Neonatal Survival 2

Evidence-based, cost-effective interventions: how many newborn babies can we save?

*Gary L Darmstadt, Zulfiqar A Bhutta, Simon Cousens, Taghreed Adam, Neff Walker, Luc de Bernis, for the Lancet Neonatal Survival Steering Team**

In this second article of the neonatal survival series, we identify 16 interventions with proven efficacy (implementation under ideal conditions) for neonatal survival and combine them into packages for scaling up in health systems, according to three service delivery modes (outreach, family-community, and facility-based clinical care). All the packages of care are cost effective compared with single interventions. Universal (99%) coverage of these interventions could avert an estimated 41–72% of neonatal deaths worldwide. At 90% coverage, intrapartum and postnatal packages have similar effects on neonatal mortality—two-fold to three-fold greater than that of antenatal care. However, running costs are two-fold higher for intrapartum than for postnatal care. A combination of universal—ie, for all settings—outreach and family-community care at 90% coverage averts 18–37% of neonatal deaths. Most of this benefit is derived from family-community care, and greater effect is seen in settings with very high neonatal mortality. Reductions in neonatal mortality that exceed 50% can be achieved with an integrated, high-coverage programme of universal outreach and family-community care, consisting of 12% and 26%, respectively, of total running costs, plus universal facility-based clinical services, which make up 62% of the total cost. Early success in averting neonatal deaths is possible in settings with high mortality and weak health systems through outreach and family-community care, including health education to improve home-care practices, to create demand for skilled care, and to improve care seeking. Simultaneous expansion of clinical care for babies and mothers is essential to achieve the reduction in neonatal deaths needed to meet the Millennium Development Goal for child survival.

Published online March 3, 2005
http://image.thelancet.com/extras/05art1217web.pdf

*Lancet Neonatal Survival Steering Team listed at end of article

Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA (G L Darmstadt MD)**; Save the Children/USA, Washington, DC, USA** (G L Darmstadt)**; Aga Khan University, Karachi, Pakistan** (Z A Bhutta PhD)**; London School of Hygiene and Tropical Medicine, London, UK** (Prof S Cousens DipMathStat)**; Departments of Health Systems Financing, Expenditure and Resource Allocation, Child and Adolescent Health and Development** (T Adam MD)**, and Reproductive Health and Research** (L de Bernis MD)**, WHO, Geneva, Switzerland; and UNICEF, New York, NY, USA** (N Walker PhD)

Correspondence to: Dr Zulfiqar A Bhutta, Department of Pediatrics and Child Health, Aga Khan University, Karachi 74800, Pakistan
zulfiqar.bhutta@aku.edu

This report is the second in a series addressing neonatal survival.[1] The first article[2] discussed the unacceptably high number of neonatal deaths that happen every year (4 million), their inequitable distribution, the increasing proportion of child deaths that take place in the neonatal period, and the importance of reducing neonatal mortality to meet the Millennium Development Goal for child survival (MDG-4). Most neonatal deaths occur at home in low-income and middle-income countries against a backdrop of poverty, sub-optimum care seeking, and weak health systems.[1–4]

Globally, neonatal deaths now account for 38% of deaths in children aged younger than 5 years.[2] Child survival and safe motherhood strategies have yet to adequately address mortality in the neonatal period. A major barrier to action on neonatal health has been the erroneous perception that only expensive, high-level technology and facility-based care can reduce mortality.[5,6] Increasing access to skilled, facility-based care is an important long-term aim, but what can be done in low-income and middle-income countries in the shorter term? Are there cost-effective interventions and health-care strategies that can be implemented now, and how many lives could be saved?

Here, we summarise the findings of a review of the evidence on the efficacy (implementation under ideal conditions) and effectiveness (implementation under conditions that pertain within health systems) of a wide range of potential interventions to reduce perinatal and neonatal mortality. We present an analysis of the cost-effectiveness of individual interventions, and of interventions packaged to facilitate their delivery by health systems. We derive estimates of the proportion and number of neonatal deaths that could be prevented with these interventions in 75 countries, and the associated cost.

Identification of effective interventions

The Bellagio child survival series[7–11] has been important in drawing attention to the unfinished child survival agenda. Writing for the series, Jones and colleagues[8] estimated that implementing existing evidence-based interventions at high coverage (99%) could avert 63% of all child deaths and 35–55% of neonatal deaths. These estimates have limitations, however, especially in terms of putting the interventions into a health systems context.[1,12] Several potential interventions, particularly those that target mothers, were not included in the Bellagio analysis because a systematic review of perinatal and neonatal health interventions was not available.[13] Of the 23 interventions listed, eight were specific to neonates, but five of the eight were assumed to need skilled care,[8] leaving few choices for settings with low coverage of skilled care.

We did a systematic review of the evidence on the efficacy and effectiveness of interventions with the potential to reduce perinatal or neonatal mortality, or both (panel 1).[13–26] Our aim was to identify interventions for use in low-income and middle-income countries. We did not, therefore, include costly, high-tech interventions, such as assisted ventilation or surfactant therapy.

Of the 46 interventions (one preconception, 20 antenatal, ten intrapartum, and 15 postnatal) reviewed, 16 (one preconception, five antenatal, five intrapartum, and five postnatal) met criteria for evidence of efficacy (table 1); three had evidence of effectiveness. All but one of the eight neonatal interventions identified by the Bellagio child survival study group were included,[8] plus nine additional interventions. From the Bellagio list, on the basis of our meta-analysis, we included intermittent presumptive treatment for

Panel 1: Methods used to assess efficacy and effectiveness of interventions in reducing perinatal or neonatal mortality

Intervention assessment

We selected interventions for review on the basis of their biological plausibility and feasibility for inclusion in maternal and neonatal health-care systems in low-income and middle-income settings. The search for evidence encompassed all available electronic health and social science reference libraries (including indexed and non-indexed journals) and manual reviews of safe motherhood and child survival monographs. We solicited further information and unpublished material directly from agencies, institutions, and leading public-health researchers involved in community-based health care in low-income and middle-income countries. Our main focus was on randomised controlled trials. However, where such data were lacking, we also considered information from other study designs. We reviewed evidence from *The Cochrane Library* and WHO's Reproductive Health Library. If a Cochrane review was not available or did not incorporate all available evidence, we assessed the suitability of the available data for meta-analysis. Only intermittent presumptive treatment for malaria met the criteria for further meta-analysis.

We gave priority to evidence of effect on perinatal or neonatal mortality. For interventions for which data on perinatal or neonatal mortality effect did not exist, but such an association was plausible, we assessed the evidence for effect on determinants of mortality. This analysis included outcomes such as prematurity or asphyxia incidence or case fatality; or reductions in low birthweight rates or infectious disease morbidity. For sources that estimate effect of interventions both singly and in packages, see webtable 1 and webtable 2, respectively.

We assessed studies for size, design, quality, and setting. We used a matrix to summarise the findings of the review, and final categorisation was arrived at by a Delphi process, involving consultation and consensus, as follows:

I. Evidence of no benefit. Interventions for which evidence exists showing they have no important benefits—either singly or in combination with other measures—for perinatal or neonatal health.
II. No evidence of benefit. Interventions for which evidence for or against an effect was absent.
III. Uncertain evidence of benefit. Interventions for which there was some evidence of benefit, but contradictory evidence, or issues such as study design, location, or size precluded any firm conclusions. These interventions merit further assessment in low-income and middle-income countries.
IV. Evidence of efficacy. Interventions effective in reducing perinatal or neonatal mortality, or primary determinants thereof, but there is a lack of data on effectiveness in large-scale programme conditions.
V. Evidence of efficacy and effectiveness. Interventions of incontrovertible efficacy and which seem feasible for large-scale implementation based on effectiveness trials.

