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Childhood Pneumonia and Diarrhoea

Executive Summary of The Lancet Childhood Pneumonia and Diarrhoea Series



"This Series identifies 15 key interventions that, if delivered at high coverage and quality, would eliminate 95% of diarrhoeal and 67% of pneumonia deaths in children younger than 5 years by 2025."

Childhood pneumonia and diarrhoea

In the past 20 years, global mortality in children younger than 5 years has decreased by 41%, from 87 deaths per 1000 livebirths in 1990, to 51 deaths in 2011. This decline is a public health success, but time trends hide the real tragedy: 6·9 million children younger than 5 years still died in 2011, mostly from preventable causes. Furthermore, the world is not on track to meet Millennium Development Goal (MDG) 4, to reduce deaths in children younger than 5 years by two-thirds between 1990 and 2015. Acceleration of the reduction in child deaths requires targeting of the leading causes of mortality. In the postneonatal period, the biggest killers of children younger than 5 years are pneumonia and diarrhoea. Childhood pneumonia and diarrhoea share many risk factors (eg, absence of exclusive breastfeeding of children younger than 6 months, undernutrition, zinc deficiency), and solutions. Integrated programmes for these illnesses can reduce the burden of both.

The Lancet Series on Childhood Pneumonia and Diarrhoea, led by Aga Khan University, Pakistan, provides evidence for integrated control efforts for childhood pneumonia and diarrhoea. The first paper assesses the global burden of these two illnesses, comparing and contrasting them, and includes new estimates of severe disease and updated mortality estimates for 2011. Findings from the second paper show that a set of highly cost-effective interventions can prevent most diarrhoea deaths and nearly twothirds of pneumonia deaths by 2025, if delivered at scale. Furthermore, the paper estimates what the cost of scale-up will be. The third paper presents the results of consultations with several hundred key stakeholders in high-burden countries and explores the barriers and enablers they face in dealing with these two diseases and potential ways forward. The final paper represents a call to action and discusses the global and country-level remedies needed to eliminate preventable deaths from these illnesses by 2025.

Ouantification of the burden to be tackled

Pneumonia and diarrhoea are the leading causes of morbidity and mortality from infectious diseases in children younger than 5 years. Although child mortality has declined substantially since 2000, these two illnesses remain important causes of avoidable deaths, especially in low-income and middle-income countries. To sustain and accelerate reductions in child mortality, the epidemiology of pneumonia and diarrhoea needs to be understood to better target programmes and interventions for prevention and treatment.

How?

In the first paper in this Series we combined 24 novel and previously published reviews to compile all evidence of incidence of infection, incidence of severe disease, mortality, sequelae, age and sex distribution, cause, and risk factors. For incidence we assessed cohort studies from countries worldwide. With appropriate epidemiological modelling techniques, we estimated

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Samarasekera U, Horton R. Continuing the child survival revival. Lancet 2013; published online April 12. http://dx.doi.org/10.1016/S0140-6736(13)60718-7.

Chan M, Lake A. Integrated action for the prevention and control of pneumonia and diarrhoea. Lancet 2013; published online April 12. http://dx.doi.org/10.1016/S0140-6736(13)60692-3.

Kikwete J, Jenkins K, Whitbread J. Playing our part to save children's lives. Lancet 2013; published online April 12. http://dx.doi.org/10.1016/S0140-6736(13)60719-9.

Walker CLF, Rudan I, Liu L, et al. Global burden of childhood diarrhoea and pneumonia. *Lancet* 2013; published online April 12. http://dx.doi.org/10.1016/S0140-6736(13)60222-6.

Bhutta ZA, Das JK, Walker N, et al, for *The Lancet* Diarrhoea and Pneumonia Interventions Study Group. Interventions to address deaths from childhood diarrhoea and pneumonia equitably: what works and at what cost? *Lancet* 2013; published online April 12. http://dx.doi.org/10.1016/S0140-6736(13)60648-0.

