive Family Planning

Providing $26.80 worth of benefits for every $1 dollar spent by governments and beneficiaries, this is the sole intervention (as opposed to a package) with the greatest absolute impact on maternal deaths. Scaling up this intervention to meet 90% of unmet need in the 59 countries with the highest maternal and newborn mortality rates would require an additional $1.2bn per year in investments, and would avert an expected additional 87,000 maternal deaths.

3. *Basic Emergency Obstetric and Newborn Care* (BEmONC) in combination with Family Planning

Providing $71.50 worth of benefits for every $1 dollar spent by governments and beneficiaries, the package of interventions with the highest BCR is BEmONC combined with Family Planning. This would require an additional $2.9bn per year in investments, and would lead to an expected additional 162,000 avoided maternal deaths, 1.21m avoided newborn deaths and 1.18m avoided stillbirths. This package would be enough for the world to finally reach Millennium Development Goal 5, reducing maternal deaths by 2/3, albeit 10 years later than hoped.

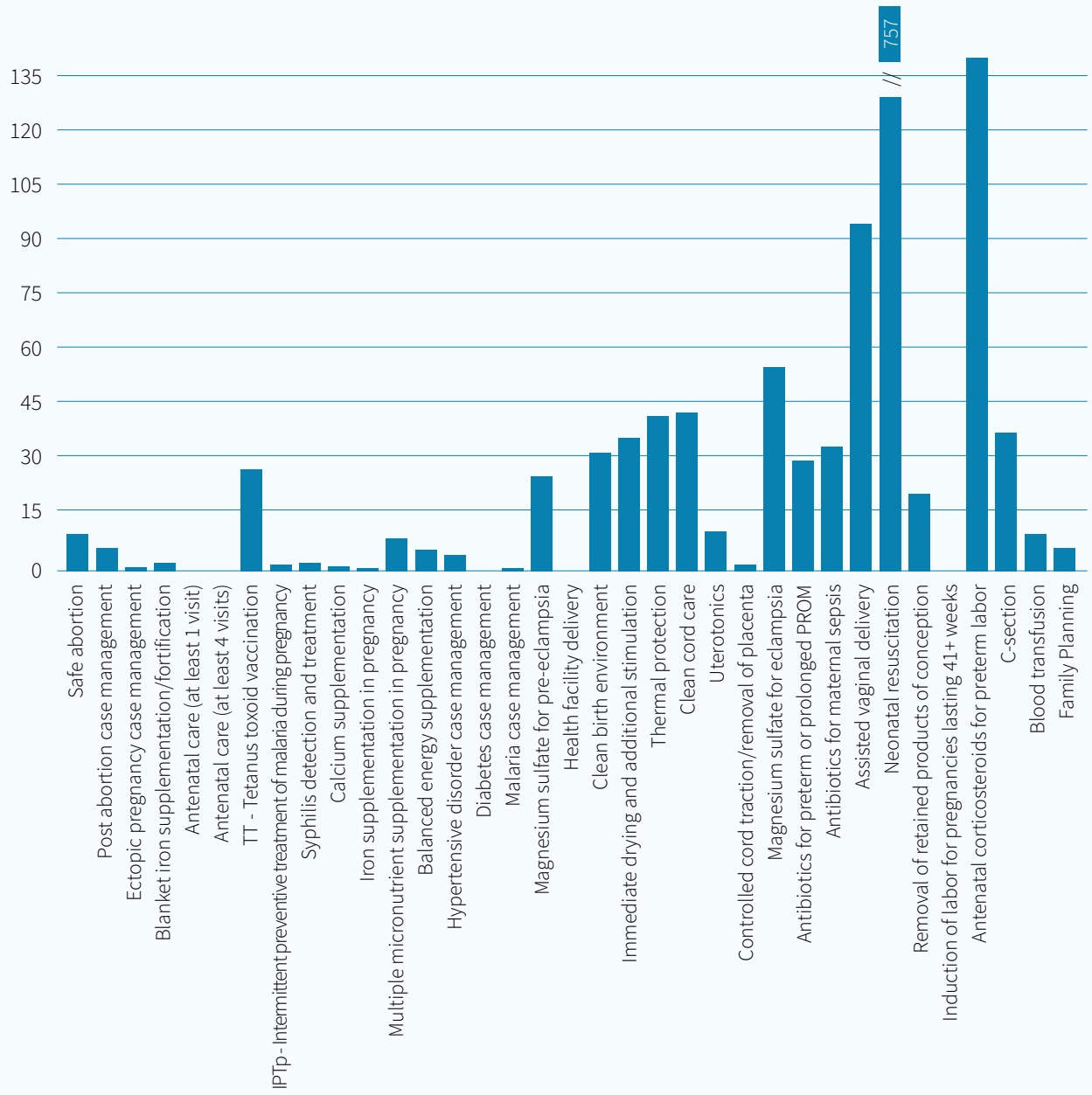
4. Among individual interventions, the strongest performing interventions in MNH:

The most cost-effective individual interventions when it comes to saving mothers' lives are the management of eclampsia and pre-eclampsia with magnesium-sulfate, which produced the largest benefit-cost ratios, at 53.0 and 20.7, respectively. This is due to the extremely high fatality rates of these conditions if left untreated and the low cost and high efficacy of the magnesium sulfate used for their treatment. Removal of retained products of conception left behind in the uterus after childbirth, a condition that if untreated can lead to hemorrhage, sepsis and death, also presented a remarkably high benefit-cost ratio of 17.1.

When taking into account life-saving impacts on both mothers and their newborns, the most cost-effective individual intervention was neonatal resuscitation, an intervention requiring only an inexpensive, reusable hand-operated resuscitator and a health care provider. The second and third most effective interventions were antenatal corticosteroids and assisted vaginal delivery, including forceps and vacuum extraction. Similarly, this finding reflects a reduction in asphyxia, and to a lesser extent deaths due to prematurity or sepsis, which are among the most common causes of death in the 59 countries analyzed.

What We Know: Interventions and Packages

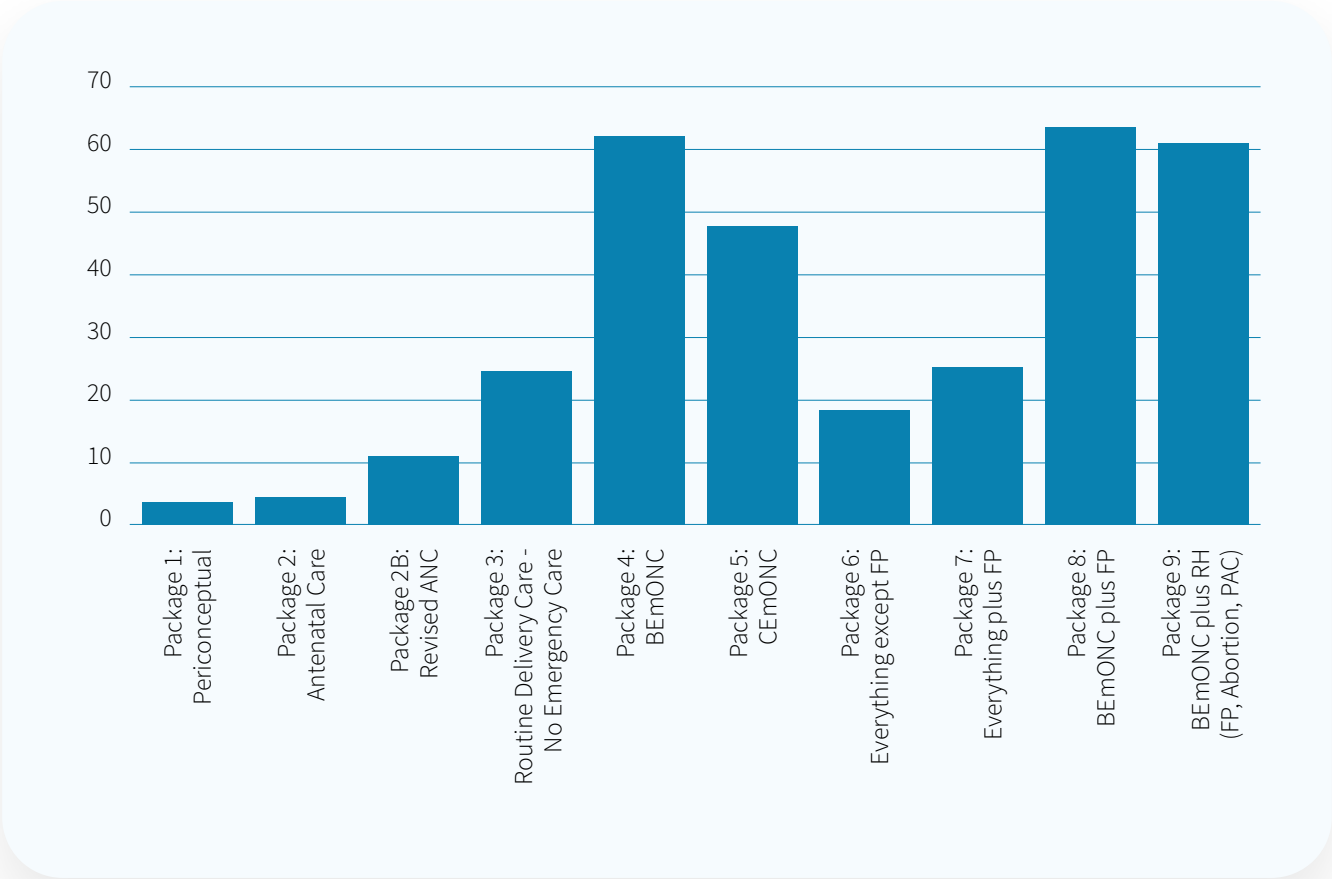
Figure 1. Benefit-Cost Ratios for Individual Interventions, Including Both Maternal and Newborn Mortality and Morbidity Averted



While costing interventions at an individual level is valuable in demonstrating the potential and scale of direct impacts and cost efficiency of an single intervention, it is not reflective of the way in which health services typically deliver interventions, as interventions such as these tend to be grouped together and delivered either at a single visit, such as antenatal care, or at single time point, such as childbirth. Grouping interventions together into combined packages compounds the benefits to each recipient, lowering time costs of the women receiving treatment as well as the salaried time costs of the person administering the treatment. Moreover, more comprehensive treatment, as provided in such package approaches accounts for the interdependency of multiple factors within pregnancy, lowering the overall likelihood of complications arising throughout and following the pregnancy, and the associated demands on the health system those complications may create.

The packages with the highest Benefit-Cost Ratios were: 1) BEmONC with basic Family Planning; 2) BEmONC with Family Planning, Abortion, and Post-Abortion Care; and, 3) BEmONC only, respectively. While basic emergency obstetric and newborn care (BEmONC) was the most cost-effective ***a priori*** package of interventions, our findings suggested that a combined package of basic emergency obstetric care and family planning or basic emergency care, family planning and abortion/post-abortion care might be more cost-effective, providing greater impact for each dollar spent. Among these broader packages, package 8, with family planning and basic emergency obstetric care was most cost-effective and had a slightly higher BCR than BEmONC alone. Package 9, as well, which included basic emergency obstetric care, family planning and abortion services had a slightly higher BCR than BEmONC alone. However, for resource-constrained nations, scaling up a package of BEmONC and family planning services is likely to be the most cost-effective first step.

Figure 2. Benefit-Cost Ratios for Interventions Delivered as Packages, Including Both Maternal and Newborn Mortality and Morbidity Averted



Trickle Up Effect: Context

Investing in maternal and newborn health goes far beyond the immediate health of a woman and her child. It is an investment in a cycle of growth and progress which has far reaching consequences and continues to yield benefits years and even decades into the future.

While many aspects of maternal and newborn health are well explored, less well studied are the impacts on a family when a mother dies. Other surviving children are at higher risk of having their schooling cut short[9] in order to support the family, which can include having to take over the mother's tasks, such as cooking, cleaning and fetching water[10]. Additional impact on a child's emotional well-being due to missing their mother[11] or of leaving the family home to live with grandmothers or other relatives have been described, but cannot be quantified[12]. Similarly, no data exists on mental health issues in the surviving husband. Economically, studies in both Africa and Asia have shown that the direct cost of a funeral and medical expenses can reach one third of a family's income[1314], and are often paid for through loans[15] or the sale of household assets[16]. Households also usually see a major reduction in both income (32% in China) and expenditure (25% in China) over the year following the maternal death[1718].

