Every Newborn 3

Can available interventions end preventable deaths in mothers, newborn babies, and stillbirths, and at what cost?

Zulfiqar A Bhutta, Jai K Das, Rajiv Bahl, Joy E Lawn, Rehana A Salam, Vinod K Paul, M Jeeva Sankar, Hannah Blencowe, Arjumand Rizvi, Victoria B Chou, Neff Walker, for The Lancet Newborn Interventions Review Group and The Lancet Every Newborn Study Group

Progress in newborn survival has been slow, and even more so for reductions in stillbirths. To meet Every Newborn targets of ten or fewer neonatal deaths and ten or fewer stillbirths per 1000 births in every country by 2035 will necessitate accelerated scale-up of the most effective care targeting major causes of newborn deaths. We have systematically reviewed interventions across the continuum of care and various delivery platforms, and then modelled the effect and cost of scale-up in the 75 high-burden Countdown countries. Closure of the quality gap through the provision of effective care for all women and newborn babies delivering in facilities could prevent an estimated 113 000 maternal deaths, 531 000 stillbirths, and 1·325 million neonatal deaths annually by 2020 at an estimated running cost of US$4·5 billion per year (US$0·9 per person). Increased coverage and quality of preconception, antenatal, intrapartum, and postnatal interventions by 2025 could avert 71% of neonatal deaths (1·9 million [range 1·6–2·1 million]), 33% of stillbirths (0·82 million [0·60–0·93 million]), and 54% of maternal deaths (0·16 million [0·14–0·17 million]) per year. These reductions can be achieved at an annual incremental running cost of US$5·65 billion (US$1·15 per person), which amounts to US$1928 for each life saved, including stillbirths, neonatal, and maternal deaths. Most (82%) of this effect is attributable to facility-based care which, although more expensive than community-based strategies, improves the likelihood of survival. Most of the running costs are also for facility-based care (US$3·66 billion or 64%), even without the cost of new hospitals and country-specific capital inputs being factored in. The maximum effect on neonatal deaths is through interventions delivered during labour and birth, including for obstetric complications (41%), followed by care of small and ill newborn babies (30%). To meet the unmet need for family planning with modern contraceptives would be synergistic, and would contribute to around a halving of births and therefore deaths. Our analysis also indicates that available interventions can reduce the three most common cause of neonatal mortality—preterm, intrapartum, and infection-related deaths—by 58%, 79%, and 84%, respectively.

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This is the third in a Series of five papers about newborn health

Center for Global Child Health, Hospital for Sick Children, Toronto, Canada (Prof Z A Bhutta PhD); **Center of Excellence in Women and Child Health, Aga Khan University, Karachi, Pakistan** (Prof Z A Bhutta, J K Das MBA, R A Salam MSc, A Rizvi MSc); **World Health Organization, Geneva, Switzerland** (R Bahl PhD); **Maternal, Adolescent Reproductive and Child Health (MARCH) Centre, London School of Hygiene & Tropical Medicine, London, UK** (J E Lawn PhD, H Blencowe PhD); **Saving Newborn Lives, Save the Children, Washington, DC, USA** (J E Lawn); **Research and Evidence Division, UK AID, London, UK** (J E Lawn); **All India Institute of Medical Sciences, New Delhi, India** (V K Paul MD, J M Sankar DM); **and Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA** (V B Chou PhD, N Walker PhD)

Correspondence to: Prof Zulfiqar A Bhutta, Center for Global Child Health, Peter Gilgan Center for Research and Learning, 686 Bay Street, Toronto, ON M5G 0A4, Canada **zulfiqar.bhutta@sickkids.ca**

See Online for appendix

Introduction

This *Lancet* Every Newborn Series shows that despite a halving of under-5 child deaths in the past two decades, progress in reducing newborn deaths has been slower, with about 3 million neonates still dying every year.[1] Reductions in neonatal mortality have averaged 2·0% annually since the Millennium Development Goals (MDG) baseline in 1990, which is much slower than corresponding reductions in maternal mortality (2·6%) or mortality in children 1–59 months of age (3·4%). Additionally, 2·6 million stillbirths (≥28 weeks or ≥1000 g) occur every year, including 1·2 million during labour.[2] These stillbirths were not counted in the MDGs and progress has been substantially slower than even that for reductions in newborn mortality.[1] Achievement of the proposed Every Newborn targets of ten or fewer neonatal deaths and stillbirths per 1000 births in every country[1,2] would need a doubling of present rates of change at a global average, and more in some high-burden countries. Such progress needs focus on the most effective interventions and intentional investment and implementation, which has been insufficient so far.[3] In this third paper of the Series, we provide an update of the evidence base for interventions since the *Lancet* 2005 Neonatal Series and 2011 Stillbirth Series, and other relevant reviews.[4–7] We estimate the potential lives saved and the running costs of implementation, and make recommendations for prioritisation linked to the Every Newborn Action Plan.

Review of interventions and delivery platforms

We identified specific interventions across the continuum of care (preconception, antenatal, intrapartum, immediate postnatal period, and thereafter), building on previous evidence reviews[4–8] (appendix pp 3–4), which could affect stillbirths and newborn outcomes (figure 1). We also reviewed delivery platforms that could augment the uptake of these interventions and methods to improve quality of care. We searched all major databases to identify available quality systematic reviews in various domains using standardised methodology. When we could not identify relevant syntheses, we did de-novo reviews (appendix pp 5–6). When we could not identify interventions from low-income and middle-income countries, we considered evidence from other contexts. Table 1 and appendix pp 8–22 summarise the evidence of interventions across the continuum of care that affect stillbirths and neonatal outcomes.

Key messages

1) Evidence is high, but coverage is low

New evidence-based interventions exist to address the main causes of newborn deaths, including:

- Innovations such as chlorhexidine cord cleansing.
- Increasing evidence of care of small and ill newborn infants in first and second level facilities.
- Increasing feasibility because of adaptation and innovation of preventive measures such as antenatal corticosteroids and care for preterm infants using training tools for resuscitation and low-cost equipment such as continuous positive airway pressure.

These interventions can be delivered within existing service delivery packages, but almost all have very low coverage at present, with less than a third of women and neonates in need receiving them. Major acceleration is needed to be able to meet targets for Every Newborn, linked to A Promise Renewed, and the post-Millenium Development Goal targets.

2) Impact is high and cost is quite low

High coverage of care by 2025 would prevent 71% of neonatal deaths, saving 1·90 million newborn babies, preventing 0·82 million stillbirths, and averting more than 0·16 million maternal deaths per year, with ongoing effects on child health beyond the first month of life. Hence, care provides a quadruple return for an investment of US$5·65 billion ($1·15 per person) and $1928 for each life saved.

Together, the most effective packages can save 87% of preventable maternal and newborn deaths:

- Care during labour and birth, plus immediate newborn care, can avert 1·49 million maternal and newborn deaths and stillbirths per year by 2025, of which almost 0·8 million are newborn lives.
- Care of the small and ill newborn can avert more than 580 000 newborn deaths per year.

Preventive care of the healthy neonate could save more than 230 000 neonatal lives, whereas immediate care of the neonate at birth alone could avert almost 190 000 deaths.

3) Quality of care gap

- Quality of care at birth: an immediately feasible opportunity is to address the quality gap for births already ocurring in facilities by 2020, resulting in an estimated 1·325 million neonates saved, 531 000 stillbirths prevented, and 113 000 women saved.
- Care of small and ill neonates: our estimates suggest the greatest effect would come from a focus on the care of small and ill neonates, which has been neglected to date and would prevent almost 600 000 newborn deaths per year by 2025. Much of this effect is potentially achievable through newborn care services in subdistrict and district level hospitals.

4) Equity gap

The 24 countries with the highest mortality (neonatal mortality rate >30) have the greatest potential for lives saved, both proportionately and in actual numbers (1·3 million or two-thirds of all newborn lives saved by 2025). Within countries, specific unreached populations need to be targeted in different ways, such as rural or urban poor populations or ethnic minority groups. To harness the power of parents, families, and communities is crucial to mobilise change. Community and primary care approaches alone could save an estimated 372 000 newborn lives by 2020, at a cost of less than US$2 billion.

Preconception: interventions before and between pregnancy

The importance of preconception interventions for improved maternal, perinatal, and neonatal health outcomes is increasingly being recognised.[9] These interventions include delaying of age at first pregnancy, meeting of unmet needs for family planning, optimisation of inter-pregnancy intervals, and enhancement of pre-pregnancy nutritional status; these approaches can be delivered across a range of possible platforms (panel 1).

Antenatal: interventions during pregnancy

The antenatal interventions reviewed included maternal immunisation, screening and management of infections (notably HIV, syphilis, other sexually transmitted infections, and malaria), interventions addressing pre-existing chronic diseases (notably diabetes and hypertension) and pregnancy-induced disorders, detection and management of significant in-utero growth retardation, prevention of rhesus (Rh) D allo-immunisation, and interventions to improve nutrition and psychosocial health and combat drug misuse during pregnancy. Some of the salient interventions are summarised in the following paragraphs and are detailed in appendix pp 8–14.

Although the importance of tetanus immunisation in pregnancy is well established,[26,27] the evidence to support other vaccines in pregnancy such as pneumococcal, haemophilus influenzae type B, and viral influenza vaccines is less robust, partly because of persistent challenges in the undertaking of immunisation trials during pregnancy. Despite reductions in maternal and infant respiratory illnesses with maternal influenza vaccination, no consistent benefits were noted on rates of preterm delivery and low birthweight (appendix p 23).

Intermittent preventive treatment of malaria in pregnancy reduces antenatal parasitemia and placental malaria, and is associated with reductions in low birthweight (by 29%) and neonatal mortality (31%) (appendix pp 24–25). The use of insecticide-treated bednets in pregnancy can reduce blood and placental parasitaemia (by 24%), low birthweight (20%), and stillbirths (32%) (appendix pp 24–25). Although the combined use of intermittent preventive treatment of malaria and insecticide-treated bednets in pregnancy can reduce the occurrence of low birthweight in the first or second pregnancy by 35% in areas of stable *Plasmodium falciparum* transmission, data for rates of prematurity and stillbirths are scarce.[28]

In syphilis-endemic countries, antenatal syphilis screening combined with penicillin treatment can reduce syphilis-specific stillbirths (by 82%), preterm births (64%), and syphilis-related neonatal mortality (80%).[29] A small amount of evidence suggests that screening for other genital tract infections and treatment programmes can also reduce respective preterm births (by 45%) and low birthweight (52%).[30] Work is underway to establish the effectiveness of these approaches in primary care health systems.

Although treatment of bacterial vaginosis with antibiotics shows no clear benefits on preterm births or neonatal infections,[31] intrapartum antibiotic prophylaxis for known group B streptococcus colonisation can reduce