Gill CJ, Young M, Schroder K, et al. Bottlenecks, barriers, and solutions: results from multi-country consultations focused on reduction of childhood diarrhoea and pneumonia deaths. *Lancet* 2013; published online April 12. http://dx.doi.org/10.1016/S0140-6736(13)60314-1.

Chopra M, Mason E, Borrazzo J, et al. Ending of preventable deaths from pneumonia and diarrhoea: an achievable goal. *Lancet* 2013; published online April 12. http://dx.doi.org/10.1016/S0140-6736(13)60319-0.

the number of new episodes of pneumonia and diarrhoea per child-year, both globally and for the six main world regions. We extracted additional data for age distribution of cases and disease severity. Furthermore, we used mortality estimates for 2011 to generate disease-specific trends in reductions in mortality rate over time. For both disorders we estimated the burden of disease for vaccine-preventable causes, reviewed the risk of long-term sequelae, and gathered the evidence for individual and joint risk factors.

What, when, and where

We estimated that in 2010, 1.7 billion diarrhoea episodes (36 million of which progressed to severe episodes) and 120 million pneumonia episodes (14 million of which progressed to severe disease) occurred in children younger than 5 years. In 2011, 700 000 children died from diarrhoea and 1.3 million from pneumonia. Many of these deaths were in the first 2 years of life (72% for diarrhoea and 81% for pneumonia; figure 1). The burden of disease for both illnesses is greatest in southeast Asia and Africa. Children in low-income and middleincome countries have higher case-fatality rates and an increased likelihood of developing long-term sequelae (such as reduced lung volume or bronchiectasis for pneumonia, or stunted growth or Guillain-Barré syndrome for diarrhoea) than do those in highincome countries. Although evidence for differences in epidemiology of disease by sex is fairly scant, data suggest that boys have a higher risk than girls of morbidity for both pneumonia and diarrhoea.

Risks

Pneumonia and diarrhoea have many risk factors. Undernutrition is the most important shared risk factor, presenting various opportunities for combined prevention. For example, absence of exclusive breastfeeding in infants aged 0–5 months increases the risk of diarrhoea mortality by 4·6 times for partially breastfed babies, and by 10·5 times for babies receiving no breast milk. No exclusive breastfeeding increases the risk of pneumonia mortality by 2·5 times for partially breastfed babies and by 14·9 times for babies receiving no breast milk. A similar dose-response relation has been noted with no appropriate breastfeeding and morbidity. Underweight (low weight-for-age), stunting (low height-for-age), and wasting (low weight-for-height)

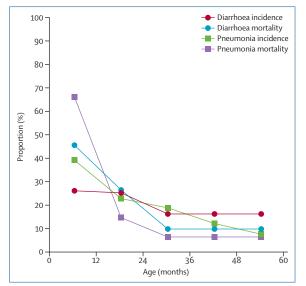


Figure 1: Distribution of cases of, and deaths from, diarrhoea and pneumonia in children aged 0-4 years

also increase the risk of morbidity and mortality from pneumonia and diarrhoea, showing a dose-response association, with the most undernourished children having the greatest risk.

Vaccine preventable disease

Vaccines are available for rotavirus and *Vibrio cholerae*, which account for 28% and 1%, respectively, of diarrhoea deaths in children younger than 5 years. Vaccines for the prevention of pneumonia are available for *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and influenza virus, which account for 33%, 16%, and 11%, respectively, of global childhood pneumonia deaths. Widespread use of these vaccines could substantially reduce the burden of pneumonia and diarrhoea deaths in the world's most vulnerable children. Increased access

Key messages

- Pneumonia and diarrhoea remain the leading causes of infectious disease mortality in children aged 0–4 years and were responsible for an estimated 1-3 million and 700 000 child deaths, respectively, in 2011
- 81% of pneumonia deaths and 72% of diarrhoea deaths occur within the first 2 years of life, and thus, prevention and treatment programmes should emphasise coverage in these young children
- The global burden of pneumonia and diarrhoea incidence is highest in southeast Asia and Africa
- Nearly three-quarters of deaths from pneumonia and diarrhoea are concentrated in 15 high-burden countries, but data sources from these countries are scant
- Undernutrition is a risk factor for both pneumonia and diarrhoea morbidity and mortality; thus, interventions to improve nutrition should be prioritised

to effective preventive and therapeutic interventions should be a priority to reduce deaths. Improved quality of clinic-based and community-based care is crucial, and new approaches to enhance quality and accessibility of care should continue to be assessed. Climate change and antibiotic resistance will continue to challenge public health efforts by changing the pathology, burden of disease, and effectiveness of the treatments we rely on. For this reason, research will remain important to monitor trends in these diseases to ensure that the interventions being used continue to reduce the global burden of childhood pneumonia and diarrhoea.

