Neonatal Survival 2

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

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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.

This report is the second in a series addressing neonatal survival.1 The first article1 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.13 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 and effectiveness of interventions with the potential to reduce perinatal or neonatal mortality, or both (panel 1).12–26 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.

This report is the second in a series addressing neonatal survival. The Bellagio child survival series7–11 has been important in drawing attention to the unfinished child survival agenda. Writing for the series, Jones and colleagues8 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.12–15 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.11 Of the 23 interventions listed, eight were specific to neonates, but five of the eight were assumed to need skilled care, leaving few choices for settings with low coverage of skilled care.

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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, plus nine additional interventions. From the Bellagio list, on the basis of our meta-analysis, we included intermittent presumptive treatment for malaria for 1000 livebirths and half the neonatal deaths in the African region—i.e., Afro-D and Afro-E. Malaria is important in this region, a necessary condition for analysing cost-effectiveness of intermittent presumptive treatment for malaria.

### 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 weblink 1 and weblink 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—i.e., 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.\(^{22}\) 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—e.g., 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.\(^{23}\) 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.\(^{24,25}\) We based medicine costs on the price of off-patent drugs, the primary source being the International Drug Price Indicator Guide.\(^{26}\) We discounted all costs and effects at 3%, consistent with the recommendations of the US panel on cost-effectiveness in health and medicine.\(^{27}\) 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,\(^{28}\) and to US$ with official exchange rates with local currencies (see also weblink 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/05art1217/webtable1.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 antihelmintic 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). 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). We derived estimates of coverage with interventions from UNICEF ChildInfo data 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, 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:

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

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. Running costs included commodities—eg, medicines, equipment, supplies—in-service 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). We obtained unit costs for in-patient care and outpatient services from the WHO CHOICE database. 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. 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.
settings—eg, intermittent presumptive treatment for malaria in endemic areas, or additional (components to be added as health systems develop). 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**
Clinical care services provided by skilled personnel, 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.
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 www.thelancet.com Published online March 3, 2005).
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/05art1217/webtable3.pdf. 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—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. 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. 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.

How many lives can be saved?

Although cost-effective interventions to prevent neonatal mortality are available, coverage of many of these
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: NMRs of

Figure 2: Reported and estimated degrees of current coverage of neonatal interventions in 75 countries, 2000...

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

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

<table>
<thead>
<tr>
<th>Implementation of packages of care that share a single common service delivery mode</th>
<th>Number (% of deaths averted (1000s) in 75 countries†</th>
<th>Low‡</th>
<th>Middle‡</th>
<th>High‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario 1: coverage with universal outreach (antenatal care) services alone increased to 90%</td>
<td>215 (6%)</td>
<td>275 (8%)</td>
<td>342 (9%)</td>
<td></td>
</tr>
<tr>
<td>Scenario 2: coverage with family-community care alone increased to 90%</td>
<td>541 (15%)</td>
<td>880 (24%)</td>
<td>1105 (32%)</td>
<td></td>
</tr>
<tr>
<td>Scenario 3: coverage with universal facility-based clinical care alone increased to 90%</td>
<td>848 (23%)</td>
<td>1363 (37%)</td>
<td>1853 (50%)</td>
<td></td>
</tr>
</tbody>
</table>

Implementations of packages of care delivered in combinations of service delivery modes

<table>
<thead>
<tr>
<th>Implementation of packages of care delivered in combinations of service delivery modes</th>
<th>Number (% of deaths averted (1000s) in 75 countries†</th>
<th>Low‡</th>
<th>Middle‡</th>
<th>High‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario 4: coverage with universal outreach and family-community care increased to 90%</td>
<td>672 (18%)</td>
<td>1038 (28%)</td>
<td>1374 (37%)</td>
<td></td>
</tr>
<tr>
<td>Coverage with universal facility-based clinical care increased to 50% (or current coverage)</td>
<td>873 (24%)</td>
<td>1338 (36%)</td>
<td>1741 (47%)</td>
<td></td>
</tr>
<tr>
<td>Scenario 5: coverage with universal outreach and family-community care increased to 90%</td>
<td>1157 (31%)</td>
<td>1755 (48%)</td>
<td>2242 (61%)</td>
<td></td>
</tr>
<tr>
<td>Coverage with universal facility-based clinical care increased to 90%</td>
<td>1157 (31%)</td>
<td>1755 (48%)</td>
<td>2242 (61%)</td>
<td></td>
</tr>
</tbody>
</table>

*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 care 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). ‡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).

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 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. 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).

Figure 3: Effect by neonatal mortality strata of interventions introduced sequentially in 75 countries, using mid-point effectiveness estimates (table 3).
(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, 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. Results of research33–37 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 sepsis35 and birth asphyxia38—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 overestimated, 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...
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 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). 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). 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.

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. The policy implications of the data presented here are considerable, since they indicate that we can do a great deal to improve...
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. Political will to spur change 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.

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

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References