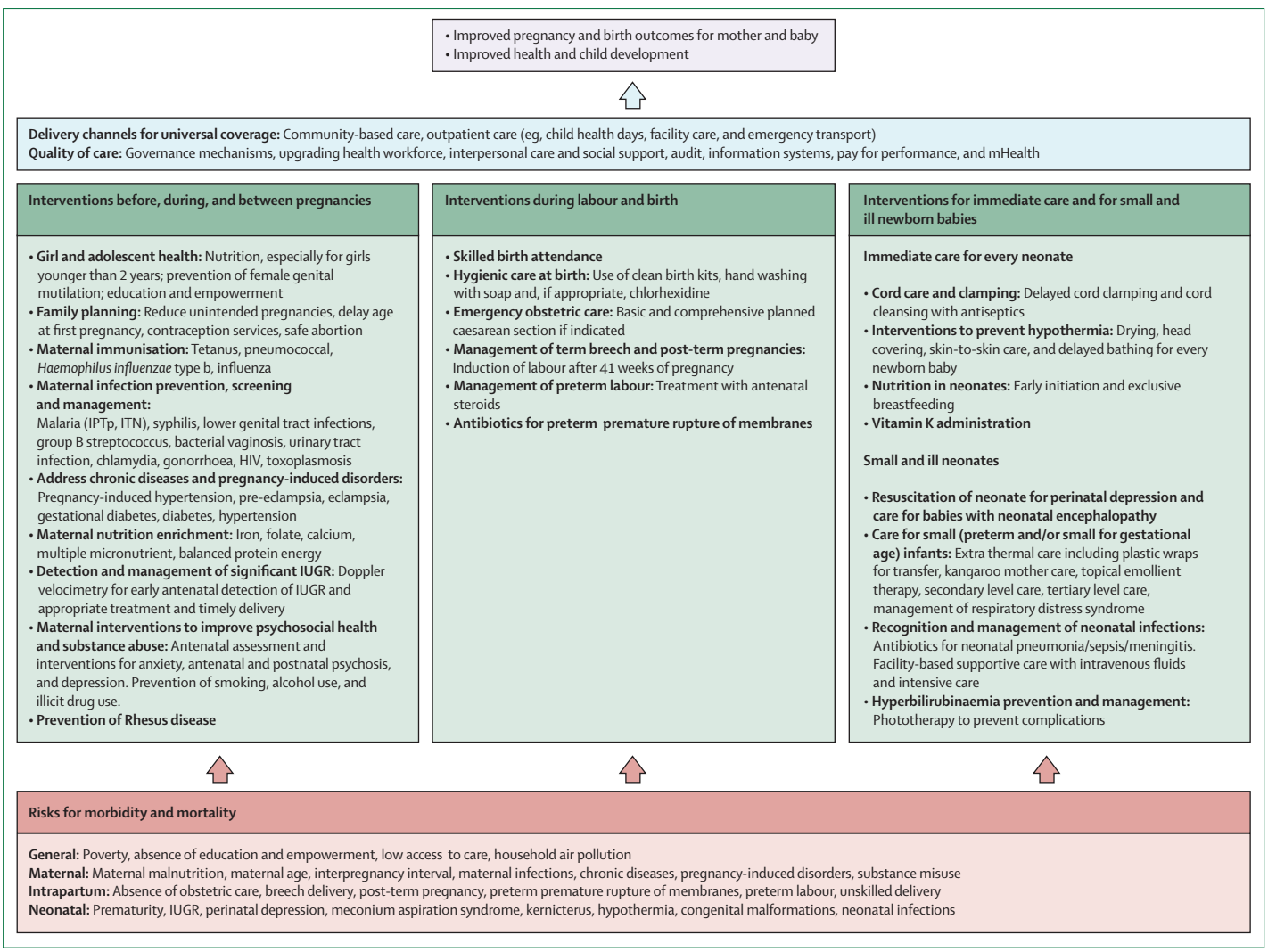


Figure 1: **Conceptual framework for risks and interventions to improve health for every newborn and other birth and maternal outcomes**
IPTp=intermittent preventative treatment in pregnancy. ITN=insecticide-treated bednets. IUGR=intrauterine growth restriction.

	Stillbirth	Preterm birth	Perinatal mortality	Small for gestational age	Neonatal mortality
Preconception and antenatal interventions					
Iron supplementation	..	0·88 (0·77–1·01)	..	..	0·90 (0·68–1·19)
Iron and folic acid supplementation	..	1·55 (0·40–6·00)	..	..	0·81 (0·51–1·30)
Multiple micronutrient supplementation	0·95 (0·85–1·06)	0·99 (0·97–1·02)	0·96 (0·84–1·10)	**0·87 (0·83–0·92)**	1·01 (0·89–1·16)
Calcium supplementation	..	**0·76 (0·60–0·97)**	0·90 (0·74–1·09)	1·01 (0·84–1·21)	1·07 (0·39–2·95)
Balanced energy protein supplementation	**0·62 (0·40–0·98)**	0·96 (0·80–1·15)	..	**0·68 (0·49–0·89)**	0·63 (0·37–1·06)
Tetanus toxoid immunisation	..	..	..	..	**0·06 (0·02–0·2)**
Haemophilus influenzae type b vaccine	1·69 (0·41–6·94)	1·37 (0·20–9·16)	..	..	..
Influenza virus vaccine	..	0·77 (0·36–1·64)	..	..	..
Syphilis screening and treatment	**0·18 (0·10–0·33)**	**0·36 (0·27–0·47)**	..	..	**0·20 (0·13–0·32)**
Intermittent preventive treatment for malaria in pregnancy	0·96 (0·72–1·27)	0·86 (0·62–1·21)	0·83 (0·66–1·05)	**0.65 (0·55 – 0·77)**	**0·69 (0·49–0·98)**
Insecticide-treated bednets	..	..	..	**0·65 (0·55 – 0·77)**	..
Maternal anthelminthic treatment	..	0·88 (0·43–1·78)	0·97 (0·68,1·40)	..	..

(Table 1 continues on next page)

	Stillbirth	Preterm birth	Perinatal mortality	Small for gestational age	Neonatal mortality
(Continued form previous page)					
Lower genital infection screening and management	..	**0·55 (0·41–0·75)**	..	..	..
Prophylactic antibiotics	..	0·96 (0·70–1·33)	0·80 (0·31–2·06)	1·29 (0·42–3·96)	..
Antibiotic prophylaxis for group b streptococcus colonisation	..	..	..	..	0·19 (0·01–3·82)
Antibiotics for bacterial vaginosis	..	0·88 (0·71–1·09)	0·71 (0·36–1·39)	..	..
Asymptomatic bacteriuria treatment	..	0·37 (0·10–1·36)	..	..	..
Periodontal disease management	**0·49 (0·26–0·94)**	..	..	..	..
Antihypertensive for mild-to-moderate hypertension	1·14 (0·60–2·17)	1·02 (0·89–1·16)	0·96 (0·60–1·54)	1·04 (0·84–1·27)	0·79 (0·14–4·34)
Magnesium sulphate for prevention of pre-eclampsia	0·99 (0·87–1·12)	..	0·98 (0·88–1·10)	..	1·16 (0·94–1·42)
Calcium supplementation for hypertension	0·90 (0·74–1·09)	**0·76 (0·60–0·97)**	0·86 (0·70–1·07)	1·05 (0·86–1·29)	..
Antiplatelets for pre-eclampsia	1·15 (0·88–1·49)	**0·92 (0·88–0·97)**	0·89 (0·74–1·08)	**0·90 (0·83–0·98)**	0·89 (0·64–1·22)
Preconception diabetes education	..	0·83 (0·62–1·12)	**0·31 (0·19–0·53)**	..	..
Optimum vs suboptimum glucose control	0·51 (0·14–1·88)	..	**0·40 (0·25–0·63)**	..	..
Education/psychotherapy to quit smoking	..	0·79 (0·52–1·21)	..	..	..
Nicotine replacement therapy	..	**0·77 (0·61–0·97)**	..	..	..
Incentives to quit smoking	..	0·49 (0·22–1·08)	..	..	..
Prenatal antidepressants	..	**1·55 (1·38–1·74)**	..	..	..
Doppler velocimetry	..	..	**0·71 (0·52–0·98)**	..	0·81 (0·53–1·24)
Fetal movement monitoring	0·65 (0·41–1·04)	1·12 (0·72–1·75)	..	..	..
Caesarean section for breech	..	..	**0·33 (0·19–0·56)**	..	..
Post-term labour induction	0·28 (0·05–1·67)	..	**0·30 (0·09–0·99)**	..	..
Antibiotics for preterm premature rupture of membrane	..	..	..	..	**0·88 (0·80–0·97)**
Steroids for preterm labour	..	..	..	0·96 (0·63–1·44)	**0·47 (0·35–0·64)**
Basic emergency obstetric care	..	..	..	..	**0·60 (0·48–0·60)**
Comprehensive emergency obstetric care	..	..	..	..	**0·15(0·12–0·32)**
Skilled birth care	..	..	..	..	**0·75 (0·70–0·85)**
Clean birth practices at home	..	..	..	..	**0·85 (0·80–0·90)**
Clean birth practices at facility	..	..	..	..	**0·73 (0·64–0·76)**
Newborn and neonatal interventions					
Delayed cord clamping in full-term neonates	..	..	..	..	0·37 (0·04–3·41)
Umbilical cord antiseptics	..	..	..	..	**0·77 (0·63–0·94)**
Neonatal resuscitation at home	..	..	..	..	**0·80 (0·75–0·85)**
Neonatal resuscitation at facility	..	..	..	..	**0·70 (0·59–0·84)**
Anticonvulsants for asphyxia	..	..	..	..	0·87 (0·54–1·40)
Hypothermia for hypoxic ischaemic encephalopathy	..	..	..	..	**0·75 (0·64–0·88)**
Continuous positive airway pressure for respiratory distress syndrome	..	..	**0·52 (0·32–0·87)**	..	..
Surfactant therapy for respiratory distress syndrome	..	..	..	..	**0·68 (0·57–0·82)**
Preventive surfactant therapy for preterm neonates	..	..	..	..	**0·60 (0·47–0·77)**
Antibiotics for meconium aspiration syndrome	..	..	..	..	1·29 (0·36–4·54)
Systemic steroids for meconium aspiration syndrome	..	..	..	..	0·61 (0·22–1·71)
Inhaled steroids for meconium aspiration syndrome	..	..	..	..	0·39 (0·08–1·94)
Surfactant lung lavage for meconium aspiration syndrome	..	..	..	..	0·38 (0·09–1·57)
Bolus surfactant for meconium aspiration syndrome	..	..	..	..	0·80 (0·39–1·66)
Topical emollient therapy	..	..	..	..	**0·73 (0·56–0·94)**
Hypothermia prevention for preterm infants	..	..	..	..	**0·80 (0·55–0·92)**
Kangaroo mother care in preterm infants	..	..	..	..	**0·60 (0·39–0·93)**
Oral antibiotics for pneumonia	..	..	..	..	**0·58 (0·41–0·82)**
Injectable antibiotics for pneumonia	..	..	..	..	**0·25(0·19· 0·30)**
Antibiotics for sepsis	..	..	..	..	**0·35 (0·30–0·50)**

Data are RR (95% CI). Numbers in bold indicate a significant effect, whereas non-bold data indicate no significant effect. .. Indicates no evidence.

Table 1: **Overview of interventions showing effect on selected outcomes**

Panel 1: Preconception and adolescent care interventions

Nearly 50% of women 20–24 years of age in Asia and Africa are married by the age of 18 years, which puts them at an increased risk of early pregnancy, maternal disability, and death. Worldwide, about 16 million girls aged 15–19 years and 2 million girls younger than 15 years old give birth every year. Half of all adolescent births occur in just seven countries: Bangladesh, Brazil, Democratic Republic of the Congo, Ethiopia, India, Nigeria, and the USA.[10] Adolescent pregnancy poses a threat to both mother and newborn baby because adolescent girls are not physically mature and might enter pregnancy with depleted nutrition reserves and anaemia.[10] Pregnancies in adolescents have a higher risk of adverse birth outcomes than do pregnancies in older women, with a 50% increased risk of stillbirths and neonatal deaths, and increased risks of preterm birth, low birthweight, and asphyxia.[11–13] Moderate preconception anaemia makes the risk of fetal growth restriction significantly higher (odds ratio [OR] 4·6, 95% CI 1·5–13·5) and increases the risk of low birthweight (6·5, 1·6–26·7).[14] Adolescents are also especially prone to complications of labour and delivery, such as obstructed and prolonged labour, vesico-vaginal fistulae, and infectious morbidity.[13] Abstinence-focused education and contraceptive availability in combination can reduce adolescent pregnancy by 15% (relative risk [RR] 0·85, 95% CI 0·74–0·98), whereas abstinence education alone can reduce repeat pregnancy in teen mothers by 37% (RR 0·63, 95% CI 0·49–0·82). Contraceptive distribution alone does not have any significant effect on either index pregnancy or repeat pregnancy in adolescent girls. Primary prevention strategies to reduce unintended pregnancies in adolescents, including sex education sessions, school-based clinics, and family planning clinics, can significantly reduce the number of unintended pregnancies (RR 0·77, 95% CI 0·64–0·92) and increase contraceptive use by adolescent girls, with a non-significant effect on delaying initiation of sexual intercourse, repeat pregnancy, and sexually transmitted infections.[15,16] School-based health centres seem to be most effective when contraception provision is made available on site and can be effective in preventing repeat adolescent pregnancies; however, the available evidence is insufficient in terms of both quality and quantity.[17,18] Adolescents taking part in a home-visiting programme and enhanced well-baby care programme are less likely to have a second birth in 2 years, and teenagers in a structured home-visiting programme are more likely to use contraception at 6 months than those who have standard home visits (OR 3·24, 95% CI 1·35–7·79).[19]

In addition to early pregnancy, studies have also shown that inter-pregnancy intervals of less than 12 months or longer than 60 months have an adverse effect on maternal and perinatal outcomes, with a J-shaped dose–response relation for perinatal outcomes.[20–22] Short inter-pregnancy intervals are associated with a 32% increased risk in maternal anaemia, a three-times higher risk of uterine rupture, and 42% increased risk for stillbirths. Short and long intervals were shown to be associated with greater risks of preterm birth (OR 1·45 and 1·21, respectively) and low birthweight (OR 1·65 and 1·37, respectively) and a slightly increased risk of infants being small for gestational age (OR 1·17 and 1·18, respectively). Interventions to communicate the effectiveness of contraceptives in preventing pregnancy have shown encouraging results but interventions vary greatly in the trials assessed. Such trials also need to include whether the methods used to assess knowledge or attitudes were tested for validity or reliability and follow-ups should also be done to assess retention of knowledge over time.[23] The effects of educational interventions for post-partum mothers about contraceptive use show that half of these post-partum interventions led to fewer repeat pregnancies or births or increased use of contraceptives and that these were more effective for interventions with several sessions but would need to be adapted for other locations and then retested.[23] Community-based interventions and antenatal contraceptive counselling improve uptake of copper intrauterine devices, which is one of the most effective reversible contraceptive methods, although a cost-benefit analysis may be needed to assess applicability.[24] A woman's nutritional status also needs to be optimised before she enters pregnancy. One such intervention—periconceptional folic acid supplementation—is associated with a 72% reduction in risk of development of neural tube defects and a 68% reduction in risk of recurrence compared with either no intervention, placebo, or micronutrient intake without folic acid.[25]

early infection. The potential overall effect in low-income and middle-income countries is uncertain.[32] Antibiotic treatment for asymptomatic bacteriuria in pregnancy is effective in clearing asymptomatic bacteriuria (by 75%), and in reducing the incidence of pyelonephritis (77%) and low birthweight (44%).[33] Despite wide prevalence, the evidence to support interventions to prevent the transmission and complications of cytomegalovirus,[34] herpes,[35] or toxoplasmosis[36,37] is inconclusive.

