Chapter **26**

Maternal and Perinatal Conditions

Wendy J. Graham, John Cairns, Sohinee Bhattacharya, Colin H. W. Bullough, Zahidul Quayyum, and Khama Rogo

The Millennium Declaration includes two goals directly relevant to maternal and perinatal conditions: reducing child mortality and improving maternal health. The fact that two out of the eight Millennium Development Goals (MDGs) are exclusively targeted at mothers and children is testament to the significant proportion of the global burden of disease they suffer and to the huge inequities within and between countries in the magnitude of their burden. Achieving these goals is inextricably linked at the biological, intervention, and service delivery levels (Bale and others 2003).

Maternal and child health services have long been seen as inseparable partners, although over the past 20 years the relative emphasis within each, particularly at a policy level, has varied (De Brouwere and Van Lerberghe 2001). The launch of the Safe Motherhood Initiative in the late 1980s, for example, brought heightened attention to maternal mortality, whereas the International Conference on Population and Development (ICPD) broadened the focus to reproductive health and, more recently, to reproductive rights (Germain 2000). Those shifts can be linked with international programmatic responses and terminology—with the preventive emphasis of, for instance, prenatal care being lowered as a priority relative to the treatment focus of emergency obstetric care. For the child, integrated management of childhood illnesses has brought renewed emphasis to maintaining a balance between preventive and curative care. The particular needs of the newborn, however, have only started to receive significant attention in the past three or four years (Foege 2001).

Although health experts agree that the single clinical interventions needed to avert much of the burden of maternal and perinatal death and disability are known, they also accept that these interventions require a functioning health system to have an effect at the population scale. Levels of maternal and perinatal mortality are thus regarded as sensitive indicators of the entire health system (Goodburn and Campbell 2001), and they can therefore be used to monitor progress in health gains more generally. What is also clear is that maternal mortality and the neonatal component of child mortality continue to represent two of the most serious challenges to the attainment of the MDGs, particularly in South Asia and Sub-Saharan Africa.

An estimated 210 million women become pregnant each year, and close to 60 million of these pregnancies end with the death of the mother (≈500,000) or the baby or as abortions. This chapter focuses on the adverse events of pregnancy and childbirth and on the intervention strategies to eliminate and ameliorate this burden.

EPIDEMIOLOGY OF MATERNAL AND PERINATAL CONDITIONS

Much has been written about the lack of reliable data on maternal and perinatal conditions in developing countries (AbouZahr 2003; Graham 2002; Save the Children 2001). Weak routine information systems, inadequate vital registration, and reliance on periodic household surveys as the main source of population-based data are all familiar obstacles to improving public health in poor countries (Godlee and others 2004). Recognizing the implications of these obstacles for prioritizing health needs and interventions is important and is now endorsed by a global movement toward evidence-based decision making for policy and practice (Evans and Stansfield 2003).

However, there has been much less appreciation of the consequences for evaluations of effectiveness—and thus cost-effectiveness—of the weaknesses in current outcomes measurement and in routine data collection. Those weaknesses also affect the monitoring of progress toward the MDGs. Initiatives for improved health surveillance are thus urgently needed (CMH 2002). For the vast majority of the world's population, the magnitude of adverse maternal and perinatal outcomes is not known reliably. It is impossible to determine whether many of the patterns apparently observed, especially at a cause-specific level, are real or are artifacts of the measurement process.

Definitions

The terms *maternal* and *perinatal* encompass a continuum of health states—from the most positive (complete physical, mental, and social well-being) to the most negative—and a huge number of clinical conditions. This chapter focuses on eight major conditions, hereafter referred to as the *focus conditions,* which are estimated to account for about 75 percent of maternal deaths and more than 60 percent of perinatal deaths. For the mother, these conditions are hemorrhage, sepsis, hypertensive disorders of pregnancy, obstructed labor, and unsafe abortion. For the baby, they are low birthweight, birth asphyxia, and infection (table 26.1).

We define *maternal conditions* as encompassing events occurring from conception to 42 days postpartum (WHO 1992a). The chapters on women's health, family planning, adolescent health, and surgery address the longer-term sequelae of pregnancy and childbirth; the preconception period; pregnancy at an early age; and specific interventions, such as repair of obstetric fistulas. Within the period from conception to 42 days postpartum, two broad categories of conditions can be distinguished: those arising specifically from pregnancy and parturition (*direct obstetric conditions*), and those aggravated by or aggravating to pregnancy (*indirect obstetric conditions*). Because the latter conditions, such as malaria, HIV/AIDS, or anemia, are not exclusive to pregnant or parturient women, they are not dealt with here but in the relevant disease-specific chapters.

Regarding perinatal conditions, we focus on those for which interventions can be directed to the baby through the mother during pregnancy or delivery. Our discussion is complemented by the discussion in chapter 27, which concentrates on the neonate, including special care of the small baby and emergency care of the sick newborn.

Formal definitions of perinatal conditions tend to vary by data source. Taken literally, they refer to conditions that arise in the perinatal period (Murray and Lopez 1998), which are not the same as events that occur in the perinatal period—that is, from 28 weeks of gestation to the end of the seventh day of life. For example, death resulting from conditions that arise in the perinatal period can happen at any age, although it tends to take place during the neonatal period (up to 28 days of life). By contrast, perinatal deaths include both stillborn babies and those who are born alive but die before the end of the seventh day. Early neonatal deaths only include live births.

Nature and Characteristics

Pregnancy and childbirth are not inherently pathological. Maintaining an effective balance, however, between preserving normality and ensuring a state of readiness to deal with abnormality represents a fundamental challenge to health systems and a tension in safe motherhood programming. Although this balance between prevention and treatment is not peculiar to maternal and perinatal conditions (or complications), the following additional characteristics are relevant to assessing the burden as well as the effectiveness of interventions:

- The principle of "first, do no harm" has particular significance in this area, because many preventive practices related to pregnancy and childbirth can readily become harmful in unskilled hands—for example, inappropriately early induction of labor or poor forceps technique. The iatrogenic burden of maternal and perinatal conditions is rarely factored into assessments of intervention effectiveness.
- The lives of two individuals, mother and baby, are potentially at stake (Stoll and Measham 2001); however, interventions will not necessarily benefit both equally, and indeed, some will be in direct conflict.
- A large number of maternal and perinatal conditions present clinically not as single entities but as complexes, such as hemorrhage and sepsis or preterm delivery and birth asphyxia. For the mother, the situation may be further complicated by the role of underlying conditions, such as HIV/AIDS underlying puerperal sepsis.
- The most extreme negative outcome, death of both the mother and the baby, is highly concentrated around the time of delivery, from the onset of labor or abortion to 48 hours postpartum or postabortion. Estimates indicate that about two-thirds of maternal deaths occur within this time window (AbouZahr 1998), and the proportion for perinatal deaths appears to be even higher (Bale and others 2003). For the mother, however, a growing number of studies highlight the contribution of direct and indirect causes of deaths, including violence, when a one-year postpartum reference period is used (Etard, Kodio, and Traore 1999; Hoj and others 2003).
- The initial clinical presentation of some conditions can be severe, with rapid escalation to a life-threatening state, and these conditions often require surgical intervention.
- A distinct clinical feature of some maternal conditions is their unpredictability (AbouZahr 1998). This fact has had a

Table 26.1 Maternal and Perinatal Focus Conditions and Risk Factors for These Conditions

Condition	Definition or complications and sequelae	Case fatality rate[a] (percent)	Average duration until death if condition fatal	Timing of presentation	Risk factors for condition		Risk factors for death from condition	
					Distal or proximate	Direct, physiological	Distal or proximate	Direct, physiological
Maternal								
Hemorrhage	*Definition* Antepartum hemorrhage: bleeding from the genital tract during the last 3 months of pregnancy	Not available	12 hours	28 weeks of gestation up to delivery	Primigravidity Grand multiparity (greater than 4) Fibroids Anemia	Placental abnormalities (including placenta previa; abruption; placenta accreta, percreta, increta; other adhesions) Polyhydramnios Multiple gestation Previous third-stage complication Previous cesarean section Preeclampsia, eclampsia Intrauterine death Hepatitis Induced labor Prolonged labor Precipitate labor Forceps delivery Cesarean section Chorioamnionitis Disseminated intravascular coagulation	Remote location Anemia Coagulopathies	Lack of blood transfusion Badly managed third stage of labor Delay or absence of oxytocic treatment
	Primary postpartum hemorrhage: excessive bleeding (more than 500 milliliters) from the genital tract following delivery	1.0[b]	2 hours	Delivery to 24 hours after delivery				
Sepsis	*Definition* Infection of the genital tract or extragenital infections following childbirth	1.3	6 days	Delivery to 6 weeks postpartum	Immunosuppression Anemia Sexually transmitted infections Inadequate prenatal care	Prolonged labor Obstructed labor Premature rupture of membranes Frequent pelvic examinations Intrauterine death Foreign body insertion (for example, herbs) Episiotomy Instrumental delivery	Delivery by untrained personnel Immunosuppression Anemia Lack of knowledge about warning signs Lack of postnatal care Cultural practices	Misdiagnosis Inappropriate use of antibiotics Lack of access to intravenous antibiotics

(Continues on the following page.)

Table 26.1 Continued

Condition	Definition or complications and sequelae	Case fatality rate[a] (percent)	Average duration until death if condition fatal	Timing of presentation	Risk factors for condition		Risk factors for death from condition	
					Distal or proximate	Direct, physiological	Distal or proximate	Direct, physiological
						Cesarean section Unhygienic delivery conditions Retained products of conception		
Hypertensive disorders of pregnancy	*Definition* Raised blood pressure with proteinuria	1.7	2 days (eclampsia)	28 weeks of gestation to 2 days postpartum	Extremes of maternal age Primigravidity Genetic predisposition Racial or geographical predisposition Diabetes and chronic hypertension Lack of prenatal care	Multiple gestations Molar pregnancy Previous history of pregnancy-induced hypertension or chronic hypertension	Cultural practices Lack of knowledge Lack of prenatal care	Appearance of complications, such as cardiovascular and cerebral complications, hemolysis, elevated liver enzyme, low platelets syndrome Disseminated intravascular coagulation Eclampsia
Obstructed labor	*Definition* Labor in which progress is arrested by mechanical factors	0.7	3 days	During labor	Malnutrition Rickets in childhood Bony deformity of pelvis Achondroplasia Short stature Primigravidity Grand multiparity Adolescent pregnancy	Cephalopelvic disproportion Malpresentation, position	Lack of access to cesarean delivery Lack of access to instrumental delivery and symphysiotomy Scarred uterus Inappropriate use of oxytocin	Uterine rupture Hemorrhage Sepsis Exhaustion, dehydration
Unsafe abortion	*Definition* Procedure for terminating an unintended pregnancy carried out by people lacking the necessary skills or in an environment that does not conform to minimal medical standards or both	0.3	6 hours to 6 days	After first missed period to 22 weeks of gestation or fetal weight of less than 500 grams	Unwanted pregnancy Adolescence Unmarried status Absence of legal abortion services Lack of access to contraception Lack of access to safe abortion services Sexually transmitted infections	Absence of aseptic technique Foreign body insertion Poisoning from abortifacients	Sociocultural factors Lack of access to safe termination services Lack of access to postabortion care	Perforated uterus Poisoning from abortifacients Peritonitis Septic shock Acute renal failure Hepatorenal failure Bowel injury, perforation Hemorrhagic shock Peritonitis

Perinatal[c]								
Low birthweight (less than 2,500 grams)[d]	*Complications or sequelae* Respiratory insufficiency in preterm infants with lung immaturity presenting as respiratory distress syndrome because of surfactant deficiency	50	5 days	Less than 24 hours	Extremes of maternal age Race, ethnicity Low socioeconomic status Unmarried status Lack of education Parity (0 or greater than 4) Smoking, alcohol use Maternal malnutrition Maternal diabetes or hypertension Genetic factors Rubella, other viral infection Poor obstetric history Diethylstilboestrol, other toxic exposure High altitude Absent or inadequate prenatal care	Multiple pregnancy Short interpregnancy interval First or second trimester bleeding Placenta previa Preeclampsia Anemia Hyperemesis Isoimmunization Fetal abnormalities Cervical incompetence Oligohydramnios or polyhydramnios	Lack of adequate neonatal care facility Lack of knowledge and understanding	Birth asphyxia Intraventricular hemorrhage Central nervous system injury Respiratory infection Respiratory distress syndrome Necrotizing enterocolitis Cholestatic liver disease Other infections Sudden infant death syndrome Neonatal coagulopathy
	Neonatal cerebral injury caused by periventricular hemorrhage mediated by perinatal stress such as hypotension or trauma	80	3 days	1–4 days				
	Severe physiological jaundice of preterm infant	50	1–5 days	2–5 days				
	Difficulties in establishing spontaneous feeding and inability to tolerate feeds resulting from prematurity	20	1–14 days	First day				
	Failure of closure of the ductus arteriosus, frequently seen in preterm babies with lung disease	70	3 days to months	3–14 days				
	Hypoglycemia and other metabolic disorders related to prematurity	2	7 days	Birth				
Birth asphyxia (excluding birth trauma)	*Complications or sequelae* Absent or depressed breathing at birth	20	20 minutes	Birth (5 minutes)	Drugs taken during labor, including anesthesia Maternal diabetes Maternal hypertension Preeclampsia Any other severe illness	Prolonged or obstructed labor Abruptio placentae Placental infarct, insufficiency Postmaturity Prematurity or low birthweight Multiple pregnancies Placenta previa or separation Cord prolapse	Badly conducted labor Lack of fetal monitoring Lack of partograph Lack of neonatal resuscitation facilities	Central nervous system injury Neonatal encephalopathy (seizures and recurrent apnea)
	Neonatal encephalopathy: clinically evident disturbance in neurological behavior, commonly with early neonatal seizures in term babies, resulting from an event causing hypoxia during delivery	30	3 days to life	Birth to first 12 hours				

(Continues on the following page.)