Combating pneumonia and diarrhoea: how and at what cost

Pneumonia and diarrhoea deaths are closely associated, with overlapping risk factors such as poverty, undernutrition, poor hygiene, and deprived home environments. In the second paper in this Series, we undertook systematic reviews of evidence for the effectiveness of a range of proven and emerging interventions to address childhood pneumonia and diarrhoea. We also assessed the various delivery strategies that could scale up the uptake of these interventions and help to deliver these interventions efficiently. We adopted a conceptual framework that outlined

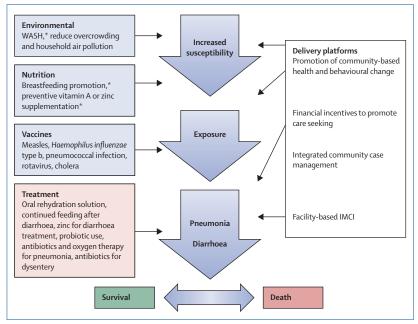


Figure 2: Conceptual framework of the effect of interventions for diarrhoea and pneumonia WASH=water, sanitation, and hygiene. IMCI=Integrated Management of Childhood Illness. *Interventions common to both diarrhoea and pneumonia.

preventive and case management interventions against pneumonia and diarrhoea (figure 2). We selected these potential interventions from several previous reports that identified the benefits and potential effects of these interventions, and specifically reviewed them to identify data of their effectiveness on pneumonia and diarrhoea incidence, morbidity, or mortality. We further projected the potential effect of delivery of these interventions to the 75 high-burden countries that are part of the Countdown to 2015 initiative, and assessed the potential effect on pneumonia and diarrhoea mortality and also the costs needed to achieve mortality reductions.

To save the most lives, care needs to be delivered at all levels of the health system and implemented with proven techniques that target key health-system interfaces. These interfaces are interactions between people in the health systems, such as health-care providers, management, patients, and policy makers.

Evidence

Findings from the reviews show the effectiveness of various interventions ranging from preventive to promotive to curative. Interventions include those that are simple to implement and already in place, to those that are promising and could make a difference. This review emphasises not only the importance of the structural changes needed to reduce environmental pollution and provide safe water and sanitation, but also the importance of behavioural changes needed for other interventions.

Interventions with proven effectiveness at the prevention level include water, sanitation, and hygiene (WASH) interventions, breastfeeding promotion, zinc supplementation, and vaccines for pneumonia (*H influenzae*, pneumococcal, and measles) and diarrhoea (rotavirus and cholera). Oral rehydration solution, zinc treatment, and antibiotic treatment for some strains of diarrhoea (cholera, shigella, and cryptosporidiosis) are effective strategies for treatment of diarrhoea, and antibiotic treatment and oxygen therapy are effective for pneumonia.

What can be achieved: vision for 2025

We used the Lives Saved Tool model to assess the potential effect on mortality when these interventions are applied, and estimated that if implemented at present annual rates of increase in each country, roughly

half (51% of pneumonia and 54% of diarrhoea deaths in children younger than 5 years) of deaths can be averted by implementation of 15 identified interventions by 2025. However, ambitious scale-up of interventions to increase global coverage of these interventions to at least 80%, and immunisations to at least 90%, could eliminate almost all diarrhoea deaths, but only twothirds of pneumonia deaths, showing the continued need to develop and implement more effective interventions for the prevention and treatment of pneumonia. Figure 3 shows all interventions modelled and their individual effects. The analysis shows that combined, WASH interventions alone could eliminate nearly 0.5 million child deaths due to pneumonia and diarrhoea by 2025, almost the same as the projected effect of H influenzae, pneumococcal, and rotavirus vaccines. Similar effects are noted with scaling up of community case management in children younger than 5 years, followed by promotion of breastfeeding.