Antiretroviral drugs reduce viral replication and can decrease mother-to-child transmission of HIV.[38] Recent studies suggest that extended duration of treatment, especially highly active antiretroviral therapy during pregnancy, might be associated with an increased incidence of preterm delivery, small for gestational age infants, and pregnancy complications, including hypertension.[39] These areas merit further research and development.

Hypertensive diseases of pregnancy, including pregnancy-induced hypertension, pre-eclampsia, and eclampsia, can complicate 5–8% of pregnancies[40] and are the second most common cause of maternal deaths worldwide.[41] Treatment of mild-to-moderate hypertension during pregnancy does not substantially affect maternal and birth outcomes,[42] although the use of magnesium sulphate can reduce the risk of eclampsia by 59%.[43] Studies of antiplatelet drugs for women at risk of developing pre-eclampsia show that these drugs reduced

risks of pre-eclampsia (by 17%), preterm birth (8%), and small for gestational age infants (10%).[44,45] These drugs might be beneficial to prevent pre-eclampsia and improve maternal care in health systems.

An estimated 60 million women of reproductive age have type 2 diabetes, and gestational diabetes affects up to 15% of pregnant women worldwide.[46] Gestational diabetes creates an excess risk of adverse birth outcomes.[47,48] Preconception dietary advice and counselling can reduce the mean concentration of glycated haemoglobin ($HbA1_c$) during the first trimester of pregnancy, and can also reduce congenital malformations (by 70%) and perinatal mortality (69%).[49] Intensified management including dietary advice, monitoring, or pharmacotherapy for women with gestational diabetes results in a 54% reduction in birth of macrosomic babies compared with conventional management.[49] Although most of the evidence is from high-income countries, these interventions can also improve maternal and newborn outcomes in low-income and middle-income countries.

Maternal undernutrition is a risk factor for infants being small for gestational age. General nutrition interventions include dietary advice to pregnant women, specific micronutrients and balanced protein energy supplements to malnourished women, and prescription of low-energy diets to overweight pregnant women or those with excessive weight gain in early pregnancy.

Iron deficiency is the most common cause of anaemia in pregnancy and iron and folic acid supplements are recommended for prevention.[50] However, in view of the widespread multiple micronutrient deficiencies in women of reproductive age worldwide,[51] replacement of iron folate supplements with multiple micronutrient supplements has been recommended and could have additional benefits on reducing small for gestational age births.[8] Calcium supplementation during pregnancy in populations with low calcium intake can lower the risk of gestational hypertension and pre-eclampsia, reduce the risk of preterm births, and improve birthweight.[52]

The causes and risk factors overlap for stillbirth and intrauterine growth restriction. Early antenatal detection of intrauterine growth restriction and then appropriate treatment and timely delivery could minimise the risks of adverse outcomes and has been shown to be cost effective for middle-income countries according to a modelling exercise.[4] One possible treatment is low-dose heparin, although this therapy is yet to be tested in low-income and middle-income countries.[53] Detection based on low maternal body-mass index, symphysial fundal height measurement, and targeted doppler ultrasonography could help in the identification of fetuses at risk of intrauterine growth restriction who should be delivered early, which could potentially reduce stillbirths by 20% according to a Delphi consensus panel.[54] However, this strategy needs further assessment in low-income and middle-income countries because of its high cost and the potential associated risks regarding increased preterm birth in the absence of high-quality neonatal intensive care.[54]

The risk of RhD alloimmunisation during or immediately after a first pregnancy is about 1% and administration of 100 µg (500 IU) anti-D to women in their first pregnancy can reduce this risk to about 0·2%.[55] Anti-D, when given within 72 h after childbirth, significantly reduces the risk of RhD alloimmunisation (by 90%),[56] whereas administration during the last trimester (usually at 28 weeks) will prevent almost all of the remaining 10% risk.[55] Prophylaxis is also recommended to be given post-abortion, although the evidence to support this treatment approach is not clear.[57] Recent estimates show a substantial burden of both death and disability caused by this preventable disorder, and new focus is needed to reduce the cost of anti-D so that it can be made universally available.[58]

Maternal mental health disorders can significantly affect the health of both the mother and the newborn baby. Although the benefit of maternal mental health interventions, especially cognitive behavioural therapy, is well recognised,[59,60] reviews about antidepressants for treatment of antenatal depression show conflicting reports about the benefits and risks.[61]

Substance misuse during pregnancy consists of the use of illicit drugs, alcohol, or smoking, and can affect maternal and fetal health and development. Although neonatal withdrawal syndrome can be managed,[62,63] few proven interventions can reduce maternal drug misuse and its effects on newborn outcomes. By contrast, promising evidence suggests that a decrease in the prevalence of smoking could reduce preterm births and low birthweight in some countries (appendix pp 26–27).

Interventions during labour and birth

Interventions during and close to labour include obstetric care (monitoring of labour and assisted vaginal delivery or caesarean section), skilled delivery, and management of preterm labour and post-term pregnancy (appendix pp 15–17).

In obstetric care, the potential benefits of partogram use and cardiotocography with intermittent auscultation of the fetal heart rate on neonatal outcomes in low-risk pregnant women are uncertain.[64,65] The presence of skilled birth attendants and provision of emergency obstetric care as needed are the cornerstone of modern obstetrics. A Delphi process among experts suggested that basic emergency obstetric care could reduce intrapartum-related neonatal deaths by 40% and comprehensive emergency obstetric care could do so by 40%, whereas skilled birth care alone without access to the emergency component was judged to have a smaller effect at 25%.[66,67]

Education and promotion of clean birth behaviours results in a 29% increase in the use of sterile cord cutting and reductions in perinatal and neonatal mortality

(14% and 21%, respectively) (appendix pp 28–29). Hand washing with soap and water by traditional birth attendants, infants' caregivers or both reduces the risk of omphalitis (by 31%) and neonatal tetanus (42%) (appendix pp 30–31). A Delphi-based expert panel suggested that clean birth practices could reduce neonatal sepsis deaths by 15% at home, by 27% in facilities, and by 40% with clean postnatal care practices. The panel also estimated that clean birth practices reduce neonatal tetanus mortality by 30% in home births, by 38% in facility births, and by 40% through clean postnatal care practices.[68]

The effect of antenatal steroids to manage preterm labour is mediated through overall acceleration of fetal maturity, and has shown to reduce respiratory distress syndrome by 34%, cerebroventricular haemorrhage by 46%, and the risk of neonatal deaths by 31%.[69,70] This intervention is also associated with reduced need for ventilation so will probably have a greater effect in settings without intensive care, and a subgroup analysis of evidence from low-income and middle-income countries suggests that the effect on neonatal mortality effect is indeed bigger than in high-income countries at 53%.[69] Antibiotics administered for preterm, premature rupture of membranes reduces the risk of respiratory distress syndrome by 12% and early-onset postnatal infection by 39%.[71]

A policy of labour induction at term or post-term (at 41 weeks or more), when compared with spontaneous labour or later induction, was associated with 69% fewer perinatal deaths and 50% reduction in risk of meconium aspiration syndrome.[72] However, the costs and increased risk associated with the detection and induction of labour for post-term pregnancies do not yet support implementation of this approach in low-income and middle-income countries.[4]

Interventions for immediate care for every newborn baby

Interventions at birth for every newborn baby include immediate drying and stimulation, provision of warmth, hygienic care, support for immediate breastfeeding, and administration of vitamin K. For babies who do not breathe at birth, neonatal resuscitation is crucial, and might also include prevention and management of meconium aspiration syndrome (appendix pp 18–20).

Cleansing of the umbilical cord with antiseptics can reduce risk of infection, and application of chlorhexidine to the cord stump in community settings is associated with a 27% reduction in the incidence of omphalitis and 23% reduction in risk of neonatal mortality.[73,74] Delayed cord clamping in preterm newborns is associated with a 39% reduction in the need for blood transfusion, a 41% reduction in the risk of intraventricular haemorrhage, and a 38% reduction in risk of nectrotising enterocolitis.[75]

In view of the raised risk of neonatal mortality with hypothermia, thermal care is important for every newborn baby. Plastic wraps, when combined with other environmental heat sources, are effective in reducing hypothermia in preterm babies during stabilisation and transfer within the hospital. Some evidence supports a beneficial effect of delayed bathing and head covering on hypothermia in term and preterm babies. However, only a few small, underpowered studies have sought to quantify the effect of common thermal care interventions on neonatal mortality in low-income and middle-income countries (appendix p 32). A Delphi-based expert panel provided estimates for the effect of three thermal care practices (delayed bathing, head covering, and skin-to-skin care) and suggested that these methods could avert 20% of neonatal deaths caused by preterm birth complications and 10% of deaths in full-term or moderately preterm babies caused by infection (appendix p 32).

Initiation of breastfeeding within 1 h of birth, exclusive breastfeeding of infants until 6 months of age, and continuation of breastfeeding until 2 years of age are strongly recommended.[76] Although descriptive analyses suggest that early initiation of breastfeeding can reduce neonatal mortality by 44%,[77] in exclusively breastfed infants the risk of all-cause neonatal mortality did not differ between early and late initiators. Education and counselling interventions have been shown to improve exclusive breastfeeding rates by 43% at day 1 and by up to 30% by 1 month of age, and this can be included in maternal and newborn home visit programmes that are presently being scaled up.[78]

When given to infants of very low birthweight, oral or intramuscular vitamin A supplementation is associated with slightly reduced neonatal mortality.[79] Asian studies have shown that neonatal vitamin A reduces the risk of mortality at 6 months of age by 14%, with evidence of benefit in populations at risk of maternal vitamin A deficiency, although results from Africa are awaited.[80] Vitamin K is given prophylactically after birth to prevent vitamin K deficiency bleeding and is especially important for babies who are exclusively breastfed. In the absence of vitamin K prophylaxis, the risk of such bleeding is 0·4–1·7% and one dose of intramuscular vitamin K can reduce this risk on days 1–7 after birth and improve coagulation indices.[81]

Interventions for small and ill newborn babies

Interventions for small and ill newborn babies include prevention of hypothermia; management of respiratory distress syndrome, neonatal pneumonia, sepsis and hyperbilirubinaemia; and innovations for skin care including emollient and massage therapy (appendix pp 21–22).

Kangaroo mother care involves a package of early and continuous skin-to-skin contact, breastfeeding support, early discharge from hospital, and supportive care in stable neonates. This care package in preterm neonates (<2000 g birthweight) in hospitals is associated with reduced risk of neonatal mortality (by 51%),[82] nosocomial infection or sepsis (by 58%), hypothermia

(by 77%), and shorter length of hospital stay.[83] Kangaroo mother care also leads to a 27% increase in breastfeeding rates at 1–4 months after birth and increased breastfeeding duration.[84] So far, insufficient evidence exists to recommend community initiation of kangaroo mother care, but strong evidence supports the use of this care approach post-discharge to reduce both later mortality and also improve breastfeeding rates. High-income countries are taking up kangaroo mother care because of its long-term developmental benefits.

Perinatal respiratory depression caused by intrapartum hypoxic events or preterm birth increases the risks of mortality, neonatal encephalopathy, and long-term disability. Resuscitation training in facilities reduces intrapartum-related neonatal deaths by 30% and early neonatal deaths by 38%.[85] Although some community-based studies of resuscitation have shown benefit, further evidence is needed from large-scale implementation efforts, especially regarding cost-effectiveness and sustainability (appendix p 33).

The use of anticonvulsants in encephalopathic asphyxiated newborns has no additional benefit[86] (appendix pp 34–35). Evidence, mostly from high-income settings, suggests that therapeutic hypothermia could reduce neonatal mortality by 25% and major neurodevelopmental disabilities by 23%.[87] A more recent review from low-income and middle-income countries suggests similar benefit, although concerns persist about scale-up in low-income and middle-income countries because of the high underlying rates of infection.[88] Meconium aspiration syndrome can accompany intrapartum complications, although evidence for effective, feasible interventions is scarce (appendix pp 36–39).