Table 26.1 Continued

Condition	Definition or complications and sequelae	Case fatality rate[a] (percent)	Average duration until death if condition fatal	Timing of presentation	Risk factors for condition		Risk factors for death from condition	
					Distal or proximate	Direct, physiological	Distal or proximate	Direct, physiological
Infection	*Complications or sequelae* Neonatal sepsis of early onset resulting from intrauterine or intrapartum infection	30–40	5 days	First 3 days	Lack of adequate prenatal care Maternal infection Lack of maternal immunization Unhygienic cultural practices	Premature rupture of membranes Preterm delivery Birth asphyxia Unhygienic delivery and cord care	Congenital HIV infection Lack of adequate neonatal care	Preterm delivery Septic shock Respiratory failure Hepatorenal failure Coagulopathies
	Neonatal sepsis of late onset resulting from nosocomial infection or lack of immunity to commensal bacteria	15	5 days	After 3 days				
	Tetanus neonatorum, commonly resulting from unhygienic cutting of the cord or care of the cord stump	80	3–7 days	3–14 days				
	Congenital syphilis resulting from transplacental infection with *Treponema pallidum* after 18 weeks gestation	30	5 days	Birth onward				
	HIV infection transmitted either intrapartum or postpartum			Direct effects mainly after neonatal period				

Source: Maternal conditions: Chamberlain 1995; case fatality rates: AbouZahr 2003; mechanical factors of obstructed labor: WHO 1994; unsafe abortion: WHO 1992b; low birthweight: Bale and others 2003, Robertson 1993, Yasmin and others 2001; birth asphyxia: Bale and others 2003, p. 324, Robertson 1993; infections: Robertson 1993; risk factors: Calder and Dunlop 1992, Murray and Lopez 1998.

a. Case fatality rates assume that no intensive care is available, because this is the norm in South Asia and Sub-Saharan Africa.

b. Case fatality for severe pph (blood loss ≥ 1000 ml).

c. Excludes stillbirths.

d. Includes preterm deliveries and small for gestational age.

profound effect on the prioritization of interventions in safe motherhood, and it is an area in urgent need of further research. The situation is confused by the alternative endpoints, such as death or disability, and by the extent to which there are clear and predictable risk factors. Table 26.1 summarizes some of these key characteristics as they relate to the eight focus conditions.

Causes and Conceptual Frameworks

One of the most frequently quoted figures in safe motherhood is that 88 to 98 percent of maternal deaths are avoidable with moderate levels of health care (WHO 1986). This advocacy statement simplifies the multiple pathways leading to death and, thus, the multiple opportunities for primary and secondary prevention. In part, this simplicity is a further reflection of the grouping together of clinical conditions that in reality are distinctly different in terms of prevalence, case fatality, and scope for intervention, such as eclampsia and puerperal sepsis or congenital anomalies and birth asphyxia. The multiple endpoints and conditions, for both the mother and the fetus or newborn, have implications for what is regarded as an antecedent (a cause, a determinant, or a risk factor)[1] and what is regarded as a consequence (an outcome or a sequela).

A large number of conceptual frameworks depict pathways to adverse maternal and perinatal outcomes (Bale and others 2003; McCarthy and Maine 1992). Several identify three levels of contributory factors, which are also found in causal models for general health outcomes (WHO 2002): (a) distal, (b) proximal or intermediate, and (c) physiological or direct. Table 26.1 highlights the risk factors for the focus maternal and perinatal conditions. The distal determinants emphasize that maternal and perinatal well-being is not just a medical issue. Improvements throughout the health sector must be complemented by attention to wider social, economic, and cultural factors as well as to reproductive rights (CMH 2002). Many conceptual frameworks also differentiate between the timing of interventions: before pregnancy, during pregnancy, during labor and delivery, or during the postpartum period. Similarly, a further distinction can be made in terms of the timing of the outcome, although from a programmatic perspective, such a temporal focus may lead to fragmented care for women and their babies.

Levels, Trends, and Differentials

The latest regional estimates of maternal mortality are for 2000–1 (table 26.2), with most of the figures for the developing world produced by modeling (WHO 2004b). More than 99 percent of annual maternal deaths occur in the developing world. At a national level, the magnitude of the differential in terms of lifetime risk is almost 500-fold between the highest figure for a developing country (1 in 6) and the lowest estimate for a developed country (1 in 29,800) (WHO 2004b). This differential is often cited as the largest discrepancy between the developing and developed world of all public health statistics, reflecting major differences both in obstetric risk, as measured by the maternal mortality ratio, and in levels of fertility, as reflected in the total fertility rate.

In terms of medical causes of maternal mortality, even greater caution is needed regarding the reliability of any patterns observed, because of their dependence on whether the data are health service based or population based and on coding conventions. Figure 26.1a shows the percentage distribution among direct causes at a crude global level. Direct causes account for about 80 percent of all maternal deaths, with indirect causes responsible for the remainder. Of the direct causes, hemorrhage is generally regarded as the most common and may be underestimated, because health facilities are unaware of many such deaths, given the short interval between onset and death (see table 26.1). In terms of indirect causes, the pattern varies enormously between different parts of the world, primarily according to the prevalence of HIV/AIDS, malaria, and tuberculosis.

The published data on severe maternal morbidity are weaker still. A recent World Health Organization (WHO) systematic review indicates how prevalence figures vary hugely according to the criteria used to identify cases (Say, Pattinson, and Gulmezoglu 2004). Using disease-specific criteria, WHO found that prevalence ranged from 0.80 to 8.23 percent. Using organ system criteria, WHO found that the range was 0.38 to 1.09 percent. Finally, using management-based criteria, WHO found that the range was 0.01 to 2.99 percent. Estimates suggest that for every maternal death, at least 16 or 17 other women suffer a life-threatening complication during pregnancy or childbirth (Gay and others 2003) and at least 30 women are left with long-term disabilities, such as an obstetric fistula (UNFPA 2003). These estimates must be regarded as crude approximations, most originating from small-scale studies and most in urgent need of updating and verification. Given the varying case fatality rates shown in table 26.1, the fact that the distributional pattern for morbidity (figure 26.1b) does not completely mirror the one for mortality is not surprising.

As concerns mortality in babies, an estimated 5.7 million perinatal deaths occur each year, 47 percent as stillbirths and 53 percent in the first week of life (J. Zupan, personal communication, August 25, 2004). Many of those deaths are linked directly with complications experienced by the mothers, and several studies have shown that the survival prospects for a baby whose mother dies are generally poor—less than 1 percent in one study in Bangladesh (Koenig, Fauveau, and Wojtyniak 1991). In 2004, neonatal deaths represented 36 percent of all deaths of children under five in developing

Table 26.2 Estimates of Maternal Mortality by Region, 2000–1

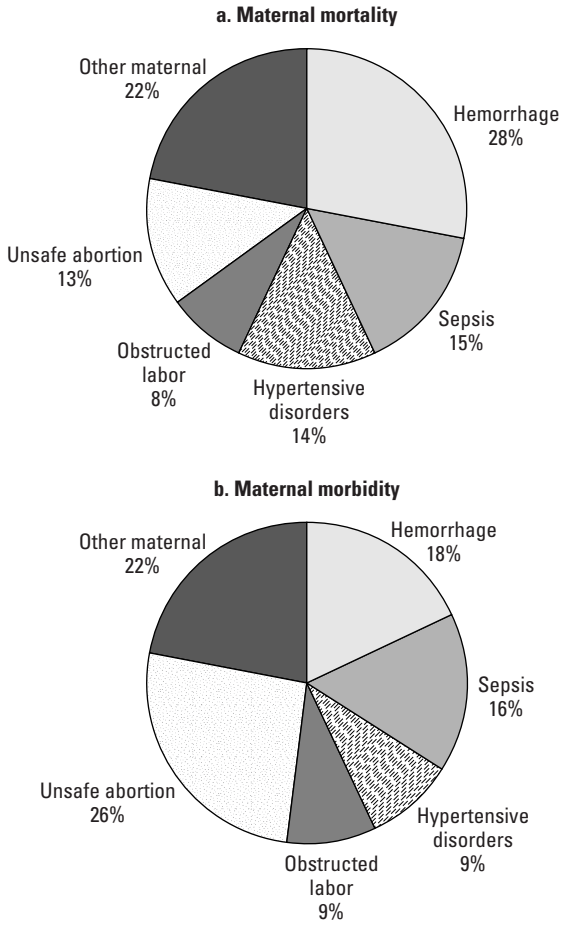
Region	Maternal mortality ratio (maternal deaths per 100,000 live births), 2000	Number of maternal deaths as modeled by WHO, 2000	Estimated number of maternal deaths, 2001	Lifetime risk of maternal death (1 in number shown)	Range of uncertainty of maternal mortality ratio estimates		Total fertility rate
					Lower estimate	Upper estimate	
Central and Eastern Europe, Commonwealth of Independent States, Baltic states, Europe, and Central Asia	64	3,400	3,000	770	29	100	1.6
East Asia and the Pacific	110	37,000	37,000	360	44	210	2.0
Eastern and Southern Africa	980	123,000	—	15	490	1,500	5.5
Latin America and the Caribbean	190	22,000	16,000	160	110	280	2.6
Middle East and North Africa	220	21,000	15,000	100	85	380	3.7
South Asia	560	205,000	199,000	43	370	760	3.5
Sub-Saharan Africa	940	240,000	237,000	16	400	1,500	5.7
Western and Central Africa	900	118,000	—	16	310	1,600	5.9
High-income countries	13	1,300	1,000	4,000	8	17	1.6
Low- and middle-income countries	440	527,000	507,000	61	230	680	3.0
Low-income countries	890	236,000	—	17	410	1,400	5.4
World	400	529,000	508,000	74	210	620	2.7

Source: WHO 2004b, 2004d; UN 2002.
— = not available.
Note: The regions are those used by the United Nations Children's Fund.

countries, with about 1 million of these 3.94 million neonatal deaths occurring in the first week of life (Jamison and others 2004). Table 26.3 presents modeled estimates for early neonatal deaths in 2001. The data on the magnitude and patterns of stillbirths remain particularly poor.

Given weak sources of information, the dearth of reliable trends data is hardly surprising. At a global level, a major difficulty arises from the need to use models to estimate maternal mortality. As the basic methodology for the models has changed over time, the data are not appropriate for trend assessment. AbouZahr and Wardlaw (2001) provide patchy support for downward trends in some parts of the world, mostly on the basis of civil registration data and mostly restricted to countries with maternal mortality ratios of less than 100 per 100,000 live births—thus notably excluding South Asia and Sub-Saharan Africa. Even where declines appear to have occurred, they did so prior to 1990. Countries with sustained falls since then, such as Argentina and China, cannot be regarded as representative of all developing countries. Cause-specific trend data are extremely rare, often gathered through small-scale hospital-based studies or special inquiries (see, for example, Pattinson 2002). Recent WHO (2004c) statistics on unsafe abortion show an apparent decrease in incidence in all world regions, although the risk of death remains high at 50 per 100,000 live births, and in parts of Sub-Saharan Africa the risk is as high as 140 per 100,000 live births (Rogo, Bohmer, and Ombaka 1999). These adverse events, however, are often also the most seriously underreported, as elaborated further in chapter 57.

The availability of reliable trends data for perinatal mortality is even more problematic. A demand for population-based estimates for newborn mortality is comparatively recent; thus, there has been insufficient time to accumulate multiple data points. Demographic and health surveys (DHSs) are a key source for tracking trends in infant and child mortality. Several DHSs now have data that can be disaggregated to show neonatal deaths, but only a few have information on stillbirths, and the quality of that information is still being assessed. Information from WHO suggests that early neonatal death rates fell slightly, from 28 per 1,000 live births around 1980 to about 25 per 1,000 in 2000, for low- and middle-income countries,



Source: Mortality: WHO 2004d; Morbidity: Murray and Lopez 1998.

Note: Nonobstetric (indirect) causes of death and morbidity, such as tuberculosis and malaria, have been excluded.

Figure 26.1 Medical Causes of Direct Maternal Mortality and Morbidity *(percentage distribution)*

and the equivalent trend for stillbirths is suggested to be a drop from 36 per 1,000 deliveries to 22 per 1,000 deliveries (J. Zupan, personal communication, August 25, 2004).

Two types of differentials are particularly relevant: geographic (or regional) and socioeconomic. Table 26.2 indicates the wide variation in the magnitude of maternal mortality across regions, and a similar difference can be seen between countries. In terms of absolute numbers of deaths, just 13 countries account for 70 percent of the global total (WHO 2004b).[2] Caution is again needed, because the poorest countries also have the weakest information systems and, therefore, have estimates derived solely from modeling. One regression model (WHO 2004b), for example, uses independent variables, such as the percentage of deliveries with health professionals present and the proportion of deaths of women of reproductive age that are maternal deaths. Those variables are themselves subject to error and likely to be least reliable where information systems are weakest. Geographic differences in maternal mortality within countries are poorly documented, although remote populations are often assumed to suffer the highest levels because of poor access to emergency obstetric care. Although this assumption seems logical, few reliable data are available to confirm or refute it, and the possibility of high levels of mortality in urban areas linked to unsafe abortion (Thonneau and others 2002) makes the topic of geographic differentials a priority for research.

Until recently, socioeconomic differentials in mortality have tended to be inferred from utilization patterns for prenatal care and health professionals at delivery. The DHSs continue to provide the main data sources in this regard, for both international and national analyses, and they demonstrate huge differences between wealth quintiles. A relevant recent development, however, is the familial technique, which can be used to examine socioeconomic differences in maternal mortality using existing survey data (Graham and others 2004). Because

Table 26.3 Early Neonatal Deaths by Gender and Cause, 2001 *(thousands)*

	World[a]			South Asia			Sub-Saharan Africa[a]		
Cause	**All**	**Male**	**Female**	**All**	**Male**	**Female**	**All**	**Male**	**Female**
Perinatal conditions[b]	2,522	1,400	1,123	1,086	596	489	573	332	241
Low birthweight[c]	1,301	710	591	757	406	351	243	141	102
Birth asphyxia (including birth trauma)	739	432	307	192	122	70	240	139	101
Other perinatal conditions[d]	482	258	225	137	68	68	90	52	38

Source: WHO 2004d.

a. Excludes the island of Mayotte.

b. Excludes stillbirths, congenital malformations, neonatal tetanus, congenital syphilis, acquired infections (respiratory and sepsis), and diarrhea.

c. Includes preterm deliveries and small for gestational age.

d. Includes all conditions originating in the perinatal period (P00–P96 codes in perinatal chapter of WHO 1992a), apart from low birthweight and asphyxia.