In total, there is no clear and quantifiable estimate available of the impact a maternal death on her family. The only aspect which has been characterized, in a wide variety of settings, is the reduced survival of a newborn in the case of the death of its mother, although much of the available literature and studies are a composite of maternal mortality in the index child, maternal mortality in older children, and non-maternal mortality[19]. For children whose mother died, the risk of dying before the age of 5 was 2 to 51 times higher than the corresponding risk for children whose mothers survived[20], with the detailed relationship dependent on many factors[21] including age of the child and the time of the mother's death, socioeconomic status (both familial and societal), cultural attitudes, availability of familial relationships, and whether the death was a maternal death (up to 42 days after childbirth) or the death of a mother (at any point)[22]. One study in Bangladesh suggested that children may be as much as four times more likely to die by age 10 than children whose mothers didn't die[23]. Much of this is likely a consequence of reduced nutrition due to lack of breastfeeding in the first years of life, but not all. The study found a notable increase in the number of deaths in older children (over age 2), suggesting that there are additional pathways to mortality beyond breastfeeding and nutrition alone[24], although this result is not universal[25]. It should also be noted that children died at higher rates in families experiencing a maternal death (up to 42 days after childbirth) than in families with a mother dying from a non-maternal cause of death (i.e., car accident, drowning, cancer)[26]. In addition, increased stunting (RR=1.3-1.4, depending on the specific analysis) has been observed in children under 2 years of age who are maternal orphans[27].

Targeted investments in maternal and newborn health stand to mitigate these impacts for those almost 300,000 women around the world who die in childbirth each year, their families, and the communities which depend on them. In addition to averting these negative impacts, significant economic, educational and environmental benefits to society, families and households could be achieved if all women who needed sexual and reproductive health care and family planning could access it.

Discussion and Conclusions

In November 2019, at the Population Summit in Nairobi, an analysis was presented which documented the cost of a package of interventions to end preventable maternal deaths, eliminate gender-based violence and harmful practices and meet the family planning needs of women in 120 countries[28]. This package would include all of the

interventions modelled here, as well as additional interventions, and amounted to a global funding ask of $115 billion in order to end preventable maternal deaths. While this ambition is both necessary and commendable, it remains the case that if those costs appear to be too prohibitive to countries, countries and donors may reduce their willingness to invest in these services at all. This current analysis complements the Nairobi Summit commitments by noting where the greatest benefits can be achieved with fewer resources, providing guidance to policy makers on where to begin investing to yield the largest possible impact.

This report is similar to other analyses conducted by UNFPA (2020) and the Guttmacher Institute (2017) that have estimated the additional investments required to significantly reduce maternal deaths and provide family planning.[29] Our costing methodology is most similar to UNFPA (2020) with results that are broadly comparable. UNFPA estimates the costs to scale up to 95% coverage of essential maternal and neonatal health across 120 countries with a population of around 1.3 billion women of a reproductive age are USD 115bn over a 10-year time period.

In this study we focus on a smaller subset of 59 countries with a population of 3.8 billion (970 million women of reproductive age), with slightly lower targets and identify a cost of $8.3bn per year for the entire suite of family planning and EmONC interventions. The value addition of this study is estimating the costs and benefits of different interventions and packages that are less than the full suite of possible interventions, providing an evidence-based approach to prioritization and planning within the global fight to end preventable maternal deaths. For example, focusing on where the greatest impact can be attained per dollar invested, this report shows that 80-90% of the benefits can be had for around $2.9bn per year - a much more realistic and achievable ask.

Although this study clearly demonstrates the potential global impact of these interventions on maternal mortality, it is critical to note that the most cost-effective packages were those which included a combination of reproductive health (specifically family planning, safe abortion and post-abortion care) and childbirth care at the basic emergency obstetric care level. Although these types of interventions have different delivery pathways, together they address the majority of the needs of a woman and her newborn. Although comprehensive obstetric care is exceedingly effective in reducing maternal deaths, the cost of delivering C-sections may be prohibitive at scale, particularly in low-income countries. In such cases, it is likely be more efficient to begin with basic emergency obstetric care and family planning, and then expand to other services once those are in place.

Detailed Analysis of Findings – Packages

This study clearly shows that the majority of the key individual interventions which are included in typical maternal and newborn care packages and family planning are cost-effective. However, with the exception of a few individual interventions with outsized BCRs, they are more cost-effective when combined into efficient packages, in the way that the global and medical communities have already been doing. Thus, somewhat broader packages of interventions, including family planning, are more likely to result in greater benefits than focusing on single interventions, through scale and through reduced numbers of contacts with the health system.

The results of this analysis indicate that the package of interventions with the highest BCR is BEmONC with family planning, yielding benefits of $71 for every dollar spent by governments and beneficiaries. This would require an additional $2.9bn per year in investments, and would lead to an expected additional 162,000 avoided maternal deaths, 1.2m avoided newborn deaths and 1.2m avoided stillbirths. It would also generate a demographic divi-

dend benefit equivalent to $25bn annually, equivalent to a 6% increase in GDP per capita over the long run.[1] While a more ambitious intervention package of all maternal and neonatal health interventions, with family planning, would avoid a ***further*** 40,000 maternal deaths, 200,000 newborn deaths and 400,000 stillbirths it would also require 3 times as large an investment per year ($8.3bn). The BCR of the full package is 29 – still a very sizeable return on investment. However, as noted earlier, for resource-constrained nations, scaling up a package BEmONC and family planning services is likely to be the most cost-effective first step.

Table 2 below presents the overall package results, in terms of lives saved, costs, and cost per life saved. While averted stillbirths are presented, they are not included in monetized benefits and the BCR. The BCRs of these packages are presented in Figures 3 and 4 below (packages 1-7) along with family planning. The most cost-effective package of interventions was Package 1: Periconceptual interventions and Package 4: Basic emergency obstetric and newborn care.

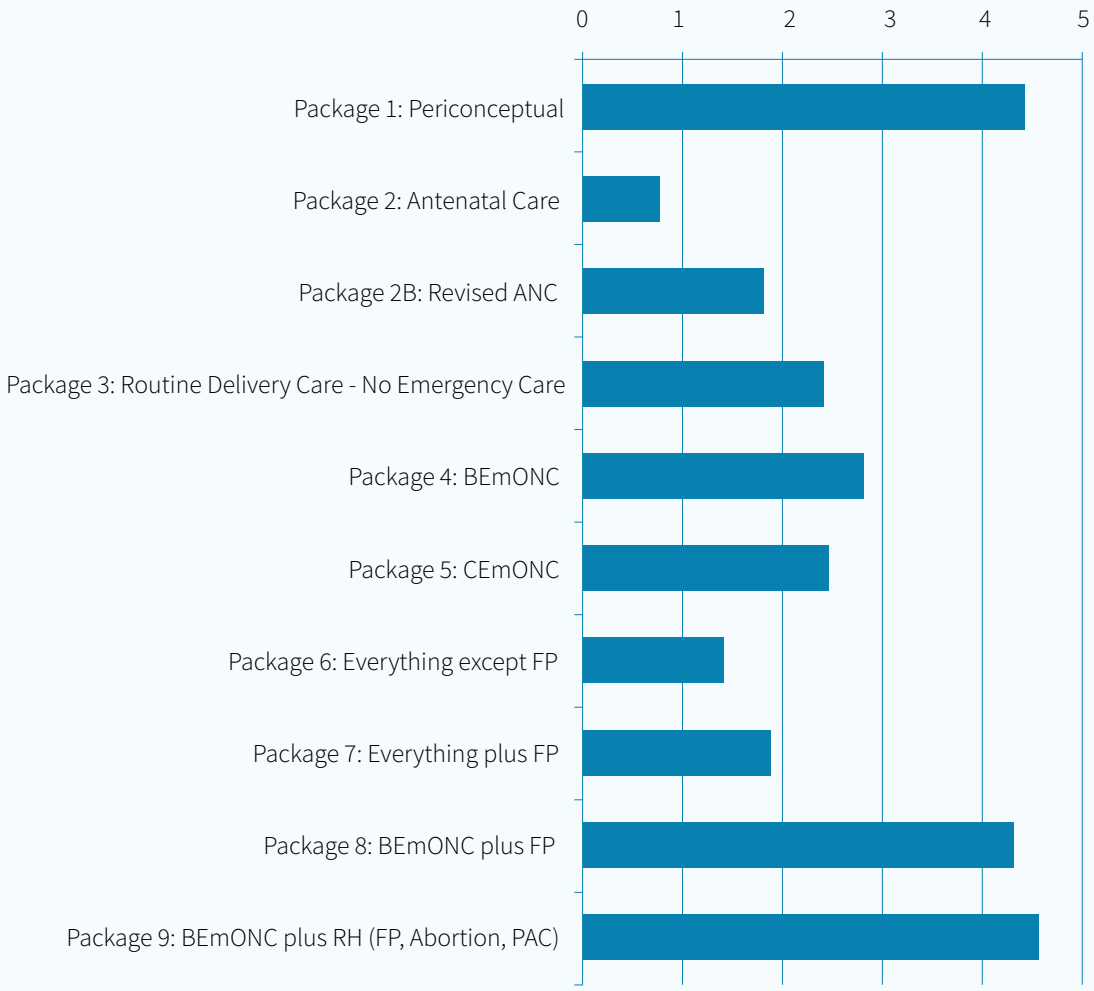
Table 2. Potential Lives Saved by Intervention Packages

	Lives Saved			Additional Cost (Mio US$)	Additional Benefits (Mio. US$)*	Cost per life saved excl. still births (Th. US$)	BCR
	Maternal	Newborn	Stillbirths				
Package 1: Periconceptual	40,000	0	0	$873	$3,767	$21.82	4.3
Package 2: Antenatal Care	56,000	160,000	782,000	$5,123	$26,516	$23.72	5.2
Package 2B: Revised ANC	49,000	121,000	767,000	$1,787	$21,545	$10.51	12.1
Package 3: Routine Delivery Care	46,000	214,000	0	$1,290	$31,355	$4.96	24.3
Package 4: BEmONC	93,000	869,000	806,000	$2,185	$134,448	$2.27	61.5
Package 5: CEmONC	118,000	990,000	806,000	$3,195	$153,652	$2.88	48.1
Package 6: Everything except FP	165,000	1,105,000	1,337,000	$9,190	$176,033	$7.24	19.2
Package 7: Every-thing including FP	205,000	1,391,000	1,587,000	$8,313	$239,509	$5.21	28.8
Package 8: BEmONC + FP	162,000	1,211,000	1,182,000	$2,890	$206,540	$2.10	71.5
Package 9: BEmONC + RH	170,000	1,211,000	1,182,000	$3,040	$207,884	$2.20	68.4

*This includes maternal and newborn lives saved, as well as demographic dividend and incentives

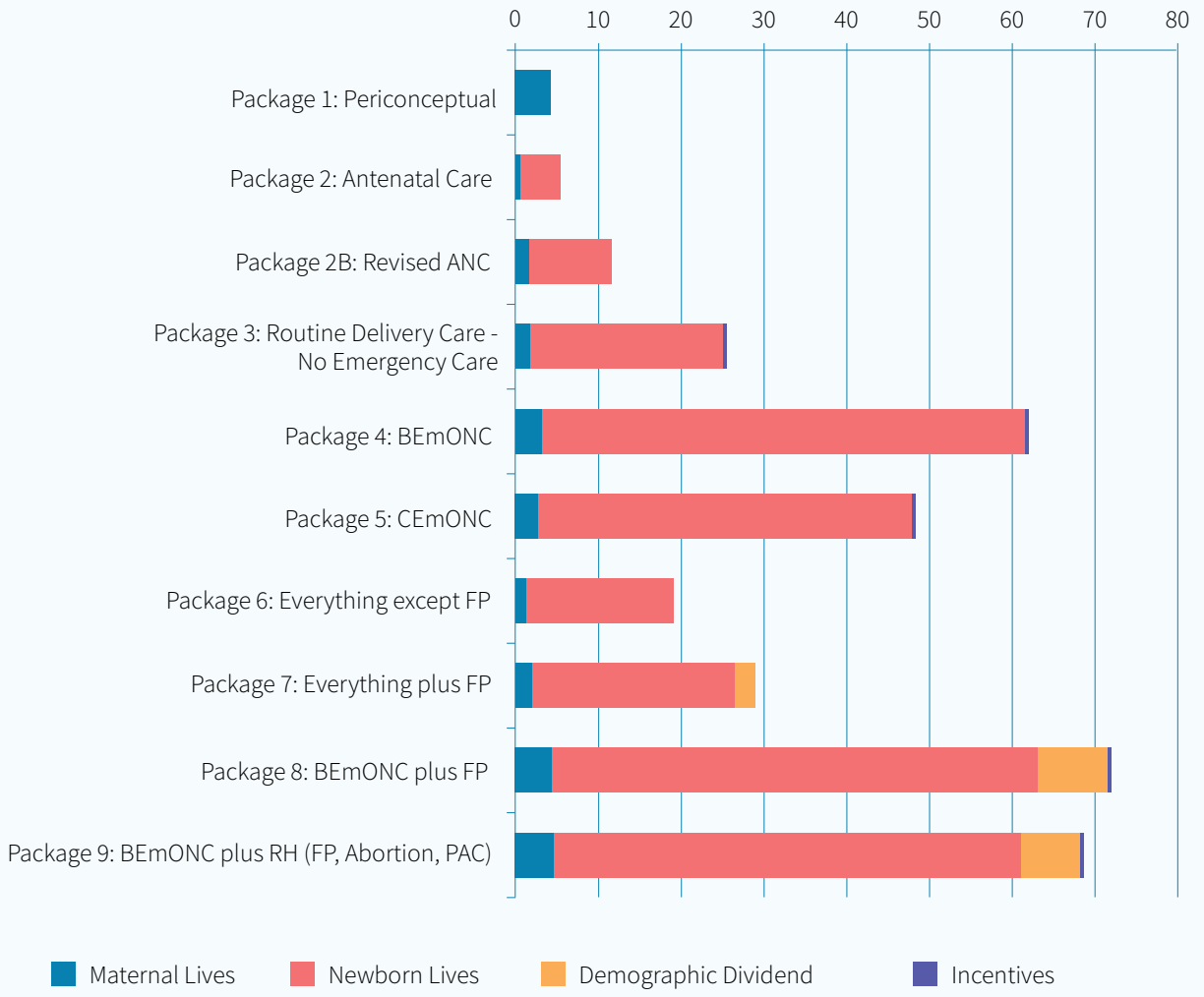
1 Taking an average over the course of 80 years, though in the short-term these impacts would be small.