Continuous positive airway pressure in spontaneously breathing preterm infants with respiratory distress syndrome reduces both intensive care admissions (by 53%) and mortality (48%).[89] Most trials of this procedure analyse specifics in the context of wide use of ventilation, such as reduced time to extubation wth continuous positive airway pressure. A few more recent but small studies have assessed the use of continuous positive airway pressure versus no ventilation in South Africa[90] and Malawi[91] with encouraging results. Further research is needed before wide-scale implementation in low-income and middle-income countries.

Prophylactic intratracheal administration of animal-derived surfactant reduces the risks of pneumothorax (by 60%), pulmonary interstitial emphysema (54%), and neonatal mortality (40%).[92] Similarly, the use of animal-derived surfactant in preterm infants with established respiratory distress syndrome is associated with substantial decreases in risks of pneumothorax (by 58%), pulmonary interstitial emphysema (55%), and neonatal mortality (32%).[93] Further research efforts are needed to develop a low-cost surfactant.

In developed countries, facility-based neonatal care is usual practice and historical trends clearly show the effect on reducing neonatal mortality. Hospital-based care of neonates has become increasingly sophisticated with improving understanding of physiology and disease, and the development of new technologies (eg, ventilators, monitoring devices, and laboratory investigations) and treatments (eg, surfactant, parenteral nutrition, indomethacin, and caffeine). Low-income and middle-income countries have followed this trend with the establishment of neonatal care units, often in the private sector or in referral hospitals in urban settings.[94]

Specific evidence for the effectiveness of the package of hospital-based care for ill and preterm infants is scarce in both high-income countries and in low-income and middle-income countries since trials tend to focus on the incremental gains of single interventions. We undertook a Delphi consultation on the effectiveness of two hospital-based supportive care packages: secondary level care (including kangaroo mother care, provision of warmth, feeding support/intravenous fluids, infection management, oxygen, and management of neonatal jaundice) and tertiary level care (including additional surfactant and/or nasal continuous positive airway pressure or intermittent positive pressure ventilation as needed). The consultation suggested that secondary and tertiary level care could prevent 70% and 90% of deaths in preterm infants, respectively (appendix pp 40–45).

The rapid detection and optimum treatment of suspected neonatal bacterial infections, such as pneumonia and sepsis, is essential. Oral antibiotics administered in community settings can reduce all-cause neonatal mortality by 25% and pneumonia-specific mortality by 42%.[95] Although the evidence for the use of injectable antibiotics in community settings shows significant reductions in mortality in infected newborn babies, implementation at scale has not yet been reported. Recent findings from studies of simplified antibiotic regimens in Asia and Africa suggest that newborn infants with potentially serious bacterial infections can be identifed by community health workers and can be successfully given injectable antibiotics in first-level facilities (Bahl R [WHO, Geneva, Switzerland], personal communication).

Premature and small for gestational age infants are at high risk of pathological hyperbilirubinaemia that can lead to bilirubin encephalopathy.[58] Phototherapy is the most common treatment for neonatal hyperbilirubinaemia and is effective in preventing the sequelae of the disorder.[96]

Topical emollient therapy can reduce the risk of hospital-acquired infections (by 50%), improve weight gain (by 98 g), and reduce neonatal mortality (by 27%).[97] Massage therapy with or without emollients might have several benefits in preterm infants in low-income and middle-income countries but this approach needs to be assessed further (appendix p 46).

Delivery platforms and strategies to reach mothers and neonates in the greatest need

Although we have a reasonable repertoire of evidence-based interventions, the effect on the population depends on the achievement of high coverage and on reaching unreached groups. The introduction of mHealth also opens the door to efficiently reaching households and health workers (appendix p 47). Several approaches could be instrumental in the scale-up of evidence-based interventions.

First, community-based delivery platforms, especially when linked to local health facilities, can not only increase the coverage of essential interventions but also reduce inequities (appendix pp 48–49). A recent review assessing the effectiveness of community-based intervention packages shows benefits on reducing maternal morbidity (by 25%), stillbirths (19%), perinatal mortality (23%), and neonatal mortality (26%).[98] Many of these effects operate through changes in household behaviours and practices, such as improved tetanus immunisation rates, use of clean birth kits, facility births, early initiation of breastfeeding, and seeking of health care for neonatal illnesses.

Community mobilisation and antenatal and postnatal home visits by community health workers should complement facility-based care and promote family contact with the health system at crucial times, with consequent reductions in neonatal mortality (by 40%).[98] Concomitant gains are provided by newborn care practices such as early initiation of breastfeeding, exclusive breastfeeding, delayed bathing, and clean cord care. When referral is not possible, home-based care of ill neonates is feasible and has been shown to be effective in India,[99] Bangladesh,[100] and Zambia.[101]

An important aspect of such community platforms is the creation of demand for services and changes in household practices. A recent review on women's groups facilitated by workers to discuss and solve related problems showed a significant effect on reducing neonatal mortality by 20%.[102] These approaches can have a huge effect on empowering communities, improving household practices, and promoting demand for better maternal and newborn care.

Notwithstanding good-quality maternal and newborn care in facilities, sufficient evidence supports scale-up of community-based packages of preventive and basic care, which can be promoted through a range of outreach workers and women's groups. A combination of these approaches, empowerment of women through community mobilisation and support groups, outreach community health workers, and promotion of transport to referral facilities are needed as a logical step to scale-up coverage.[74]

Child health days have been introduced in some contexts as a strategy to rapidly scale-up essential child survival interventions, including vitamin A supplements, immunisations, insecticide-treated bednets, and deworming, among others. Several new elements can be included within such approaches, for example, maternal antenatal care, micronutrient supplements, birth registration, and behavioural change communication to support early initiation of breastfeeding and exclusive breastfeeding.[103]

Although integrated management of childhood illness initially excluded the first week of life, the strategy was explicitly modified in some countries to include this period. This new approach has now been shown to have good sensitivity for the diagnosis and referral of young infants with severe illnesses[104,105] and for improving the quality and cost-effectiveness of ambulatory care.[106,107] Although information about newborn outcomes and effects is scarce, integrated management of neonatal and childhood illnesses has been shown to reduce neonatal mortality when implemented at scale.[106]

Financial incentives are used widely as policy strategies to ameliorate poverty, reduce financial barriers, and improve health outcomes in poor populations. A review of financial platforms to improve basic and emergency obstetric care showed that maternal voucher schemes improved the use of a range of maternal and newborn health services and outcomes,[108] including increased institutional births with voucher schemes, community-based health insurance, and exemptions from user fees. Voucher schemes led to increased use of antenatal care and higher skilled birth attendance.[108] Evidence exists for the benefits of conditional cash transfers on maternal care seeking and improved rates of institutional deliveries.[109] India's conditional cash transfer scheme (the Janani Suraksha Yojana) had an impressive effect on increasing the number of births in facilities, but was only associated with a modest reduction in perinatal and neonatal mortality, possibly because the quality of facility care provided was low.[110] Conditional and unconditional cash transfers have also improved birth registration[111] and hold promise in reducing inequities.

Improvement of quality of maternal and newborn care

Despite existing evidence-based interventions to prevent and successfully manage major causes of maternal and newborn morbidity and mortality,[112] the delivery and distribution of these services is often inadequate.[112,113] The quality of care received by women and newborn babies in poor and marginalised populations is insufficient and could contribute to low use of services and high rates of morbidity and mortality.[114–116] Although evidence from formal trials is scarce, improvement of the quality of care at all tiers of the health system could offer a major opportunity for change (panel 2).

Modelling of the cost and effect on stillbirths and maternal and neonatal mortality

Methods

We selected interventions from those reviewed, based on evidence of benefits as described here and extensively in previous publications. The cause-specific effects of

Panel 2: Quality of care

Audits and feedback mechanisms

A review showed that audits and feedback mechanisms led to an absolute increase in health-care professionals' compliance with desired practice.[117] The median adjusted percentage change compared with control was 1·3% (IQR 1·3–28·9), and feedback mechanisms also positively affected various patient outcomes, with a median percentage change of 17% (IQR 1·5–17).[117] Multivariate meta-regression indicated that these mechanisms might be more effective when repetitive, with low baseline performance, and when feedback is provided by a supervisor or colleague and is given in both verbal and written formats, including both explicit targets and an action plan.

Training of care providers

A review found two randomised controlled trials, the first of which showed that newborn resuscitation training was associated with a significant improvement in performance of adequate initial resuscitation steps (relative risk [RR] 2·45, 95% CI 1·75–3·42) and a reduction in the frequency of inappropriate and potentially harmful practices (mean difference 0·40, 95% CI 0·13–0·66).[118] In the second trial included in the review, assessment of breathing and newborn care practices in the delivery room improved following implementation of essential newborn care training. Implementation of the Helping Babies Breathe programme in eight health facilities in Tanzania was associated with a significant reduction in neonatal deaths (RR 0·53, 95% CI 0·43–0·65) and rates of fresh stillbirths (RR 0·76, 95% CI 0·64–0·90).[119]

Paying health workers for performance

A review of interventions including target payments linked to coverage and quality of care or conditional cash transfers without quality measures showed that these approaches have some benefits. Most of the interventions used a wide range of targets covering inpatient, outpatient, and preventive care, including a strong focus on services for women and children. Almost all dimensions of potential effect remain understudied, including intended and unintended effects on health outcomes, equity, organisational change, user payments and satisfaction, resource use, and staff satisfaction.[120]

Safe childbirth checklist

This approach tries to emulate the success of aviation industry in improving quality and reducing the risk of accidents through the use of checklists. A safe childbirth checklist has been shown to improve quality of maternal and newborn care in pilot settings.[121] The effectiveness of this checklist is being assessed in a large trial in India.

Information systems

Information technology has been used to educate mothers and families, send reminders to health providers or mothers and families, support health providers in clinical management, and to improve supervision and monitoring,[122,123] all of which have the potential to improve quality of care. Several assessments of this approach are underway.

Social support during pregnancy and labour

Standardised or individualised programmes of additional social support throughout pregnancy and during labour, including emotional support and provision of information about labour and coping techniques, can reduce the risk of antenatal hospital admission (RR 0·79; 95% CI 0·68–0·92), caesarean birth (0·87; 0·78–0·97), intrapartum analgesia (0·90; 0·84–0·97), dissatisfaction (0·69; 0·59-0·79), labour duration (mean difference –0·58 h; 95% CI –0·86 to –0·30), instrumental vaginal birth (RR 0·90; 95% CI: 0·84-0·96) with an increase in spontaneous vaginal birth (1·08; 1·04–1·12) although it did not show any effect on preterm birth, low birthweight, or perinatal mortality.[124,125]

Breastfeeding support interventions

These interventions, including reassurance, praise, information, and staff training to improve the supportive care, have been shown to increase the duration and exclusivity of breastfeeding (RR for stopping any breast feeding before 6 months 0·91; 95% CI 0·88–0·96). However, the effectiveness is reportedly higher in settings with high initiation rates; hence, strategies to increase the uptake of breastfeeding should be in place.[126] Training of traditional birth attendants might lead to improved referrals and early breastfeeding with reductions in perinatal and neonatal mortality but are not yet integrated with other health systems interventions.

these interventions on stillbirths and neonatal mortality are presented in table 2 and appendix pp 50–64. We used the Lives Saved Tool (LiST) to model the effect of these interventions within the health systems of 75 Countdown countries that together account for more than 95% of maternal, neonatal, and child deaths worldwide. LiST works by estimating the country-by-country cause-specific effects of increasing coverage of individual interventions from baseline levels of 2012 on stillbirth and neonatal and maternal mortality (panel 3) (appendix pp 65–67).

To calculate the costs of these packages of care we used an ingredient-based approach for each of the 75 Countdown countries to estimate the incremental running cost of the higher coverage for selected interventions in terms of people time, commodites, amortised facility costs, and other inputs as detailed in panel 3 and appendix pp 68–80). This calculation does not include specific infrastructure investments that might be needed since these are more specific to context. These methods are broadly consistent with other recent multi-country costing work, except for one recent model[127] in which general health system strengthening costs were included for a wide range of interventions and scenarios (table 3 and appendix pp 68–80).