Table 26.4 DALYs for Perinatal and Maternal Conditions by Gender, Selected Regions, 2001
(thousands)

	World[a]			South Asia			Sub-Saharan Africa[a]		
Condition	**All**	**Male**	**Female**	**All**	**Male**	**Female**	**All**	**Male**	**Female**
Maternal	26,789	n.a.	26,789	10,069	n.a.	10,069	9,743	n.a.	9,743
Hemorrhage	3,928	n.a.	3,928	1,718	n.a.	1,718	1,643	n.a.	1,643
Sepsis	5,348	n.a.	5,348	1,857	n.a.	1,857	1,843	n.a.	1,843
Hypertensive disorders of pregnancy	1,895	n.a.	1,895	742	n.a.	742	842	n.a.	842
Obstructed labor	2,506	n.a.	2,506	1,185	n.a.	1,185	919	n.a.	919
Unsafe abortion	3,507	n.a.	3,507	1,467	n.a.	1,467	1,557	n.a.	1,557
Perinatal[b]	90,505	49,384	41,117	37,721	20,442	17,279	20,046	11,351	8,697
Low birthweight[c]	43,073	23,241	19,832	25,015	13,292	11,723	7,891	4,501	3,391
Birth asphyxia (including birth trauma)	31,972	17,945	14,025	8,283	4,957	3,326	9,256	5,195	4,062
Other perinatal conditions[d]	15,460	8,198	7,260	4,423	2,193	2,230	2,899	1,655	1,244

Source: WHO 2004d.
n.a. = not applicable.
a. Excludes the island of Mayotte.
b. Excludes stillbirths, congenital malformations, neonatal tetanus, congenital syphilis, acquired infections (respiratory and sepsis), and diarrhea.
c. Includes preterm deliveries and small for gestational age.
d. Includes all conditions originating in the perinatal period (P00–P96 codes in perinatal chapter of WHO 1992a) apart from low birthweight and asphyxia.

maternal health and health care are clearly associated with stillbirths and early neonatal deaths, the same differentiating factors are likely to apply to perinatal outcomes. Indeed, data from many DHSs show large gaps between rich and poor in relation to neonatal mortality, with the greatest average disparity being found in Latin American and the Caribbean (http://www.worldbank.org/poverty/health/).

Attributable Burden

The estimation of maternal and perinatal conditions as part of international assessments of the burden of disease has long been controversial, and much has been written about the problems and potential distortions of priorities (AbouZahr 1998; Sadana 2001). Some of those criticisms relate to methods of valuation based on disability-adjusted life years (DALYs), especially in relation to discounting and the omission of stillbirths, and others to the inaccuracies and selectivity of the base data on the incidence of complications, on case fatalities, and on disabilities. Table 26.4 presents DALYs for South Asia and Sub-Saharan Africa for the focus conditions for 2001. Those two regions together account for 74 percent of the global burden of maternal conditions and 64 percent of the global burden of perinatal conditions.

The significance of the burden of maternal and perinatal conditions is clear from two recent global assessments (CMH 2002; WHO 2002). The approaches the two initiatives adopted have led to different conclusions about public health priorities. The former focused on avoidable mortality resulting primarily from direct obstetric conditions, whereas the latter considered population risk assessments and highlighted the contribution of indirect obstetric problems—especially micronutrient deficiencies—and the role for preventive strategies. Clearly, the choice between different measures of burden has a crucial influence both on the strategic approach to achieving health gains and on the prioritization of interventions.

INTERVENTIONS

Given the scope and nature of the burden of maternal and perinatal conditions, no quick fix is available and, thus, no single intervention warrants exclusive attention. Rather, clusters or packages of interventions need to be considered, and this understanding has long been reflected in maternity services throughout the world (Milne and others 2004). Even though these clusters can be characterized or differentiated solely on the basis of content—namely, the component interventions—in practice, the health system or implementation context is also a defining factor.

Levels and Types of Interventions

Box 26.1 presents one example of a comprehensive strategy for safe motherhood. It illustrates the range of programmatic

Box 26.1

Components of a Comprehensive Safe Motherhood Strategy

The following are part of a comprehensive safe motherhood strategy:

- community education on safe motherhood and newborn care
- evidence-based prenatal care and counseling
  - — nutritional advice
  - — iron and folate supplements (multivitamins and micronutrients)
  - — iodization of edible oils and salt and vitamin A in areas of endemic deficiency
  - — blood pressure screening
  - — screening and treatment for syphilis
  - — antiretrovirals, where voluntary counseling and testing undertaken, and breastfeeding advice
  - — tetanus toxoid immunization
  - — treatment of urinary tract infections
- skilled assistance at delivery
- care of obstetric complications and emergencies
- postpartum care
- safe abortion and postabortion services
- family-planning information and services
- adolescent reproductive health education and services

Source: Dayaratna and others 2000.

issues raised by maternal and perinatal conditions:

- the scope for both primary and secondary prevention
- the difference between the individual receiving specific interventions (here, the mother) and the beneficiary (the baby)
- the multiple effects of single (component) interventions on different outcomes
- the multiple benefits to the same outcome of different interventions
- the short- and long-term time frames for interventions and outcomes
- the balance between supply-side and demand-side interventions
- the role for interventions outside the health sector.

Three main pathways are available for averting adverse outcomes: preventing pregnancy, preventing complications, and preventing death or disability from complications. The first pathway is the only truly primary preventive strategy. It requires intervention to avert the occurrence or mistiming of pregnancy by means of effective family-planning methods, as discussed in chapter 57. This preventive approach is relevant for those women who are able to and wish to avoid or delay pregnancy, but it has a limited role for those not in this position, estimated at between 15 and 57 percent of women age 15 to 29 (WHO 2002). As concerns the primary prevention of complications, comparatively limited reliable evidence is available on the true size of the avoidable fraction for many conditions at a population level. The emphasis in this preventive pathway is on maintaining normality and on managing mild complications—and thus on good quality of care. Finally, maternal death and disability may be avoided by effective, timely, and appropriate clinical interventions, often referred to as *emergency obstetric care.*

Given this complexity and the multiple approaches used to address maternal and perinatal conditions, no perfect framework for categorizing interventions exists. We, therefore, cluster the alternative intervention pathways on the basis of the following three parameters:

- level of care—home, primary, and secondary
- time period—pregnancy, labor and delivery, and postpartum
- strategic approach—population-based versus personal interventions.

Quality of Evidence

Pregnancy and childbirth have been the subjects of medical investigation for centuries and, indeed, are among the oldest clinical specialties. As a consequence, a substantial body of opinion exists on the signs, symptoms, etiology, prognosis, natural history, and management and treatment options for many maternal and perinatal complications, particularly in developed countries. Much of it can be regarded as conventional wisdom acquired through practice. In contrast, a comparatively small proportion of interventions can be regarded as based on evidence, by contemporary scientific standards, and arrived at through the conduct of robust research. Thus, in specification of the content of intervention clusters, a built-in tension exists between using the best available knowledge and using only evidence that passes minimum quality criteria. Equally important

is recognizing the fundamental distinction between knowing what is effective at an individual case-management level, for which an evidence base exists for maternal and perinatal conditions, and demonstrating effectiveness at the aggregate levels of composite strategies and entire countries or regions, for which robust evidence is extremely limited (Graham 2002).

Population-Based Interventions

The primary aim of population-based interventions is to reduce the risks leading to adverse outcomes at the population level rather than at the individual level (WHO 2002). Population-based interventions are essentially preventive and seek to promote healthy behaviors, thereby reducing incidence in the entire population. In the case of maternal and perinatal conditions, such an approach could be adopted for two major risk factors: lack of contraception and maternal undernutrition. The grade of evidence for these population-based interventions is primarily level C for the former, but a mixture of A and B for the latter.[3]

Fertility Behavior Change. Fertility behavior is ultimately the primary exposure factor for both maternal and perinatal conditions. Investigators have shown that the frequency (number and spacing), the timing with regard to age, and the desirability of pregnancy are associated with increased risks, although some dispute remains about the effect of birth intervals. Researchers have also investigated the influence of those factors on perinatal conditions, finding clear associations with old or young maternal age, short interpregnancy intervals, and high or first birth order, with many of those variables also being interrelated (Bale and others 2003).

Lack of effective use of contraception may result in unwanted or mistimed pregnancies. Unintended pregnancies are known to be associated with adverse maternal outcomes, including unsafe abortion. Contraceptive behavior is clearly determined by a host of socioeconomic, cultural, religious, and medical factors (Hussain, Fikree, and Berendes 2000; Marston and Cleland 2003; Mwageni, Ankomah, and Powell 2001), which also have a bearing on intervention options. Most of the options on the demand side focus on information, education, and communication; those on the supply side focus on client-friendly services. At a macro level, those intervention options have been credited with the substantial increase in contraceptive use in developing countries over the past 40 years, which, in turn, is seen as a contributor to the overall fall in the total fertility rate from 6 to 3 (Cleland and Ali 2004). Nevertheless, a significant unmet need for contraception persists in many developing countries, with high levels of unsafe abortion as a proxy indicator of that need.

As regards evidence of the effectiveness of family planning in explicitly reducing maternal mortality or disability, no primary sources are available, but there are a variety of modeled estimates, such as Prata and others (2004), Walsh and others (1993), and Winikoff and Sullivan (1987). Model estimates vary enormously in terms of the size of the effect, depending primarily on assumptions about the proportion of maternal deaths caused by unsafe abortion. Investigators estimate the potential gain from the avoidance of unintended or mistimed pregnancies to be a 20 percent decrease in maternal deaths in developing countries (Donnay 2000; Kurjak and Bekavac 2001; UNICEF 1999).

Nutritional Interventions. Maternal undernutrition encompasses two main dimensions: underweight and micronutrient deficiencies (principally iron and vitamin A). Unlike many of the direct maternal complications, which are acute at onset and of relatively short duration, these nutritional problems are chronic and long term and, indeed, are intergenerational (Tomkins 2001). The physiological mechanisms by which undernutrition exerts an influence on outcomes in the mother and baby are not entirely understood, but a large body of epidemiological evidence supports associations with, for example, fetal growth or length of pregnancy (Villar and others 2002). Those findings have originated mostly from populations with either severe levels of undernutrition or significant cofactors, such as malaria and other infections.

Considerable uncertainty surrounds the issue of timing potential interventions, with conflicting opinions about making targeted interventions during pregnancy; addressing undernutrition among girl children or adolescents, and applying strategies for women of reproductive age, including periconceptual women (Gay and others 2003; Rush 2000). Further debate relates to the use of supplements versus food fortification. A systematic review by Villar and others (2002) of randomized controlled trials to prevent or treat adverse maternal outcomes and preterm delivery concludes that limited evidence supports large-scale interventions with multivitamins, minerals, or protein-energy supplementation, but that iron and folic acid are effective against anemia. Rouse (2003) emphasizes the potential cost-effectiveness of vitamin A or beta-carotene supplementation in reducing maternal mortality if the findings of West and others (1999) from Nepal are replicable elsewhere.

Personal Interventions

When we consider interventions directed at individuals rather than whole populations, the need for a continuum of care for mother and baby in terms of time (before and after delivery), place (linking home and health services through an effective referral chain), and person (the provider of care) is important. A variety of conceptual frameworks emphasize this continuum and the dangers of fragmentation. Care to prevent or treat the vast majority of maternal and perinatal conditions can be

provided at home, at the primary level (clinic or health center), and at the secondary level (district hospital),[4] with the district or equivalent regarded as the essential planning unit for service delivery (WHO 1994). This system is comparable to the "close-to-client" health system that the Commission on Macroeconomics and Health (CMH 2002) has proposed, whereby trained staff members other than doctors provide much of the care, with an emphasis on primary prevention and management of acute conditions.

Home-Based Care. Two topical interventions that fall into the category of home-based care are (a) information, education, and communication and birth preparedness and (b) male involvement (for home-based newborn care, see chapter 27). Evidence in this cluster of interventions falls predominantly into the level C category.

Birth Preparedness Many descriptive studies indicate that women, relatives, and other members of the community frequently do not recognize danger signs in pregnancy, childbirth, or the puerperium, and that lack of recognition can have serious consequences for mother and baby (Gay and others 2003). Health education interventions at prenatal clinics appear to be less successful at raising awareness and increasing the use of emergency obstetric care than the use of pictorial cards (Khanum and others 2000) or community education (Bailey, Szaszdi, and Schieber 1995).

Birth preparedness includes planning for the place and the attendant at delivery, as well as arranging for rapid transfer to a health center or hospital, when needed, and sometimes identifying a compatible blood donor in the case of hemorrhage (Portela and Santarelli 2003). Initiatives to promote birth preparedness can clearly be home or community based, but studies have emphasized the importance of linkages with prenatal care so as to include appropriate recommendations for intrapartum care (Shehu, Ikeh, and Kuna 1997). In circumstances in which prenatal services are of poor quality or are underused, traditional birth attendants or relatives are often the only source of information; thus, initiatives need to reach those individuals too.

Male Involvement Many studies have observed positive benefits from the involvement of male partners in care-seeking behavior related to pregnancy and delivery (Gay and others 2003). That involvement is now advocated as an essential element of WHO's Making Pregnancy Safer Initiative (WHO 2003). Models and mechanisms for achieving this involvement have not been robustly evaluated, and considerable controversy concerns those that are based on behavioral and social cognitive theories that presume lack of knowledge as the root problem (Portela and Santarelli 2003; Raju and Leonard 2000).

Primary-Level Care. Primary-level care is widely regarded as the crucial entry point to maternity services—and also to care before and after pregnancy. The focus here is essentially preventive, but with the capacity to detect problems, to manage mild complications appropriately, and to stabilize and then refer cases that require higher-level care. Although the name used for primary care facilities varies from country to country, we employ the commonly used term *health center*. In terms of functionality in relation to maternal and perinatal care, the health center should provide prenatal, delivery (including management of complicated abortion), and postpartum care (including family planning and postabortion counseling), as well as care of the newborn.

The management of complicated cases is usually discussed at two levels: basic emergency obstetric care (BEmOC) and comprehensive emergency obstetric care (CEmOC), the distinction being made on the basis of the number of signal or essential clinical functions performed.[5] This distinction forms the basis of a set of process indicators that the United Nations (UN) has endorsed for program monitoring (UNFPA 2003). The capacity of health centers to provide BEmOC depends on the availability of supplies, drugs, infrastructure, and skilled providers. Some of the signal functions may not always be performed by midwives or nurses, sometimes because of the regulation of roles by the government or professional bodies. For this reason, a further distinction can be made between full BEmOC, which comprises six functions, some of which may require a doctor, and obstetric first aid, which includes two signal functions universally performed by midwives and nurses: the administration of antibiotics or oxytocics, intravenously or intramuscularly.

Routine Prenatal Care The literature available on routine prenatal care is extensive, and there is a long history of assessing the component interventions (Hall, MacIntyre, and Porter 1985; Rooney 1992). In safe motherhood programs, prenatal care provides one of the rare examples of robust assessment of an intervention package (Villar and others 2001). As Bale and others (2003) note, even though many of the component clinical interventions are effective in terms of perinatal outcomes (Bergsjo and Villar 1997), reliable evidence of an effect on maternal mortality in developing countries is not available (McDonagh 1996). However, where early detection is followed by appropriate treatment, prenatal care does seem to reduce adverse outcomes from specific maternal conditions, including hypertensive disorders of pregnancy, urinary tract infections, and breech presentations (Carroli, Rooney, and Villar 2001; Villar and Bergsjo 1997). Conversely, the limited effectiveness of prenatal risk screening at a population level is now widely acknowledged (Graham 1998). The poor predictive value of many screening tools for maternal complications reinforces the importance of access to emergency obstetric care for all women

who develop a need for it and underlies calls for skilled attendance at all deliveries. Many health experts, however, do accept screening and treatment for syphilis and immunization with tetanus toxoid as important prenatal interventions (Bale and others 2003). Similarly, the prevention and treatment of anemia and of malaria, with prophylaxis or bednets, are widely regarded as essential elements of routine prenatal care. Nutritional supplementation, however, remains more controversial.