Figure 3. Benefit-Cost Ratios for Interventions Delivered as Packages including Family Planning, Considering only Maternal Mortality and Morbidity



When combining the effects on mothers and newborns plus the demographic dividend, basic emergency obstetric and newborn care (BEmONC) was found to be the most cost-effective ***a priori*** package of interventions. This was followed by comprehensive emergency obstetric care and then routine delivery (Figure 6.) A visual inspection of these sets of results, combined with consideration of the types of cadres that deliver services (i.e. physicians and surgeons are required only for comprehensive emergency obstetric care, while midwives and community health workers can typically deliver basic obstetric care and family planning), suggested that a combined package of basic emergency obstetric care and family planning or basic emergency care, family planning and abortion care might be cost-effective. Among these broader packages, package 8, with family planning and basic emergency obstetric care was most cost-effective and had a slightly higher BCR than BEmONC alone. There was only a modest difference from package 9, which included basic emergency obstetric care, family planning and abortion services.

Figure 4. Benefit-Cost Ratios for Interventions Delivered as Packages including Family Planning, Considering Maternal and Newborn Mortality and Morbidity as well as Demographic Dividend



Packages Explained

Table 1 shows all the interventions analyzed, as well the composition of nine packages of interventions. Several of these packages were agreed a priori as packages which seemed sensible based on place or time of delivery (i.e., during antenatal care) (packages 1-7) or were identified as results of further analyses (packages 2B, 8 and 9), as presented below.

Once each of the individual analyses were done, the packages were created grouping those interventions that could be delivered at specific points in time (periconceptually, antenatally, as part of routine delivery care (clean birth environment, immediate drying and additional stimulation, thermal protection, clean cord care and controlled cord traction), basic emergency obstetric care (routine care plus antibiotics for preterm or prolonged premature rupture of membranes, parenteral administration of antibiotics, assisted vaginal delivery, neonatal resus-

citation, parenteral administration of uterotonics, removal of retained products of conception, induction of labor for pregnancies lasting 41+ weeks, and antenatal corticosteroids for preterm labor) or comprehensive emergency obstetric care (all childbirth interventions). Antenatal care attendance and facility delivery were not included as interventions per se but as delivery vehicles for the interventions when delivered as part of the packages. Finally, upon review of the results, additional packages were created which could be feasible to implement and which could maximize cost-effectiveness.

Detailed Analysis of Findings - Individual Interventions

The specific health and family planning interventions modeled were those that would be delivered to the mother over the course of her pregnancy, or to the mother and the baby during childbirth and are included in the Lives Saved Tool (see benefits below for details). We also scaled up coverage of family planning methods to meet 90% of need (current user + unmet need). Neither HIV-related interventions nor postpartum or child interventions were included in the analysis.

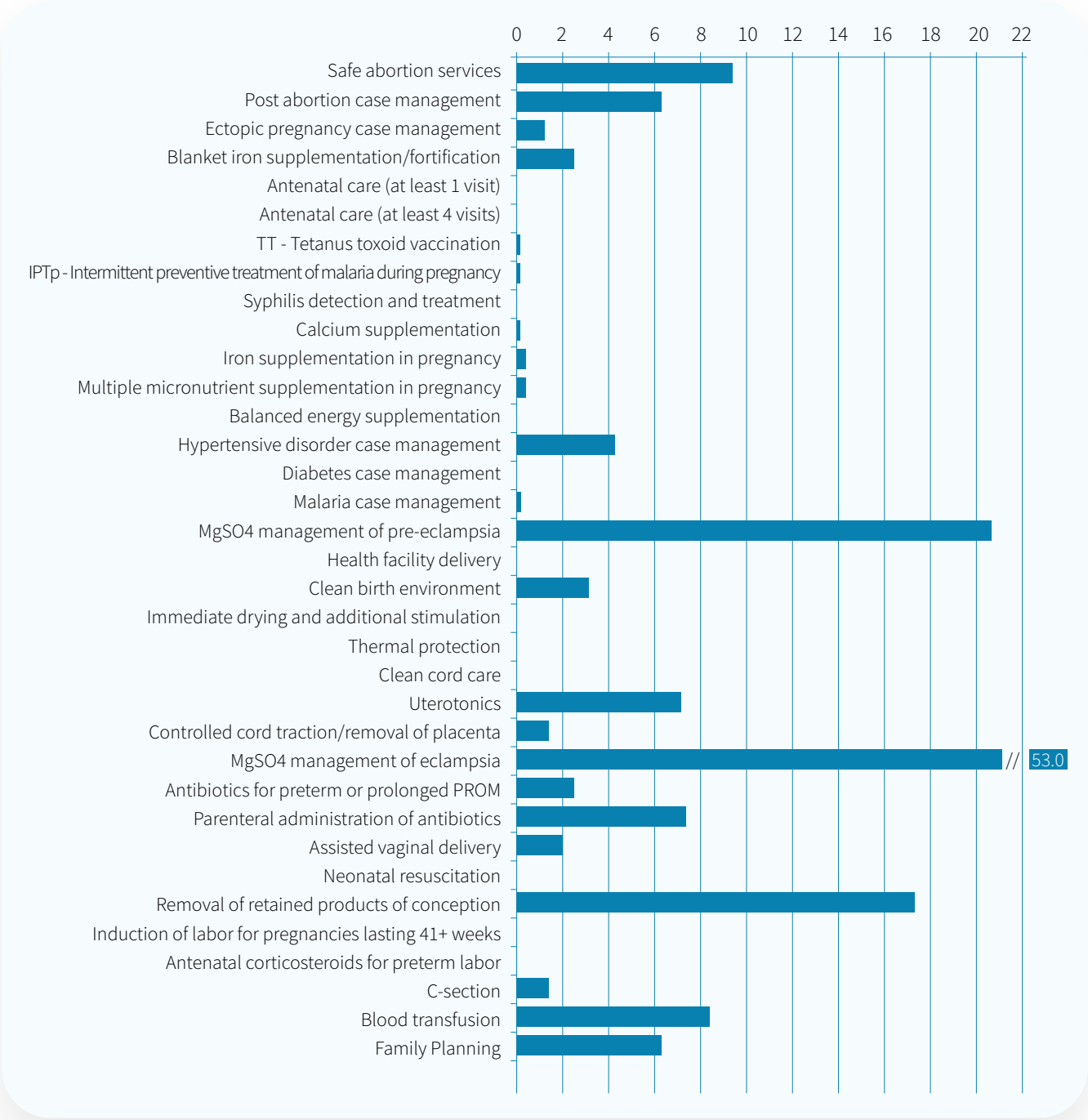
Scaling up individual health or family planning interventions to 90% coverage (or 90% of unmet need for family planning) was found to avert up to 87,000 maternal deaths or 357,000 newborns deaths annually, using a 2025 population (Table 3). However, these numbers cannot be added together to calculate the total number of deaths that could be averted by scaling up maternal health interventions as many interventions target the same deaths and causes of death.

Table 3. Potential Lives Saved by Interventions Delivered Individually

		Lives Saved			Additional Cost (Mio US$)	Cost per life saved (Th. US$)
		Maternal	Newborn	Stillbirths		
Periconceptual	Safe abortion†	14,000			$219	$16
	Post abortion case management	12,000			$135	$11
	Ectopic pregnancy case management	2,800			$163	$58
	Blanket iron fortification	16,000			$473	$30
Antenatal	Tetanus vaccination	100	12,000		$55	$5
	Intermittent preventive treatment of malaria	1,400	3,800	47,000	$269	$52
	Syphilis detection and treatment		5,900	6,600	$374	$63
	Calcium supplementation	7,900	39,000		$3,508	$75
	Iron supplementation in pregnancy	15,000			$1,194	$80
	Multiple micronutrient supplementation	21,000	80,000	182,000	$1,719	$17
	Balanced energy supplementation		14,000	134,000	$388	$28
	Hypertensive disorder case management	18,000		389,000	$240	$13
	Diabetes case management			21,000	$940	n/a
	Malaria case management	1,900			$397	$209
	MgSO4 management of pre-eclampsia	20,000		55,000	$60	$3
Childbirth	Clean birth environment	11,000	48,000		$232	$4
	Immediate drying and stimulation of newborn		49,000		$185	$4
	Thermal protection		58,000		$189	$3
	Clean cord care		60,000		$177	$3
	Uterotonics	26,000			$200	$8
	Controlled cord traction/removal of placenta	12,000			$496	$41
	MgSO4 for eclampsia	18,000			$21	$1
	Antibiotics for premature rupture of membranes	6,000	28,000		$147	$4
	Antibiotics	18,000	28,000		$154	$3
	Assisted vaginal delivery	8,600	177,000	722,000	$276	$1
	Neonatal resuscitation		152,000		$28	$<1
	Removal of retained products of conception	12,000			$49	$4
	Induction of labor for post-term pregnancies			50,000	$57	n/a
	Antenatal corticosteroids		357,000		$415	$1
	C-section	23,000	217,000		$919	$4
	Blood transfusion	30,000			$250	$8
Family Planning	Family Planning	87,000			$1,232	$14

Looking only at maternal deaths, benefit-cost ratio were calculated for each of the 31 individual health and family planning interventions listed above which can be delivered during pregnancy and childbirth (Figure 5). The most cost-effective individual intervention for mothers is the management of eclampsia with magnesium-sulfate, which had a benefit-cost ratio of 53. Second and third are the management of pre-eclampsia with magnesium sulfate during the antenatal period and removal of the retained products of conception, during childbirth. It should be noted that many of the interventions which are delivered during pregnancy and childbirth have no impact on maternal deaths but do have measurable effects on newborns and the fetus.