Cost-effectiveness analysis

The Afro-D subregion of WHO is used for illustrative purposes. The 26 countries in this region have high NMRs (median 40 per 1000 livebirths) and half the neonatal deaths in the African region—ie, Afro-D and Afro-E. Malaria is important in this region, a necessary condition for analysing cost-effectiveness of intermittent presumptive treatment for malaria.

We applied a generalised cost-effectiveness framework called CHOICE, which allows comparison of interventions and programmes across more than one disease area; not only within maternal and child health programmes, but also across other communicable and non-communicable diseases.[14] Effectiveness was based on the mid-point of the effect estimates presented in table 3. We divided costs into two categories: programme-level costs are those associated with running the programme—eg, administration, supervision, and training—and patient-level costs include such items as primary or referral care visits, home visits, diagnostic tests, and medicines. We based costs on a standardised ingredients approach across interventions.[14–16] We identified the physical inputs needed from the published work with additional information provided by authors, a wider circle of consultants, and WHO programme staff worldwide. Unit costs for programme-level and patient-level inputs, such as the salaries of central administrators, the capital costs of vehicles, or the cost per outpatient visit were based on country-specific estimates developed by the WHO CHOICE project, based on unit cost data for more than 75 countries and incorporating cost multipliers to account for increased costs with increasing degrees of coverage.[17–19] We based medicine costs on the price of off-patent drugs, the primary source being the *International Drug Price Indicator Guide*.[20] We discounted all costs and effects at 3%, consistent with the recommendations of the US panel on cost-effectiveness in health and medicine.[21] We used international dollars (Intl$) to account for differences in purchasing power parity across countries. Conversion to local currency was done as described on the WHO CHOICE website,[22] and to US$ with official exchange rates with local currencies (see also webtable 3).

malaria, but excluded insecticide-treated bed nets because of lack of evidence for added benefit (see webtable 1 at http://image.thelancet.com/extras/05art1217webtable1.pdf). There was a general lack of evidence from randomised controlled trials in representative populations—31 community-based randomised controlled trials reported perinatal or neonatal mortality effect and 74 community-based studies reported effect on morbidity or major risk factors for mortality—and especially from effectiveness trials in health system settings (n=10).

We chose to focus on the interventions listed in table 1 because of their effect on neonatal mortality. However, there was evidence of health benefits later in childhood and for mothers for several other interventions initiated in the antenatal or neonatal period—eg, maternal and infant use of insecticide-treated bed nets, maternal anthelmintic therapy, prevention of mother-to-child-transmission of HIV, and maternal and infant micronutrient supplementation (panel 2). Despite their exclusion here, these interventions are important for programmes across the continuum of maternal, neonatal, and child health.

Cost-effective delivery of interventions

In a health-systems context, to package interventions according to their target populations and service delivery modes is logical (panel 3).[27–29] We therefore considered how to deliver these interventions for home births and neonatal care in settings where access to health services is poor, as well as how to integrate them into facility-based maternal and child health care. We packaged interventions according to common service delivery mode and time of implementation (table 2). Moreover, to facilitate programme planning, we designated them as universal (for all settings), situational (for all relevant

Panel 1: **(continued)**

Effect estimation

To estimate the numbers and proportions of neonatal deaths that could be averted, we derived the effect of components of intervention packages on specific causes of neonatal mortality, using available published work and expert opinion (table 3). The input data for cause-specific neonatal deaths by country was based on the work of the Neonatal Group of the Child Health and Epidemiology Reference Group (CHERG).[23] We derived estimates of coverage with interventions from UNICEF ChildInfo data[24] or by consensus expert opinion among ourselves and external consultants. These effects were then applied to estimates of the current numbers of neonatal deaths due to each cause (unpublished data) in every one of the 75 countries included in this analysis and derived from the WHO 2005 world health report,[25] assuming that the population effect increased linearly with coverage. Thus, the number of deaths that would be expected to be prevented for a given cause of death by a given intervention was calculated as:

$$\text{Deaths prevented}=\frac{N\times I\times(P_1-P_0)}{(1-I\times P_0)}$$

where: N=number of deaths at existing coverage; I=percentage by which intervention reduces deaths; P_0=existing coverage of intervention; P_1=target coverage for intervention. We then subtracted the number of deaths due to a specific cause and prevented by the intervention from the current number of deaths, before calculating the effect of the next intervention. See webtable 2 for coverage estimates and assumptions underlying effect estimates.

Cost estimation

We calculated costs for current (based on the year 2000) and expanded (90%) coverage of neonatal interventions in the 75 countries of our database.[25] Running costs included commodities—eg, medicines, equipment, supplies—inservice training, salaries, and supervision of the health-care providers, as well as depreciation and maintenance costs of the health-care facilities. We did not include initial investments for scaling up coverage to 90%, including building new facilities and strengthening health-systems' capacity and management.

For every intervention, we defined current coverage and need/incidence of all relevant health conditions targeted by the intervention (webtable 4). Our target coverage of all interventions was 90% of those in need, which in turn was defined by identifying the general target population—eg, all newborn babies, pregnant women—and multiplying by the incidence or proportion of the target population with the condition of interest.

We estimated the health-service delivery inputs needed to provide the interventions, either in domiciliary settings by a community health worker, at a clinic by a health-care provider, or in a hospital (including number of days of admission). Drug costs were calculated on the basis of the amount of first-line drug that would be used for treatment, and the estimated current price, largely derived from the UNICEF supply website (http://www.supply.unicef.dk/catalogue1).[26] We obtained unit costs for in-patient care and outpatient services from the WHO CHOICE database.[18] Unit costs for service provision increased with degree of coverage to show the increasing unit costs for providing services to those harder to reach, using a scaling-up factor from the WHO CHOICE database.[17] We calculated costs using the year 2000 US$ applied to the base populations from that year. Therefore, all costs have to be increased to reflect population growth to estimate the actual costs for target levels of service provision based on the year the targets would be reached.

	Amount of evidence†	Reduction (%) in all-cause neonatal mortality or morbidity/major risk factor if specified (effect range)
Preconception		
Folic acid supplementation	IV	Incidence of neural tube defects: 72% (42–87%)
Antenatal		
Tetanus toxoid immunisation	V	33–58% Incidence of neonatal tetanus: 88–100%
Syphilis screening and treatment	IV	Prevalence-dependent[13]
Pre-eclampsia and eclampsia: prevention (calcium supplementation)	IV	Incidence of prematurity: 34% (–1 to 57%) Incidence of low birthweight: 31% (–1 to 53%)
Intermittent presumptive treatment for malaria	IV	32% (–1 to 54%) PMR: 27% (1–47%) (first/second births)
Detection and treatment of asymptomatic bacteriuria	IV	Incidence of prematurity/low birthweight: 40% (20–55%)
Intrapartum		
Antibiotics for preterm premature rupture of membranes	IV	Incidence of infections: 32% (13–47%)
Corticosteroids for preterm labour	IV	40% (25–52%)
Detection and management of breech (caesarian section)	IV	Perinatal/neonatal death: 71% (14–90%)
Labour surveillance (including partograph) for early diagnosis of complications	IV	Early neonatal deaths: 40%
Clean delivery practices	IV	58–78% Incidence of neonatal tetanus: 55–99%
Postnatal		
Resuscitation of newborn baby	IV	6–42%
Breastfeeding	V	55–87%
Prevention and management of hypothermia	IV	18–42%[13]
Kangaroo mother care (low birthweight infants in health facilities)	IV	Incidence of infections: 51% (7–75%)
Community-based pneumonia case management	V	27% (18–35%)

PNR=perinatal mortality rate. *See webtable 1. †See panel 1 for definitions.