Prenatal care has been assessed not only in terms of content, but also in relation to alternative models of the number and timing of visits (Munjanja, Lindmark, and Nystrom 1996). Strong evidence exists on the cost-effectiveness of a targeted, four-visit schedule (Villar and others 2001) that includes an educational element on the recognition of danger signs and the use of skilled attendance at delivery.

The principal sources of international data on levels, trends, and differentials in prenatal care coverage are the DHSs. The latest statistics show comparatively high coverage levels when measured in terms of one or more visits—levels average 71 percent for Sub-Saharan Africa—but comparatively little improvement between 1990 and 2000. Within countries, wide socioeconomic differentials in uptake are apparent.

Delivery Care As indicated earlier, the risks of adverse outcomes in mother and baby are usually highest during the intrapartum period. Even though health experts have long appreciated this fact, prioritization of this element of safe motherhood is comparatively recent. Much has been written both on this shift in emphasis and on the underlying rationale, as well as on what skilled attendance at delivery should comprise (De Brouwere and Van Lerberghe 2001). Investigators have suggested a variety of conceptual models for defining content, with varying degrees of emphasis on the attendant and on the enabling environment (Bell and others 2003). All these models recognize that skilled attendance encompasses both normal and complicated deliveries, with the focus on the former and on the management of mild complications at the primary level, as is consistent with BEmOC, and with referral to CEmOC at the secondary level when necessary.

Key unresolved issues at the primary level relate to the skills and scope of work of the attendant, especially in relation to being a multipurpose health worker, and to the potential role of nonprofessionals, such as auxiliaries and trained traditional birth attendants (Buttiens, Marchal, and De Brouwere 2004). Work by Koblinsky and Campbell (2003) has helped to inform this debate by proposing four basic models of delivery care that vary according to configurations of place of delivery and attendant. Evidence on the effectiveness of the alternative models at a population level is lacking, and support for skilled attendance at delivery is, thus, based primarily on historical and contemporary ecological analysis (De Brouwere and Van Lerberghe 2001). Conversely, high-grade evidence supports a number of clinical interventions, such as active management of the third stage of labor, as well as essential newborn care.

Once again, the principal sources of data on levels and trends in coverage of skilled attendants at delivery are the DHSs. The data, however, are based on women's self-reports of who attended their deliveries, include only live births, and have major definitional uncertainties. Some countries, for example, use terms such as *supervised deliveries* and include as attendants both auxiliaries and trained traditional birth attendants (see Bell, Curtis, and Alayon 2003 for a critique of these data). A global analysis of trends in deliveries by skilled attendants showed wide variations in progress across different regions, with the latest figures for Sub-Saharan Africa, Asia, and Latin America and the Caribbean for 1990–2003 being 48, 59, and 82 percent, respectively (AbouZahr and Wardlaw 2001; WHO 2004a). The proportion of deliveries with health professionals present (doctors, midwives, nurses) is one of the proxy indicators for the MDG on maternal health (Graham and Hussein 2004). It demonstrates not only major differentials between countries, but also wide variation in uptake across socioeconomic groups within countries (De Brouwere and Van Lerberghe 2001). Although skilled attendants do not necessarily operate only in fixed health facilities such as health centers, the DHS data show low levels of professional attendance in the community. Promoting skilled attendance is thus essentially advocating for institutionalizing deliveries.

Postpartum Care Primary care services continue to neglect the postpartum period despite significant morbidity among mothers and babies during this time. Routine performance of postnatal checks is not widespread, and most contacts with services after delivery tend to focus on educational messages on, for example, danger signs, breastfeeding, nutrition, and lifestyle.

Postabortion Care One significant area of service delivery that does not fit well with descriptive frameworks based on prenatal, intrapartum, and postpartum care is the management of complicated abortions. Unsafe abortion accounts for a significant proportion of the burden of maternal conditions, but it is still treated as the poor relation in the debate on intervention strategies (De Brouwere and Van Lerberghe 2001). In particular, with the prioritization in recent years of skilled attendance at delivery, both the service base for and the provider of postabortion care have become less well defined (Dayaratna and others 2000). This crucial element of obstetric care falls into BEmOC in the case of mild complications and CEmOC for more serious cases, but whether it is regarded as part of prenatal, delivery, or postnatal services appears to vary from setting to setting. Moreover, postabortion care illustrates the dangers of the fragmentation of broader reproductive health

care, because primary prevention and counseling after treatment for complications tend to fall within the remit of family-planning services, whereas emergency care at the primary level is usually provided as part of maternity services and at the secondary level may fall within obstetrics or gynecology services.

Secondary-Level Care. Secondary-level care is hospital-based care, generally at the district level, including CEmOC. As a center for referral, this level of care needs to be linked to the primary level through an effective chain of communications (Murray and others 2001). The focus at the district hospital is on secondary prevention, with the ability to manage the principal maternal and perinatal conditions discussed earlier; thus, district hospitals must be able to provide surgical interventions and the requisite backup, such as blood banks (Kusiako, Ronsmans, and Van der Paul 2000). In many countries, however, the district hospital is also the local provider of preventive services, including prenatal and normal delivery care; as such, it is responsible for attending to a wide mix of uncomplicated and complicated cases.

Although no high-grade evidence of the effectiveness of CEmOC is available, many health experts agree that maternal mortality cannot be significantly reduced in the absence of such care (Bale and others 2003). The issue thus becomes one of the cost-effectiveness of other strategies, given the presence of CEmOC. The UN agencies have endorsed the threshold of one CEmOC facility per 500,000 people. Data indicating the attainment of this ratio—and, indeed, the percentage of met need for CEmOC—are not widely available. Similarly, reliable information on geographic or socioeconomic differentials in access to CEmOC is extremely limited.

Policy Considerations and Approaches

The health of mothers and babies is a human right and needs to be underpinned by policies and laws that increase access to information and good-quality, affordable health services (Germain 2000). A positive policy environment is crucial for promoting maternal health and reducing the burden of maternal and perinatal conditions. Such policy considerations need to go beyond the health sector to include related issues, such as transportation, nutrition, girls' access to education, and gender biases in the control of economic resources. Through a human rights–based approach, programs can be fashioned to ensure that every woman has the right to make informed decisions about her own health and has access to quality services before, during, and after childbirth (Freedman 2001).

The ICPD marked a dramatic shift not only by putting the concepts of rights and choice center stage, but also by introducing the reproductive health paradigm. The first decade of the ICPD plan of action was marked by major improvements in policies related to maternal health in most of the 179 signatory countries. However, as observed at the ICPD + 10 Conference, many promised changes remain at the level of policy pronouncement and have not yet been implemented. The stagnation is most notable in relation to maternal mortality and the HIV pandemic, especially in Sub-Saharan Africa. The failure to fully implement the ICPD consensus can be attributed to lack of political will, inadequate funding for programs to further reproductive health, and weak health systems. It is too early to judge the effect of the MDG proclamation (Johansson and Stewart 2002), although it could well suffer the same fate unless special attention is given to maternal and child health in the context of sectorwide approaches and Poverty Reduction Strategy Papers (UNFPA 2003). Some suspect that both these modalities may not give reproductive health the focus and attention it requires, because competing needs may crowd it out. Others argue, however, that sectorwide approaches can be a boon for maternal health because they offer a more effective platform for addressing ailing health systems (Goodburn and Campbell 2001).

Whether at the national or international level, advocacy for maternal and perinatal health should focus on the following seven key message areas:

- magnitude of the problem
- factors influencing maternal and perinatal outcomes
- functions of maternal health programs and which interventions work
- consequences of not addressing maternal and perinatal health
- costs of improving maternal and perinatal health
- responsibilities at each level of the health system and beyond
- policy and legal impediments to implementing comprehensive safe motherhood and newborn health programs.

Major advocacy networks, such as the Partnership for Safe Motherhood and Newborn Health, the White Ribbon Alliance, and the Healthy Newborn Partnership, seek to promote maternal and newborn health at the global level. Their purpose is to create awareness by changing the language of discourse, building international political commitment, developing global guidelines, and improving access to technical information for providers and program managers.

COST-EFFECTIVENESS OF SELECTED INTERVENTION PACKAGES

Cost-effectiveness analysis (CEA) faces several major challenges with respect to evaluating the prevention and treatment of maternal and perinatal conditions. First is the sheer range of conditions and potential interventions. The breadth of the clinical area implies the need to make tough choices with

respect to which packages of interventions to compare. A second and related challenge is the lack both of reliable data on the burden of conditions and of high-grade evidence on the effectiveness and costs of packages. As a result, we can assess only the relative cost-effectiveness of different packages of interventions by means of modeling. Thus, the third set of challenges is associated with modeling, which makes the analysis vulnerable to all the usual criticisms of the modeling of cost-effectiveness—in particular, uncertainty about the direction of any bias introduced and the difficulty of establishing the validity of the model (Sheldon 1996). Finally, there are the related issues of the appropriateness to maternal and perinatal conditions of standard outcome measures used in the model—in particular, DALYs, which exclude stillbirths and indirect maternal conditions (AbouZahr 1999; De Brouwere and Van Lerberghe 2001).

Selected Intervention Packages

For some of the reasons mentioned in the previous subsection, researchers have made few attempts to model packages of interventions for maternal and perinatal conditions, and many of those attempts do not specify content in sufficient detail to replicate the package. Our approach is to define content by beginning with a literature search of best practices in preventing and managing the focus maternal and perinatal conditions, acknowledging that, by excluding conditions that impose a lesser burden, we ignore interventions that might be highly effective and cost-effective. We then grouped those interventions that are considered effective and that are either being or likely to be implemented on a substantial scale into packages of care, bearing in mind previous CEA work, such as the WHO mother-baby package (WHO 1994). Expert panels then reviewed the component interventions and the packages and assisted with identifying resource requirements. Given the complementary CEA elsewhere in this volume on interventions relevant to maternal and perinatal conditions such as family planning, we focus on care during pregnancy, postpregnancy care, and care immediately postdelivery—in other words, on clusters or packages of interventions typically referred to as *prenatal care, delivery* or *intrapartum care,* and *emergency obstetric care.* Table 26.5 outlines the content of those packages.

When one considers the intervention packages, contextual factors are clearly crucial. Given the particularly high burden in South Asia and Sub-Saharan Africa, we chose those two regions as the specific health system scenarios for this chapter. Those regions are also characterized by high levels of poverty and encompass some of the most heavily indebted countries in the world.

Comparison of Alternative Intervention Package Scenarios. Following the approach of generalized CEA (Hutubessy and others 2003), we evaluated intervention packages with respect to a counterfactual (base scenario), varying the content and coverage. We also performed sensitivity analyses to examine the effects of changing the values of key variables for costs, effectiveness, or both. Each intervention package scenario specifies different dimensions of prenatal and intrapartum care provided at primary and secondary care facilities. As regards the assumed pathways through which women with normal or complicated pregnancies may or may not access care, the crucial entry point in our model is prenatal care. That choice influences the detection and treatment of mild and severe complications during the antepartum period at both the primary and the secondary levels, as well as the proportion of women delivering with a health professional present and with improved access to emergency care for intrapartum or abortion-related complications. In our CEA model, these effects are achieved primarily through two types of interventions:

- improvements in the quality of care, incorporating the technical content or the proportion of women in receipt of the care needed (that is, met need)
- increases in the coverage of care—namely, the proportion of women accessing care.

Routine prenatal care can be characterized in terms of whether it is a basic or an enhanced package—in other words, its technical content (table 26.5)—and by the percentage of women accessing the package—in other words, its coverage. Delivery at a primary-level health center is viewed as having a single quality dimension in terms of content—namely, whether BEmOC is available for women who develop mild complications, including complicated abortion (table 26.5). BEmOC is assumed to require the presence of a doctor at the health center; otherwise, only obstetric first aid is presumed to be available, covering just the two signal functions described earlier.

A percentage of women with severe complications who access primary care will go on to secondary care. This percentage is assumed to be 20 or 50 percent of complicated cases attending primary care. Our model makes no provision for women who access secondary care directly in the event of a serious complication, although it does allow for those who were attending the hospital as their local provider of primary care. Of those women who access the secondary care facility from the primary level, a proportion will receive the CEmOC that they need (assumed to vary between 50 and 90 percent of complicated cases that reach secondary care). This figure reflects such issues as staff skills and motivation and the availability of drugs and equipment. For the other quality-of-care element—namely, the technical content of CEmOC—we consider two levels: with (enhanced package) and without (base package) selected interventions for high-risk babies (table 26.5).

Table 26.5 Care Packages at the Primary and Secondary Levels

Level of care and condition	Content	Base package	Enhanced package
Routine prenatal care at the primary level[a]	Clinical examination, including for severe anemia, height and weight, blood pressure	√	√
	Obstetric examination for gestational age estimation and uterine height, fetal heart, detection of malpresentation and position, and referral	√	√
	Gynecological examination	√	√
	Urine test (multiple dipstick)	√	√
	Laboratory tests: hemoglobin, blood type and rhesus status, syphilis and other symptomatic testing for sexually transmitted diseases	√	√
	Advice on emergencies, delivery, lactation, and contraception	√	√
	Education about clean delivery, warning signs, and premature rupture of membranes	√	√
	Iron and folic acid supplementation	√	√
	Multivitamin supplementation	—	√
	Tetanus toxoid immunization	√	√
	HIV voluntary testing and counseling	—	√
	Antimalarial chemoprophylaxis in endemic areas	—	√
	Screening and treatment for syphilis	√	√
	Balanced protein-energy supplementation for all women	—	√
Delivery care at the primary level[b]	Clean delivery technique, clean cord cutting, clean delivery of baby and placenta	√	√
	Active management of the third stage of labor, including oxytocics	√	√
	Episiotomy in appropriate cases	√	√
	Recognition and first-line management of delivery complications (for example, obstructed labor, early detection of cephalopelvic disproportion, malposition and malpresentation, previous cesarean delivery, postpartum hemorrhage, and preeclampsia or eclampsia) and referral	√	√
	Intravenous fluid	√	√
	Intravenous uterotonics, if bleeding occurs	√	√
	Partograph	√	√
	Essential newborn care	√	√
	Intravenous antibiotics	√	√
	Magnesium sulfate	—	√
	Forceps or vacuum extraction	—	√
	Manual removal of placenta	—	√
	Removal of retained products of conception	—	√
	Corticosteroids for preterm labor	—	√
	Antiretrovirals for prevention of mother-to-child transmission of HIV	—	√
	Antibiotics for premature rupture of membranes	—	√
CEmOC package at the secondary level[c]			
Postpartum hemorrhage	Recognition of high-risk cases and arrangements for delivery in a facility	√	√
	Grouping of blood	√	√
	Iron and folate supplementation	√	√
	Blood transfusion	√	√
	Uterotonic drugs, oxytocics	√	√
	Bimanual compression of uterus	√	√
	Manual removal of placenta	√	√
	Uterine packing or balloon tamponade	√	√
	Fluid replacement	√	√
	Hysterectomy	√	√
	Removal of products of conception	√	√
	Secondary postpartum hemorrhage management (antibiotics, uterotonics, removal of products of conception, and fluid and blood replacement)	√	√

(Continues on the following page.)