Figure 5. Benefit-Cost Ratios for Individual Interventions, Considering Maternal Mortality and Morbidity Only



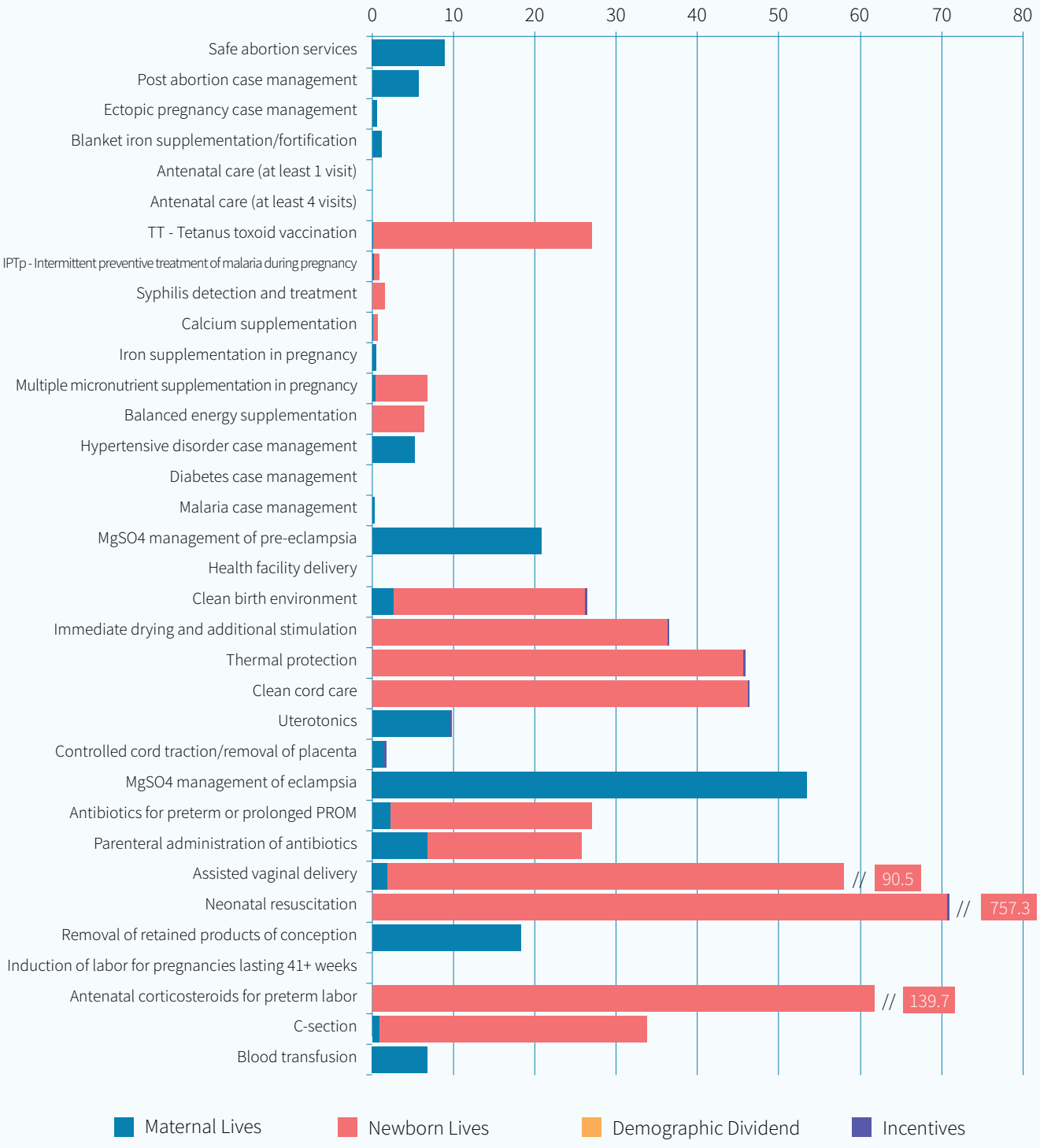
The four most cost-effective individual interventions when only maternal deaths averted were included were interventions that prevented deaths due to hypertensive diseases in pregnancy and hemorrhage (both intrapartum and postpartum), among the most common causes of maternal death. The other top interventions reduced mortality due to sepsis and abortion. Family planning led to a large decrease in the number of maternal deaths by preventing unintended and risky pregnancies.

Table 4. Top Ten Individual Benefit Cost Rations, Considering only Maternal Mortality and Morbidity.

	Maternal Lives Saved	Additional Costs (Mio. US$)	Additional Benefits (Mio. US$)	BCR
MgSO4 management of eclampsia	18,249	$21	$1,118	53.0
MgSO4 management of pre-eclampsia	20,129	$60	$1,250	20.7
Removal of retained products of conception	12,055	$49	$838	17.1
Uterotonics	26,117	$196	$1,818	9.3
Safe abortion services	14,283	$219	$1,997	9.1
Blood transfusion	30,353	$250	$2,114	8.5
Parenteral administration of antibiotics	18,212	$153	$1,174	7.7
Family Planning	86,522	$1,232	$7,793	6.3
Post abortion case management	12,275	$135	$833	6.2
Hypertensive disorder case management	18,308	$240	$1,156	4.8

When taking into account life-saving impacts on both mothers and their newborns, the most cost-effective individual intervention was neonatal resuscitation, an intervention requiring only an inexpensive, reusable hand-operated resuscitator and a health care provider. (Figure 6) The second and third most effective interventions were antenatal corticosteroids and assisted vaginal delivery. Although we also calculated estimates for stillbirths, these are not shown due to the controversy of how to consider them, since some could survive outside the womb while others may not. See the discussion section for additional consideration of antenatal corticosteroids.

Figure 6. Benefit-Cost Ratios for Individual Interventions, Considering Maternal and Newborn Mortality and Morbidity as well as Demographic Dividend



The interventions which were the most cost-effective for the combination of mothers and newborns reduced asphyxia, and to a lesser extent deaths due to prematurity or sepsis. (Table 5) These are among the most common causes of death in the 59 countries analyzed. It should also be noted that all of these interventions are delivered during the childbirth period, and are part of routine care, BEmONC or CEmONC.

Table 5. Top Ten Individual Benefit Cost Rations, Considering Maternal and Newborn Mortality and Morbidity as well as Demographic Dividident and Incentives.

Top ten Interventions	Lives Saved			Additional costs (Mio. US$)	Additional Benefits (Mio. US$)	BCR
	Maternal	Newborn	Stillbirths			
Neonatal resuscitation	0	152,385	0	$28	$21,267	751.2
Antenatal corticosteroids for preterm labor	0	356,647	0	$415	$57,828	139.5
Assisted vaginal delivery	8,552	177,416	722,076	$276	$25,492	92.4
Magnesium sulfate for eclampsia	18,249	0	0	$21	$1,118	53.0
Clean cord care	0	60,241	0	$177	$7,489	42.4
Thermal protection	0	57,890	0	$189	$7,859	41.6
Immediate drying and additional stimulation	0	48,726	0	$185	$6,594	35.7
C-section	23,319	216,876	0	$919	$32,145	35.0
Antibiotics	18,212	28,433	0	$154	$5,044	32.8
Clean birth environment	11,356	48,435	0	$232	$6,937	29.9

Country-specific results

Although we present these results in aggregate, each country will need to take into account the state of its health system when assessing the potential impact of these packages. In some settings, the staffing required to provide the interventions may be in place, while the medications and drugs might be in short supply, while in others, the opposite may be true. Both situations will affect the potential number of lives that can be saved as they will affect either the quantity or the quality of the intervention or package delivered. Any shortfalls in staff, drugs or supplies needed will either make it difficult for a country to achieve the 90% target coverage rate or reduce the quality and thus the impact of the intervention provided.

The results presented above represent the composite results for all 59 countries under evaluation in this analysis. Country-specific results were generated, although they are not presented specifically here as it was not feasible to dive into country-specific data on the specific costs, and thus the results may be imprecise at a country level. However, a few observations can be made. First, the most cost-effective package was family planning combined with basic emergency obstetric care. However, this result was not different than the cost effectiveness for a package

of family planning, abortion and post-abortion services and basic emergency obstetric care. For countries where abortion is legal, it would be prudent to consider this as part of the most cost-effective package.

Regional analysis also showed that the countries which are likely to be the most cost-effective to implement in, are those which have the highest human development index. This counterintuitive result may be a factor of the underlying analysis, or it may be the impact of having higher levels of current contact with women and children, requiring less intensive scale up. These options should be considered whenever an implementation based on these results is contemplated.

The cost-effectiveness results were also assessed based on the HDI (Health Development Index) of the different countries[30] (Table 6). In all cases, the most cost-effective interventions were in higher HDI countries, likely because the incremental increase relates to increases in the range of services delivered rather than increases in contacts between women and health care providers. An additional reason is that the monetized benefits of lives saved were estimated based upon country-specific Gross National Income (GNI) per capita, resulting in higher benefits for countries with higher GNI per capita, the same countries as have higher HDI values.

We additionally assessed cost-effectiveness when categorizing countries by population size and by region (Africa, Asia and Other). No notable differences were found that would alter the suggestions from the national analysis (Table 7). The only interesting point is that both family planning and periconceptual interventions were most cost-effective in Africa, relative to in other areas, suggesting that if packages need to be implemented, perhaps implementing these packages in Africa and then adding in basic emergency obstetric care would be more efficient than in other areas where BEmONC might be implemented first, and then family planning and reproductive health added on. This could be due to regional differences in baseline fertility and unmet need, resulting in a higher than average benefit in the Africa region.

Table 7. Average BCRs according to Region, Population Size and Human Development Index*

	Family Planning	Package 1: Periconceptual	Package 2: Antenatal Care	Package 2B: Revised ANC	Package 3: Routine Delivery Care - No Emergency Care	Package 4: BEmONC	Package 5: CEmONC	Package 6: Everything except FP	Package 7: Everything plus FP	Package 8: BEmONC plus FP	Package 9: BEmONC plus RH (FP, Abortion, PAC)
All Countries	$26.79	$4.32	$5.18	$12.06	$24.30	$61.53	$48.10	$19.15	$28.81	$71.47	$68.38
All Africa	$28.16	$6.23	$4.39	$10.59	$19.23	$46.23	$35.56	$14.54	$27.12	$64.39	$63.11
All Asia	$28.21	$3.12	$5.83	$14.12	$36.57	$100.99	$68.50	$23.48	$27.93	$82.30	$74.00
All other	$55.75	$2.15	$2.35	$6.29	$9.15	$23.39	$18.01	$8.29	$20.06	$43.43	$41.19
20 largest	$24.86	$4.17	$5.64	$13.57	$32.57	$88.25	$61.04	$21.67	$27.71	$77.14	$70.65
19 middle	$40.45	$3.99	$2.89	$7.53	$14.96	$34.63	$27.18	$10.44	$22.68	$58.78	$57.17
20 smallest	$99.94	$3.91	$3.67	$9.36	$19.56	$49.05	$34.14	$13.52	$39.89	$93.68	$91.06

Middle/High HDI	$27.81	$3.33	$5.80	$14.23	$35.61	$99.82	$67.40	$23.37	$28.88	$83.78	$75.87
Low HDI	$30.80	$6.15	$4.02	$9.29	$17.26	$35.95	$30.12	$12.51	$24.19	$55.60	$54.81

* Considering both Maternal and Newborn Mortality and Morbidity

Methods

Overall

In order to estimate the cost-effectiveness of 31 of the most high-impact maternal health interventions and family planning, we constructed a cost-benefit model that looked at the scale-up of these services from current coverage levels to 90% coverage in the 59 countries suffering from the highest burden of maternal morbidity and mortality. Costs included were for providing the interventions (specifically, health care provider salaries, drugs, medical supplies and clinic overhead), the cost to women of accessing the care (travel cost, lost time/productivity) as well as the cost of incentives assumed necessary to stimulate demand for these services. Benefits included were lives saved and averted morbidity and treatment costs along with any potential incentives. They were converted into international dollars and juxtaposed with the cost of the different interventions. Final results are presented as benefit-cost ratios (BCR).

Scenarios

We created multiple individual scenarios for 59 of the highest burden countries and formulated the analysis similarly to Bartlett et al's paper[31] assessing the impact of health and family planning interventions delivered by midwives and doctors on maternal and newborn deaths and stillbirths. For each country, we scaled up each of the 31 interventions and family planning (Table 1 and Annex 2) separately and independently to full coverage (90%), unless coverage was already above 90%, in which case the coverage level was kept constant. The analysis was run over a 5-year time period in order to ensure that the full effect of the interventions was achieved, as is standard for Lives Saved Tool (LiST) analyses affecting children; however, the final analysis only reports on the impact in the fifth year, in this case 2025. Family planning was scaled up to the point where unmet need for family planning services was 90% satisfied.

Once each of the individual analyses were done, we also created packages of interventions, specifically packages that could be delivered at specific points in time (periconceptually, antenatally, as part of routine delivery care (clean birth environment, immediate drying and additional stimulation, thermal protection, clean cord care and controlled cord traction), basic emergency obstetric care (routine care plus antibiotics for preterm or prolonged premature rupture of membranes, parenteral administration of antibiotics, assisted vaginal delivery, neonatal resuscitation, parenteral administration of uterotonics, removal of retained products of conception, induction of labor for pregnancies lasting 41+ weeks, and antenatal corticosteroids for preterm labor) or comprehensive obstetric care (all childbirth interventions). Antenatal care attendance and facility delivery were not included as interventions per se but as delivery vehicles for the interventions when delivered as part of the packages. Finally, upon review of the results, additional packages were created which could be feasible to implement and which could maximize cost-effectiveness.

Costs

In order to estimate the cost-effectiveness of the different interventions and intervention combinations, we calculated the cost of providing the interventions, from the provider as well as the woman's perspective and added in costs of demand generation.