Table 1: **Evidence of efficacy for interventions at different time periods***

Panel 2: Interventions not included in evidence-based neonatal health-care packages that are of benefit for infant, child, or maternal health

Infant or child benefit

Birth spacing
Maternal zinc supplementation
Maternal iron and folic acid supplementation
Maternal iodine supplementation
Neonatal vitamin A supplementation
Insecticide-treated bed nets for malaria prevention
Maternal anthelmintic treatment
Prevention of maternal-to-child transmission of HIV
Delayed umbilical cord clamping
Prevention of ophthalmia neonatorum
Hepatitis B vaccination and immunoprophylaxis

Maternal benefit

Birth spacing
Promotion of smoking cessation in pregnancy
Antenatal iron and folic acid supplementation
Antenatal vitamin A supplementation
Insecticide-treated bed nets for malaria prevention
Maternal anthelmintic treatment
Maternal vaginal chlorhexidine cleansing
Antepartum haemorrhage management
Emergency transportation

settings—eg, intermittent presumptive treatment for malaria in endemic areas), or additional (components to be added as health systems develop).[30] We then reviewed the evidence for efficacy and effectiveness of packages of interventions, and identified the biologically plausible pathways for effect on perinatal or neonatal mortality, or both (table 3; see also webtable 2 at http://image.thelancet.com/extras/05art1217webtable2.pdf).

Panel 3: Service delivery modes for neonatal health interventions

Facility-based clinical care[28,29]

Clinical care services provided by skilled personnel,[28] typically at health facilities, should be available around-the-clock to manage acute clinical problems. Provision of individual-oriented clinical care requires that providers: be adequately trained, equipped, and supervised; respond promptly to complaints from individuals; and exercise discretion in assigning a diagnosis and choosing a treatment. Examples include skilled maternal and immediate neonatal care, emergency obstetric care, and emergency neonatal care.

Outreach

These population-oriented services can be standardised to meet common needs of a population—ie, the appropriate action is the same for a specific group or population—and need less skill and training than for clinical care services. Interventions can be delivered on a periodic basis, either through static health facilities or during visits within the community. Some examples of outreach include routine antenatal care, immunisation programmes, and provision of intermittent presumptive treatment for malaria.

Family-community care

Family-oriented and community-oriented services support self care, including the adoption of improved care practices and appropriate care seeking for illness. With the widespread barriers to care seeking for neonatal illness, an important aspect of family-community care is community mobilisation and the empowerment of individuals and communities to demand quality services that respond to their needs. These services can be provided by various workers, and should be tailored to the community's social and cultural environment. Examples of family-community care include: behaviour change communications; community mobilisation and engagement to stimulate adoption of improved antenatal, intrapartum, and postnatal care practices; care seeking for illness; and, in some settings, community-based case management of illness—eg, pneumonia—by community health workers.

	Interventions		
	Universal	Situational	Additional
Periconceptual	..		Folic acid supplementation
Antenatal/intrapartum/postnatal	Family care package (family-community care) • Community mobilisation and engagement, and antenatal and postnatal domiciliary behaviour change communications to promote: evidence-based neonatal care practices (breastfeeding, thermal care, clean cord care), care seeking, and demand for quality clinical care • Promotion and practice of clean delivery and referral of complications (for home births)		
Antenatal	Antenatal care package • Outreach visits, including history and physical examination, with assessment of blood pressure, weight gain, and fundal height; urine screen for protein; screen for anaemia; two doses of tetanus toxoid immunisation; syphilis screening and treatment; counselling on plan for birth, emergencies, breastfeeding; referral in case of complication	Intermittent presumptive treatment for malaria	Detection and treatment of asymptomatic bacteriuria
Intrapartum	Skilled maternal and immediate neonatal care package • Skilled attendant at birth; labour surveillance; encouragement of supportive companion; assistance to birth (including vacuum extraction); early detection, clinical management and referral of maternal or fetal complications (emergency obstetric care at first level); resuscitation of the newborn baby		Antibiotics for preterm premature rupture of membranes
	Emergency obstetric care package • Detection and clinical management of obstetric complications, including the provision of instrumental delivery, caesarian section, blood transfusion		Corticosteroids for preterm labour
Postnatal	Extra community-based care of low birthweight infants (family-community care) • Extra home visits; support for breastfeeding, thermal care, and hygienic cord care; early recognition and care seeking for illness Community-based case management of pneumonia (family-community care) • Algorithm-based diagnosis and management of pneumonia, including treatment with oral antibiotics Emergency neonatal care package • Facility-based clinical care of ill newborn babies, particularly those with infections, prematurity (eg, very low birthweight infants), birth asphyxia		

Table 2: **Evidence-based packages of interventions at different periods**

To corroborate the packaging of interventions in table 2, we examined their cost-effectiveness delivered singly (four single interventions) or in combination (ten packages), using the choosing interventions that are cost-effective (CHOICE) model developed by WHO (panel 1; see also webtable 3 at

	Nature of intervention (main elements of intervention packages)	Reduction: all-cause neonatal mortality (or in other indicators if data on NMR unavailable)	Cause-specific mortality reduction					
			Serious infections	Diarrhoea	Tetanus	Birth asphyxia	Prematurity	Congenital anomalies
Antenatal/ intrapartum/ postnatal	Family care: clean home delivery, hygienic cord care, thermal care, breastfeeding promotion	10–50%	20–50%	25–60%	75–85%	0	0	0
Preconception	Folic acid supplementation	Incidence of neural tube defects: 40-85%	0	0	0	0	0	1–10%
Antenatal	Antenatal care: physical exam, tetanus toxoid, detection and treatment of syphilis and pre-eclampsia	10–20%	<1–5%	0	80–95%	10–20%	<1–5%	0
	Malaria (intermittent presumptive treatment)	10–30%	10–20%	0	0	0	0	0
	Detection and treatment of asymptomatic bacteriuria	Incidence of prematurity or low birthweight: 20–55%	0	0	0	0	5–14%	0
Intrapartum	Skilled maternal and immediate neonatal care	Skilled birth care: 20–30%; resuscitation: 5–20%	10–20%	0	50–70%	30–45%	5–10%	0
	Emergency obstetric care: management of complications—obstructed labour, haemorrhage, hypertension, infection	10–15%	0	0	0	20–60%	0	0
	Antibiotics for preterm premature rupture of membranes	Incidence of infections: 15–45%	3–9%	0	0	0	0	0
	Antenatal corticosteroids for preterm labour	25–50%	0	0	0	0	25–50%	0
Postnatal	Extra care for low birthweight infants: extra warmth, hygiene, feeding	20–40%	1–10%	0	0	0	20–50%	0
	Case management for pneumonia	10–35%	20–55%	0	0	0	0	0
	Emergency neonatal care: management of serious illness (infections, asphyxia, prematurity, jaundice)	15–50%	30–70%	0	0	0–5%	15–40%	0

*See webtable 2.