Table 26.5 Continued

Level of care and condition	Content	Base package	Enhanced package
Antepartum hemorrhage	Early detection of major placenta previa and abruption	√	√
	Grouping and saving blood	√	√
	Iron and folate supplementation	√	√
	Cesarean section for major-degree placenta previa, abruption with a live baby	√	√
	Blood and fluid replacement	√	√
	Oxytocics	√	√
Sepsis	Antibiotics for premature rupture of membranes, cesarean section	√	√
	Fluid and blood transfusion	√	√
	Intravenous antibiotics	√	√
	Evacuation of products of conception	√	√
	Drainage of abscess	√	√
	Treatment of shock with fluids or blood, nitroglycerine	√	√
Pregnancy-induced hypertension	Early detection and management of preeclampsia	√	√
	Calcium supplementation in high-risk cases	√	√
	Aspirin to prevent preeclampsia	√	√
	Antioxidants to prevent preeclampsia	√	√
	Intravenous magnesium sulfate	√	√
	Antihypertensive drugs to reduce blood pressure	√	√
	Immediate delivery if more than 36 weeks	√	√
	Magnesium sulfate and antihypertensives for postpartum eclampsia	√	√
Obstructed labor	Partograph	√	√
	Cesarean section	√	√
	Symphysiotomy	√	√
	Destructive operation	√	√
	Antibiotics	√	√
	Fluid and blood transfusion	√	√
	Hysterectomy	√	√
Abortion	Evacuation of retained products of conception	√	√
	Intravenous antibiotics	√	√
	Fluid or blood transfusion	√	√
	Postabortion contraceptive advice	√	√
Ectopic pregnancy	Proof puncture (culdocentesis)	—	—
	Laparotomy and salpingectomy	—	—
	Blood transfusion (autotransfusion)	√	√
High-risk infant	Forceps or vacuum extraction[d]	√	√
	Corticosteroids for preterm labor	—	√
	Antiretrovirals for prevention of mother-to-child transmission of HIV	—	√
	Antibiotics for premature rupture of membranes	—	√

Source: Authors.

— = not available.

a. The base package includes the four-visit schedule recommended by WHO (Villar and others 2001).

b. The base package includes the provision of obstetric first aid (intravenous or intramuscular antibiotics and oxytocics). The enhanced package includes the availability of a doctor, and thus the full range of BEmOC (UNFPA 2003). In some settings, experienced midwives or clinical officers may perform all six BEmOC functions.

c. At the hospital level, prenatal or delivery care will also be provided for normal, uncomplicated cases and, thus, also includes all care listed in the first two panels of the table.

d. Forceps or vacuum delivery can also be used for several other conditions, such as prolonged labor (not obstructed), fetal distress, preterm birth, aftercoming head of breech, and preeclampsia to speed up delivery.

The base case for our CEA model assumes the following:

- basic technical content for the prenatal care package
- prenatal care coverage for 50 percent of pregnancies
- only obstetric first aid (two signal functions) available in health centers
- 20 percent of women with severe complications accessing secondary care
- 50 percent of those severe cases receiving the CEmOC that they need.

The different assumptions regarding quality of care and coverage can be combined in many different ways, yielding a large number of potential packages and a larger number of potential comparisons between those and the base package. However, not all possible scenarios are meaningful. For example, because the base prenatal care package does not screen for HIV, matching that package with enhanced delivery care that provides antiretrovirals to reduce vertical transmission would be inappropriate. We identified six packages for comparison with the base case, representing a range of safe motherhood strategies and focusing on prenatal and delivery care. Table 26.6 summarizes these alternatives and indicates their essential characteristics from a safe motherhood perspective.

Resource Use and Costs

We adopted an ingredients approach (Creese and Parker 1994) to identify resource use. For this type of bottom-up costing, we prepared lists for primary- and secondary-level care facilities of types of personnel, drugs, supplies (medical and nonmedical), medical and surgical equipment relevant for the interventions, and capital items (vehicles, buildings, building space). For most of the scenarios, our identification of resources was based on the WHO mother-baby package costing tool (WHO 1999), with necessary modifications because of the content of care packages indicated in table 26.5. We estimated the costs for clinical personnel on the basis of salaries for different grades according to the guidelines provided by the volume editors for the two selected regions. The time required by different staff members for each care intervention and the changes in time and personnel because of varying content and coverage of packages were informed by expert panel reviews, and we then calculated the costs. We valued the other nontraded inputs using information primarily provided by WHO-CHOICE (2004).

Cost-Effectiveness Ratios

The CEA involves a number of fixed and variable assumptions (see annex 26.A). The most important assumptions concern the reducible burden of these conditions, the effectiveness of the interventions, and the availability of appropriate human resources. We have assumed that increases in care can be achieved without major capital investments and that human resources are not in short supply; therefore, more could be used (with given wage rates) as required for increased activity and enhanced coverage.

Table 26.7 summarizes the findings of the CEA in terms of incremental cost-effectiveness ratios (ICERs) for the six primary comparisons between the base scenario and alternative intervention packages for a population of 1 million. Table 26.8 gives details of total costs, deaths averted, life years saved, and DALYs averted. Table 26.9 shows the findings of the sensitivity analysis in terms of how the ICERs change when different assumptions (see annex 26.A) are made with respect to effectiveness, met need, and inpatient costs.

In interpreting the results, note that they are point estimates. Even though they are based on the best information currently available, all the inputs into the model are subject to some degree of uncertainty. Without access to robust data on individual costs and effects or without specifying distributions for each variable, it is impossible to identify confidence limits for the estimated ICERs. Thus, we do not know, for example, whether the difference in the incremental cost per DALY averted for Sub-Saharan Africa between increased coverage at the primary level (US$92) and improved quality of CEmOC (US$151) reflects a genuine difference in cost-effectiveness or whether there are overlapping confidence intervals (table 26.7).

With those important caveats in mind, at first sight the results for South Asia and Sub-Saharan Africa appear quite different. For each intervention package, regardless of the specific assumptions made, the cost per DALY averted is always lower in Sub-Saharan Africa. The higher costs of care in Sub-Saharan Africa (see annex 26.A) are thus more than compensated for by the higher effectiveness, which is a result of the region's greater burden. However, some important similarities are apparent between South Asia and Sub-Saharan Africa. Leaving aside options 3b and 5b (the options without nutritional supplements), the results for both regions show a consistent pattern. Improvements in the overall quality of care, especially at the primary level through the provision of BEmOC (option 3a), together with increased overall coverage (option 5a), are the most cost-effective intervention packages—and both include nutritional supplements. They are followed by increased coverage at the primary level (option 2). Improved quality of CEmOC (option 4) is the least cost-effective option. Removing nutritional supplements from the packages makes relatively little difference in Sub-Saharan Africa, slightly increasing cost-effectiveness, but in South Asia, options 3b and 5b become less cost-effective with the nutritional supplements removed. The explanation lies in the ICERs of nutritional supplements as such, which are US$48 or US$45 in South Asia and US$118 or US$110 in Sub-Saharan Africa, depending on whether the

Table 26.6 Comparisons Undertaken for CEA

Abbreviated description of package	Option number	Primary level		Secondary level			Interpretation	Safe motherhood strategy	Resource implications
		Coverage	Quality of care: technical content	Coverage[a]	Quality of care: Percentage receiving care needed	Quality of care: technical content			
Routine maternity care	Base	50 percent of pregnant women attend prenatal care; 50 percent of pregnant women have professional intrapartum care[b]	See first two panels of table 26.5	20 percent of complicated cases at the primary level referred to the secondary level	50 percent of those reaching the secondary level receive the CEmOC needed	See table 26.5[c]	Basic package of prenatal and delivery care	Content of package essentially the same as WHO mother-baby package, plus magnesium sulfate and active management of labor	Costs typical of WHO mother-baby package
Increased primary-level coverage	2	70 percent prenatal care; 70 percent delivery care	No change from base	No change from base	No change from base	No change from base	Benefit from increasing coverage	Information, education, and communication for increasing uptake of prenatal and delivery care	Costs of information, education, and communication; increased personnel; drugs
Improved overall quality of care with nutritional supplements	3a	No change from base	Enhanced prenatal and delivery care (BEmOC)	No change from base	70 percent	Enhanced CEmOC (adds interventions for high-risk babies)	Benefit from enhancing quality (content and receipt of care needed) at the primary and secondary levels	Provision of BEmOC at the primary level	Costs of doctors and equipment at the primary level, training for BEmOC and CEmOC, costs of BPS
Improved overall quality of care without nutritional supplements	3b	No change from base	Enhanced prenatal and delivery care (BEmOC) without BPS	No change from base	70 percent	Enhanced CEmOC (adds interventions for high-risk babies)	As for 3a without BPS	As for 3a	As for 3a without costs of BPS

Improved quality of CEmOC	4	No change from base	No change from base	No change from base	80 percent	No change from base	Benefit from increased percentage of women with severe complications receiving the CEmOC needed	Improved quality of CEmOC	Cost of additional personnel time and drugs
Improved overall quality of care and coverage with nutritional supplements	5a	70 percent prenatal care; 70 percent delivery care	Enhanced prenatal and delivery care (BEmOC)	50 percent	90 percent	Enhanced CEmOC (adds interventions for high-risk babies)	Benefit from improved quality (technical content and percentage receiving care needed) and coverage at the primary and secondary levels	Comprehensive package: improved coverage and content with BPS	Costs of providing and running ambulances, costs of additional personnel and drugs, training for BEmOC and CEmOC, costs of BPS
Improved overall quality of care and coverage without nutritional supplements	5b	70 percent prenatal care; 70 percent delivery care	Enhanced prenatal and delivery care (BEmOC) without BPS	50 percent	90 percent	Enhanced CEmOC (adds interventions for high-risk babies)	Benefit from improved quality and coverage at the primary and secondary levels without BPS	Improved coverage and content without BPS	As for 5a without the costs of BPS

Source: Authors.

BPS = balanced protein-energy supplementation.

a. Defined in terms of the percentage of complicated cases at the primary level referred to and reaching the secondary level.

b. Includes obstetric first aid for complicated cases, including abortion and postpartum complications.

c. The secondary level will also provide some prenatal and delivery care for normal cases, as defined in the first two panels of table 26.5 for the base package at the primary level.

Table 26.7 ICERs per Million Population, South Asia and Sub-Saharan Africa
(U.S. dollars)

Option number	Alternative compared with the base package	Incremental cost per death averted		Incremental cost per life-year saved		Incremental cost per DALY averted	
		South Asia	Sub-Saharan Africa	South Asia	Sub-Saharan Africa	South Asia	Sub-Saharan Africa
2	Increased primary-level coverage	6,129	3,337	217	119	148	92
3a	Improved overall quality of care with nutritional supplements	5,017	2,729	165	90	142	83
3b	Improved overall quality of care without nutritional supplements	8,975	2,538	296	84	240	77
4	Improved quality of CEmOC	10,532	5,089	372	195	255	151
5a	Improved overall quality of care and coverage with nutritional supplements	5,297	2,915	177	98	144	86
5b	Improved overall quality of care and coverage without nutritional supplements	7,944	2,865	269	96	203	84

Source: Authors' calculations.

Table 26.8 Costs and Effectiveness of Intervention Packages per Million Population, South Asia and Sub-Saharan Africa

Option number	Intervention package	Total costs (US$)	Number of deaths averted	Number of life years saved	Number of DALYs averted	Percentage of DALYs averted that are maternal
South Asia						
1	Routine maternity care	408,976	79	2,240	3,273	50
2	Increased primary-level coverage	603,071	111	3,136	4,582	50
3a	Improved overall quality of care with nutritional supplements	829,505	163	4,793	6,225	26
3b	Improved overall quality of care without nutritional supplements	757,433	118	3,415	4,727	35
4	Improved quality of CEmOC	420,918	80	2,272	3,320	50
5a	Improved overall quality of care and coverage with nutritional supplements	1,287,354	245	7,201	9,354	26
5b	Improved overall quality of care and coverage without nutritional supplements	1,186,123	177	5,131	7,103	35
Sub-Saharan Africa						
1	Routine maternity care	602,646	192	5,406	6,969	47
2	Increased primary-level coverage	859,027	269	7,568	9,757	47
3a	Improved overall quality of care with nutritional supplements	1,164,833	398	11,652	13,753	24
3b	Improved overall quality of care without nutritional supplements	1,049,209	368	10,733	12,770	26
4	Improved quality of CEmOC	617,724	195	5,483	7,069	47
5a	Improved overall quality of care and coverage with nutritional supplements	1,785,971	597	17,508	20,664	24
5b	Improved overall quality of care and coverage without nutritional supplements	1,633,956	552	16,127	19,188	26

Source: Authors' calculations.

Table 26.9 Sensitivity Analysis Results, South Asia and Sub-Saharan Africa
(incremental cost per DALY averted, US$)

Option number	Alternative compared with base package	Best estimate	Effectiveness assumption		Met need assumption		Inpatient cost assumption	
			High	Low	High	Low	High	Low
South Asia								
2	Increased primary-level coverage	148	113	163	147	150	213	109
3a	Improved overall quality of care with nutritional supplements	142	100	163	143	144	142	143
3b	Improved overall quality of care without nutritional supplements	240	180	326	241	242	240	240
4	Improved quality of CEmOC	255	193	311	373	260	446	204
5a	Improved overall quality of care and coverage with nutritional supplements	144	104	164	144	149	152	136
5b	Improved overall quality of care and coverage without nutritional supplements	203	153	250	203	210	227	189
Sub-Saharan Africa								
2	Increased primary-level coverage	92	70	104	91	93	191	84
3a	Improved overall quality of care with nutritional supplements	83	64	90	83	84	83	83
3b	Improved overall quality of care without nutritional supplements	77	61	85	77	78	77	77
4	Improved quality of CEmOC	151	114	166	228	151	326	130
5a	Improved overall quality of care and coverage with nutritional supplements	86	66	94	86	89	123	82
5b	Improved overall quality of care and coverage without nutritional supplements	84	66	93	84	87	123	79

Source: Authors' calculations.

comparison is with or without increased coverage (options 5a and 3a, respectively). This difference reflects the high burden from low birthweight in South Asia and, thus, the gain from nutritional supplements.