	Cause of death or risk factor	Neonatal mortality		Stillbirths		Average coverage at baseline (%)	2020 coverage target (%)	2025 coverage target (%)
		Effect size	Affected fraction*	Effect size	Affected fraction*			
Preconception nutrition care								
Folic acid fortification	Congenital anomalies (neural tube defects)†	0·35	0·3	0·4	1	··‡	70%	90%
Multiple micronutrient supplementation	Term and preterm small for gestational age	0·09	1	··	··	··‡	70%	90%
Balanced energy supplementation	Term and preterm small for gestational age	0·32	Percentage of population living on less than US$1·25 per day	··	··	··‡	70%	90%
Antenatal care								
Tetanus toxoid vaccination	Tetanus†	0·94	1			68·2%	90%	90%
Pregnant women exposed to falciparum malaria protected via intermittent preventive treatment of malaria during pregnancy or by sleeping under an insecticide-treated net	Term and preterm small for gestational age†	0·35	Percentage of exposed women having their first or second birth	0·22	Percentage of women having their first or second birth	37·5%	90% (in relevant countries)	90% (in relevant countries)
Syphilis detection and treatment	Sepsis†	0·97	Based on estimated prevalence by country	0·82	Based on estimated prevalence of syphilis by country	22·9%	70%	90%
Advanced antenatal care								
Detection and management of hypertensive diseases of pregnancy (including treatment with magnesium sulphate)	Antepartum stillbirths†	··	Not estimated separately to obstetric care	0·20	Based on estimated prevalence of hypertensive disorders by country	··§	90%‖	90%‖
Detection and management of diabetes during pregnancy	Antepartum stillbirths†	··	Not estimated separately to obstetric care	0·10	Based on estimated prevalence of diabetes by country	··§	90%‖	90%‖
Detection and management of fetal growth restriction	Antepartum and intrapartum stillbirths†	··		0·20	1	··§	90%‖	90%‖
Induction of labour for pregnancy >41 weeks	Antepartum and intrapartum stillbirths†	··	CEmOC facility births	0·69	0·04	··§	90%‖	90%‖
Care during labour and childbirth								
Clean birth practices								
Births at home	Sepsis† and tetanus†	Sepsis: 0·23; tetanus: 0·35	1	··	··	··§	90%	90%
Facility births (clinic, BEmOC, or CEmOC level)	Sepsis† and tetanus†	Sepsis: 0·27; tetanus: 0·38	1	··	··	··§	90%	90%
Labour and delivery management								
Births at home	Intrapartum-related† and prematurity†	Intrapartum-related: 0·25; prematurity: 0·10	1	0·22	1	··§	90%	90%
BEmOC facility births	Intrapartum-related† and prematurity†	Intrapartum-related: 0·40; prematurity: 0·10	1	0·40	1	··§	90%	90%
CEmOC facility births	Intrapartum-related† and prematurity†	Intrapartum-related: 0·85; prematurity: 0·10	1	0·70	1	··§	90%	90%
Antenatal corticosteroids for preterm labour in facility births (clinic, BEmOC, or CEmOC level)	Prematurity†	0·53	0·8	··	··	··§	70% of facility birth	90%
Antibiotics for PPROM in facility births (clinic, BEmOC, or CEmOC level)	Prematurity† and sepsis†	Prematurity: 0·12; sepsis: 0·08	0·3 (proportion of PPROM among preterm infants)	··	··	··§	70% of facility birth	90%

(Table 2 continues on next page)

	Cause of death or risk factor	Neonatal mortality		Stillbirths		Average coverage at baseline (%)	2020 coverage target (%)	2025 coverage target (%)
		Effect size	Affected fraction*	Effect size	Affected fraction*			
(Continued from previous page)								
Immediate newborn care								
Immediate assessment and stimulation: home births	Intrapartum-related† and prematurity†	Intrapartum-related: 0·10; prematurity: 0·05	1	··	··	··§	90%	90%
Neonatal resuscitation								
Home births	Intrapartum-related† and prematurity†	Intrapartum-related: 0·20; prematurity: 0·05	1	··	··	··§	70%	90%
Facility births (clinic, BEmOC or CEmOC level)	Intrapartum-related† and prematurity†	Intrapartum-related: 0·30; prematurity: 0·10	1	··	··	··§	90%	90%
Care of the healthy neonate								
Breastfeeding	Diarrhoea, pneumonia, and sepsis	Relative risks for diarrhoea: exclusive breastfeeding (1·00); partial breastfeeding (2·28); predominant breastfeeding (4·62); not breastfeeding (10·53). Relative risks for pneumonia and sepsis: exclusive breastfeeding (1·00); partial breastfeeding (1·66); predominant breastfeeding (2·50); not breastfeeding (14·97)	See previous column	··	··	62·2%	90%	90%
Clean postnatal practices	Sepsis† and tetanus†	0·40 for both	1	··	··	··¶	90%	90%
Chlorhexidine for cord care	Sepsis†	0·12	1	··	··	··¶	70%	90%
Care of the small and ill neonate								
Thermal care: home births	Prematurity†	0·20	1	··	··	··¶	70%	90%
Kangaroo mother care (clinic or facility level)	Prematurity†	0·40	0·58	··	··	··‡	90%	90%
Oral antibiotics (home or outpatient clinic)	Pneumonia†	0·42	1	··	··	··‡	70%	90%
Injectable antibiotics (outpatient clinic)	Pneumonia† and sepsis†	Pneumonia: 0·75; sepsis: 0·65	1	··	··	··‡	70%	90%
Full supportive care for sepsis and asphyxia (facility births: clinic, BEmOC, or CEmOC level)	Intrapartum-related events†, pneumonia†, and sepsis†	Intrapartum-related events: 0·05; pneumonia: 0·9; sepsis: 0·8	1	··	··	··§	90%	90%
Secondary level preterm newborn care, including kangaroo mother care, warmth, feeding/intravenous fluids, oxygen during stabilisation, antibiotics, jaundice care, etc (clinic/facility births)	Prematurity†	0·70	1	··	··	··§	90%	90%
Full supportive care of preterm newborns, including treatment with CPAP and surfactant, etc, in addition to secondary level care (clinic/facility births)	Prematurity†	0·90	1	··	··	··§	90%	90%
Oral rehydration solution	Diarrhoea†	0·93	1	··	··	35·1%	90%	90%

BEmOC=basic emergency obstetric care. CEmOC=comprehensive emergency obstetric care. PPROM=preterm premature rupture of membranes. CPAP=continuous positive airway pressure. *Fraction affected=the proportion of the target population that the intervention will affect. †Three values corresponding to low, moderate (shown), and high estimates of efficacy for the interventions were applied. For interventions with meta-analyses, the 95% confidence bounds defined the low and high estimates of efficacy. For interventions when efficacy was estimated with a Delphi approach, the IQR was used to provide the low and high estimates. ‡‡Estimates were used because baseline coverage data were not available. §Baseline estimates were linked to facility delivery and/or skilled birth attendance coverage. ¶Baseline estimates were linked to coverage for visit to a health professional within 2 days of delivery. ||In countries with neonatal mortality rates <30.

Table 2: **Interventions modelled for effect**

Results for estimates of lives saved

On the basis of the coverage listed in figure 2 and the interventions' effects and targets (table 2), we estimate that with high coverage by 2025, 71% (range 56–76%) of neonatal mortality, 33% (23–38%) of stillbirths, and 51% (44–53%) of maternal deaths could be averted. A breakup of the analysis in the modelled countries according to neonatal mortality rates[1] shows that the largest effects of

Panel 3: **Methods for modelling and costing**

Modelling methods

We modelled the potential effect of introducing these interventions within health systems of the 75 high-burden Countdown countries. We used a standard sequential introduction of the interventions using the Lives Saved Tool (LiST), which estimates the effect of increased coverage of interventions on deaths from one or more causes, or in reduction of the prevalence of a risk factor (appendix p 65). For each of the 75 Countdown countries, baseline scenarios were created that represent the most up-to-date details about health status, including mortality rates,[1] stunting and wasting rates,[51] and median coverage of interventions and other maternal and child health indicators based on the most recent data from the United Nations (figure 2). We estimated the effects of scale-up of a set of interventions that fall into six packages along the continuum of care:

- Preconception nutrition care (balanced energy protein supplementation, folic acid supplementation/fortification, and micronutrient supplementation [multiple micronutrients, including iron and folic acid])
- Antenatal care (calcium supplementation in at-risk populations, intermittent preventive treatment in pregnancy, syphilis detection and treatment, and tetanus toxoid vaccination). We also modelled an additional set of more complex antenatal care interventions (diabetes case management, fetal growth restriction detection and hypertensive disease prevention and case management, induction of labour for pregnancies lasting longer than 41 weeks) for possible effect on stillbirths in only in a few countries with neonatal mortality rates lower than 30 per 1000 livebirths
- Care during labour and childbirth (active management of the third stage of labour, clean birth practices, labour and delivery management, antenatal corticosteroids for preterm labour, antibiotics for preterm premature rupture of membranes, and magnesium sulphate for pre-eclampsia
- Immediate newborn care (immediate assessment and stimulation, and neonatal resuscitation)
- Care of the healthy neonate (breastfeeding, chlorhexidine cord application, and clean postnatal practices)
- Care of the small and ill neonate (thermal care, hospital care of preterm babies including kangaroo mother care, case management of severe neonatal infections, oral antibiotics for neonatal infections, and oral rehydration solution for diarrhoea)

Table 2 shows the intervention packages and modelled coverage targets for 2020 and 2025. For the period before birth, the coverage targets for the seven core intervention packages were set at 70% for 2020 and 90% for 2025. For interventions at birth, we had a more complex scale-up that addressed the quality of service provided and the overall coverage of births occurring in a facility. We systematically scaled up the quality of services by scaling up assumptions of coverage of the component services that could be provided at a low level facility, at a higher level secondary care facility, and at a hospital able to provide a full range of tertiary care services. Finally, we also scaled up preventive and curative interventions after birth. Here, as was the case with birth care, we increased the coverage of quality of care at an appropriate level of care. For example, for a premature baby we have three options of care that could be provided at different levels of facilities—ie, basic thermal care in lower level facilities, followed by kangaroo mother care alone in some of the primary care facilities, and then quality secondary and tertiary care at higher level facilities in both rural and urban settings. We also ascertained the effect by levels of care at various time points. Sensitivity analyses to produce different scenarios were done for the results estimating effect (eg, deaths averted and number of deaths). The specific scale-up functions are shown in appendix pp 66–67.

Sensitivity analyses to produce different scenarios were done for the results estimating effect (eg, deaths averted and number of deaths). The sensitivity analyses were based upon varying the assumptions of efficacy for the modelled interventions. Three different scenarios were created using the same levels of baseline coverage, scale-up patterns, and achieved targets but the effectiveness of the interventions to reduce cause-specific maternal, neonatal, or stillbirth deaths was varied according to the ranges reported for specific interventions. These ranges represent the lowest, intermediate, and highest estimates of efficacy or effect for the interventions. For estimates of intervention effectiveness derived from meta-analyses, the 95% CIs were used to define the upper and lower bounds. For interventions in which efficacy was estimated with a Delphi approach, the interquartile range (IQR) was used to define the low and high estimates.

Costing methods

We used the LiST costing sub-module to assess the running costs of the interventions for which we used an ingredients-based approach. The costing sub-module draws its assumptions about staffing, drugs, and need for services from the the United Nation's OneHealth Tool database—another module within the overall Spectrum software package.[127] As with OneHealth, the costing module adjusts personnel costs based on regional variation in costs and costs by location and type of service provider. This approach has been used in previous studies building on others to analyse costs for interventions to address interventions for stillbirths,[4] childhood pneumonia and diarrhoea,[128] and maternal and childhood malnutrition.[8] A similar approach that used the OneHealth Tool was published recently in a report that developed a global investment case for maternal and child health and survival.[127] More details about the costing approach and inputs are available in appendix pp 68–80. The cost estimates reported incremental costs for increasing coverage to the target levels in 2020 and 2025 from the levels of coverage in 2012. All the costs are reported in US$.

Clear limitations exist to the estimated effect and costs of scaling up of the package of interventions to reduce neonatal mortality. Although we believe that the levels of coverage are achievable, they are not rapidly achievably in all countries. To reach the levels of coverage in 2025, many countries will need to scale-up coverage at a rate many times higher than they have done in the past. This goal is challenging since hospital-based services such as comprehensive emergency obstetric care, and inpatient care of preterm newborns and neonatal sepsis need more investment in reliable referral system and in infrastructure and especially human resources if they are to reach the coverage levels used in these analyses. Illustrative financing for these costs at various amounts of coverage have recently been published[127] and, similar to other recent reports,[4,8,128] the main focus of our paper is on running costs.

the interventions are in countries with high neonatal mortality rates; since 24 countries with rates higher than 30 per 1000 livebirths account for about two-thirds (1·3 million) of the neonatal deaths averted (figure 3). The top ten countries with maximum lives saved are distributed equally between Asia and Africa (appendix

p 81). Our analysis suggests that India, Nigeria, and Pakistan would benefit the most in terms of absolute lives saved, and the top five countries account for 57% of the total reduction in mortality. An important aspirational goal relates to the scale-up of quality secondary and tertiary newborn care in facility settings (appendix p 83) and the missed opportunity and quality gap around maternal and newborn care. If 90% of all women giving birth in facilities in 2020 were recipients of the highly effective interventions that they and their babies should receive, this would contribute to the prevention of an estimated 113 000 maternal deaths (84% of the total deaths averted by 2020), 531 000 stillbirths (76%), and 1·325 million neonatal deaths (77%), including 300 000 preterm deaths (table 4).