Table 3: **Cause-specific effect of intervention packages delivered at different periods***

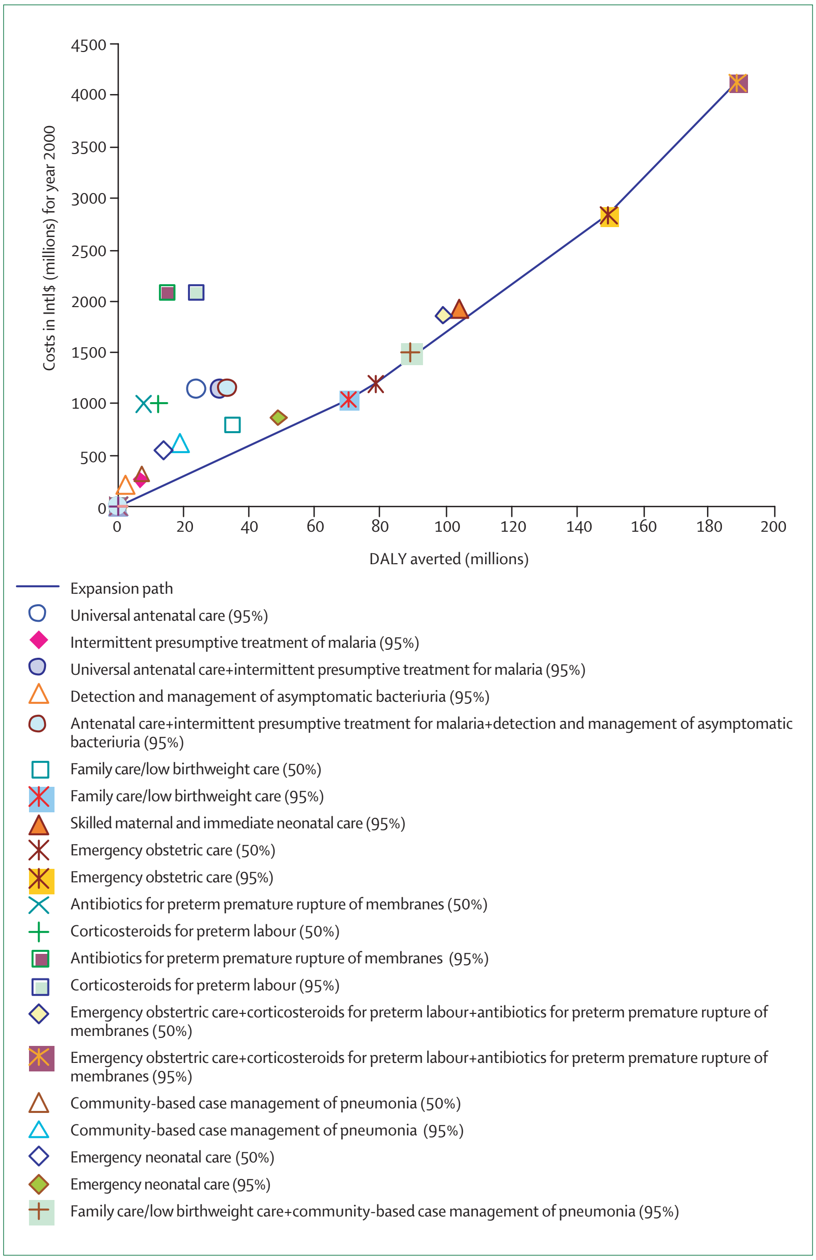

Figure 1: **Cost-effectiveness of neonatal health interventions singly and in packages of care in the Afro-D region**
DALY=neonatal YLL and maternal YLL+years lived with disability. See webtable 3 for additional data.

http://image.thelancet.com/extras/05art1217webtable3.pdf).[15,22] Cost-effectiveness is expressed as the cost per disability-adjusted life year (DALY) averted through implementation of interventions at the indicated degree of coverage, in international dollars (Intl$) for the year 2000 (see webtable 3 for conversion to US$). The DALY measure used here includes years of life lost (YLL) for both neonatal and maternal outcomes, and also includes a small contribution from maternal years lived with disability but no neonatal years lived with disability since few reliable data are available from low-income and middle-income countries. This DALY measure (or neonatal YLL plus maternal DALYs) largely relates to neonatal mortality reductions, since most of the interventions save only neonatal lives and, for those with maternal benefit, maternal deaths make up less than a quarter of the total deaths averted (see webtable 3). Since neonatal morbidity and disability averted are not taken into account, our cost-effectiveness estimates might underestimate the true benefits of these interventions.

Figure 1 shows estimates of the costs per DALY averted in the 26 countries of the WHO Afro-D subregion (Africa with high child and high adult mortality), where average gross domestic product (GDP) per person is Intl$1391. On the basis of their common delivery mode—ie, through the same cadre of worker at the family-community level—the family-care package and extra community-based care of low birthweight infants were combined and labelled family care/low birthweight care in this analysis. Interventions shown along the expansion path (the diagonal line in figure 1) are the most cost-effective, whereas those that fall above the expansion path are less cost-effective.

The universal packages (table 2) all fall on or close to the expansion path (figure 1). Most importantly, all the universal care packages (Intl$15–47 per DALY averted) in this analysis are very cost effective—ie, below average per-person GDP, or Intl$1391 for Afro-D countries, which, for example, in Nigeria, would be US$349—as defined by cost-effectiveness thresholds of the Commission on Macroeconomics and Health.[31] Cost-effectiveness of emergency neonatal care, seen just above the line, would increase on integration with maternal and child clinical care services. By comparison, the costs per DALY averted of providing antiretroviral therapy and preventing mother-to-child transmission of HIV/AIDS in the Afro-E (Africa with high child and very high adult mortality) region (average regional GDP per person of Intl$1576—which in Kenya, for example, would be US$351) have been estimated at about 20–100-fold greater at Intl$1661 and Intl$1134, respectively.[31]

The results of our cost-effectiveness analysis emphasise the benefits of combining interventions into packages with a common service delivery mode, rather than providing single interventions in a vertical manner, since all single interventions fall above the expansion path. Thus, the additional interventions (table 2) only become cost effective when added to universal packages delivered at high coverage in a more developed health system. However, against the efficiency gains of packaging should be balanced the potential for over-bundling interventions and exacerbating inequities in the availability of these services for the poor.[32]

How many lives can be saved?

Although cost-effective interventions to prevent neonatal mortality are available, coverage of many of these interventions is low (figure 2), especially in resource-poor settings. The number of neonatal deaths that could be prevented through wider implementation of evidence-based interventions in the 75 countries included in the WHO 2005 world health report[25] was estimated as described in panel 1. These 75 countries include the 42 analysed by the Bellagio child survival study group, plus additional countries with high maternal mortality burden.[8] The data and assumptions about degrees of coverage and the cause-specific effect of packages of interventions are shown in webtable 2.

If all the interventions in table 2, including situational and additional elements, were implemented at full coverage (99%), an estimated 41–72% of neonatal deaths could be averted in the 75 countries in our analysis (table 4). Our estimate of a 59% reduction, obtained on the assumption that the true effectiveness of the interventions lies in the middle of the ranges we have used, is close to the figure of 55% estimated by the Bellagio child survival group.[8] We included several interventions not considered by the Bellagio group—eg, expanded maternal care—while excluding only one that they did include—insecticide-treated bed nets-—suggesting our effectiveness assumptions might have been more conservative than theirs. Our results show that the largest percentage reductions in neonatal deaths would be achieved in African (Afro), Eastern Mediterranean (Emro), and southeast Asia (Searo) regions of WHO, which have the highest NMRs and the largest numbers of neonatal deaths.