Provider costs

Costs were calculated using bottom-up costing, with detailed lists drawn up detailing the needs for drugs, supplies and medical staff time required per case for each of the interventions. Treatment was based on most recent World Health Organization (WHO) guidelines[32,33]. Drugs and supplies were costed based on prices in the United Nations Children's Fund (UNICEF) supply catalogue[34]. For each intervention, the types of medical staff and time required to provide the intervention were estimated and then multiplied by country-specific salaries, taken from WHO's CHOICE database[35], updated to 2018 dollars. A facility overhead cost was added to each cost per case estimate, again using WHO CHOICE data and based on the length of a woman's interaction with the health system. For ambulatory care provided at the health center level, costs were calculated for the length of the individual visits, while for hospital stays, overhead cost was calculated per day of hospitalization[36]. It was assumed that all outpatient maternal interventions, such as antenatal care, would be provided at the health center (no beds) level, while all delivery-related intervention would take place at a primary-level hospital able to carry out emergency obstetric care (EmOC) functions.

Finally, 15% were added to the direct cost of service provision for supervision, a critical activity required to ensure that services are provided according to national standards and with high quality.

Social costs

In addition to provider costs, we also included the social costs to women accessing this care. Based on the small number of studies available on the topic[37,38], travel times to health centers and hospitals were estimated for women in both rural and urban areas. We assumed a trip to the health center would take 30 minutes (round trip) in urban areas, 1 hour in rural areas and trips to a hospital/EmOC facility would take 1 and 4 hours respectively. These times were then multiplied by a factor of 3 (health center) and 2 (hospital), respectively, to account for often substantial waiting time at the health facilities. The time was monetized using country-specific GNI per capita[39], converted to an hourly value assuming an annual 2,000 work hours (50 work weeks x 40 hours).

Demand generation

To account for the cost of stimulating demand and care seeking, we included the cost of a financial incentive program for deliveries at facilities, based on recent success with this kind of program in India and other countries. We included costs for the 37 countries whose current delivery rate at facilities was below 70%, and which we assumed would benefit from incentives to get that rate up to the target rate of 90%. Based on India's conditional cash transfer program as described in Randive B et al[40], we assumed that all women living under the national poverty level in these 37 countries would be entitled to an average incentive of 0.35% of GDP per capita for delivering at a facility. The cost of incentives was calculated for the entire total eligible population, not just the additional deliveries estimated under the scale-up scenario. In addition to the cost of the incentives, we added a 30% add-on cost for the administration of the program.

Service provision and cost to women were calculated for each intervention separately, and then also in the context of interventions being delivered as packages, which substantially reduced the number of visits, staff and travel time required. For details, see spreadsheet model[41].

Benefits

Four types of benefits linked to the scaling up of the health interventions were included in the analysis: a) lives saved; b) morbidity and treatment costs averted; c) the incentives paid to the women accessing institutional deliveries; and d) demographic dividends.

Lives saved

Lives saved were calculated using the using the Lives Saved Tool (LIST), a module within the Spectrum suite of modelling tools (including FamPlan (family planning) and AIM (the AIDS impact model)), which projects the number of maternal, newborn, and child deaths and stillbirths that would be saved through an increase in coverage of individual health interventions. The module uses the most recent available data on women's health status (mortality and nutrition), causes of death and cause-specific effectiveness of the different interventions. Then, based on the current coverage of each intervention and the target coverage, the model calculates the most likely change in causes of deaths and nutrition, and assigns those deaths averted to a specific intervention, based on relative coverage change for all interventions scaled up along with the cause-specific effectiveness of the intervention. For additional details, see Annex 3. All analyses were done in Spectrum 5.8[42].

To put a value on the number of lives saved, we used the value of a statistical life approach. The value of a statistical life lost due to the death of a woman in pregnancy or childbirth has two components, a) an economic one, which represents the contribution to the economy a women would have made through the production of goods or services if she hadn't died and b) the social value of her life – as a woman, mother, member of her family and community.

To put a dollar value on the lives lost we used the approach recommended in the ***Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development.***[43] We used the current Value of a Statistical Life in the US (of roughly $10 million per life saved in 2018 dollars), which we then converted to different country-specific values based on the PPP GNI per capita relationship of the respective countries to the US[44].

VSL Country A = VSL US x (GNI per capita Country A/GNI per capita US) ^ Elasticity of 1.5

The value of a life-year saved (VSLY) was then calculated by dividing the Value of a Statistical Life (VSL) by the difference between the average population age and life expectancy[45].

Maternal lives saved were valued by multiplying the value of a statistical life-year with half the life expectancy at birth (a proxy for average remaining life expectancy at maternal death) while newborn lives saved were monetized multiplying the VSLY by the average life expectancy at birth. Stillbirths are not valued in this cost-benefit analysis due to uncertainty surrounding the willingness-to-pay to avoid a stillbirth.

Treatment costs averted

We also included an estimate of the number of pregnancy and delivery complications averted by interventions where applicable. They were monetized using treatment costs averted for those interventions included in this analysis and using monetized disability-adjusted life years (DALYs) for sequela that fell outside of the 31 interventions (such as infertility). Family planning in particular has a significant impact on the incidence of maternal complications and deaths, especially in countries with high maternal mortality rates, by reducing the number of wom-

en who become pregnant and are thus exposed to the risk of dying in pregnancy and childbirth in the first place. Other key interventions that reduce the burden of maternal morbidity and mortality are the active management of the third stage of labor with uterotonics, which is highly effective at reducing the chances of women of developing postpartum hemorrhage and severe anemia, as well as safe abortion services, which not only save lives but also prevent women from suffering from long-term complications that might affect quality of life, such as infertility and pelvic inflammatory disease (PID).

Treatment Costs Averted = Cases averted x treatment cost per case

Morbidity cost of sequelae such as anemia and infertility = Disability-Adjusted Life Years Saved x Value of a Life-Year Saved

Incentives

The incentives paid to women to encourage them to give birth at facilities equipped to provide safe and clean delivery services and giving them access to life-saving emergency obstetric care when needed, constitute a cost (to the government) as well as a benefit to the women who receive them. The money they receive can be spent on travel to the facility, coverage of any potential treatment costs and any additional purposes as needed.

Other benefits

Family planning not only reduces the incidence of maternal deaths by preventing unintended or risky pregnancies, it also has effects that go beyond the individual level, affecting societies as a whole. Examining the ways in which family planning can affect economic growth especially in low- and middle-income countries, Ashraf et al.[46] found that a reduction in fertility can lead to a potentially significant increase in income per capita. Table 6 below spells out some of the pathways through which this can happen. One of the best known is the so-called Malthus effect – reducing the size of the population will ease the strain on limited resources, such as land and food. Several of the pathways interact with the age-structure of the population which is in turn based on past fertility and mortality rates. If fertility rates decline, children make up a lower share of the total population, decreasing the dependency effect, increasing available income per family and society overall. A higher proportion of the total population in the workforce leads to higher productivity and savings. Having fewer children lowers the amount of time women spend on childrearing, freeing their time to participate in the labor market. When families have fewer children, they also have more money available to spend on any individual's health and education.

Table 6. Summary of potential impacts of fertility reduction on economic growth

Malthus effect	Congestion of fixed factors such as land
Solow effect	Capital shallowing
Age-structure effects:	
Dependency effect	Higher ratio of working age population to dependents (in particular, fewer children) Even if income per worker stays constant – increase in available income per household and overall income
Life-cycle savings effect	Higher number of people in the workforce leads to > higher capital accumulation and output > raise in national savings
Experience effect	Age distribution of workers shifting towards older, more experienced workers

Life-cycle labor supply effect	Higher overall labor participation (particularly of women, see childcare effect)
Childcare effect	Lowers the amount of time devoted to childrearing, freeing up time for productive labor
Child-quality effect	Increase in parental investment in education per child
Health improvement effect	Similar to education, shift from quantity to quality (with fewer children, parents can spend more on health care per child)

Applying their model to Nigeria, Ashraf et al. found that a sustained decrease in total fertility rate by 0.5 lead to an increase in the GDP per capita of 5.6 percent after twenty years, and 11.9 percent after fifty years.[47] We use this relationship to project the boost to GDP per capita across the 59 countries analyzed in this study. Baseline GDP and population projections until 2070 were sourced from the UN's middle-of-the-road scenario under the Shared Socio-economic Pathways.[48] We assume the % reduction in total fertility rate from the scale up of family planning, is the equal to the % reduction in annual births from the LiST output. From there we project the intervention scenario GDP per capita using the reported relationship between TFR and GDP per capita output from Ashraf et al. with linear interpolation between years 2020-2040 (from 0 percent to 5.6 percent) and then from years 2041-2070 (from 5.6 percent to 11.9 percent). The demographic dividend benefit is simply:

Demographic Dividend Benefit = Population * GDP per capita boost

This is estimated for every year and the net present value is calculated using a country-specific discount rate equal to two times the average of the first five years of growth following recommendations in ***Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development.***[49] For the purposes of this report, we use the annualized value over 50 years in the cost-benefit analysis.

Limitations and Methodological considerations

This analysis, combining the impacts estimated by the Lives Saved Tool with detailed costing profiles, must be considered in light of the limitations of each methodology. The Lives Saved Tool is a linear tool which estimates the impact an increase in coverage of an intervention has on the number of lives saved based on the assumption that all necessary drugs and supplies needed to provide the intervention are available and effective, that appropriate providers are available and well trained, that health facilities have all required equipment, water and electricity and that the intervention is delivered according to standard treatment guidelines. The costing uses the same assumptions and costs out all inputs required to provide an intervention based on WHO guidelines, using the same treatment assumptions for all countries. An in-depth assessment of individual health systems and their current facility and staff shortcomings in the 59 countries covered and a costing of the resources required to remedy the gaps was beyond the scope of this study. The costing thus assumes that countries have the facilities and staff to provide the interventions included in this study and costs out the inputs required to provide the intervention in a functioning setting. The cost of a C-section, for instance, includes the costs of the anesthesia, drugs and medical supplies required plus the time of an obstetrician and other staff needed to provide proper care before, during and after the procedure as well as overhead cost of the facility (including amortized building and equipment cost). Not included is the cost of training the obstetrician or any initial investment cost to scale up the number of EmOC facilities in a country.

It should also be recognized that LiST only includes those health interventions whose live-saving impacts have been proven and quantified across multiple settings. Other interventions, which might be highly recommended as they might improve quality of life or increase the attendance of individuals at care, are not part of LiST, which

focuses on interventions that have an impact on mortality. While antenatal care, for instance, has been shown to increase facility-based delivery, that impact is not modeled in the LiST tool. In addition, other interventions may exist which have similar impacts that are not currently analyzed in LiST.

An example is the use of heat-stable carbetocin (HSC), which has recently been recommended by WHO as an alternative to oxytocin for the prevention of post-partum hemorrhage. Carbetocin has the advantage over oxytocin that it is heat-stable, which means it does not need a functioning cold chain, which makes the drug much easier to deliver to hard to reach rural areas which have the highest burden of maternal mortality. Several recent studies have shown that oxytocin and other uterotonics that need refrigeration are often not reliably effective due to transport and storage problems. At the current price point of $20 a dose, carbetocin, however, is still at least 50 times the cost of the more widely used oxytocin, which makes it not competitive even when considering its potentially higher effectiveness. In a recent agreement with WHO, though, the producers of the drug committed to providing carbetocin to low- and lower-middle income countries at a subsidized “Access Price” similar to the price at which UNFPA procures oxytocin, which would make carbetocin as cost-effective, if not more cost-effective than oxytocin.

One of the most cost-effective interventions for newborns was antenatal corticosteroids (See Table 5), which are given to women who are in pre-term labor, in order to mature the lungs and prevent respiratory distress in the newborn. Although this intervention has been widely used globally in both humans and animals for more than 50 years, recent analyses suggest that it may be less beneficial in places with lower human and physical resources and less oversight[50]. As a result, it is no longer included in the Lives Saved Tool as a standard intervention. We included it in this analysis due to the high potential benefit and the assumption that any implementation based on these results would incorporate the high level of resources needed to deliver corticosteroids in a safe and effective manner. Excluding this intervention would reduce the cost-effectiveness of all of the packages which include basic emergency obstetric care, but would not affect the ranking of the packages, as corticosteroids are included in all of the most effective packages.

An additional limitation to this study is the uncertainty around the underlying incidence of several of the conditions. For example, reputable sources indicate that incidence of eclampsia could range from 0.11% to 1.4% of all births, while incidence of severe pre-eclampsia could range from 0.75 to 4.6%[51]. These have notably different implications for the cost-effectiveness of interventions which affect deaths due to hypertensive diseases in pregnancy; sensitivity analysis (data not shown) around these values on the final packages (as opposed to the individual intervention) had no noticeable impact on the package cost-effectiveness. This suggests that while tailoring of the results to a country specific context, where better data may be available, it may also not be necessary for decision making at broader levels.