	Countries	Interventions	Year of baseline coverage (endline year)	Target coverage (%)	Costing methods	Total additional annual cost	Cost per person (total population)
Child survival series (2005)[129]	42	23 neonatal and child interventions	2000 (2015)	99%	Ingredients-based running costs with human resource time based on normative delivery schedule and amortised facility costs, plus additional training supervision and M&E time	$5·1 billion (2004 US$)	$1·23
Neonatal series (2005)[5]	75	16 neonatal interventions (7 of the 8 neonatal in the child survival series)	2000 (2015)	90%	Ingredients-based running costs with human resource time based on normative delivery schedule and and amortised facility costs, plus additional training supervision, M&E time	$4·1 billion (2004 US$)	$0·96
Countdown to 2015 (2005)[130]	60	32 maternal, neonatal, and child interventions	2005 (2015)	99%	Ingredients-based running costs with human resource time based on normative delivery schedule and amortised facility costs , plus additional training supervision, M&E time	$7 billion (range $4·6 billion–10·7 billion) (2004 US$)	$1·62
World Health Report (2005)[131]	75	67 maternal, newborn, and child health interventions and services (23 for maternal and newborn)	2005 (2015)	95%	Bottom-up ingredients-based approach	$7·8 billion (2004 US$)	$1·05
Guttmacher Institute (2009,[132] revised in 2010[133])	United Nations Development Programme developing countries (all countries except for Australia, Canada, Japan, New Zealand, USA, and all European nations)	26 reproductive, maternal, and newborn interventions	2008 (2015)	Universal coverage (100% met need for family planning interventions)	Direct costs based on theUnited Nation Population Fund's Reproductive Health Costing Tool. Indirect costs include overhead costs for programme management, supervision, health education, monitoring and assessment, advocacy, human resources training, information systems, commodity supply systems, and capital costs for maintenance and expansion of the physical capacity of health facilities	$12·8 billion ($3·6 billion for family planning, $9·2 billion for maternal and neonatal care) (2008 US$)	$2·23
Taskforce for Innovative International Financing for Health Systems (2010)[134]	49 low-income countries (not including China and India)	135 maternal, newborn, child, and infectious disease interventions	2008 (2015)	No specified target	WHO normative approach and MBB tool. Ingredients-based approaches are for health systems strengthening (eg, new facilities) and demand-side financing (eg, incentives). These costs include costs for health systems strengthening (74% of WHO normative and 62% of MBB estimated costs)	$18·6–36·5 billion (MBB) $45·2–58 billion (WHO normative) (2005 constant costs)	$24 (MBB) $29 (WHO normative)
Commission of Macroeconomics and Health[135]	All low-income and middle-income countries	Interventions not defined	2002 (2015)	No specified target	··	$94 billion additional ($38 billion from donors) (US$; year not clear)	··
Stillbirth series (2011)[4]	68	15 maternal and perinatal interventions (10 with effects on stillbirths)	2008 (2015)	99%	Ingredients-based running costs with human resource time amortised facility costs based on the Lives Saved Tool costing method, UNICEF drug costs, and WHO-CHOICE inputs	$10·9 billion (2008 US$)	$2·32
Diarrhoea and Pneumonia Series (2013)[128]	75	15 child interventions	2011 (2025)	80% for all interventions except vitamin A supplementation and vaccines, for which 90% target coverage was used	The costs were based on four components: personnel and labour, drugs and supplies, other direct costs, and indirect costs. Assumptions were obtained for time needed for an intervention and costs for drugs and supplies from the One Health Model developed by the UN	$6·715 billion (2011 US$)	NA
Nutrition Series (2013)[8]	75	10 maternal and child nutrition interventions	2011	90%	Ingredients approach to work out the cost of nutrition interventions, based on the United Nations OneHealth Tool	$9·6 billion (2011 US$)	NA

(Table 3 continues on next page)

	Countries	Interventions	Year of baseline coverage (endline year)	Target coverage (%)	Costing methods	Total additional annual cost	Cost per person (total population)
(Continued from previous page)							
Investment Framework for Women's and Children's Health (*Lancet Global Health* 2035) (2013)[122]	74	Health systems strengthening and six investment packages for maternal and newborn health, child health, immunisation, family planning, HIV/AIDS, and malaria. Nutrition was a cross-cutting theme	2012 (2035)	95%	OneHealth Tool, which takes an integrated approach to the assessment of costs and health benefits and incorporates interlinked epidemiological reference models such as the Lives Saved Tool, the AIDS Impact Model for HIV/AIDS interventions, and the FamPlan model which computes the association between contraceptive use and the total fertility rate	$30 billion (2011 US$)	$5 per person per year up to 2035
Every Newborn Series 2014 (current)	75	27 reproductive, maternal, and newborn interventions	2012 (2025)	90%	Lives Saved Tool model estimated basic running costs for provision of services without including additional infrastructure costs	$5·65 billion (2012 US$)	$1·15 per person

M&E=monitoring and evaluation. MBB=marginal budgeting for bottlenecks. NA=not available.

Table 3: **Comparison of multi-country costing exercises of relevance to maternal, newborn, and child health**

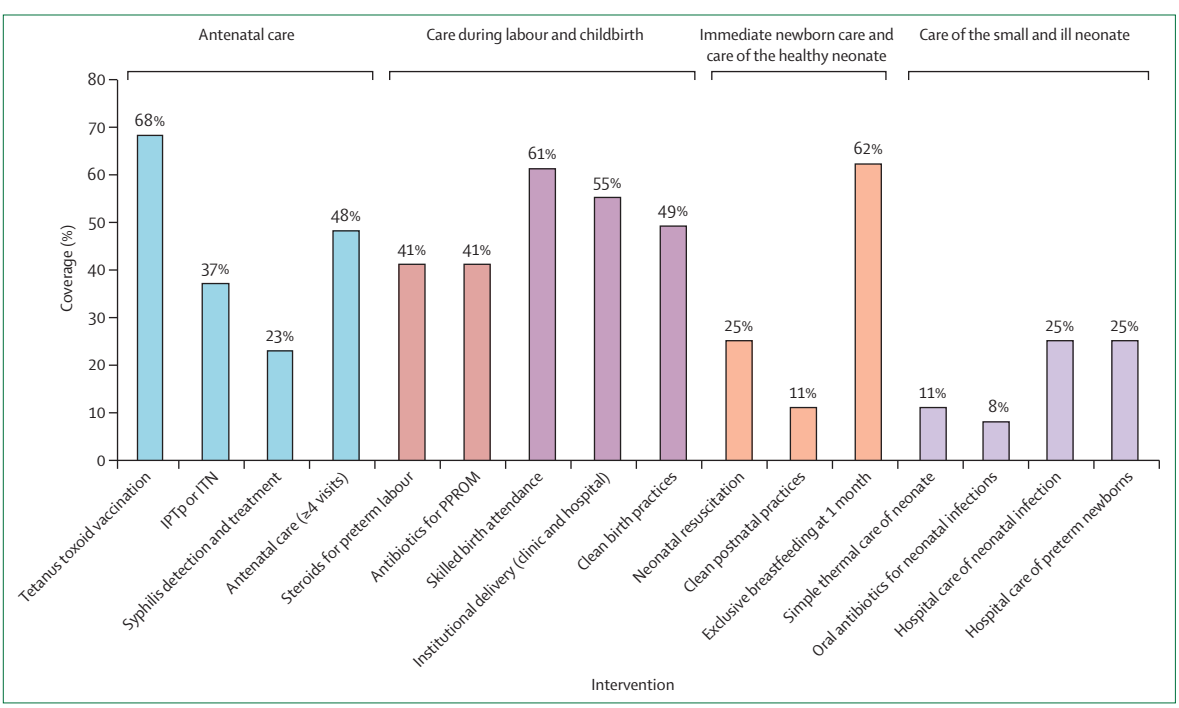
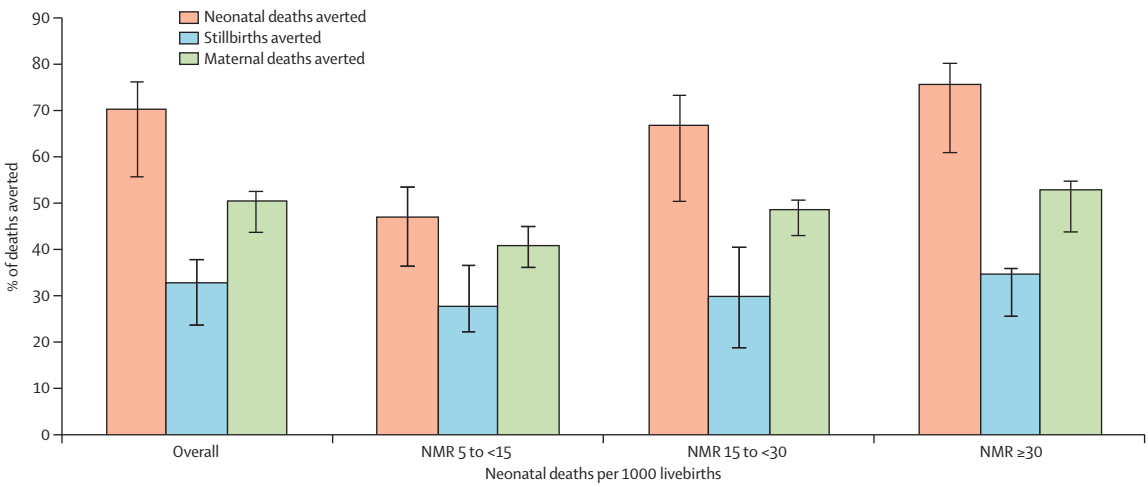


Figure 2: **Coverage of selected interventions* in the 75 Countdown countries (weighted average)**
IPTp=intermittent preventive treatment in pregnancy. ITN=insecticide-treated bednets. PPROM=preterm premature rupture of membranes. *Interventions modelled and not shown on graph have estimated coverage below 10% in the 75 Countdown countries.

In a comparison of the effects across the continuum of care, about half of the effect on neonatal mortality is from interventions delivered to the mother (48%) and the remainder from interventions delivered to the newborn infant (52%). The maximum gains (41% of all neonatal deaths averted) occurred with interventions delivered during labour and childbirth, followed by care of the small and ill neonate (30%), care of the healthy neonate (12%), and immediate newborn care (10%), which emphasises the importance of interventions during the period around birth (figure 4). Similarly, for stillbirths, the maximum benefit was noted from appropriate care during labour and childbirth including complications (70% of all stillbirths averted), followed by enhanced antenatal care focused on the detection of complications (21%).

In terms of the effect of intervention scale-up by 2025 on major causes of neonatal mortality, deaths caused by prematurity could be reduced by 58%, intrapartum-related deaths by 79%, and those related to serious infections by 84% (appendix p 82). Assessment of



	Overall		NMR 5 to <15		NMR 15 to <30		NMR ≥30	
	Count (range)	% Reduction (range)	Count (range)	% Reduction (range)	Count (range)	% Reduction (range)	Count (range)	% Reduction (range)
Neonatal deaths averted	1 900 000 (1 558 300–2 103 000)	71% (56–76%)	95 000 (65 900–112 600)	47% (36–54%)	550 000 (431 100–598 500)	67% (51–73%)	1 300 000 (1 061 400–1 391 900)	76% (61–81%)
Stillbirths averted	820 000 (601 100–932 400)	33% (23–38%)	38 000 (26 000–57 900)	28% (22–36%)	260 000 (186 500–341 700)	30% (19–40%)	510 000 (388 600–532 800)	35% (26–36%)
Maternal deaths averted	160 000 (143 900–168 100	51% (44–53%)	4200 (3500–4800)	41% (36–45%)	59 000 (53 100–60 700)	49% (43–51%)	100 000 (87 300–102 700)	53% (45–55%)

Figure 3: **Estimated effect of scale-up of interventions on stillbirths and neonatal and maternal deaths by the year 2025 from the baseline year 2012**
NMR=neonatal mortality rate. Error bars represent ranges.

specific interventions affecting these three major causes of neonatal mortality shows that appropriate care at birth (70%) and neonatal resuscitation (22%) are responsible for most intrapartum-related deaths averted, whereas hospital care of preterm babies including kangaroo mother care (50%) and scale-up of antenatal steroids (31%) are responsible for most preterm-related deaths averted. Appropriate case management of serious infections (24%) and clean postnatal care practices (24%) were responsible for most of the reduction in infection-related deaths (figure 5).