Implementation of the universal packages only—ie, excluding additional interventions but including intermittent presumptive treatment for malaria (situational)—at full (99%) coverage would avert an estimated 35–66% of neonatal deaths (data not shown). Thus, much of the reduction in mortality can be achieved even in the absence of a fully developed health system. Similarly, if coverage of all interventions were increased from their current levels to 90% rather than 99%, mortality would be reduced by an estimated 36–67% (table 5).

A halving of neonatal mortality would result in a global neonatal mortality rate (NMR) (about 15 per 1000) similar to that in high-income countries in the era immediately before the widespread institution of neonatal intensive care. Thus, the results of our analysis are compatible with historical experience:[6] NMRs of

	Number of countries[25]	Median NMR (per 1000 livebirths)	Current (2000) number of deaths (1000s)	Predicted number of neonatal deaths averted (1000s) after intervention (% reduction)		
				Low†	Middle†	High†
Africa	40	40	1084	465 (43%)	656 (61%)	793 (73%)
Americas	8	18	114	29 (25%)	47 (42%)	63 (55%)
E Mediterranean	9	39	556	254 (46%)	353 (64%)	420 (76%)
Europe	5	25	45	10 (23%)	17 (38%)	23 (51%)
Southeast Asia	7	39	1413	576 (41%)	850 (60%)	1045 (74%)
Western Pacific	6	27	478	161 (34%)	245 (51%)	313 (66%)
Total	75	37	3690	1496 (41%)	2169 (59%)	2657 (72%)

*See table 2 for a description of interventions. †Degree of effectiveness derived by taking low, middle point, and high end of estimated range of intervention effect as per table 3 (see reduction: all-cause neonatal mortality).

Table 4: **Estimated number of neonatal deaths in 75 countries by region that could be averted by universal (99% coverage) delivery of all* evidence-based interventions**

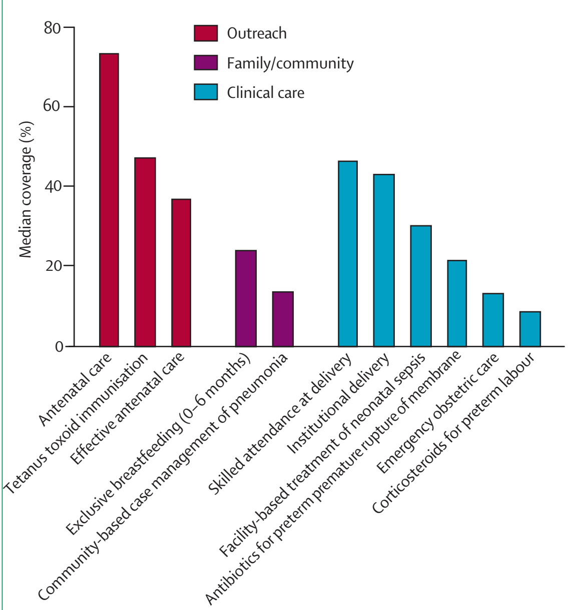

Figure 2: **Reported and estimated degrees of current coverage of neonatal interventions in 75 countries, 2000[29]**
See webtable 2 for assumptions.

	Predicted number of deaths averted (1000s) after intervention (% reduction)†		
	Low‡	Middle‡	High‡
All interventions	1340 (36%)	1980 (54%)	2470 (67%)
Universal/situational	1157 (31%)	1755 (48%)	2242 (61%)
All antenatal care	246 (7%)	337 (9%)	432 (12%)
Universal antenatal care	215 (6%)	276 (8%)	342 (9%)
All intrapartum	648 (18%)	968 (27%)	1285 (35%)
Universal intrapartum	434 (12%)	638 (17%)	841 (23%)
Postnatal	615 (17%)	1061 (29%)	1426 (39%)

All interventions=universal/situational and additional interventions for the periconceptual, antenatal, intrapartum, and postnatal periods. All=includes universal/situational and additional interventions; additional interventions shown below by period in italics. Antenatal care=antenatal care package, intermittent presumptive treatment for malaria, *detection and treatment of asymptomatic bacteriuria*. Intrapartum=family care package (clean home delivery only), skilled maternal and immediate neonatal care, emergency obstetric care, *antibiotics for preterm premature rupture of membranes, corticosteroids for preterm labour*. Postnatal=family care package (all minus clean home delivery), extra community-based care of low birthweight infants, community-based case management for pneumonia, emergency neonatal care. *See table 2 for description of intervention packages. †Calculations based on 2000 estimates of global neonatal deaths in 75 countries (n=3690000).[25] ‡Degree of effectiveness derived by taking low, middle point, and high end of estimated range of intervention effect as per table 3 (see reduction: all-cause neonatal mortality).

Table 5: **Estimated number of neonatal deaths that could be averted by delivering packages of interventions* during the indicated periods at 90% coverage in 75 countries**

	Number (%) of deaths averted (1000s) in 75 countries†		
	Low‡	Middle‡	High‡
Implementation of packages of care that share a single common service delivery mode			
Scenario 1: coverage with universal outreach (antenatal care) services alone increased to 90%	215 (6%)	276 (8%)	342 (9%)
Scenario 2: coverage with family-community care alone increased to 90%	541 (15%)	880 (24%)	1195 (32%)
Scenario 3: coverage with universal facility-based clinical care alone increased to 90%	848 (23%)	1363 (37%)	1853 (50%)
Implementation of packages of care delivered in combinations of service delivery modes			
Scenario 4: coverage with universal outreach and family-community care increased to 90%	672 (18%)	1038 (28%)	1374 (37%)
Scenario 5: coverage with universal outreach and family-community care increased to 90%. Coverage with universal facility-based clinical care increased to 50% (or current coverage)	873 (24%)	1338 (36%)	1741 (47%)
Scenario 6: coverage with universal outreach and family-community care increased to 90%. Coverage with universal facility-based clinical care increased to 90%	1157 (31%)	1755 (48%)	2242 (61%)

*Universal outreach=antenatal care package, intermittent presumptive treatment for malaria; family and community care=family care package, extra community-based care of low birthweight infants, community-based case management for pneumonia; clinical care=skilled maternal and immediate neonatal care, emergency obstetric care, emergency neonatal care . †Calculations based on 2000 estimates of global neonatal deaths in 75 countries (n=3 690 000).[25] ‡Degree of effectiveness derived by taking low, middle point, and high end of estimated range of intervention effect as per table 3 (see reduction: all-cause neonatal mortality).

Table 6: Effect of interventions packaged by service delivery mode* and delivered in programmatically relevant models of implementation in 75 countries

about 15 per 1000 are achievable with the basic intervention packages outlined in table 2.

Packages of intrapartum and postnatal care implemented at 90% coverage have broadly similar effects: two-fold to three-fold higher than that of antenatal care (table 5). The higher effect of intrapartum and postnatal care relative to antenatal care is due to the higher current coverage of antenatal care (figure 2), as well as the lower effect of the interventions that make up the antenatal package on neonatal mortality (table 3, figure 1).