How best to deliver interventions

Although most of these interventions are within present health systems of many countries, their coverage and availability to poor and marginalised populations varies greatly. Little consensus exists about the strategies to employ to deliver these interventions to reduce disparities and provide equitable access to marginalised populations. One such method is to provide these amenities through community health workers through home visitation and community-based sessions for education and promotion of care seeking. Financial incentives are becoming widely used policy strategies to alleviate poverty, promote care seeking, and improve the health of populations. Such incentives have been recommended as an important strategy to reduce barriers to access to health care. Our review shows the effectiveness of these strategies not only for improved coverage and uptake, but also for reducing overall burden and ensuring equitable delivery to those who need it most.

At what costs?

We estimate that US\$3.8 billion would be needed to save 51% of pneumonia deaths and 54% of diarrhoea deaths in children younger than 5 years at present annual rates of increase in each country, and \$6.715 billion would be needed for the ambitious scale-up plan; an extra \$2.914 billion is needed to save an additional

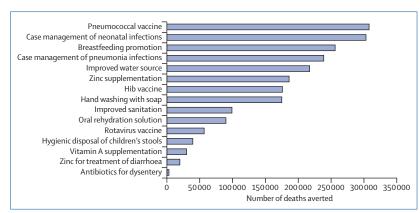


Figure 3: Sequential effect of individual interventions on deaths due to diarrhoea and pneumonia Lives saved by interventions show the conjoint effect of interventions delivered together in the Lives Saved Tool.

Key messages

- This Series identifies 15 key interventions that, if delivered at high coverage and quality, would eliminate 95% of diarrhoeal and 67% of pneumonia deaths in children younger than 5 years by 2025, at an additional cost of US\$2.914 billion over projected levels of spending at present rates
- Interventions with the maximum effect include water, sanitation, and hygiene interventions, breastfeeding, oral rehydration solution, and community case management
- With an increasing number of countries deploying programmes with community health workers to reach unreached populations, real opportunities exist to scale up community advocacy and education programmes and early case detection and management strategies, and to reduce the disproportionate burden of diarrhoea and pneumonia mortality therein

557 163 lives between the two approaches, representing 95% of diarrhoeal deaths and 67% of pneumonia deaths. Drugs and supplies consumed the most costs.

Barriers and enablers: findings from consultations in countries

In the first paper in this Series, we noted the staggering residual burden of preventable morbidity and mortality due to pneumonia and diarrhoea in low-income and middle-income countries. Similarly, in the second paper, we noted that the present situation is avoidable: with the techniques available, millions of lives could be saved. The focus of the third paper was to examine this problem from a programmatic perspective, and critically assess the barriers to progress and chart a way forwards. This paper asks the essential questions: why are so many children still dying of these preventable

causes? And more importantly, what can be done to improve this situation?

To answer these questions, we gave voice to our colleagues on the front lines of child survival efforts in high-burden countries in Africa and Asia, and combined information obtained from three overlapping, but autonomous, work streams. These groups were the Global Action Plan for Pneumonia (GAPP), spearheaded by WHO and UNICEF; the Diarrhea Global Action Plan (DGAP), led by academic institutions; and the Diarrhea and Pneumonia Working Group (DPWG), a public-private partnership co-led by UNICEF and the Clinton Health Action Initiative. In GAPP and DGAP, qualitative data were solicited from several hundred key informants, convened at workshops and assigned to working groups according to a set of predefined activities, in 39 countries in Africa and Asia. The participants at these workshops included representatives from country Ministries of Health, non-governmental organisations, privatesector companies, academics, and the medical community, plus representatives from UNICEF and WHO. By giving voice to individuals working so closely to the situation, whose main focus is programmatic implementation and management, we hoped to identify key programmatic barriers to improvements in child survival, and to identify priority areas that need improvement to enable progress. The work from DPWG was in turn focused on the specific issue of how to assure a reliable source of the key commodities needed for programme implementation. For diarrhoea, these commodities are oral rehydration salts and zinc; for pneumonia the focus was on oral antibiotics, notably amoxicillin.