Comparing the content of the three most cost-effective intervention packages (3a, 5a, and 2) suggests that much can be achieved through improvements at the primary care level. Improved quality in relation to managing complications—in other words, the provision of BEmOC—and increases in coverage (a combination of options 3a and 2) at the primary level are likely to have even lower ICERs than those shown in table 26.7. This finding is consistent with the Commission on Macroeconomics and Health's emphasis on close-to-client services (CMH 2002), and it is highlighted further in chapter 53. As noted earlier, given the importance of prompt intervention in the event of obstetric complications, the effectiveness of intervention packages that may reduce delays by bringing services closer to communities is hardly surprising.

The benefits from option 2 were achieved essentially by increasing prenatal care coverage from 50 to 70 percent, because our model assumes that those women taking advantage of professional delivery are those who have also had prenatal contact. Prenatal care is, thus, a crucial entry point to the health system. Small changes in prenatal care coverage (20 percent) lead to larger numbers of women also benefiting from the rest of the care package in terms of obstetric first aid and CEmOC.

This issue is important for safe motherhood and newborn health, because the role of prenatal care has been subject to intense debate about its benefits relative to resource use (De Brouwere and Van Lerberghe 2001; Maine and Rosenfield 1999). Much of this discussion has focused on the lack of evidence on the direct contribution of prenatal care to reducing maternal mortality (McDonagh 1996; Rooney 1992), which, in turn, is explained partly by the poor performance of at-risk screening tools. However, differentiating the contribution to the prevention of maternal deaths of the prenatal care component alone is difficult. Ultimately, life-saving interventions depend on the functioning of the entire health system, including an effective referral network.

Our model also made assumptions about women's willingness and capacity to respond to referral to higher levels of care in case of complications. This willingness and capacity depend on many factors and are undoubtedly also driven by communities' perceptions of quality of care. As noted earlier, coverage rates of prenatal care are already high in many Sub-Saharan African countries, but significant socioeconomic differentials are apparent within countries. Our model does not address this

equity dimension but, given the recent work showing higher risks of maternal death among the poorest groups (Graham and others 2004), targeting disadvantaged women for improvements in uptake might be worth considering (Gwatkin and Deveshwar-Bahl 2002; De Brouwere and Van Lerberghe 2001).

Whereas option 2, increased primary-level coverage, relates predominantly to the demand side of the health system (Williams 1987), the most cost-effective packages (3a and 5a) focus on the supply side, particularly at the health center level. The latter packages are particularly relevant to the baby, including screening of the HIV status of the mother and treatment with antiretrovirals at the time of delivery to reduce the risk of mother-to-child transmission, as well as provision of antimalarials. As a consequence, these options have a particularly marked effect on the burden from perinatal conditions, accounting for two-thirds to three-fourths of the total DALYs averted (table 26.8). Note that these cost-effective options include a doctor at the health center level to provide all six BEmOC functions. In some situations, highly skilled midwives will be able to act in this capacity, which would reduce costs and further increase cost-effectiveness.

The most comprehensive packages in our model provide for improved quality of care and coverage at both the primary and the secondary levels (options 5a and 5b). Costing US$1.79 and US$1.63 per capita, respectively, in Sub-Saharan Africa (as calculated from the total costs of these packages shown in table 26.8, and divided by the base of 1 million people), these are also the most expensive packages. Not surprisingly, therefore, these two options avert much higher numbers of DALYs, with the package that includes nutritional supplementation averting nearly three times as many DALYs as the base package (table 26.8). In CEA, generally the most comprehensive packages—that is, those that result in the greatest gain in quality and coverage and, thus, cost the most—are often not cost-effective, and yet our analysis found otherwise. This finding may partly be explained by the linear assumptions about effectiveness in the model and the assumption that the marginal cost of care is constant. Such a finding also stresses both the importance of a well-functioning health system (rather than an excessive focus on one element) and the absence of any quick fix. Moreover, we did not model these more comprehensive options as perfect but unrealistic scenarios. We also still allowed for 30 percent of pregnant women not attending prenatal care, 50 percent of severe complications at a primary level not reaching CEmOC, and 10 percent of those reaching secondary care not receiving the emergency treatment they need.

Finally, a note of caution is warranted on the interpretation of the CEA results. First, our model has necessarily used a number of assumptions for which data are extremely limited, and it remains fairly crude, having been subject to only a limited sensitivity analysis. Second, many comparisons are possible from our model, but we have selected only six. Thus, we may not have identified even more cost-effective intervention packages, such as a combination of options 3a and 2.

ECONOMIC BENEFITS OF INTERVENTION

A narrow definition of the economic benefits of safe motherhood interventions would focus primarily on the impact of maternal mortality and morbidity on household investment and consumption. Investment in this context refers not so much to financial investment as to investment in improving housing conditions, agricultural productivity, education, and so on. The key elements to capture include the loss of productivity and the disruption of planned investment and consumption. In addition to the loss of a woman's own productivity, consequent effects are likely on the productivity of other household members—effects that may be particularly long lived in the case of young children whose health and education suffer because of their mother's death. The household will also be worse off because it will have diverted resources from preferred consumption and investment activities in response to the health crisis. Thus, recognizing the dynamic consequences of maternal death and disability and selecting an appropriate time horizon for the analysis are important.

The potential benefits to individual households arising from investments in safe motherhood are relatively clear, although challenges in quantifying and valuing them remain. The benefits may, however, be more widely spread in that improvements in safe motherhood may reduce poverty, which in turn may stimulate economic development. Increased economic development may then feed back into further improvements in maternal health, generating a virtuous cycle. The mechanisms whereby changes in maternal health affect other parts of the economy may be identified by a close examination of the influence of maternal health on productivity and educational attainment.

A number of links may exist between safe motherhood and the performance of the health care system; therefore, strategies to improve safe motherhood may be a means of achieving wider health service improvements (Goodburn and Campbell 2001). Jowett (2000, 213) notes that "to improve a facility's capacity to respond to obstetric emergencies, it is necessary to have the skills and supplies to deal with trauma, give blood transfusions and anesthesia, and have a functional operating theatre." Thus, initiatives in safe motherhood could be an entry point for wider health sector reform and improvement.

LESSONS FOR IMPLEMENTATION

The findings from the CEA indicate potential health gains and the reduced burden that may be achieved by implementing selected packages of interventions. Such implementation

assumes, first, that decision makers accept the evidence and are willing and able to act and, second, that an enabling health system environment exists within which the requisite scale and quality of care can be effectively delivered. These factors are not peculiar to safe motherhood, but they undoubtedly help explain the significant gap between evidence and action that many argue is one of the main obstacles to progress (Godlee and others 2004; Villar and others 2001). The gains from bridging this gap would be significant: the MDGs for child survival and maternal health might become more than mere rhetoric for poor regions if intervention packages of the scope and nature described here were implemented. The most cost-effective of the packages averted nearly 50 percent more direct maternal deaths than the base package. This gain would be encouraging, but the prospects for achieving it by 2015 are weak (Johansson and Stewart 2002).

At the macro level, a supportive policy environment clearly is crucial, as noted earlier. At the micro level, an enabling health system implies a reduction in the disequilibrium between the demand and supply sides (Williams 1987), with particular attention to three interrelated issues: access, quality, and finance. The CEA reported in this chapter emphasizes the potential benefits to mother and baby of improved access to care, particularly the importance of entry to the health system through primary-level services. The increases in coverage could be achieved by a variety of mechanisms but clearly require both demand- and supply-side interventions.

On the supply side, this chapter has shown that improved quality of care at both the primary and the secondary levels encompassing technical, infrastructural, and human resource dimensions (Pittrof, Campbell, and Filippi 2002) is a particularly cost-effective option. The widespread call for all women to deliver with skilled attendance immediately raises major questions about quality of care and capacity, because much of the developing world faces an acute shortage, as well as an unequal geographic distribution, of health professionals.

Our CEA assumes that redistributing human resources within countries will accommodate the increased uptake of care by women, although the most effective mechanisms for achieving this goal, such as incentives, use of nonphysicians, and increased private sector involvement, have not yet been established (De Brouwere and Van Lerberghe 2001). What is clear, however, is the importance of the interplay between supply and demand, with the supply of quality care stimulating demand for care and vice versa. Quality care includes an effective referral system (Murray and others 2001) to ensure the required match between the various levels of care different women and their babies need at different times (De Brouwere and Van Lerberghe 2001). Such systems require not only financial resources to support transportation, communications, and feedback mechanisms, but also structured fee and exemption strategies to reduce both inappropriate self-referral to hospitals and financial barriers to access on the part of the poor.

The financing of prenatal and delivery care services at an adequate and sustainable level is a subject of much debate and uncertainty, given the difficulty of distinguishing these elements from broader health expenditure categories (De Brouwere and Van Lerberghe 2001). Given the low level of overall per capita expenditure on health in developing countries—estimated at US$13 in 2002 for the poorest 49 countries (Bale and others 2003)—attaining our base intervention package (costing approximately US$0.41 per capita in South Asia and US$0.60 in Sub-Saharan Africa) does not sound unrealistic at current resource levels (see table 26.8, and divide by base population of 1 million people).

The effects of health sector reforms, particularly decentralization of management and budget holding, appear to be mixed in terms of increasing resource flows into maternity services, with both apparent positive benefits, as in Bolivia (De Brouwere and Van Lerberghe 2001), and negative effects through the exacerbation of inequities (Russell and Gilson 1997). Effective management decisions on finance, access, and quality require information, an essential ingredient for stimulating action. To allocate scarce resources where they are likely to achieve the greatest gain, countries need information to assess the burden of ill health, evaluate the performance of current intervention strategies, identify the scope for improvement and implement changes, and close the loop by evaluating effects and cost-effectiveness (Lawn, McCarthy, and Ross 2001).

Even though the challenges that the poorest countries face today clearly differ in many respects from those that developed or transition countries experienced in the past, six historical lessons provide particularly relevant insights. First, examples abound of supportive policy contexts and individual champions of progress in addressing maternal and newborn health, such as those reported by De Brouwere and Van Lerberghe (2001). Second, historical data on the uptake of prenatal care demonstrate that community-based providers and advocates played a crucial role. Third, the role of various professionals and professional bodies has not always been positive, particularly as regards the "war" between advocates for home and institutional deliveries (Koblinsky and Campbell 2003). Moreover, good historical evidence indicates that excessive rates of forceps deliveries and other interventions were significant contributors to maternal mortality in countries such as the United Kingdom and the United States (Buekens 2001). Fourth, primary-level care depends on an effective referral system being in place to maintain the confidence of both women and providers (Loudon 1997). Fifth, to reduce the burden of maternal and perinatal conditions, the system of health care financing must facilitate access for the poorest groups and guarantee service quality (De Brouwere and Van Lerberghe 2001). Finally, the role of population-based information on births and maternal deaths was

crucial in ensuring that actions were locally relevant (Sorenson and others 1998), in demonstrating progress, and thus in stimulating further action. This crucial role is particularly apparent in the literature on several European countries in the past century (Graham 2002; De Brouwere and Van Lerberghe 2001).

RESEARCH AND DEVELOPMENT NEEDS

The priorities for research and development arising from this chapter need to be put in the context of wider requirements for safe motherhood and newborn health that have been well articulated elsewhere (see, for example, Bale and others 2003). The general heading under which the specific needs emerging from this chapter can be grouped is evidence-based decision making, which has five crucial requirements:

- recognizing the weakness of current approaches to allocating scarce health care resources in poor countries
- making efforts to improve the scope and quality of data on the burden from maternal and perinatal conditions
- carrying out robust evaluation of the costs and effectiveness of intervention strategies
- using reliable evidence to inform the decision-making process
- implementing prioritized strategies and robust, continuous assessment of their performance.

Within those major areas, specific topics relevant to the CEA undertaken here include the following:

- *Ascertaining the burden of maternal and perinatal conditions.* Greater clarity and consensus are needed on the scope of this important burden category and the implications of significant current exclusions, such as indirect maternal conditions and stillbirths. Practical assessment tools are needed to enable meta-analysis and other modeling approaches to systematically factor in data constraints. Huge gaps in knowledge exist with regard to the levels and consequences of maternal morbidity (Say, Pattinson, and Gulmezoglu 2004), the contribution of iatrogenic factors, the unpredictability of maternal complications, and the levels of mortality. Most of those gaps require significant developments in relation to available measurement tools and in poor countries' capacity to use them as part of routine health surveillance. These improvements not only are needed to inform future CEA but also have wider implications for global health monitoring.
- *Implementing change.* In addition to evidence on the content of intervention strategies, assessments of how to implement changes are urgently needed. A limitation of our analysis is that, even though the model may be a reasonable representation of the resource and health consequences of different intervention packages, the way to achieve the required change, such as a particular increase in the uptake of prenatal care, may not be known. Thus, the ICERs may be too low, in that they do not fully capture the costs of the intervention.
- *Estimating cost-effectiveness.* More sophisticated economic models need to be developed to facilitate the evaluation of a wider range of safe motherhood strategies, particularly as better primary evidence becomes available from other studies and initiatives using a variety of outcome measures (Cairns, McNamee, and Hernandez 2003). Similarly, probabilistic sensitivity analysis would be a valuable development that would permit fuller exploration of the uncertainties regarding the model's parameters.

CONCLUSIONS

In 2001, maternal and perinatal conditions represented the single largest contributor to the global burden of disease, at nearly 6 percent of total DALYs (Mathers and others 2004). Reducing that burden is widely stated as a priority at both national and international levels, but the track record of translating the rhetoric into action on a sufficiently large and equitable scale to make a difference at the population level remains disappointing. The literature abounds with examples of this disappointment (see, for example, Maine and Rosenfield 1999; Weil and Fernandez 1999). Many reasons account for the limited progress, especially in the poorest regions of the world, and researchers offer many interpretations of the bottlenecks. Lack of evidence on the size of the burden and on the effectiveness of alternative intervention strategies figures prominently in these interpretations.

The modeling in this chapter is, therefore, based on imperfect knowledge and needs to be supplemented with data from primary evaluations. The findings do, however, provide some tentative insights into programmatic options that may represent the optimal use of resources in South Asia and Sub-Saharan Africa. In this context, three issues deserve emphasis. First, for intervention packages to achieve the degree of cost-effectiveness shown here, improvements are needed across health systems, and both the supply and the demand sides need to be addressed. Second, crucial entry points to this system can be achieved at the primary level, particularly through prenatal care. The effect of increasing the volume of women in contact with these services is likely to manifest itself in an increased proportion of deliveries with skilled attendance and of deliveries in which women obtain access to emergency obstetric care. Finally, the quality of these services is crucial, and even with only 50 percent uptake of care, benefits can still be achieved in terms of overall DALYs averted and of reduced maternal and perinatal mortality.