Although the cost-effectiveness results presented were calculated both in aggregate for the 59 countries, and individually for each country, we have chosen to only present the aggregate in this analysis. Many countries do not have complete data available on either costs or benefits of scaling up maternal health interventions, leading to wide uncertainty around country-specific results. A more local analysis could perhaps pinpoint additional unexpected areas of gain, however this would not be reliable without more local and tailored data. In general, however, the results from individual analyses were similar to those presented at the aggregate level (data not shown). Regional analysis also showed that the countries which are likely to be the most cost-effective to implement in, are those which have the highest human development index. This counterintuitive result may be a factor of the underlying analysis, or it may be the impact of having higher levels of current contact with women and children, requiring less intensive scale up. These options should be considered whenever an implementation based on these results is contemplated.

It is critical to note that this analysis explicitly does not include the likely additional benefits of antenatal care processes on increasing trust in the health system and increasing access to safe delivery care. Significant amounts of cross-sectional data across Asia and Africa, among other settings, demonstrate that women who attend antenatal care are more likely to deliver in a facility or with a skilled attendant[52]. A much smaller body of evidence, using regression techniques and propensity score analyses[53], confirms these results, but do not yet reach a high level of confidence in causation rather than correlation. One review including data from Zambia, Laos and Mali[54], and confirmed in later research in Ghana[55] suggested that a key factor may be lack of information about labor and delivery, which antenatal care has the ability to improve. But as always, the evidence is not strong enough to assume causation. If true, the cost-benefit results presented for antenatal care would be much stronger than they appear in this analysis.

A separate, but relevant point is that if women have positive experiences delivering in a facility, then they are likely to do the same for a future pregnancy, so the positive impact of increased antenatal care attendance and increased quality of antenatal care may be long lasting, throughout a woman's reproductive life. Both qualitative and quantitative studies point to this impact. The inverse has already been shown. Poor quality care, including abuse, at antenatal care leads to lower rates of facility delivery, while positive experiences lead to women seeking out the same provider at a later point in time[56].

ANNEXES

ANNEX 1: DESCRIPTION OF KEY MATERNAL AND NEWBORN INTERVENTIONS

Selected Interventions with highest impact on maternal mortality

Below we present a brief description of the key interventions impacting maternal mortality.

	Name Used in this Report
1	Management of pre-eclampsia with magnesium sulfate
2	Removal of retained products of conception
3	Management of eclampsia with magnesium sulfate
4	Management of third stage of labor with uterotonics
5	Safe abortion services
6	Blood transfusion
7	Management of maternal sepsis
8	Post abortion case management
9	Family Planning
10	Hypertensive Disorder Case Management

1. Management of Pre-eclampsia with Magnesium Sulfate

Condition requiring this Intervention

Hypertensive disorders of pregnancy are an important cause of severe morbidity, long-term disability and death among both mothers and their babies. In Africa and Asia, nearly one tenth of all maternal deaths are associated with hypertensive disorders of pregnancy, whereas one quarter of maternal deaths in Latin America have been associated with those complications. Among the hypertensive disorders that complicate pregnancy, pre-eclampsia and eclampsia stand out as major causes of maternal and perinatal mortality and morbidity. The majority of deaths due to pre-eclampsia and eclampsia are avoidable through the provision of timely and effective care to the women presenting with these complications.
World Health Organization. 2011. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia.

Description of Intervention

Magnesium sulfate (MgSO4) has been used throughout the 20th century for prevention of eclamptic seizures and continues to be used extensively. Empirical evidence supports the effectiveness of MgSO4 in preventing and treating eclamptic seizures, in addition to recent controlled clinical trials. For eclamptic seizure prophylaxis in preeclamptic women, MgSO4 is superior to phenytoin, nimodipine, diazepam, and placebo. In the multinational Collaborative Eclampsia Trial, MgSO4 reduced the risk of recurrent seizures in eclamptic women by 52% when compared to diazepam and by 67% when compared to phenytoin.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2663594/

Magnesium sulfate is administered through injections and on an IV. Delivery should be induced as soon as possible.

Need
Pre-eclampsia affects approximately 1% of pregnant women.

Treatment Guidelines
WHO. 2017. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed. P. S-57
WHO. 2015. Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice – 3rd ed., B-13

NOTE: It should be noted that interventions 1 and 2 in this list both use magnesium sulfate. However, they are delivered at different locations (i.e. during ANC for severe pre-eclampsia and during childbirth for eclampsia) as well as for slightly different indications. When given for pre-eclampsia, the goal is to prevent the development of convulsions and signs of eclampsia, given for eclampsia, it is given as a first-line treatment for convulsions in order to prevent direct mortality.

2. Treatment of Eclampsia with Magnesium Sulfate

Condition requiring this Intervention
Eclampsia: convulsions occurring ante-, intra- or postpartum, associated with high blood pressure and proteinuria.

Description of Intervention
Magnesium sulfate administered through injections and IV.

Need
Eclampsia occurs in about 0.5% of all deliveries

Treatment Guidelines
WHO. 2017. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed. P. S-57
WHO. 2015. Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice – 3rd ed., B-13

3. Removal of Retained Products of Conception

Condition requiring this Intervention
Retained products of conception are common complications after abortion or delivery. Postpartum RPOC may cause short-term complications such as massive vaginal bleeding or endometritis. They are also associated with the development of intrauterine adhesions (IUAs), secondary infertility, recurrent abortions, and other placental pathologies.

Description of Intervention
Evacuation of retained products of conception involves the removal of any remaining products of conception that are still inside the uterus following a miscarriage, termination of pregnancy or childbirth. This is usually done by manual vacuum aspiration.

Need
Approximately 1% of women will require this intervention.

Treatment Guidelines
WHO. 2015. Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice – 3rd ed.p. B-11

4. Uterotonics

Uterotonics are one of the key components of Active management of the third stage of labor (AMTSL), which includes the administration of uterotonics, along with uterine massage and controlled cord traction designed to lead to the expulsion of the placenta after delivery of the child. Evidence suggests that the majority of the benefits of AMTSL is derived from the uterotonics component.

Condition requiring this Intervention
All women who deliver should receive this intervention.

Description of Intervention
Active management of the third stage of labor involves giving a prophylactic uterotonic, early cord clamping and controlled cord traction to deliver the placenta. Oxytocin is the most commonly used uterotonic agent and the primary drug of choice for the management of the third stage of labor and the one evaluated in this report. Prophylactic administration of oxytocin (Pitocin) reduces rates of postpartum hemorrhage by over 77 percent.

Need
WHO recommends that all women giving birth receive a dose of a uterotonic (oxytocin, ergometrine/methylergometrine, carbetocin or misoprostol) as part of the active management of the third stage of labor.

Treatment Guidelines
WHO. 2015. Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice – 3rd ed., p. D-12

5. Safe Abortion

Key Facts on Unsafe Abortion and Abortion Complications

- Between 2010–2014, on average, 56 million induced (safe and unsafe) abortions occurred worldwide each year.
- There were 35 induced abortions per 1000 women aged between 15–44 years.
- 25% of all pregnancies ended in an induced abortion.
- The rate of abortions was higher in developing regions than in developed regions.
- Around 25 million unsafe abortions were estimated to have taken place worldwide each year, almost all in developing countries (1).
- Among these, 8 million were carried out in the least- safe or dangerous conditions.
- Over half of all estimated unsafe abortions globally were in Asia.
- 3 out of 4 abortions that occurred in Africa and Latin America were unsafe.
- The risk of dying from an unsafe abortion was the highest in Africa.
- Each year between 4.7% – 13.2% of maternal deaths can be attributed to unsafe abortion (2).
- Around 7 million women are admitted to hospitals every year in developing countries, as a result of unsafe abortion (3).
- The annual cost of treating major complications from unsafe abortion is estimated at US$ 553 million (4).
- Safe abortion must be provided or supported by a trained person using WHO recommended methods appropriate for the pregnancy duration.
- Almost every abortion death and disability could be prevented through sexuality education, use of effective contraception, provision of safe, legal induced abortion, and timely care for complications (5).

Source: https://www.who.int/news-room/fact-sheets/detail/preventing-unsafe-abortion

Condition requiring this Intervention
Abortions are safe if they are done with a method recommended by WHO that is appropriate to the pregnancy duration and if the person providing or supporting the abortion is trained. Such abortions can be done using tablets (medical abortion) or a simple outpatient procedure.

Unsafe abortion occur when a pregnancy is terminated either by persons lacking the necessary skills or in an environment that does not conform to minimal medical standards, or both. The people, skills, and medical standards considered safe in the provision of induced abortions are different for medical abortion (which is performed with drugs alone), and surgical abortion (which is performed with a manual or electric aspirator).

Need
We assumed that 1% of women having induced abortions under safe conditions and 42% of women having induced abortions under unsafe conditions have complications requiring medical treatment.[57]

6. Blood transfusion

Condition requiring this Intervention

Deliveries involving excessive blood loss (hemorrhage)

Need
An estimated 6.5% of women delivering will experience post-partum hemorrhage and require a blood transfusion.

Description of Intervention
2 liters of blood plus 2 liters of Ringer's lactate.

Treatment Guidelines
WHO. 2015. Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice –3rd ed.p. B-11

7. Parenteral administration of antibiotics

Condition requiring this Intervention
Bacterial infections around the time of childbirth account for about one tenth of the global burden of maternal death. Although the majority of these deaths are recorded in low-income countries, childbirth-related infections are also an important direct cause of maternal mortality in high-income countries. Apart from severe morbidity and death, women who experience peripartum infections can experience long-term disabilities such as chronic pelvic pain, fallopian tube blockage and secondary infertility. Maternal infections before or during childbirth are also associated with an estimated 1 million newborn deaths annually.
WHO. 2015. WHO recommendations for prevention and treatment of maternal peripartum infections.

Description of Intervention
IV antibiotics

Need
An estimated 2.5% of deliveries require management of sepsis.

Treatment Guidelines
WHO. 2017. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed. P. S-49

8. Family Planning

Current use of family planning
% of women of reproductive age (age 15-49) using modern and traditional family planning methods based on LiST model/most recent DHS data.
Methods included:

- Condoms
- Pills
- Injectables
- Implants
- IUD
- Female sterilization
- Male sterilization
- Traditional methods such as periodic abstinence, withdrawal

Projected need for family planning
Projected need for family planning was estimated as current % of women using plus 90% of Unmet need for family planning.

Unmet need for family planning is defined as the percentage of women of reproductive age, either married or in a union, who have an unmet need for family planning. Women with unmet need are those who are want to stop or delay childbearing but are either using an ineffective/traditional method or no method of contraception.

9. Management of Abortion Complications (PAC)

Condition requiring this Intervention
Women experiencing complications from unsafe abortions

Need
Based on information from country studies conducted between 2008 and 2012 in Colombia, Ethiopia, Rwanda and Uganda, we estimated that 82.3% of women requiring care for complications of induced abortion have incomplete abortion, 6.8% of patients require treatment for shock, 4.5% require care for uterine perforation and/or cervical lacerations and 15.2% have sepsis. The percentages sum to more than 100% because some women need care for more than one of these complications. [58]

10. Hypertensive Disorder Case Management

Condition requiring this Intervention
Hypertensive disorders of pregnancy (HDP) represent a group of conditions associated with high blood pressure during pregnancy. Women with pregnancy-induced hypertension disorders may progress from mild disease to a more serious condition such as pre-eclampsia and eclampsia.

Description of Intervention
Weekly monitoring for blood pressure and proteinuria for women showing signs of hypertension. Assumption that hypertensive disorders of pregnancy are usually discovered around week 35 of a pregnancy, with the average woman with hypertension needing four monitoring visits through the end of pregnancy.[59]

Need
An estimated 2.5% of women require this treatment.

Treatment Guidelines
WHO. 2017. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed. P. S-55

Selected additional Interventions with high impact on maternal and newborn mortality

Two additional interventions of interest are described below, to facilitate understanding of these interventions.

1. Neonatal Resuscitation

Condition requiring this Intervention
Neonatal resuscitation also known as newborn resuscitation is an emergency procedure focused on supporting the approximately 10% of newborn children who do not readily begin breathing, putting them at risk of irreversible organ injury and death.

Description of Intervention
Positive pressure ventilation with a mask and self-inflating bag. The average cost of equipment was estimated as the total cost divided by average caseload of a midwife (50 births per year).

Need
An estimated 3% of newborns experience asphyxia or other breathing difficulties.[60]

Treatment Guidelines
WHO. 2017. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed. P. S-167

2. Antenatal corticosteroids for preterm labor

Condition requiring this Intervention

Preterm birth is defined as live births occurring before 37 completed weeks of gestation.1 An estimated 14.9 million neonates were born preterm in 2010, accounting for 11.1% of live births worldwide.2 The majority of all preterm births occur in the late preterm period (34 to <37 weeks)—for example, in the USA more than 70% of preterm births in 2014 were born in the late preterm period.3 It is estimated that more than 60% of the world's preterm births occur in sub-Saharan African and South Asian countries.