The workshops yielded many programmatic insights regarding barriers and solutions pertinent to reducing childhood pneumonia and diarrhoea deaths. After coding and ranking of these items, five priority areas emerged as most essential for programmatic improvement. First, increases in human resources are needed. Fundamentally, the entire system for prevention of pneumonia and diarrhoea deaths relies on the assumption of a clinical encounter between an acutely ill child and a competent health worker. This system is in crisis because of the low level of support for these essential workers. The solution is to pay health-care workers a living wage; make this vocation attractive

and competitive; invest in their training; reward them for excellence; and ensure that managers are available who are similarly trained, motivated, and compensated.

Second, is to improve coordination of activities. Presently, several agencies exist that all work towards the shared goal of eliminating preventable childhood deaths; however, their effectiveness is diluted by waste, redundancy of effort, and the failure to capture potential synergies. This issue was dealt with effectively in how we coordinated responses to malaria, tuberculosis, and particularly HIV/AIDS, and there is no reason why these successes could not be replicated for paediatric pneumonia and diarrhoea.

Third, monitoring and evaluation activities need to be rationalised. Without accurate data, the effectiveness of programmes in bearing results is unclear. At present, data collection systems are antiquated; data items are redundant across programmes and the data are slow to be harvested, collated, aggregated, analysed, and disseminated, because of a reliance on inefficient paper-based capture systems. Use of electronic systems for data capture, including those that can be operated with hand-held devices, could substantially reduce the cost of data collection, reduce the time from collection to dissemination, and be more responsive than systems are at present. Low-cost solutions exist that can solve this issue and should be used.

Fourth, is to modernise systems of supply-chain management. There is a saying in programmatic circles: without a drug, you have no programme. Again, one can use the example of our responses to HIV/AIDS and malaria in that no intrinsic reason exists as to why oral rehydration solution, zinc, and antibiotics could not be supplied where needed. In fact, the solution is far simpler in the present case, because these commodities are cheap, off-patent, need no laboratory monitoring for toxic effects or efficacy, need no cold chains, and cost little per treatment course. We can solve this issue if we choose to.

Finally, is investment in child survival programmes. This point is somewhat the unifying theme. Our response to HIV/AIDS has been an undeniably brilliant success, for which one of the key reasons was that we, as a global public health community, chose to make the necessary investments to develop the human resource workforce, coordinate responses across various sectors

Key messages

Key barriers include:

- Poor coordination within ministries and other stakeholders at country level to deliver interventions
- · Restricted financial resources
- Inadequate training and support for health workers
- Poor systems for monitoring and assessment of key programmatic indicators
- · Sporadic availability of key commodities

Key recommendations include:

- Improve coordination between groups working on prevention and treatment of pneumonia and diarrhoea
- Substantially increase resources for child survival programmes, with emphasis on pneumonia and diarrhoea control efforts
- Enhance efforts to attract, train, and retain a competent workforce of caregivers
- Invest in better systems to harmonise the collection of essential programmatic indicators
- Strengthen supply systems that deliver essential commodities

and stakeholders, to build systems to monitor the key inputs and outputs that allow us to know whether we are winning or losing the fight or just treading water, and to make sure that life-saving drugs get to the patients that need them, where they are, and when they are needed.

Notably, the participants at these workshops were not calling for a technological fix to solve these issues. Rather, their attention was on the mundane: management, human resources, commodities, programming monitoring, and data feedback, and resources commensurate with the magnitude of the challenge. Should we choose to do so, these issues can be solved.