Table 6 presents estimates of effect by service delivery mode (scenarios 1–3), and the incremental effects that might be achieved by introducing intervention packages in combination and in a sequence (scenarios 4–6) that takes into account their delivery mode, the expansion path identified by the cost-effectiveness analysis (figure 1), current coverage, and programmatic realities with respect to scaling up care within resource-poor countries. Figure 3 shows the results of this analysis for countries grouped by NMR.[2] This analysis models a situation in which initial emphasis in health-systems' development is placed on the establishment of effective outreach—ie, antenatal care—and family-community care to promote improved domiciliary care practices, care seeking, and demand for good clinical care. Steps are also taken to enhance clinical care capacity, including skilled attendance at deliveries and facility-based care of maternal and neonatal emergencies, but recognition is given to the lag in time needed to establish high degrees of effective coverage with these interventions.

An estimated 18–37% of neonatal deaths could be averted through expanded coverage (90%) with a combination of effective outreach and family-community care (scenario 4). Most of this initial effect is achieved through increased coverage with family-community care (scenario 2). For countries with high NMRs (⩾30 per 1000), outreach and family-community care assume even greater importance (figure 3). Outreach is especially important early in health-systems' development—in countries with NMRs greater than 45 where tetanus remains an important cause of death.[2] As the health system develops and coverage of universal facility-based clinical care increases (scenarios 5 and 6), the proportion of deaths averted rises to 31–61%. Inclusion of the additional packages further increases this effect to 36–67% (table 5).

Cost of saving newborn babies

We estimated annual running costs for current degrees of coverage (US$1·97 billion) with evidence-based interventions, and the additional costs for expansion of coverage (excluding initial investments for scaling up coverage, such as building new facilities) from current levels to 90% ($4·11 billion) for the 75 countries included in our analyses (panel 1, webtable 4 [http://image.thelancet.com/extras/05art1217webtable4.pdf]). Of the additional expenditures needed to maintain expanded coverage of all interventions (universal, situational, and additional), delivery of outreach

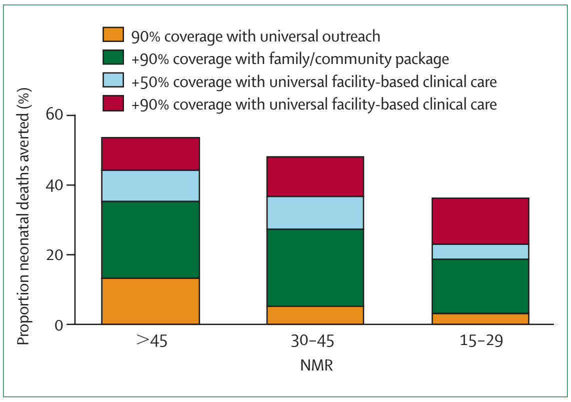

Figure 3: Effect by neonatal mortality strata of interventions introduced sequentially in 75 countries, using mid-point effectiveness estimates (table 3)[25]

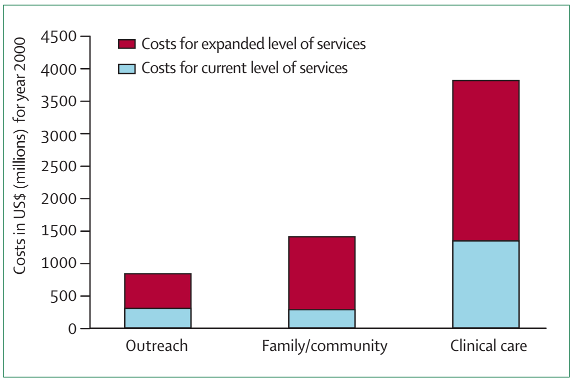

Figure 4: **Estimated current expenditures by service delivery category for implementation of evidence-based interventions, and additional costs to implement these interventions at expanded coverage of 90% in 75 countries[25]**
See webtable 4 for assumptions.

(antenatal care package and periconceptual folic acid) and family-community care (family care package, extra community-based care of low birthweight infants, community-based case management of pneumonia) (table 2) account for 13% and 27%, respectively, of the total (figure 4). For the running costs of all the packages at 90% coverage, outreach and family-community care consist of 14% and 23%, respectively, of total costs—ie, current plus additional costs. The costs for these components are low, in part because they do not depend on hospital care and the human resources costs are less. Facility-based clinical care—ie, skilled maternal and immediate neonatal care package, emergency obstetric care package, emergency neonatal care package—accounts for 60% of additional costs to maintain expanded coverage of all interventions from current levels, and facility-based clinical care makes up 63% of total running costs (current plus additional) to maintain expanded services for all interventions. Intrapartum care—ie, clean home delivery component of the family care package, skilled maternal and immediate neonatal care package, emergency obstetric care package—makes up 50% of additional costs for all interventions, which is double that of postnatal care (25%)—ie, postnatal component of family-community care, emergency neonatal care package. Of total annual programme expenditures at expanded coverage, all intrapartum care makes up 52% and postnatal care 26%.

Discussion

Analyses of the evidence base for efficacy and effectiveness of interventions, cost-effectiveness, and the potential to avert neonatal deaths if implemented at increased coverage indicate that feasible, highly cost-effective interventions are available that could avert up to 72% of neonatal deaths. These interventions can be packaged according to service delivery modes and provided to populations in need in a complementary way within health systems.

Our data further suggest that emphasis on antenatal and postnatal care through family-community interventions—including health education to improve domiciliary neonatal care practices and care-seeking for illness, as well as creation of demand for skilled care—could yield early success in advancing neonatal survival, especially in settings with weak health systems and high NMRs. Family-community care has similar costs to outreach but greater potential effect. However, in settings where tetanus remains an important cause of neonatal deaths, early development of outreach services, including tetanus toxoid immunisation, might be most strategic.[2] Results of research[33–37] suggest that intervention programmes delivered through outreach and family-community care not only save neonatal lives directly, but also act as a platform for development of a more comprehensive, effective neonatal health programme. Outreach and family-community care could also work together to link communities with health facilities, and lay a foundation for improved care seeking and demand for clinical care, which are essential for the effect of clinical care services to be fully realised. Effect at the family-community level might also be increased through more comprehensive community case management of illnesses in newborn babies, such as neonatal sepsis[35] and birth asphyxia[38]—effectively taking more clinical care into the home and community. Questions remain, however, about the feasibility and effectiveness of such approaches, which are especially relevant for settings with very poor health-systems' development.

There is a limit to the effect that can be achieved with outreach and family-community services alone—an 18–37% reduction in neonatal deaths in our analysis. The development of expanded coverage with quality clinical care (skilled maternal and immediate neonatal care, emergency obstetric care, and emergency neonatal care), alongside outreach and family-community services, is needed to achieve reductions in neonatal mortality that exceed about 50%. Achievement of MDG-4 will therefore depend on wide availability and improved quality of clinical care services for mothers and newborn babies. In general, clinical care services are more costly to implement than outreach or family-community services and also more challenging in terms of human resource management. However, given greater effect compared with outreach or family-community care packages, clinical care interventions are also very cost-effective, particularly when compared with many other maternal and child health programmes. The relative cost-effectiveness of clinical care, however, might be over-estimated, since costs for demand creation and promotion of care seeking through health education and behaviour change communications are borne in our analysis by the family care package. Health-systems' strengthening, including the provision of good clinical care and the establishment of effective links between communities

Panel 4: Key knowledge gaps for neonatal survival

- Effective approaches for promotion of (a) best household and community neonatal care practices and (b) care seeking for neonatal illness by improving recognition of illness, increasing demand for quality care, and overcoming cultural barriers.
- Measurement of community engagement and mobilisation, and demand for care.
- Methods to improve community-based identification and management of serious infections, birth asphyxia, and preterm or low birthweight babies.
- Content and optimum timing of postnatal care for the benefit of neonates and mothers.
- Burden of neonatal morbidities, including the long-term effect of interventions on post-neonatal mortality, illness, growth, and developmental disability.
- Ways to monitor health-systems' performance, including perinatal audit; simplified indicators for assessing neonatal health and programme implementation; and improved verbal autopsy methods to assess cause-specific effect.

and health facilities (with referral pathways), should be addressed early in programme development, even though success with comprehensive clinical care services might only be apparent in the long term.