Initiatives to improve the quality of care, particularly at a primary level, thus appear to be cost-effective options for the

poorest regions of the world. Overall those findings appear to lend support to a safe motherhood and newborn health strategy that is close to the client and boosts community confidence in health systems.

ANNEX 26.A: CEA MODEL ASSUMPTIONS

We assumed that there are four primary-level health facilities (health centers) and one secondary-level care facility (district hospital) for every 500,000 people. We estimated the numbers of pregnancies and births from the crude birth rate for each region. We assumed that pregnant mothers attending for routine prenatal care are equally distributed between the five facilities and that each facility provides similar routine prenatal and delivery care. Routine prenatal care is assumed to comprise four visits—except for mothers with complications, who make six visits. Mothers with complications are referred to the district hospital after their first visit if they cannot be treated at the health center. We assumed that complications such as anemia and sexually transmitted diseases are treated without referral to secondary care, as are preeclampsia and incomplete abortion, if a doctor is present at the facility. The average number of bed days is assumed to be three days for normal deliveries and six days for cesarean section and other complications. Table 26.A1 shows the U.S. dollar costs per inpatient bed day used in the main analysis and in the sensitivity analysis.

We assumed the existence of excess capacity, so that an increase in prenatal care coverage from 50 to 70 percent would not require an increase in the number or capacity of existing health care facilities, and the increased costs would mostly be increases in variable costs. For increased coverage of prenatal care, we assumed a need for increased expenditure on education, information, and communication. Enhanced prenatal care and comprehensive emergency obstetric care are assumed to require additional expenditures on training, assumed to be 10 percent of total personnel costs. We assumed that the additional costs of basic emergency obstetric care compared with obstetric first aid are largely due to providing doctors at each health center. We also assumed that 8 percent of mothers require cesarean section as a result of either maternal or perinatal complications. About 2 percent of mothers are assumed to require treatment for preterm delivery, and 1 percent for premature rupture of membranes.

In practice, the proportion of women with serious complications receiving comprehensive emergency obstetric care varies widely, from 3 percent in Cameroon to 75 percent in Sri Lanka (Averting Maternal Death and Disability Working Group on Indicators 2003). The scenarios considered in this chapter assume that either 20 or 50 percent of women with serious complications reach secondary care, and that 50, 70, 80, or 90 percent of those women receive the elements of comprehensive emergency obstetric care that they need, depending on which intervention package is being considered. For the sensitivity analysis, we used low values of 30, 50, 60, and 70 percent and high values of 70, 80, 90, and 95 percent. We assumed that ambulances are available, so that when the proportion of mothers with severe complications reaching secondary care is increased, the additional costs are only the additional driver time and the increased costs of running and maintaining the vehicle.

The prevalence and incidence of different maternal conditions are taken from the WHO mother-baby package (WHO 1994). World Health Organization estimates of the burden of different maternal and perinatal conditions (WHO 2004d) have been applied to a population of 1 million, with a particular crude birth rate to generate an estimate of the potential number of deaths that could be avoided, the years of life that could be saved, and the DALYs that could be averted. The assumptions regarding the effectiveness of the interventions with respect to maternal and perinatal conditions were based primarily on the WHO's mother-baby package and a review of the literature; they are shown in table 26.A2. We assumed that each intervention has the same effect on the number of deaths, years of life saved, and DALYs. The effectiveness of interventions is assumed to be additive.

ACKNOWLEDGMENTS

We would like to thank the many individuals who helped prepare this chapter. In particular, we acknowledge the expert input regarding perinatal conditions from Joy Lawn and Jelka

Table 26.A1 Costs Per Inpatient Bed Day, South Asia and Sub-Saharan Africa
(U.S. dollars)

	South Asia		Sub-Saharan Africa	
Cost of inpatient bed day	**Primary level**	**Secondary level**	**Primary level**	**Secondary level**
Best estimate	6.51	8.50	6.17	8.05
Low	2.64	3.45	1.92	2.51
High	14.52	18.94	41.79	54.52

Source: DCPP2: Guidelines for Authors.

Table 26.A2 Assumed Effectiveness of Interventions
(percentage of DALYs, deaths, and years of life lost averted)

Condition	Best estimate	Low	High
Maternal			
Hemorrhage	85	80	90
Sepsis	75	70	90
Hypertensive disorders of pregnancy (including eclampsia)	76	71	95
Obstructed labor	80	75	95
Unsafe abortion	75	70	90
Perinatal			
Low birthweight			
In context without nutritional supplements[a]	8	3	14
In context with nutritional supplements[a]	28	23	44
Birth asphyxia (including birth trauma)			
In context without enhanced delivery care package[a]	40	35	60
In context with enhanced delivery care package[a]	70	65	90
Infections, including tetanus	60	55	80
Sepsis (newborn)	40	35	60
HIV/AIDS	60	55	80

Source: expert panels; WHO 1994, 2004d; Steketee and others 2001; Prendiville, Elbourne, and Chalmers 1998; Eclampsia Trial Collaborative Group 1995.
Note: Two extra interventions added to WHO mother-baby package: active management of the third stage of labor and magnesium sulfate for hypertensive disorders of pregnancy.
a. See table 26.6.

Zupan. Thanks are also given to our colleagues at the University of Aberdeen, particularly Joyce Boor, Julia Hussein, Emma Pitchforth, Nara Tagiyeva-Milne, and Karen Witten. We acknowledge and thank our colleagues Paul McNamee and Rodolpho Hernandez from the Health Economics Research Unit at the University of Aberdeen for their thorough review of the cost-effectiveness analysis. Thanks also to our expert panel members: Deanna Ashley, Gary Darmstadt, Catherine Hauptfleisch, Jilly Ireland, Joy Lawn, Cecil Klufio, Elizabeth Molyneux, Ashalata Shetty, Sribala Sripad, Vijay Kumar Tandle, Sumesh Thomas, and Jelka Zupan.

NOTES

1. *Antecedent* is here defined as a factor that changes the probability of an adverse outcome or sequela, either positively (protecting) or, more usually, negatively (aggravating). A risk factor may be a leading contributor to the global burden because of high prevalence in the population or because of a large increase in the probability of adverse outcomes (WHO 2002).

2. Afghanistan, Angola, Bangladesh, China, the Democratic Republic of Congo, Ethiopia, India, Indonesia, Kenya, Nigeria, Pakistan, Tanzania, and Uganda.

3. We use a simple three-way distinction for levels of evidence. *Level A* refers to evidence from randomized clinical trials or systematic overviews of trials; *level B* relates to nonrandomized studies, often with multivariate analyses; and *level C* is assigned to case series, case studies, or expert opinion.

4. This chapter does not deal with tertiary and specialist levels of care or with rehabilitative care or care for chronic conditions.

5. The six functions of BEmOC are (a) administering antibiotics intravenously or intramuscularly, (b) administering oxytocics intravenously or intramuscularly, (c) manually removing the placenta, (d) administering anticonvulsants intravenously or intramuscularly, (e) carrying out instrumental delivery, and (f) removing retained products of conception. The two additional functions in CEmOC are blood transfusion and cesarean section. For a facility to be regarded as a BEmOC or CEmOC site, respectively, it must perform all six or all eight functions regularly and must be assessed every three to six months (UNFPA 2003).

REFERENCES

AbouZahr, C. 1998. "Maternal Mortality Overview." In *Health Dimensions of Sex and Reproduction,* ed. C. J. Murray and A. D. Lopez, 111–64. Geneva: World Health Organization.

———. 1999. "Disability-Adjusted Life Years and Reproductive Health: A Critical Analysis." *Reproductive Health Matters* 7 (14): 118–29.

———. 2003. "Global Burden of Maternal Death and Disability." *British Medical Bulletin* 67: 1–11.

AbouZahr, C., and T. Wardlaw. 2001. "Maternal Mortality at the End of a Decade: Signs of Progress?" *Bulletin of the World Health Organization* 79 (6): 561–68.

Averting Maternal Death and Disability Working Group on Indicators. 2003. "Program Note: Using UN Process Indicators to Assess Needs in Emergency Obstetric Services: Morocco, Nicaragua, and Sri Lanka." *International Journal of Gynaecology and Obstetrics* 80: 222–30.

Bailey, P., J. Szaszdi, and B. Schieber. 1995. "Analysis of the Vital Events Reporting System of the Maternal and Neonatal Health Project: Quetzaltenango, Guatemala." MotherCare Technical Working Paper 3, John Snow, Arlington, VA.

Bale, J., B. Stoll, A. Mack, and A. Lucas, eds. 2003. *Improving Birth Outcomes: Meeting the Challenges in the Developing World.* Washington, DC: National Academy of Sciences and Institute of Medicine.

Bell, J., S. L. Curtis, and S. Alayon. 2003. "Trends in Delivery Care in Six Countries." Department of Homeland Security Analytical Studies 7, Opinion Research Corporation and Macro International Research Partnership for Skilled Attendance for Everyone (SAFE), Calverton, MD.

Bell, J., J. Hussein, B. Jentsch, G. Scotland, C. Bullough, and W. J. Graham. 2003. "Improving Skilled Attendance at Delivery: A Preliminary Report of the SAFE Strategy Development Tool." *Birth* 30 (4): 227–34.

Bergsjo, P., and J. Villar. 1997. "Scientific Basis for the Content of Routine Antenatal Care: II. Power to Eliminate or Alleviate Adverse Newborn Outcomes; Some Special Conditions and Examinations." *Acta Obstetrica et Gynecologica Scandinavica* 76 (1): 15–25.

Buekens, P. 2001. "Is Estimating Maternal Mortality Useful?" *Bulletin of the World Health Organization* 79 (3): 179.

Buttiens, H., B. Marchal, and V. De Brouwere. 2004. "Skilled Attendance at Childbirth: Let Us Go beyond the Rhetorics." *Tropical Medicine and International Health* 9 (6): 653–54.

Cairns, J., P. McNamee, and R. Hernandez. 2003. "Measurement and Valuation of Economic Outcomes." Economic Outcomes Work Program, Draft Concept Paper, IMMPACT (Initiative for Maternal Mortality Programme Assessment), Dugald Baird Centre, University of Aberdeen, Scotland.

Calder, A. A., and W. Dunlop, eds. 1992. *High Risk Pregnancy.* Oxford, U.K.: Butterworth-Heinemann.

Carroli, G., C. Rooney, and J. Villar. 2001. "How Effective Is Antenatal Care in Preventing Maternal Mortality and Serious Morbidity? An Overview of the Evidence." *Paediatric and Perinatal Epidemiology* 15 (Suppl. 1): 1–42.

Chamberlain, G., ed. 1995. *Turnbull's Obstetrics.* 2nd ed. London: Churchill Livingstone.

Cleland, J., and M. Ali. 2004. "Reproductive Consequences of Contraceptive Failure in 19 Developing Countries." *Obstetrics and Gynecology* 104 (2): 314–20.

CMH (Commission on Macroeconomics and Health). 2002. *Improving the Health Outcomes of the Poor.* Report of Working Group 5 of the Commission on Macroeconomics and Health. Geneva: World Health Organization.

Creese, A., and D. Parker. 1994. *Cost Analysis in Primary Care: A Training Manual for Programme Managers.* Geneva: World Health Organization.

Dayaratna, V., W. Winfrey, W. McGreevey, K. Hardee, K. Smith, E. Mumford, and others. 2000. *Reproductive Health Interventions: Which Ones Work and What Do They Cost?* Washington, DC: Policy Project.

De Brouwere, V., and W. Van Lerberghe, eds. 2001. *Safe Motherhood Strategies: A Review of the Evidence.* Vol. 17 of Studies in Health Services Organisations and Policy. Antwerp, Belgium: ITG Press.

Donnay, F. 2000. "Maternal Survival in Developing Countries: What Has Been Done; What Can Be Achieved in the Next Decade." *International Journal of Gynecology and Obstetrics* 70 (1): 89–97.

Eclampsia Trial Collaborative Group. 1995. "Which Anticonvulsant for Women with Eclampsia? Evidence from the Collaborative Eclampsia Trial." *Lancet* 345 (8963): 1455–63.

Etard, J. F., B. Kodio, and S. Traore. 1999. "Assessment of Maternal Mortality and Late Maternal Mortality among a Cohort of Pregnant Women in Bamako, Mali." *British Journal of Obstetrics and Gynaecology* 106 (1): 60–65.

Evans, T., and S. Stansfield. 2003. "Health Information in the New Millennium: A Gathering Storm?" *Bulletin of the World Health Organization* 81 (12): 856.

Foege, W. 2001. "Managing Newborn Health in the Global Community." *American Journal of Public Health* 91 (10): 1563–64.

Freedman, L. P. 2001. "Using Human Rights in Maternal Mortality Programs: From Analysis to Strategy." *International Journal of Gynecology and Obstetrics* 75 (1): 51–60.

Gay, J., K. Hardee, N. Judice, K. Agarwal, K. Flemming, A. Hairston, and others. 2003. *What Works: A Policy and Program Guide to the Evidence on Family Planning, Safe Motherhood, and STI/HIV/AIDS Interventions.* Safe Motherhood Module 1. Washington, DC: Policy Project.

Germain, A. 2000. "Population and Reproductive Health: Where Do We Go Next?" *American Journal of Public Health* 90 (12): 1845–47.

Godlee, F., N. Pakenham-Walsh, D. Ncayiyana, B. Cohen, and A. Packer. 2004. "Can We Achieve Health Information for All by 2015?" *Lancet* 364 (9430): 295–300.

Goodburn, E., and O. Campbell. 2001. "Reducing Maternal Mortality in the Developing World: Sector-Wide Approaches May Be the Key." *British Medical Journal* 322 (7291): 917–20.

Graham, W. J. 1998. "Every Pregnancy Faces Risks." *Planned Parenthood Challenges* 1: 13–14.

———. 2002. "Now or Never: The Case for Measuring Maternal Mortality." *Lancet* 359 (9307): 701–04.

Graham, W. J., A. E. Fitzmaurice, J. S. Bell, and J. A. Cairns. 2004. "The Familial Technique for Linking Maternal Death and Poverty." *Lancet* 363 (9402): 23–27.

Graham, W. J., and J. Hussein. 2004. "The Right to Count." *Lancet* 363 (9402): 67–68.

Gwatkin, D., and G. Deveshwar-Bahl. 2002. "Socioeconomic Inequalities in Use of Safe Motherhood Services in Developing Countries." Paper presented at the Inter-Agency Safe Motherhood Meeting, London, February 6.