The way forward: ending preventable child deaths from pneumonia and diarrhoea

The effects of a small number of cost-effective interventions are such that, if applied, would prevent most diarrhoeal pneumonia deaths in children younger than 5 years. Knowledge about how to best deliver these interventions would allow countries to plan to eliminate preventable deaths from pneumonia and diarrhoea by 2025 (ie, fewer than three deaths per 1000 livebirths from pneumonia and less than one death per 1000 livebirths from diarrhoea). These targets are reasonable because the values constitute rates at which preventable deaths from these diseases have been previously avoided by other

countries in Africa and Asia. Thus, the goal is bold, but achievable. Indeed, such low mortality rates have already been reached in China and Mexico.

Large-scale success has been achieved with a consistent focus to overcome restrictions against increased coverage. For example, in Niger, such success required strengthening of primary-care posts that prioritised the provision of essential interventions, such as oral rehydration solution. For larger countries, such as Bangladesh, provision through public health systems was insufficient and the role of non-governmental providers has been crucial. However, a range of challenges remain if declines in mortality rates are to be accelerated. New research and innovation have led to the development of new and powerful cost-effective interventions, ranging from zinc for the treatment of diarrhoea, to bacterial protein-polysaccharide conjugate vaccines for pneumonia. Yet, the rate of adoption of these interventions is highly variable and often slow, especially in settings with the greatest need, as shown by high rates of child mortality. Therefore, inequities have widened, with stagnant and increasing rates of mortality in large groups in populations. Increases in inequalities in outcomes also emphasise the differences in exposure to underlying determinants. For example, 1.1 billion people still practice open defecation.

Promoted approaches that focus on behavioural drivers to increase demand for sanitation, such as community-led total sanitation, and on the creation of sustainable markets in sanitation products show promise, but still need to be implemented on a large scale and proven as sustainable in the long term. The Lancet Study Group suggests several priority actions to address these challenges. (1) Global and national leadership. The Integrated Global Action Plan for the Prevention and Control of Pneumonia & Diarrhoea, launched to coincide with the Series, offers a policy framework and important opportunities to engage with political and civil society leaders about the importance of these two leading preventable causes of childhood deaths. Intersectoral action—the importance of an intersectoral approach—is widely recognised. Greater innovation and evaluation is needed across different parts of government to address a common public health concern. (2) Prioritise interventions. With the increasing number of interventions and programme strategies, policy makers encounter difficulties in

setting of evidence-based priorities. Moreover, the cost-effectiveness of interventions can vary with context, which emphasises the need for a planning process that can take the local context into account. We have developed a simple and practical analytical framework to prioritise interventions and identify key sources of information to support a systematic and evidence-based approach to scaling up. The framework is centred around an equity-focused situation analysis and planning process to identify high-risk groups, determinants to coverage, and key bottlenecks. Such analysis leads to the identification of possible alternative delivery and demand creation strategies and their potential effectiveness and cost to overcome existing bottlenecks for high-risk groups. (3) Health systems research. Overall research funding for pneumonia and diarrhoea is very low and urgently needs to be increased. For example, funds for diarrhoea are estimated to be roughly US\$10 per disability-adjusted life-year, compared with more than \$100 per disability-adjusted life-year for diabetes. Extensive research methods for priority setting have identified the most important research gaps. Within both short and long timeframes for diarrhoea, improvements in the acceptability and effectiveness of oral rehydration solution and zinc were the most urgent research priorities. For pneumonia, in a short timeframe, studying of barriers to health-care seeking and access; increase of coverage with available vaccines; and assessment of the potential to scale up antibiotic treatment through community health workers, were all main priorities. (4) Accountability for results. Accountability for results and resources is crucial for transparency and good governance and for the effective implementation of the adopted policies. Countries are encouraged to use core indicators, such as coverage of essential pneumonia and diarrhoea interventions, in their annual national health sector reviews, and to do national countdowns to monitor coverage subnationally on a district-bydistrict basis. This technique will enable adjustment in implementation on the basis of the districts or areas with the greatest need, and will thus enhance both equity and local accountability.

Key message

 The goal of ending preventable deaths from pneumonia and diarrhoea by 2025, with a target of fewer than three deaths per 1000 livebirths for pneumonia and one death per 1000 livebirths for diarrhoea, is achievable

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