The potential for postnatal care to have substantial effect, greater than that of antenatal care and similar to that of intrapartum care but at lower estimated cost, is noteworthy. Care for mothers and neonates after birth has received little emphasis in public health programmes and, typically, has neither been monitored in demographic and health surveys nor included among key programme indicators. Findings of studies[39] in five south Asian and sub-Saharan African countries indicate that only 3–12% of children born at home received care from a trained provider within 3 days of birth. These findings emphasise both the challenges and the opportunities that exist with respect to postnatal care.

Our analysis has several limitations. Because of lack of evidence from robust, large-scale effectiveness trials, many of our effect estimates are derived from only a few efficacy trials. We identified only ten effectiveness trials that addressed neonatal survival in low-income and middle-income settings (webtable 1).[40] Since studies have generally reported effect on all-cause neonatal mortality, estimates of cause-specific mortality had to be extrapolated from these data for many interventions. Consideration of other sources of evidence, including trials in high-income settings, unpublished work, programme experience, and expert opinion, however, enabled clear identification of effective and feasible interventions, and estimation of effect on all-cause and cause-specific mortality. We attempted to take account of the lack of effectiveness data by assigning effect ranges to interventions, and by being conservative when working these ranges out. We did not include neonatal morbidity or mutual benefits of interventions for maternal or child health, and our cost-effectiveness analyses and cost estimates did not include the expense of filling current gaps in health facility infrastructure and the availability of qualified staff. Thus, we underestimate the full benefits as well as the costs of developing effective neonatal health programmes. However, since neonatal health cannot be addressed through vertical programmes, but depends on integration with safe motherhood and child survival initiatives, to place the entire financial burden of these challenges on neonatal health programmes would not be appropriate. Although vertical approaches might historically reach higher coverage, our results show that to integrate these interventions within maternal care and child survival programmes is more effective. Finally, we did not take into full account the resources needed to achieve high uptake, and hence coverage, of clinical care services. Other health system interventions to subsidise care seeking for the very poor might be essential to prevent pushing them further into poverty in case of catastrophic illness and to increase the effectiveness of the family-community and clinical care packages through actual use of services.

Although our findings emphasise that we already know enough to save many neonatal lives, major evidence gaps still exist. Thus, for many interventions, an absence of evidence should not be misconstrued as evidence of absence (webtable 1). Some knowledge gaps and priority areas for research are listed in panel 4. There is a need for translational research or programme learning to ascertain how to scale up what we know works, and to develop improved methods for monitoring effect (panel 4).[2,27] Although we did not include other effective interventions that are more high-tech and costly than those considered, such as surfactant administration or nasal continuous positive airway pressure, as health systems and access improve, additional interventions such as these might assume increased importance. Although we have mostly considered the public sector of health systems, in many countries much of the health care is provided by the private sector. There is a clear need for integrated management strategies and innovative approaches to promote public-private partnerships for providing maternal and neonatal care.[41]

In conclusion, we have described the evidence base for interventions that improve neonatal survival (panel 5), but the real challenge is to deliver these at high coverage in countries with weak health systems. In many countries, coverage with the cost-effective interventions identified in this analysis is poor, and tremendous challenges need to be overcome to achieve their implementation at high coverage.[41] The policy implications of the data presented here are considerable, since they indicate that we can do a great deal to improve

Panel 5: Key messages

- Effective interventions are available to save lives of newborn babies.
- These interventions can be bundled in very cost-effective packages for delivery in health systems through outreach, family-community care, and facility-based clinical care.
- Current coverage rates for many of these interventions are extremely low.
- Universal implementation of these packages of interventions could avert up to 72% of neonatal deaths in 75 countries. Variation in potential effect ranges from 41% to 72%, depending on baseline NMR and programme effectiveness.
- Outreach and health education of families and communities to promote adoption of evidence-based home-care practices, create demand for skilled care, and improve care seeking can bring early success in averting neonatal deaths, particularly in settings with high mortality and weak health systems.
- Simultaneous expansion of clinical care for newborn babies and their mothers is essential to achieve the global reductions in neonatal mortality needed to meet MDG-4.

neonatal care, even within existing suboptimum health systems. Our analyses based on running costs also indicate that doing so would require a continuing investment that is affordable and necessary to achieve the MDGs. Improving neonatal care requires a clear implementation process and framework for applying these interventions at the country level within existing programmes.[41] Political will to spur change[42] is essential. Generating this political will and leadership is the real challenge that policy makers and health systems face to translate our estimates into reality.

Lancet Neonatal Survival Steering Team
Joy E Lawn, Simon Cousens, Zulfiqar A Bhutta, Gary L Darmstadt, Jose Martines, Vinod Paul, Rudolph Knippenberg, and Helga Fogstad.

Interventions working group
Gary L Darmstadt, Simon Cousens, Rachel A Haws, Zulfiqar A Bhutta, Joy E Lawn, Taghreed Adam, Neff Walker, Luc de Bernis.

Global price tag working group
Neff Walker, Gary L Darmstadt, Joy E Lawn, Zulfiqar A Bhutta, Simon Cousens, Agnes Soucat, Rudolph Knippenberg.

Cost-effectiveness working group
Taghreed Adam, Gary L Darmstadt, Zulfiqar A Bhutta, Joy E Lawn.

Conflict of interest statement
We declare that we have no conflict of interest.

Acknowledgments
We thank Stephen Lim and Sumi Mehta (WHO, Geneva, Switzerland) for contributing to the cost-effectiveness analysis of maternal interventions, and Matthews Mathai and Ornella Lincetto (WHO) for reviewing the effect assumptions; Helga Fogstad (WHO) and Jennifer W Bryce for technical assistance to the costing analysis; Victor Yu (Monash University, Melbourne, Australia) and Chewe Luo (UNICEF, New York, NY, USA) who acted as critical discussants and reviewers of the article at a review meeting in Geneva; Robert Black (Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA) and Anne Tinker (Saving Newborn Lives/Save the Children-USA, Washington, DC, USA) who also reviewed the manuscript; and Julia Ruben (Saving Newborn Lives/Save the Children-USA) who provided editorial assistance.

Work for this paper was supported by the Bill & Melinda Gates Foundation, through a grant to WHO, and by the Office of Health, Infectious Diseases and Nutrition, Global Health Bureau, United States Agency for International Development, Washington, DC, USA (award number GHS-A-00-03-00019-00 given to the Department of International Health at The Johns Hopkins Bloomberg School of Public Health). GLD was supported by the Saving Newborn Lives initiative of Save the Children-USA through a grant from the Bill & Melinda Gates Foundation. SC received some salary support from the Bill & Melinda Gates Foundation through WHO for his contribution to this work. The funding sources did not influence the content of this article. The opinions expressed herein are those of the authors and are not necessarily the views of any of the agencies.