Hall, M., S. MacIntyre, and M. Porter. 1985. *Antenatal Care Assessed.* Aberdeen, Scotland: Aberdeen University Press.

Hoj, L., D. da Silva, K. Hedegaard, A. Sandstrom, and P. Aaby. 2003. "Maternal Mortality: Only 42 Days?" *British Journal of Obstetrics and Gynaecology* 110 (11): 995–1000.

Hussain, R., F. F. Fikree, and H. W. Berendes. 2000. "The Role of Son Preference in Reproductive Behaviour in Pakistan." *Bulletin of the World Health Organization* 78 (3): 379–88.

Hutubessy, R. C., R. M. Baltussen, T. Tan-Torres Edejer, and D. Evans. 2003. "Generalised Cost-Effectiveness Analysis: An Aid to Decision Making in Health." In Making Choices in Health: WHO *Guide to Cost-Effectiveness Analysis*, ed. T. Tan-Torres Edejer, R. M. Baltussen, T. Adam, R. Hutubessy, A. Acharya, D. B. Evan, and C. J. L. Murray, 277–88. Geneva: World Health Organization.

Jamison, D. T., J. S. Jamison, J. Lawn, S. Shahid-Salles, and J. Zupan. 2004. "Incorporating Deaths Near the Time of Birth into Estimates of the Global Burden of Disease." Working Paper 26, Disease Control Priorities Project, Bethesda, MD.

Johansson, C., and D. Stewart. 2002. "The Millennium Development Goals: Commitments and Prospects." Working Paper 1, Human Development Report Office Working Papers and Notes, United Nations Development Programme, New York.

Jowett, M. 2000. "Safe Motherhood Interventions in Low-Income Countries: An Economic Justification and Evidence of Cost Effectiveness." *Health Policy* 53 (3): 201–28.

Khanum, P. A., M. A. Quaiyum, A. Islam, and S. Ahmed. 2000. "Complication of Pregnancy and Childbirth: Knowledge and Practices of Women in Rural Bangladesh." Working Paper 131, International Centre for Diarrhoeal Disease Research, Dhaka.

Koblinsky, M. A., and O. Campbell, eds. 2003. *Reducing Maternal Mortality: Learning from Bolivia, China, Egypt, Honduras, Indonesia, Jamaica, and Zimbabwe.* Washington, DC: World Bank.

Koenig, M. A., V. Fauveau, and B. Wojtyniak. 1991. "Mortality Reductions from Health Interventions: The Case of Immunization in Bangladesh." *Population and Development Review* 17 (1): 87–104.

Kurjak, A., and I. Bekavac. 2001. "Perinatal Problems in Developing Countries: Lessons Learned and Future Challenges." *Journal of Perinatal Medicine* 29 (3): 179–87.

Kusiako, T., C. Ronsmans, and L. Van der Paul. 2000. "Perinatal Mortality Attributable to Complications of Childbirth in Matlab, Bangladesh." *Bulletin of the World Health Organization* 78 (5): 621–27.

Lawn, J. E., B. J. McCarthy, and S. R. Ross. 2001. *The Healthy Newborn: A Reference Manual for Program Managers.* Atlanta, GA: Centers for Disease Control and Prevention and CARE. http://www.cdc.gov/reproductivehealth/health_newborn.htm.

Loudon, I. 1997. "Midwives and the Quality of Maternal Care." In *Midwives, Society and Childbirth: Debates and Controversies in the Modern Period,* ed. H. Marland and A. M. Rafferty, 180–200. London and New York: Routledge.

Maine, D., and A. Rosenfield. 1999. "The Safe Motherhood Initiative: Why Has It Stalled?" *American Journal of Public Health* 89 (4): 480–82.

Marston, C., and J. Cleland. 2003. "Do Unintended Pregnancies Carried to Term Lead to Adverse Outcomes for Mother and Child? An Assessment in Five Developing Countries." *Population Studies* 57 (1): 77–94.

Mathers, C. D., A. Lopez, C. Stein, D. Ma Fat, C. Rao, M. Inoue, and others. 2004. "Deaths and Disease Burden by Cause: Global Burden of Disease Estimates for 2001 by World Bank Country Groups." Working Paper 18, Disease Control Priorities Project, Bethesda, MD.

McCarthy, J., and D. Maine. 1992. "A Framework for Analyzing the Determinants of Maternal Mortality." *Studies in Family Planning* 23 (1): 23–33.

McDonagh, M. 1996. "Is Antenatal Care Effective in Reducing Maternal Morbidity and Mortality?" *Health Policy and Planning* 11 (1): 1–15.

Milne, L., G. Scotland, N. Tagiyeva-Milne, and J. Hussein. 2004. "Safe Motherhood Program Evaluation: Theory and Practice." *Journal of Midwifery and Women's Health* 49 (4): 338–44.

Munjanja, S. P., G. Lindmark, and L. Nystrom. 1996. "Randomised Controlled Trial of a Reduced-Visits Programme of Antenatal Care in Harare, Zimbabwe." *Lancet* (North American ed.) 348 (9024): 364–69.

Murray, C. J. L., and A. D. Lopez, eds. 1998. *Health Dimensions of Sex and Reproduction.* In Vol. 3 of *Global Burden of Disease and Injury.* Cambridge, MA: Harvard University Press.

Murray, S. F., S. Davies, P. Kumwenda, and A. Yusuf. 2001. "Tools for Monitoring the Effectiveness of District Maternity Referral Systems." *Health Policy and Planning* 16 (4): 353–61.

Mwageni, E., A. Ankomah, and R. Powell. 2001. "Sex Preference and Contraceptive Behaviour among Men in Mbeya Region, Tanzania." *Journal of Family Planning and Reproductive Health Care* 27 (2): 85–89.

Pattinson, B. 2002. *Saving Mothers: Second Report on Confidential Enquiries into Maternal Deaths in South Africa, 1999–2001.* Pretoria: Department of Health.

Pittrof, R., O. Campbell, and V. Filippi. 2002. "What Is Quality in Maternity Care? An International Perspective." *Acta Obstetrica et Gynecologica Scandinavica* 81 (4): 277–83.

Portela, A., and C. Santarelli. 2003. "Empowerment of Women, Men, Families, and Communities: True Partners for Improving Maternal and Newborn Health." *British Medical Bulletin* 67 (1): 59–72.

Prata, N., F. Greig, J. Walsh, and M. Potts. 2004. "Setting Priorities for Safe Motherhood Interventions in Resource Scarce Settings." Paper submitted to the Population Association of America, 2004 Annual Meeting, School of Public Health, University of California–Berkeley, April 1–3.

Prendiville, W. J., D. Elbourne, and I. Chalmers. 1988. "The Effects of Routine Oxytocics Administration in the Management of the Third Stage of Labour: An Overview of the Evidence from Controlled Trials." *British Journal of Obstetrics and Gynaecology* 95 (1): 3–16.

Raju, S., and A. Leonard. 2000. *Men as Supportive Partners in Reproductive Health: Moving from Rhetoric to Reality.* New Delhi: Population Council South and East Asia Regional Office.

Robertson, N. R. C. 1993. *A Manual of Normal Neonatal Care.* London: Arnold.

Rogo, K., L. Bohmer, and C. Ombaka. 1999. "Developing Community-Based Strategies to Decrease Maternal Morbidity and Mortality Due to Unsafe Abortion: Pre-intervention Report." *East African Medical Journal* 76 (11 Suppl.): S1–71.

Rooney, C. 1992. *Antenatal Care and Maternal Health: How Effective Is It? A Review of the Evidence.* WHO/MSM/92.4. Geneva: World Health Organization.

Rouse, D. J. 2003. "Potential Cost-Effectiveness of Nutrition Interventions to Prevent Adverse Pregnancy Outcomes in the Developing World." *Journal of Nutrition* 133 (Suppl.): 1640S–44S.

Rush, D. 2000. "Nutrition and Maternal Mortality in the Developing World." *American Journal of Clinical Nutrition* 72 (Suppl.): 212–40.

Russell, S., and L. Gilson. 1997. "User Fee Policies to Promote Health Service Access for the Poor: A Wolf in Sheep's Clothing." *International Journal of Health Services* 27 (2): 359–79.

Sadana, R. 2001. "Quantifying Reproductive Health and Illness." Ph.D. dissertation, Harvard School of Public Health, Boston, MA.

Save the Children. 2001. *State of the World's Newborns: Saving Newborn Lives.* Washington, DC: Save the Children.

Say, L., R. Pattinson, and M. Gulmezoglu. 2004. "WHO Systematic Review of Maternal Morbidity and Mortality: The Prevalence of Severe Acute Maternal Morbidity (Near Miss)." *Reproductive Health* 1: 3. http://www.reproductive-health-journal.com/content/1/1/3.

Shehu, D., A. T. Ikeh, and M. J. Kuna. 1997. "Mobilizing Transport for Obstetric Emergencies in Northwestern Nigeria." *International Journal of Gynecology and Obstetrics* 59 (2): 173–80.

Sheldon, T. A. 1996. "Problems of Using Modeling in the Economic Evaluation of Health Care." *Health Economics* 5: 1–11.

Sorensen, G., K. Emmons, H. K. Hunt, and D. Johnston. 1998. "Implications of the Results of Community Intervention Trials." *Annual Review of Public Health* 19: 379–416.

Steketee, R. W., B. L. Nahlen, M. E. Parise, and C. Mendez. 2001. "The Burden of Malaria in Pregnancy in Malaria-Endemic Area." *American Journal of Tropical Medicine and Hygiene* 64 (1.2 Suppl.): 28–35.

Stoll, B. J., and A. R. Measham. 2001. "Children Can't Wait: Improving the Future for the World's Poorest Infants." *Journal of Pediatrics* 139 (5): 729–33.

Thonneau, P., N. Goyaux, S. Goufodji, and J. Sundby. 2002. "Abortion and Maternal Mortality in Africa." *New England Journal of Medicine* 347 (24): 1984–85.

Tomkins, A. 2001. "Nutrition and Maternal Morbidity and Mortality." *British Journal of Nutrition* 85 (2): 93–99.

UN (United Nations). 2002. *UN Population Division Population Estimates and Projections*, 2000 rev.

UNFPA (United Nations Population Fund). 2003. *Maternal Mortality Update 2002: A Focus on Emergency Obstetric Care.* New York: UNFPA.

UNICEF (United Nations Children's Fund). 1999. "World Summit for Children Goals: End of Decade Indicators for Monitoring Progress." Executive Directive EXD/1999-03, New York.

Villar, J., H. Ba'aqeel, G. Piaggio, P. Lumbiganon, J. M. Belizan, U. Farnot, and others. 2001. "WHO Antenatal Care Randomized Trial for the Evaluation of a New Model of Routine Antenatal Care." *Lancet* (North American ed.) 357 (9268): 1551–64.

Villar, J., and P. Bergsjo. 1997. "Scientific Basis for the Content of Routine Antenatal Care I." *Acta Obstetrica et Gynecologica Scandinavica* 76 (1): 1–14.

Villar, J., M. Merialdi, A. M. Gulmezoglu, E. Abalos, G. Carroli, R. Kulier, and M. de Oni. 2002. "Nutritional Interventions during Pregnancy for the Prevention or Treatment of Maternal Morbidity and Preterm Delivery: An Overview of Randomized Controlled Trials." *Journal of Nutrition* 133 (5): 1606S–25S.

Walsh, J., A. Fiefer, A. Measham, and P. Gertler. 1993. "Maternal and Perinatal Health." In *Disease Control Priorities in Developing Countries,* ed. D. Jamison, H. Mosley, A. Measham, and J. Bobadilla, 363–90. Oxford, U.K.: Oxford Publications.

Weil, O., and H. Fernandez. 1999. "Is Safe Motherhood an Orphan Initiative?" *Lancet* 354 (9182): 940–43.

West, K. P. Jr., J. Katz, S. K. Khatry, S. C. LeClerq, E. K. Pradhan, S. R. Shrestha, and others. 1999. "Double Blind, Cluster Randomised Trial of Low Dose Supplementation with Vitamin A or Beta Carotene on Mortality Related to Pregnancy in Nepal." *British Medical Journal* 318 (7183): 570–75.

WHO (World Health Organization). 1986. "Maternal Mortality: Helping Women off the Road to Death." *World Health Organization Chronicle* 40: 175–183.

———. 1992a. *International Classification of Diseases and Related Health Problems,* 10th rev. Geneva: WHO.

———. 1992b. *The Prevention and Management of Unsafe Abortion.* WHO/MSM/92.5. Report of a Technical Working Group. Geneva: WHO.

———. 1994. *Mother-Baby Package.* WHO/FHE/MSM/94.11. Geneva: WHO.

———. 1999. *Mother-Baby Package Costing Spreadsheet.* WHO/FCH/RHR/99.17. Geneva: WHO.

———. 2002. *Reducing Risks, Promoting Healthy Life: The World Health Report 2002.* Geneva: WHO.

———. 2003. *Making Pregnancy Safer: Global Action for Skilled Attendants for Pregnant Women.* WHO/RHR/02.17. Geneva: WHO.

———. 2004a. "Global Monitoring and Evaluation, Proportion of Births Attended by Skilled Health Personnel: Global, Regional, and Subregional Estimates." Geneva, WHO, Department of Reproductive Health and Research. http://www.who.int/reproductive-health/global_monitoring/data_regions.html.

———. 2004b. *Maternal Mortality in 2000: Estimates Developed by WHO, UNICEF, UNFPA.* Geneva: WHO.

———. 2004c. *Unsafe Abortion: Global and Regional Estimates of the Incidence of Unsafe Abortion and Associated Mortality in 2000.* 4th ed. Geneva: WHO.

———. 2004d. *Global Burden of Disease for the Year 2001 by World Bank Region, for Use in Disease Control Priorities in Developing Countries,* 2nd ed. Bethesda, MD: National Institutes of Health. http://www.fic.nih.gov/dcpp/gbd.html.

WHO-CHOICE (Choosing Interventions That Are Cost Effective). 2004. "Choosing Interventions That Are Cost Effective." Geneva. http://www3.who.int/whosis/menu.cfm?path=whosis,cea&language=english.

Williams, A. 1987. "Health Economics: The Cheerful Face of the Dismal Science?" In *Health and Economics,* ed. A. Williams. 1–11. Basingstoke and London: Macmillan.

Winikoff, B., and M. Sullivan. 1987. "Assessing the Role of Family Planning in Reducing Maternal Mortality." *Studies in Family Planning* 18 (3): 128–43.

Yasmin, S., D. Osrin, E. Paul, and A. Costello. 2001. "Neonatal Mortality of Low Birth-Weight Infants in Bangladesh." *Bulletin of the World Health Organization* 79 (7): 608–14.