Prematurity can be a lethal condition, particularly for those newborns born at earlier gestational ages. Complications of preterm birth are the leading cause of death in children under 5 years of age globally, accounting for 1.06 million deaths (uncertainty range 0.935 to 1.179 million) of the 5.9 million deaths estimated to have occurred in 2015. Those preterm neonates who survive are at increased risk of a wide range of respiratory, infectious, metabolic and neurological morbidities. Preterm infants experience higher rates of respiratory distress syndrome, bronchopulmonary dysplasia, necrotising enterocolitis, kernicterus, hypoglycaemia, periventricular leucomalacia, seizures, intraventricular haemorrhage, cerebral palsy, infections, feeding difficulties, hypoxic ischaemic encephalopathy, retinopathy of prematurity, as well as visual and hearing loss. Preterm birth and its sequelae can have significant negative psychosocial and financial impacts on families of preterm newborns. (Adding It Up 2018)

Intervention Description

Corticosteroid administration before anticipated preterm birth. Treatment consists of two doses of betamethasone 12 mg IM, 24 hours apart, and if necessary, expedited birth.

Need

WHO. 2017. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed. P. S-63

ANNEX 2: INTERVENTION NAMES IN LiST

The intervention names in the LiST model are geared towards the scientific community and are not necessarily obvious to a more general public. We here present the names used in the paper, the formal names in the Lives Saved Tool, and additional notes for clarity.

Intervention name in LiST	Intervention name in this report	Notes
Safe abortion services	Safe abortion	Modeled in all countries; recommended in countries where it is legal.
Post abortion case management	Post abortion case management	
Ectopic pregnancy case management	Ectopic pregnancy case management	
Blanket iron supplementation/fortification	Blanket Iron fortification	Iron fortification at the population level
Antenatal care (at least 1 visit)	-	No health impact. Used for calculating packages
Antenatal care (at least 4 visits)	-	No health impact. Used for calculating packages
TT - Tetanus toxoid vaccination	Tetanus vaccination	Calculated as percent of newborns protected at birth against tetanus, through maternal vaccination strategies
IPTp - Intermittent preventive treatment of malaria during pregnancy	Intermittent preventive treatment of malaria	
Syphilis detection and treatment	Syphilis detection and treatment	
Calcium supplementation	Calcium supplementation	
Iron supplementation in pregnancy	Iron supplementation in pregnancy	
Multiple micronutrient supplementation in pregnancy	Multiple micronutrient supplementation in pregnancy	Supplementation with iron, folate, vitamin A and other nutrients during pregnancy
Balanced energy supplementation	Balanced energy supplementation	Protein energy supplementation
Hypertensive disorder case management	Hypertensive disorder case management	This is the comprehensive package of screening for
Diabetes case management	Diabetes case management	
Malaria case management	Malaria case management	
MgSO4 for pre-eclampsia	Management of pre-eclampsia with magnesium sulfate	Magnesium sulfate: MgSO4; Use of MgSO4 at the pre-eclampsia stage, prior to development of eclampsia
Health facility delivery	-	No health impact. Used for calculating packages
Clean birth environment	Clean birth environment	
Immediate drying and additional stimulation	Immediate drying and stimulation of newborn	Rubbing and drying of the newborn
Thermal protection	Thermal protection	
Clean cord care	Clean cord care	

Parenteral administration of uterotonics	Uterotonics	Formerly called active management of the third stage of labor, now includes only the administration of uterotonics
Manual removal of placenta	Controlled cord traction/removal of placenta	Together with the administration of uterotonics makes up Active Management of the Third Stage of Labor (AMTSL)
Parenteral administration of anti-convulsants	Management of pre-eclampsia with magnesium sulfate	Magnesium sulfate: MgSO4; Use of MgSO4 to treat convulsions and other consequences of eclampsia
Antibiotics for preterm or prolonged PROM	Antibiotics for premature rupture of membranes	pPRoM: preterm or prolonged premature rupture of membranes
Parenteral administration of antibiotics	Antibiotics for management of maternal sepsis	For all causes other than pPRoM
Assisted vaginal delivery	Assisted vaginal delivery	
Neonatal resuscitation	Neonatal resuscitation	Using a simple bag-and-mask
Removal of retained products of conception	Removal of retained products of conception	This is invasive removal of any remnants from the placenta and other tissues in the body after delivery.
Induction of labor for pregnancies lasting 41+ weeks	Induction of labor for pregnancies lasting 41+ weeks	
Antenatal corticosteroids for preterm labor	Antenatal corticosteroids	Antenatal corticosteroids are a controversial intervention, with some studies showing that use in the field by less-skilled and less-supported staff may result in negative consequences to the mother.
Cesarean delivery	C-section	Caesarean section
Blood transfusion	Blood transfusion	
Family Planning	Family planning	Country-specific method mixes of family planning were altered, and kept at the same relative proportions to reduce the unmet need for family planning to 10% of current.

ANNEX 3: LIVES SAVED TOOL – DESCRIPTION AND ASSUMPTIONS

Brief Description

The Lives Saved Tool is a multi-cause model of mortality. It uses change in coverage and effectiveness of interventions to estimate the resultant change in the cause-specific mortality - specifically maternal, newborn, child and fetal (stillbirth) mortality. The model relies on three general types of data, which can all be modified if available or needed.

1. Population size over time
    1. Derived from the interaction between the population size and structure and the family planning methods and changes
2. Cause-specific effectiveness of health and/or nutrition interventions
3. Affected fractions
    1. The proportion of a cause of death which can benefit from a specific intervention
4. Coverage of health and/or nutrition interventions
    1. At, at least, two different time points

Modeling methodology

For a single intervention, the model assumes linear impacts over time. Thus a 10 percent change from 5 percent coverage or from 80 percent coverage would result in very similar impacts. When more than one intervention is changed, the impacts are assumed to be independent of one another, with no synergies or antagonies between the two interventions. That means that there is no boost to effectiveness of an intervention if another intervention is also present.

For multiple interventions, in general, interventions are applied to the residual deaths remailing when other interventions have been applied. Steps are taken to ensure that there is no over-estimating of the impacts. The first is assuming a timeline for when an individual intervention is applied. Interventions delivered to women during antenatal care have their benefits calculated before interventions that are delivered during childbirth and childbirth interventions have their benefits calculated before postpartum interventions. This ensures that the biological timeline is considered for the benefits. Secondly, when two interventions are applied during the same time period, the total benefits are calculated on the residual deaths remaining from other interventions. This total number is identical regardless of the order in which interventions are applied. However, to isolate the individual impact of one intervention within a package, the lives saved are weighted by the coverage change and effectiveness of each intervention. For more details see references listed below.

Data sources

The data used to populate the Lives Saved Tool, by default, is publicly available. The effectiveness of each intervention on each cause of death is visible within the Spectrum software. Additional details are available in the peer-re-

viewed sources for each of these interventions, as listed below under references. Note that the sources for the most recent estimates for the effectiveness of the maternal modules have not been put in the public domain, but should be available in the next few months. The cause of death profiles for women are from Say et al[61] while those for newborns are from Liu et al[62]. All LiST default assumptions were used unless otherwise stated, including 2017 maternal mortality ratio estimates[63], 2018 neonatal mortality rate estimates[64], and 2015 stillbirth rate estimates[65].

Limitations

The LiST model is designed to replicate the health of populations as much as possible, but as with all models it is a simplification of reality. It is beneficial if it helps to understand the overall picture of how deaths can be averted and what is causing them. It is very different than a Stochastic model which can look at extreme detail for one disease. In addition, the LiST methodology assumes linear changes regardless of the underlying coverage of the interventions. This is a simplification of the real world where we assume that the effort to reach the final people in need is notably more difficult than reaching other more accessible populations.

References

For more detailed and comprehensive methodology and description, see the following key papers.

Walker N, Tam Y, Friberg IK. Overview of the Lives Saved Tool (LiST). BMC Public Health. 2013;13 Suppl 3:S1.

Fox MJ, Martorell R, van den Broek N, Walker N. Assumptions and methods in the Lives Saved Tool (LiST). BMC Public Health. 2011.

Winfrey W, McKinnon R, Stover J. Methods used in the Lives Saved Tool (LiST). BMC Public Health. 2011;11 Suppl 3:S32.

Stover J, McKinnon R, Winfrey B. Spectrum: a model platform for linking maternal and child survival interventions with AIDS, family planning and demographic projections. Int J Epidemiol. 2010;39 Suppl 1:i7-10.

For more methodology and utilization of the Lives Saved Tool software, please see the following website and journal supplements.

The Lives Saved Tool website: livessavedtool.org

The LiST Visualizer: listvisualizer.org

NOTE: This website has not yet been updated with the newest maternal modeling details.

Walker N, Friberg IK, The Lives Saved Tool in 2017: Updates, Applications, and Future Directions, BMC Public Health, 2017;17 Suppl 4.

Walker N, Clermont A. Nutrition Modeling in the Lives Saved Tool (LiST), J Nutr. 2017;147(11).

Walker N. The Lives Saved Tool in 2013: new capabilities and applications, BMC Public Health, 2013;13 Suppl 3.

Fox MJ, Reynaldo M, van den Broek N, Walker N. Technical inputs, enhancements and applications of the Lives Saved Tool (LiST), BMC Public Health. 2011;13 Suppl 2.

Sachdev HPS, Hall A, Walker N, Development and use of the Lives Saved Tool (LiST): A model to estimate the impact of scaling up proven interventions on maternal, neonatal and child mortality, Int J Epidemiol, 2010;39 Suppl 1.

ANNEX 4: LIST OF 59 COUNTRIES CONSIDERED IN THIS ANALYSIS

Afghanistan
Bangladesh
Benin
Bhutan
Bolivia
Botswana
Burkina Faso
Burundi
Cambodia
Cameroon
Central African Republic
Chad
Comoros
Côte d'Ivoire
Democratic Republic of the Congo
Djibouti
Ethiopia
Gabon
Gambia
Ghana
Guinea
Guinea-Bissau
Guyana
Haiti
India
Indonesia
Kenya
Lao People's Democratic Republic
Liberia
Madagascar
Malawi
Mali
Mauritania
Morocco
Mozambique
Myanmar
Nepal
Nicaragua
Niger
Nigeria
Pakistan
Papua New Guinea
Rwanda
Senegal
Sierra Leone
Somalia
South Africa
South Sudan
Sudan
Tajikistan
Timor-Leste
Togo
Uganda
United Republic of Tanzania
Uzbekistan
Viet Nam
Yemen
Zambia
Zimbabwe

REFERENCES

1 https://www.un.org/millenniumgoals/

2 https://sustainabledevelopment.un.org/?menu=1300

3 https://www.familyplanning2020.org/

4 https://www.who.int/life-course/partners/global-strategy/en/

5 The Millennium Development Goals report 2015 (https://www.un.org/en/development/desa/publications/mdg-report-2015.html)

6 Trends in maternal mortality: 1990 to 2015 Estimated by WHO, UNICEF, UNFPR, World Bank Group and the United Nations Population Division (https://www.unfpa.org/publications/trends-maternal-mortality-1990-2015)

7 Trends in estimated of maternal mortality ratio 2000-2017. Source: WHO WHO, UNICEF, UNFPA, World Bank Group and UNPD (MMEIG) - September 2019; Note: calculations used the 2015 estimate for 1990 as this was not published with the most up-to-date estimates for 2017. (https://www.unfpa.org/featured-publication/trends-maternal-mortality-2000-2017)

8 For example, the following three costing exercises: A) Jowett M. (2000). Safe motherhood interventions in low-income countries: an economic justification and evidence of cost effectiveness. Health Policy. B) Adam, T., Lim, S.S., Mehta, S., Bhutta, Z.A., Fogstad, H., Mathai, M., Zupan, J. and Darmstadt, G.L. (2005), "Cost effectiveness analysis of strategies for maternal and neonatal health in developing countries", British Medical Journal, Vol. 331 No. 7525, pp. 1107-1110, available at: www.bmj.com/content/331/7525/1107 (accessed 11 April 2016). C) Goldie SJ, Sweet S, Carvalho N, Natchu UCM, and Hu D Alternative Strategies to Reduce Maternal Mortality in India: a CEA. https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000264

9 Pande RP, Ogwang S, Karuga R, Rajan R, Kes A, Odhiambo FO, Laserson K, Schaffer K. *Continuing with "…a heavy heart" – consequences of maternal death in rural Kenya* 2015 **Repro Health** 12:S2