References

1 Lawn J, Cousens S, Bhutta Z, Darmstadt G, Martines J, Paul V. Why are 4 million newborn babies dying each year? *Lancet* 2004; **364:** 399–401.

2 Lawn JE, Cousens S, Zupan J for the Lancet Neonatal Survival Steering Team. 4 million neonatal deaths: When? Where? Why? Published online March 3, 2005. http://image.thelancet.com/extras/05art1073web.pdf.

3 Costello A, Osrin D, Manandhar D. Reducing maternal and neonatal mortality in the poorest communities. *BMJ* 2004; **329:** 1166–68.

4 Bhutta Z, Ali N, Hyder A, Wajid A. Perinatal and newborn care in Pakistan: seeing the unseen. In: Bhutta Z, ed. Maternal and child health in Pakistan: challenges and opportunities. Karachi: Oxford University Press, 2004.

5 McKeown T, Record R, Turner R. An interpretation of the decline in mortality in England and Wales during the twentieth century. *Pop Stud* 1975; **29:** 391–422.

6 MacFarlane A, Johnsone A, Mugford M. Epidemiology. In: Rennie J, Roberton N, eds. Textbook of neonatology (3rd edn). Cambridge: Churchill Livingstone, 1999: 3–33.

7 Black R, Morris S, Bryce J. Where and why are 10 million children dying every year? *Lancet* 2003; **361:** 2226–34.

8 Jones G, Steketee R, Black R, Bhutta Z, Morris S. How many child deaths can we prevent this year? *Lancet* 2003; **362:** 65–71.

9 Victora C, Wagstaff A, Schellenberg J, Gwatkin D, Claeson M, Habicht J. Applying an equity lens to child health and mortality: more of the same is not enough. *Lancet* 2003; **362:** 233–41.

10 Claeson M, Gillespie D, Mshinda H, Troedsson H, Victora C. Knowledge into action for child survival. *Lancet* 2003; **362:** 323–27.

11 Bryce J, el Arifeen S, Pariyo G, Lanata C, Gwatkin D, Habicht J. Reducing child mortality: can public health deliver? *Lancet* 2003; **362:** 159–64.

12 Bhutta Z. Beyond Bellagio: addressing the challenge of sustainable child health in developing countries. *Arch Dis Child* 2004; **89:** 483–87.

13 Bhutta Z, Darmstadt G, Hasan B, Haws R. Community-based interventions for improving perinatal and neonatal outcomes in developing countries: a review of the evidence. *Pediatrics* 2005; **115:** 519–617.

14 Edejer T, Baltussen R, Adam T, Hutubessy R, Acharya A, Evans D, eds. Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: World Health Organization, 2003.

15 Baltussen R, Adam T, Edejer T-T, Hutubessy R, Acharya A, Evans D. Methods for generalized cost-effectiveness analysis. In: Edejer T, Baltussen R, Adam T, Hutubessy R, Acharya A, Evans D, eds. Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: World Health Organization, 2003.

16 Adam T, Evans D, Koopmanschap M. Cost-effectiveness analysis: can we reduce variability in costing methods? *Int J Technol Assess Health Care* 2003; **19:** 407–20.

17 Mulligan J, Fox-Rushby J, Adam T, Johns B, Mills A. Unit costs of health care inputs in low and middle income regions. DCPP Working Paper No 9, 2003. http://www.fic.nih.gov/dcpp/wps/wp9.pdf (accessed Jan 17, 2005).

18 Adam T, Evans D, Murray C. Econometric estimation of country-specific hospital costs. *Cost Eff Resour Alloc* 2003; **1:** 3.
19 Johns B, Baltussen R, Hutubessy R. Programme costs in the economic evaluation of health interventions. *Cost Eff Resour Alloc* 2004; **1:** 1.
20 Management Sciences for Health. International drug price indicator guide. Boston: Management Sciences for Health, 2004.
21 Drummond M, O'Brien B, Stoddard G, Torrance G. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1997.
22 WHO. Choosing Interventions that are Cost-Effective (CHOICE). Geneva: World Health Organization, 2004.
23 Lawn J, Cousens S, Wilczynska K. Estimating the causes of four million neonatal deaths in the year 2000: statistical annex—the World Health Report 2005. Geneva: World Health Organisation, 2005.
24 UNICEF. Child info project: New York: UNICEF, 2004.
25 WHO. The World health report 2005: making every mother and child count. Geneva: World Health Organization, 2005.
26 UNICEF. UNICEF supply division catalogue. New York: UNICEF, 2005. http://www.supply.unicef.dk/catalogue1 (accessed Feb 1, 2005).
27 Travis P, Bennett S, Haines A, et al. Overcoming health-systems constraints to achieve the Millennium Development Goals. *Lancet* 2004; **364:** 900–06.
28 WHO. Making pregnancy safer: the critical role of the skilled attendant: a joint statement by the WHO, ICM and FIGO. Geneva: World Health Organization, 2004.
29 The World Bank. The World development report 2004: making services work for the poor. Washington: The World Bank, 2004.
30 Lawn J, Zupan J, Knippenberg R, Bekyorian G. Newborn survival and health. In: Jamison D, Measham A, Alleyne G, Breman J, Claeson M, Evans D, eds. Disease control priorities in developing countries (2nd edn). Washington: Oxford University Press, 2005.
31 WHO. Report of the Commission on Macroeconomics and Health. Geneva: World Health Organization, 2002.
32 Gwatkin D, Bhuiya A, Victora C. Making health systems more equitable. *Lancet* 2004; **364:** 1273–80.
33 Manandhar D, Osrin D, Shreshtha B, et al. Effect of a participatory intervention with women's groups on birth outcomes in Nepal: cluster-randomized controlled trial. *Lancet* 2004; **364:** 970–79.
34 Howard-Grabman L, Seone G, Davenport C. The Warmi project: a participatory approach to improve maternal and neonatal health: an implementer's manual. Westport: John Snow International MotherCare Project, Save the Children, 2002.
35 Bang A, Bang R, Baitule S, Reddy M, Deshmukh M. Effect of home based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. *Lancet* 1999; **354:** 1955–61.
36 Sazawal S, Black R, Group PCMT. Effect of pneumonia case management on mortality in neonates, infants, and preschool children: a meta-analysis of community-based trials. Review. *Lancet Infect Dis* 2003; **3:** 547–56.
37 Fullerton J, Killian R, Gass P. Community partnerships for safe motherhood: the PRIME II project—final evaluation report. Chapel Hill: INTRAH, 2003.
38 Saving Newborn Lives. Birth asphyxia: report of a meeting. Cape Town: Save the Children/USA, 2002.
39 Seims L. Newborn care and survival. American Public Health Association 132nd Annual Meeting and Exposition 2004, Washington.
40 Bhutta Z, Lassi S. Child health: how can health research make a difference? In Matlin S, ed. Global forum update on research for health 2005: health research to achieve the Millennium Development Goals. London: Pro Book, 2004: 107–12.
41 Knippenberg R, Lawn JE, Darmstadt GL, et al. Systematic scaling up of neonatal care in countries. Published online March 3, 2005. http://image.thelancet.com/extras/05art1164web.pdf.
42 Martines J, Paul VK, Bhutta ZA, et al. Neonatal survival: a call for action. Published online March 3, 2005. http://image.thelancet.com/extras/05art1216web.pdf.