The effect of provision of these additional elements of quality care for ill newborn infants beyond basic preventive strategies and care in community settings is huge and supports the importance of such approaches. Our analysis also supports immediate scaling up of various community-based and primary care interventions because they have the potential to avert almost a third of all neonatal deaths by 2017, along with better secondary and tertiary facility-based care. Although scaling up of quality and secondary and tertiary care to 90% coverage by 2025 would prevent around 80% of all neonatal deaths averted, community-based strategies would still account for 20% of deaths prevented (appendix p 84).

Costing results

The incremental annual costs of providing our recommended packages of care would be close to US$4·5 billion (US$0·91 per person) by 2020, rising to US$5·65 billion (US$1·15 per person) in 2025. This amount represents a cost of about US$1928 for each maternal and neonatal life saved, including stillbirths averted. Table 5 shows the breakdown of these costs by intervention packages and suggests that scale-up of appropriate care during labour and child birth by 2025 would cost US$2·29 billion, followed by food and micronutrient supplements for pregnant women at US$1·88 billion. Of the various components of the respective costs, the bulk is related to human resources and commodities including drugs.

When costs per newborn life saved are considered, immediate care of the newborn infant and care of the healthy neonate have the best return on investment, followed by care of the small and ill neonate and labour and delivery management. However, when a wider range of benefits to maternal, fetal, and newborn deaths are considered, labour and delivery management and antenatal care are as good as neonatal interventions in terms of returns on investment (figure 4).

We recognise that these calculations underestimate the full economic cost, especially when existing facilities and

	2017			2020		
	Maternal deaths	Stillbirths	Neonatal deaths	Maternal deaths	Stillbirths	Neonatal deaths
Pre-eclampsia/eclampsia management	4200	16 400	..	6900	26 000	..
Diabetes case management	..	5500	..	..	8700	..
Antenatal steroids	..	..	130 000	..	..	214 300
Antibiotics for PPROM	9000	..	13 300	14 000	..	22 000
Detection and management of IUGR	..	20 500	..	..	32 500	..
Induction after 41 weeks of pregnancy	..	8300	..	..	19 000	..
Labour and delivery management	39 100	216 500	191 700	82 700	464 200	389 200
Clean birth practices	5100	..	35 900	9200	..	67 000
Neonatal resuscitation	..	..	111 100	..	..	170 600
Case management of prematurity and severe infection	..	..	361 800	..	..	461 800
Total	57 400 (80% of total deaths averted by 2017)	267 200 (72% of total stillbirths averted by 2017)	843 800 (74% of total neonatal deaths averted by 2017)	112 800 (84% of total deaths averted by 2020)	531 400 (76% of total stillbirths averted by 2020)	1 324 900 (77% of total neonatal deaths averted by 2020)

PPROM=preterm premature rupture of membranes. IUGR=intrauterine growth restriction.

Table 4: **Effect of provision of facility care on lives saved by 2020, hence reducing the quality gap**

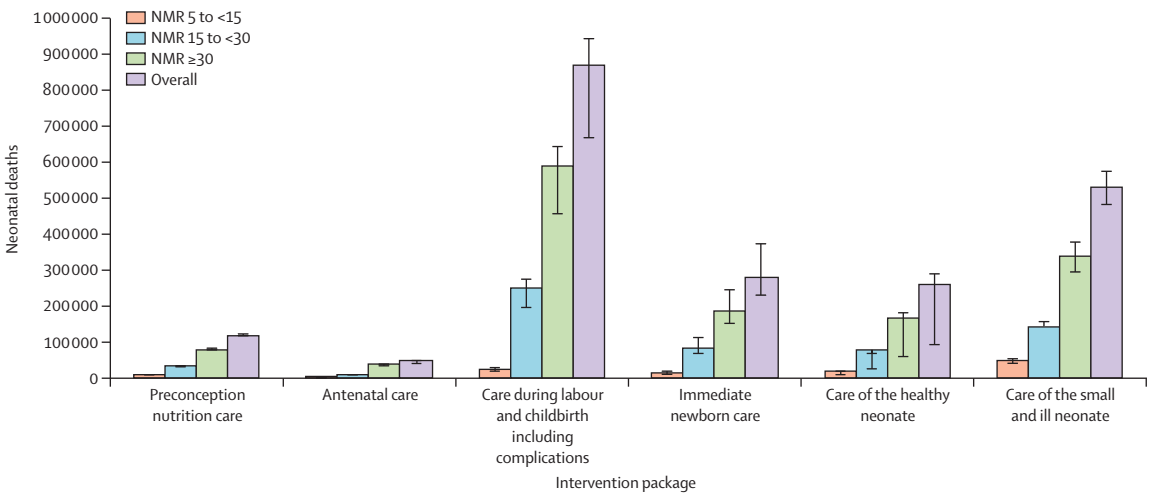
human resources need major replanning and scale-up investment. Table 3 and appendix pp 68–80 compare this costing with other exercises during the past decade, most of which are also based on incremental running costs. Our estimate is consistent with others that have taken a similar approach, noting that the various exercises have had narrower or wider remits. For example, the Investment Framework for Women's and Children's Health estimated costs per person to be US$5 per annum by 2035,[127] and this analysis covered the whole range of reproductive, maternal, and child health interventions,[131] including family planning, additional interventions for water and sanitation, and additional infrastructure costs for general health systems strengthening at scale.

Discussion

Our review is the first comprehensive analysis of the evidence base and strategies to address global newborn health and survival and delivery strategies since our analyses in 2005, and has the additional strength of considering maternal and stillbirth outcomes.[5,136] During the past decade, notable advances have been made in the breadth and depth of the evidence base for newborn interventions,[1] especially in the context of essential interventions and packages of care.[137] Some highlights include new interventions such as cord cleaning with chlorhexidine, additional evidence of the potential benefits of known interventions such as kangaroo mother care and antenatal steroids, expansion of access to treatment of neonatal infections, and the improved feasibility of more advanced care such as neonatal resuscitation and continuous positive airway pressure devices because of adaptation and innovation of equipment and training methods. We now have more experience with large-scale community-based projects to scale-up care in Asia and Africa[98] and strategies to improve access to universal care. Despite this enhanced evidence, overall coverage of interventions remains low, reductions in neonatal mortality very poor, and progress for stillbirths even more inadequate.[3,138]

High coverage of available interventions by 2025 could prevent almost three-quarters of neonatal deaths, saving around 2 million lives per year, at a running cost of $1·15 per person, and would put countries on track to achieve the "Every Newborn" and "A Promise Renewed" targets for neonatal mortality reduction by 2030 and 2035, respectively. Packages for care during labour and childbirth (including complications and immediate care of the neonate) and for the care of small and ill neonates have the potential to save 1·9 million newborn infants (almost 92% of all newborn deaths averted). These two packages are the main focus of the call for action in the Every Newborn Action Plan.[139] Indeed, even if by 2020 every woman delivering a newborn in a facility received recommended care, our estimates suggest that 1·325 million newborn infants, 0·531 million stillbirths, and 0·112 million women could be saved every year at annual running costs of US$4·5 billion, or less than a dollar per person in the 75 highest burden countries. This closure of the quality gap for facility births must become imperative for every country and is surely one of the best investments in health and also human rights.

According to the *Lancet* Global Investment Framework,[127] an even greater effect is possible with universal coverage in 2035. Especially important is to address unmet need for family planning, which would reduce births, further reduce deaths and also reduce the load on the health-care system. This framework suggests that an investment of US$5 per person per year up to 2035 in 74 high-burden countries could yield up to nine-times that value in economic and social benefits, and



	Preconception nutrition care	Antenatal care	Care during labour and childbirth including complications	Immediate newborn care	Care of the healthy neonate	Care of the small and ill neonate
Estimated maternal lives saved by 2025	0	7500 (6700–9100)	150 000 (137 100–158 900)	NA	NA	NA
Estimated stillbirths prevented by 2025	23 000 (17 800–26 500)	240 000 (150 800–374 500)	550 000 (432 500–531 400)	NA	NA	NA
Estimated neonatal lives saved by 2025	110 000 (111 800–118 300)	43 000 (36 500–46 900)	790 000 (588 500–865 000)	190 000 (136 300–280 400)	230 000 (64 300–261 500)	580 000 (531 000–621 000)
Estimated additional child lives (post-neonatal) saved by 2025	7500	1200	0	0	1900	0
Costs by 2025 (in billion US$)	1·88	0·4	2·29	0·035	0·11	0·96
Costs (billion US$) per 100 000 maternal and newborn lives, and stillbirths saved	1·38	0·16	0·15	0·02	0·05	0·17
Costs (billion US$) per 100 000 newborn babies saved	1·65	0·92	0·29	0·02	0·05	0·17

Figure 4: **Estimated effect of the intervention packages on numbers of neonatal lives saved and costs according to levels of care by the year 2025**
Error bars represent ranges. NMR=neonatal mortality rate. NA=not applicable.

would prevent the needless deaths of 147 million children, 32 million stillbirths, and 5 million women by 2035. The analysis also suggested that scaling up of family planning could lead to a 47% reduction in child deaths and a 64% reduction in stillbirths. Their estimate for running costs—excluding those for health system strengthening, new human resources, programme management, and conditional cash transfers—was US$2·1 per person, which suggests that our estimated running costs of US$1·15 per person for maternal and newborn interventions are plausible.

The high proportionate reduction in neonatal mortality suggests that the major killers of newborn babies in low-income and middle-income countries can be addressed—a notion supported by the dramatic reduction in these deaths in high-income countries. New trend data suggest that in some low-income and middle-income countries, deaths caused by neonatal infections have fallen during the past decade at a rate faster than have deaths due to intrapartum complications and substantially more than preterm deaths.[1] This finding might be indicative of inadequate attention to care of small babies in facilities in low-income and middle-income countries. Importantly, since many of these interventions are delivered in the antenatal period and around childbirth, they have the potential to reduce stillbirths by a third and reduce maternal deaths by 50%—a triple return on investment with additional benefits on later child survival, improved growth, reduced disability, and non-communicable diseases. The effect on stillbirths is smaller and more work is needed to increase the scope and scaleability of interventions, especially for antepartum stillbirths. The

effect on maternal mortality would be higher with the inclusion of some other postnatal interventions to address maternal mortality, such as the prevention and management of maternal haemorrhage and infections.

Our scale-up scenarios for the care of the small and ill neonates are deliberately ambitious but not unrealistic. Our analysis also challenges the view that newborn care is prohibitively expensive once intensive care is added.[140] With the scaling up of secondary and tertiary care for 90% of newborn infants in need by 2025, the model suggests that although the costs are substantial, the effect is huge. These benefits do not yet take into account potential long-term gains for human capital by lower disability.[3]

The rapid increase in facility births in many settings in recent years gives credence to opportunities for impact with more focus on facility care[110] but also emphasises the crucial need to match the supply-side interventions to provide quality maternal and newborn care in health systems with ongoing promotion of demand for care. Our analysis here, consistent with the 2005 *Lancet* Neonatal Series, estimated that community and primary care approaches will save about a third of newborn lives over the next 5–6 years. Even when facility-based care coverage exceeds 90%, community interventions will still continue to contribute to reducing a fifth of all newborn deaths. The maximum benefits would be accrued through a focus on integrated delivery and scale-up of both community-based and primary care strategies while clinical care in facilities and transport systems are strengthened (figure 6). We continue to support the importance of community-based strategies, including women's groups and the key role that community health workers have in preventive and promotive care and in delivering basic care in primary care settings.[98] However, in view of the effect at community level, especially for intrapartum-associated complications and preterm infants, improvement of the quality of care in referral facilities through evidence-based interventions should also be prioritised.

A key programme challenge is to reduce the equity gap, to reach those women and newborn infants in the greatest need. Although classic equity analysis relies largely on tracking differentials using income or asset quintiles,[141] many of these differentials relate to issues of ethnicity, geography, and other forms of social marginalisation. We limited our repertoire of interventions to those that address the distal pathways within the health sector while fully recognising the importance of social determinants. We should emphasise that these technological advancements and interventions have to be layered on approaches to address social determinants, education and empowerment of women in society, and human rights, especially the health and wellbeing of girls.