10 Bazile J, Rigodon J, Berman L, Boulanger VM, Maistrellis E, Kausiwa P, Yamin AE. *Intergenerational impacts of maternal mortality: Qualitative findings from rural Malawi* 2015 **Repro Health** 12:S1

11 Knight L and Yamin AE. *"Without a mother": caregivers and community members' views about the impacts of maternal mortality on families in KwaZulu-Natal, South Africa* 2015 **Repro Health** 12:S5

12 Pande RP, Ogwang S, Karuga R, Rajan R, Kes A, Odhiambo FO, Laserson K, Schaffer K. *Continuing with "…a heavy heart" – consequences of maternal death in rural Kenya* 2015 **Repro Health** 12:S2

13 Ye F, Wang H, Huntington D, Zhou H, Li Y, You F, Li J, Cui W, Yao M, Wang Y, the study team for Economic Impact of Maternal Deaths in China. *The Immediate Economic Impact of Maternal Deaths on Rural Chinese Households* 2012 **Plos ONE** 7(6): e38467

14 Kes A, Ogwang S, Pande RP, Douglas Z, Karuga R, Odhiambo FO, Laserson K, Schaffer K. *The economic burden of maternal mortality on households: evidence from three sub-counties in rural western Kenya* 2015 **Repro Health** 12:S3

15 Ye F, Wang H, Huntington D, Zhou H, Li Y, You F, Li J, Cui W, Yao M, Wang Y, the study team for Economic Impact of Maternal Deaths in China. *The Immediate Economic Impact of Maternal Deaths on Rural Chinese Households* 2012 **PloS ONE** 7(6): e38467

16 Kes A, Ogwang S, Pande RP, Douglas Z, Karuga R, Odhiambo FO, Laserson K, Schaffer K. *The economic burden of maternal mortality on households: evidence from three sub-counties in rural western Kenya* 2015 **Repro Health** 12:S3

17 Wang H, Ye F, Wang Y, Huntington D, the study group for economic Impact of Maternal Deaths in China. *Economic Impact of Maternal Death in Households in Rural China: A Prospective Cohort Study* 2013 **PLoS ONE** 8(10):e76624

18 Kes A, Ogwang S, Pande RP, Douglas Z, Karuga R, Odhiambo FO, Laserson K, Schaffer K. *The economic burden of maternal mortality on households: evidence from three sub-counties in rural western Kenya* 2015 **Repro Health** 12:S3

19 Nguyen DTN, Hughes S, Egger S, LaMontagne DS, Simms , Castle PE, Canfell K. *Risk of childhood morality associated with death of a mother in low-and-middle income countries: a systematic review and meta-analysis.* 2019 **BMC Pub Health** 19(1):1281; Ronsmans C, Chowdhury ME, Dasgupta SK, Ahmed A, Koblinsky M. *Effect of a parent's death on child survival in rural Bangaldesh: a cohort study* 2010 **Lancet** 375(9730):2024-31; Moucheraud C, Worku A, Molla M, Finlay JE, Learning J, Yamin AE. *Consequences of maternal mortality on infant and child survival: a 25-year longitudinal analysis in Butajira Ethiopia (1987-2011).* 2015 **Repro Health** 12:S4; Finlay JE Moucheraud C, Goshev S, Levira F, Mrena S, Canning D, Masanja H, Yamin AE. *The effects of maternal mortality on infant and child survival in rural Tanzania: a cohort study.* 2015 **Matern Child Health J** 19(11):2393-402; Katz J, West KP Jr, Khatry SK, Christian P, LeClerq SC, Pradhan EK, Shrestha SR. *Risk factors for early infant mortality in Sarlahi district, Nepal*. 2003. **Bull World health Organ**. 81(10):717-25; Scott S, Kendall L, Gomez P, Howie SR, Zaman SM, Ceesay S, D'Alessandro U, Jasseh M. *Effect of maternal death on child survival in rural West Africa: 25 years of prospective surveillance data in The Gambia.* 2017 **PLoS One.** 12(2):e0172286.

20 Chikungu LC, Newell M-L, Rollins N. *Under-five mortality according to maternal survival: a systematic review and meta-analysis* 2017. **Bull World Health Organ** 95:281-287; Moucheraud C, Worku A, Molla M, Finlay JE, Learning J, Yamin AE. *Consequences*

of maternal mortality on infant and child survival: a 25-year longitudinal analysis in Butajira Ethiopia (1987-2011). 2015 **Repro Health** 12:S4

21 Houle B, Clark SJ, Lahn K, Tollman S, Yamin AE. *The impacts of maternal mortality and cause of death on children's risk of dying in rural South Africa: evidence from a population based surveillance study (1992-2013)*. 2015. **Repro Health** 12(S1):S7

22 Chikungu LC, Newell M-L, Rollins N. *Under-five mortality according to maternal survival: a systematic review and meta-analysis* 2017. **Bull World Health Organ** 95:281-287.

23 Ronsmans C, Chowdhury ME, Dasgupta SK, Ahmed A, Koblinsky M. *Effect of a parent's death on child survival in rural Bangaldesh: a cohort study* 2010 **Lancet** 375(9730):2024-31

24 Ronsmans C, Chowdhury ME, Dasgupta SK, Ahmed A, Koblinsky M. *Effect of a parent's death on child survival in rural Bangaldesh: a cohort study* 2010 **Lancet** 375(9730):2024-31

25 Chikungu LC, Newell M-L, Rollins N. *Under-five mortality according to maternal survival: a systematic review and meta-analysis* 2017. **Bull World Health Organ** 95:281-287.

26 Pande RP, Ogwang S, Karuga R, Rajan R, Kes A, Odhiambo FO, Laserson K, Schaffer K. *Continuing with "…a heavy heart" – consequences of maternal death in rural Kenya* 2015 **Repro Health** 12:S2

27 Finlay JE, Fink G, McCoy DG, Tavarz LC, Chai J, Danaei G, Ezzati M, Fawzi W, Fawzi MCS. *Stunting risk of orphans by caregiver and living arrangement in low-income and middle-income countries*. 2016 **J Epidemiol Community Health** 70:784-90.

28 The cost of the transformative results that UNFPA is committed to achieving by 2030: Fact Sheets; https://sites.google.com/unfpa.org/costing30s/home; United nationals population Fund, Nairobi Summit fact Sheets, November 2019.

29 United Nations Population Fund (2019). Costing the Three Transformative Results. New York, New York.; Guttmacher Institute, Adding it Up: Investing in Contraception, Maternal and Newborn Health, 2017 https://www.guttmacher.org/fact-sheet/adding-it-up-contraception-mnh-2017

30 http://hdr.undp.org/en/content/health-index

31 Bartlett L, Weissman E, Gubin R, Patton-Molitors R, Friberg IK. *The Impact and Cost of Scaling up Midwifery and Obstetrics in 58 Low- and Middle-Income Countries* 2014 **PLoS ONE** 9(6):e98550

32 WHO. 2017. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed.

33 WHO. 2015. Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice – 3rd ed

34 https://supply.unicef.org/

35 **CHOICE (CHO**osing Interventions that are **C**ost-**E**ffective) project. https://www.who.int/choice/cost-effectiveness/inputs/en/

36 All data was updated to 2018 dollars. As WHO's overhead estimates include staff costs, which we calculated separately in this study, we deducted the personnel cost share from the WHO estimates and only included utility costs and the amortized costs of the hospital building and equipment. The separation of costs was done based on a prior study carried out in LiST, which separated out the different cost components of the WHO CHOICE hospitalization costs.

37 Gething et al. Geographical access to care at birth in Ghana: a barrier to safe motherhood. BMC Public Health 2012, 12:991

38 Samuel H. Masters et al. Travel time to maternity care and its effect on utilization in rural

Ghana: A multilevel analysis. Social Science & Medicine 93 (2013) 147-154

39 GNI per Capita, Atlas method and % of women living in urban vs. rural areas were downloaded from World Bank databases

40 Randive B, Diwan V, De Costa A. 2013. India's Conditional Cash Transfer Programme (the JSY) to Promote Institutional Birth: Is There an Association between Institutional Birth Proportion and Maternal Mortality? PLoS ONE 8(6): e67452. doi:10.1371/journal.pone.0067452

41 Provided on request.

42 https://avenirhealth.org/software-spectrum.php

43 Robinson LA. et al 2019. Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development. https://sites.sph.harvard.edu/bcaguidelines/guidelines/

44 GNI per capita, PPP (current international $), World Bank World Development Indicator Database. https://data.worldbank.org/indicator/NY.GNP.PCAP.PP.CD

45 https://data.worldbank.org/indicator/SP.DYN.LE00.IN

46 Ashraf QH et al. 2013. The Effect of Fertility Reduction on Economic Growth. Population and Development Review 39(1): 97–130 (March 2013)

47 Ashraf QH et al. 2013. The Effect of Fertility Reduction on Economic Growth. Population and Development Review 39(1): 97–130 (March 2013)

48 Riahi K, van Vuuren DP, Kriegler E et al., *The Shared Socioeconomic Pathways and their energy, land use, and greenhouse gas emissions implications: An overview*, **Global Environment Change**, 2018, 42, 153-168

49 Robinson LA. 2019. Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development. https://sites.sph.harvard.edu/bcaguidelines/guidelines/

50 Althabe F, Belizan JM, McClure EM et al. *A population-based , multifaceted strategy to implement antenatal corticosteroid treatment versus standard care for the reduction of neonatal mortality due to preterm birth in low-income and middle-income countresi: the ACT cluster-randomised trial.* 2015 **Lancet** 385(9968):629-639.

51 Examples include: Darroch JE, *Adding It Up: Investing in Contraception and Maternal and Newborn Health, 2017—Estimation Methodology*, New York: Guttmacher Institute, 2018; the Spectrum software suite (www.avenirhealth.org)

52 Fekadu GA, Kassa GM, Behre AK, Muche AA, Katiso NA. *The effect of antenatal care on use of institutional delivery service and postnatal care in Ethiopia: a systematic review and meta-analysis*. 2018 ***BMC Health Serv Res*** *18:577*; Anastasi E, Borchert M, Campbell OM, Sondorp E, Kaducu F, Hill O, Okeng D, Odong VN, Lange IL. *Losing women along the path to safe otherhood: why is there such a gap between women's use of antenatal care and skilled birth attendance? A mixed methods study in northern Uganda* 2015 **BMC Preg Child** 15:287; Boah M, Mahama AB, Ayamga EA. *They receive antenatal care in health facilities, yet do not deliver there: predictors of health facility delivery by women in rural Ghana* 2018 **BMC Preg Child** 18:125

53 Ryan BL, Krishnan RJ, Terry A, Thind A. *Do four or more antenatal care visits increase skilled birth attendant use and institutional delivery in Bangladesh? A propensity-score matched analysis* 2019 **BMC Public Health** 19:583

54 Gabrysch S and Campbell OMR. *Still too far to walk: Literature review of the determinants of delivery service use*. 2009 **BMC Preg Child** 9:34

55 Boah M, Mahama AB, Ayamga EA. *They receive antenatal care in health facilities, yet do not deliver there: predictors of health facility delivery by women in rural Ghana* 2018 **BMC Preg Child** 18:125

56 Moyer CA and Mustafa A. *Drivers and deterrents of facility delivery in sub-Saharan Afria: a systematic review* 2013 **Repro Health** 10:40

57 Darroch JE, *Adding It Up: Investing in Contraception and Maternal and Newborn Health, 2017—Estimation Methodology,* New York: Guttmacher Institute, 2018.

58 Darroch JE, *Adding It Up: Investing in Contraception and Maternal and Newborn Health, 2017—Estimation Methodology*, New York: Guttmacher Institute, 2018.

59 Darroch JE, *Adding It Up: Investing in Contraception and Maternal and Newborn Health, 2017—Estimation Methodology*, New York: Guttmacher Institute, 2018.

60 Darroch JE, *Adding It Up: Investing in Contraception and Maternal and Newborn Health, 2017—Estimation Methodology*, New York: Guttmacher Institute, 2018.

61 Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, Gülmezoglu AM, Temmerman M, Alkema L. *Global causes of maternal death: a WHO systematic analysis*. 2014 **Lancet Glob Health**; 2(6):e323-33.

62 Liu L, Oza S, Hogan D, et al. *Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals*. 2016 **Lancet** 388(10063):3027-3035

63 WHO, UNICEF, UNFPA, World Bank, UN Population Division. Trends in maternal mortality: 2000 to 2017. Geneva: World Health Organization, 2019.

64 UN Inter-agency Group for Child Mortality Estimation. Levels & trends in child mortality report 2019. New York: United Nations Children's Fund, 2019.

65 Healthy Newborn Network. Numbers. 2019. https://www.healthynewbornnetwork.org/numbers/ (accessed Jan 6, 2020).