Strategies to overcome these obstacles include addressing of financial barriers[105] and deliberate targeting of patient groups through community outreach programmes.[98] The evidence from the role of women's groups from various settings also underscores the need for continued community engagement, demand creation, and empowerment of communities—especially women—as a continued adjunct to interventions within the health sector. The transition

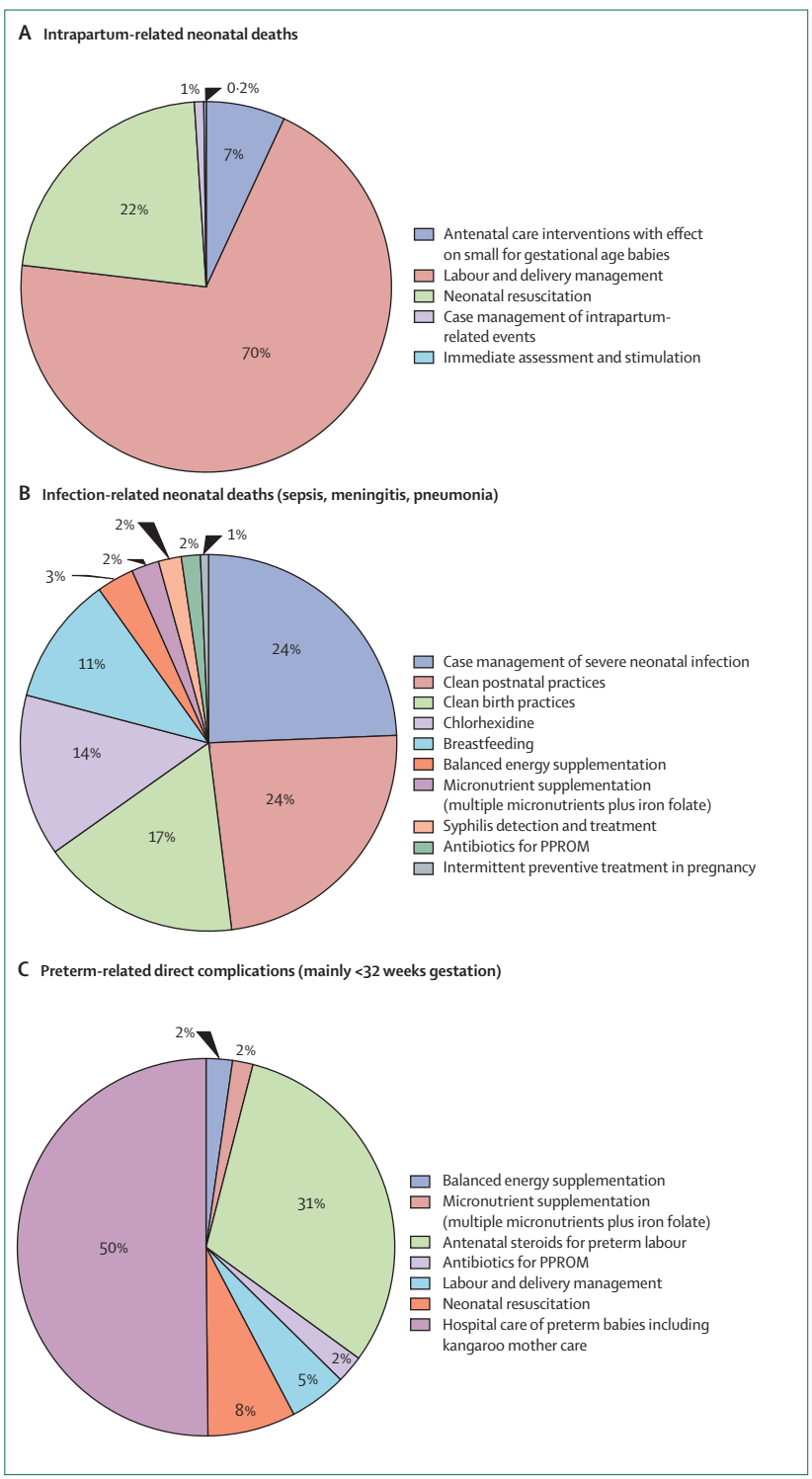


Figure 5: **Estimated effect of interventions on the three largest causes of neonatal deaths**
(A) Intrapartum-related neonatal deaths. (B) Infection-related neonatal deaths. (C) Preterm-related direct complications. PPROM=preterm premature rupture of membranes.

	Annual costs in 2020 (US$)				Annual costs in 2025 (US$)			
	Capital costs	Drug and supply costs	Labour costs	Other recurrent costs	Capital costs	Drug and supply costs	Labour costs	Other recurrent costs
Preconception nutrition care	231 093 000	1 031 434 000	99 201 000	66 645 000	302 619 000	1 356 250 000	132 059 000	87 272 000
Antenatal care	60 508 000	38 413 000	41 791 000	17 450 000	58 279 000	50 952 000	57 102 000	16 807 000
Advanced antenatal care	67 518 000	31 983 000	104 604 000	21 061 000	64 848 000	31 571 000	103 539 000	20 227 000
Care during labour and childbirth, including complications	267 028 000	382 064 000	1 020 568 000	88 051 000	335 856 000	555 408 000	1 286 525 000	110 648 000
Immediate neonatal care	1 877 000	3000	1 570 000	601 000	1 869 000	1000	1 017 000	598 000
Care of the healthy neonate	..	25 125 000	80 291 000	..	..	32 586 000	79 965 000	..
Care of the small and ill neonate	378 825 000	77 991 000	283 164 000	101 376 000	423 789 000	88 706 000	335 126 000	111 749 000
Total	1 006 849 000	1 587 013 000	1 631 189 000	295 184 000	1 187 260 000	2 115 474 000	1 995 333 000	347 301 000

Table 5: **Incremental cost of the scale-up plan by intervention package for the years 2020 and 2025**

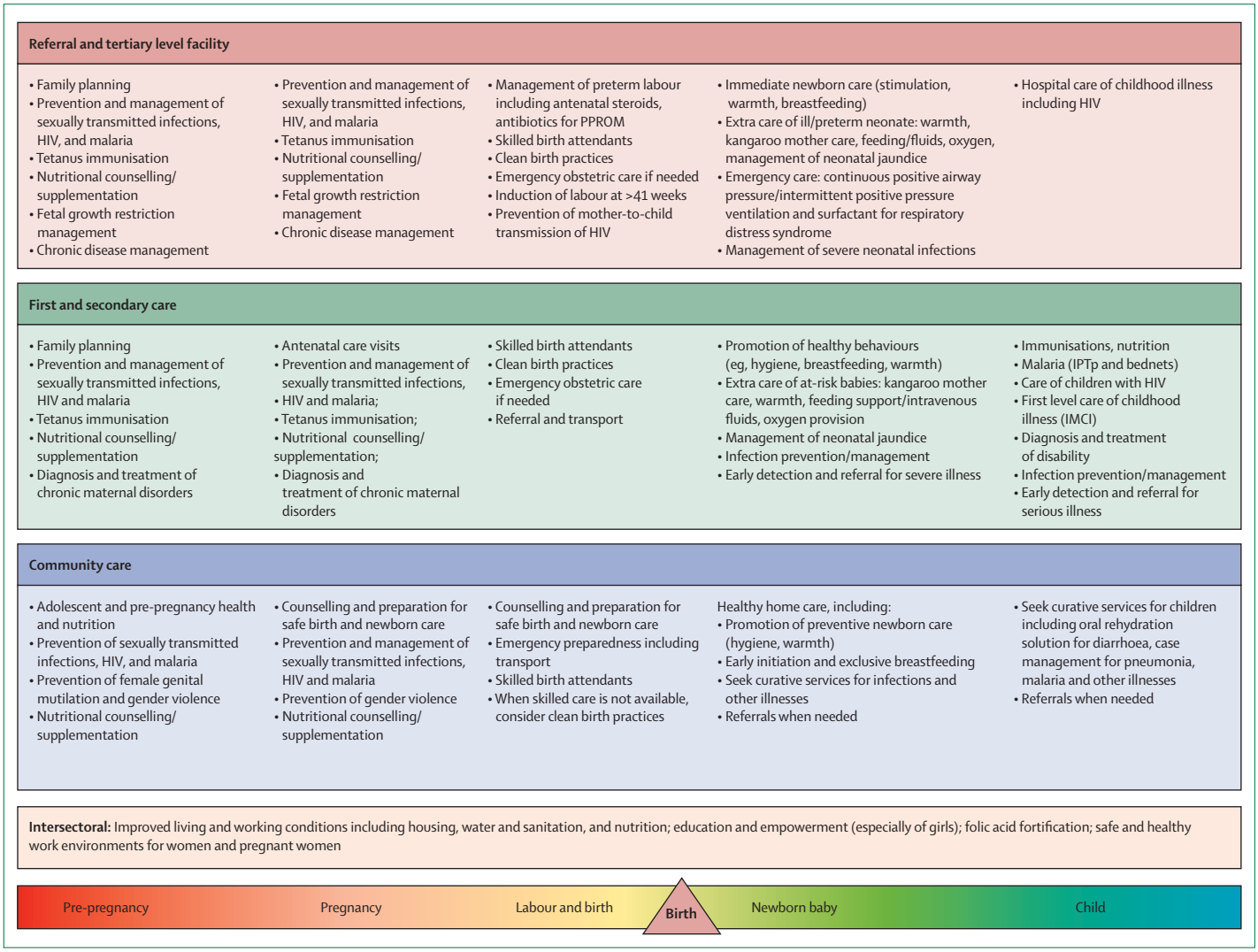


Figure 6: **Intervention packages by level of care**

PPROM=preterm premature rupture of membranes. IPTp=intermittent preventive treatment in pregnancy. IMCI=integrated management of childhood illnesses.

from home deliveries to facility births can be accelerated through incentives that increase coverage of skilled care in facility settings. The latter also necessitates consideration of strategies to move beyond community care and task shifting to appropriate quality care in district and referral health facilities. So far, this approach has not received sufficient

attention and is crucially important, especially in view of the longer time frame post-MDGs to 2035. Given the burden of preterm births in low-income and middle-income countries, low-cost strategies to manage preterm infants with respiratory distress syndrome as an adjunct to preventive strategies, such as the use of antenatal steroids and management of complications in pregnancy, could potentially save many lives. The mortality reduction targets of the Every Newborn strategy would not be achievable without the rational development of high-quality facility-based newborn care. An urgent need therefore exists to develop acceptable standards, norms, and protocols for facility-based newborn care, and enhance capacity in this crucial area of newborn health care. The vital role of health care professionals, especially well-trained midwives, in achieving these goals must be recognised.[142]

Our findings have several limitations that should be recognised. We still struggle with the level and quality of evidence for many of the interventions considered here, with relatively few effectiveness assessments of packages of care. We have used LiST to estimate effect and have provided uncertainty ranges that do draw attention to the wide uncertainty, more so for partial estimates. Our cost estimates are also consistent with those in several recent studies (table 3 and appendix pp 68–80) and are based on estimated annual running costs. Contextual factors and assessment of specific health systems gaps are essential for planning, and further analysis of the full costs should be based on actual country-specific planning for human resources and infrastructure gaps. The incremental running cost approach is also more comparable across countries and does provide a basis for more detailed national and subnational planning for additional specific investments.

Integration and further scale-up of these interventions in health systems will benefit women, babies, development outcomes, and economic capital—a quadruple return on investment. The key is to prioritise implementation to overcome context-specific bottlenecks.[143] Universal health coverage, which entitles every citizen and every family to a package of health care services guaranteed by the state is the lens through which equitable provision of maternal and newborn care should be viewed. No country can afford to ignore this investment case to change survival and health for every newborn baby and future generations.

Contributors

ZAB was responsible for overall coordination and oversight of the review and writing process; JKD for coordination of reviews and substantial contribution to the writing process; RAS for reviews of maternal vaccination, emollient and massage therapy, adolescent interventions, and quality of care reviews; ZL for community delivery platforms, management of gestational diabetes mellitus; VKP, RA, and JMS for respiratory distress syndrome, meconium aspiration syndrome, and continuous positive airway pressure reviews; HB and JEL for folate supplementation or fortification, syphilis, tetanus vaccine, hypothermia management, kangaroo mother care, obstetric care, and neonatal resusciation; AI for maternal calcium and balanced energy protein supplementation, cord care and intrauterine growth restriction; SA and AL for contributing the section on mHealth; JEL, VBC, and AR for working on the LiST and cost analysis; and NW for overseeing the modelling and costing process. All named authors contributed to the conceptualisation, writing, and finalisation of the paper. ZAB is the overall guarantor.

***The Lancet* Every Newborn Interventions Review Group**

Rehana A Salam, Zohra Lassi, Jai K Das (Aga Khan University, Karachi, Pakistan); Zulfiqar A Bhutta (Aga Khan University, Karachi, Pakistan, and Sick Kids Centre for Global Child Health, Toronto, Canada); Hannah Blencowe, Joy Lawn (London School of Hygiene & Tropical Medicine, London, UK); Vinod K Paul, Jeeva M Sankar, Ramesh Agarwal (All India Institute of Medical Sciences, New Dehli, India); Venkatnarayan Kannan (Command Hospital Eastern Command, Kolkata, India); Rajiv Bahl (World Health Organization, Geneva, Switzerland).

***The Lancet* Every Newborn Study Group**

Joy E Lawn, Zulfiqar Bhutta, Gary Darmstadt, Kim Dickson, Mary Kinney, Liz Mason, and Lori McDougall.

Declaration of interests

We declare no competing interests.

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