Comparative impact assessment of child pneumonia interventions

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Objective To compare the cost-effectiveness of interventions to reduce pneumonia mortality through risk reduction, immunization and case management.

Methods Country-specific pneumonia burden estimates and intervention costs from WHO were used to review estimates of pneumonia risk in children under 5 years of age and the efficacy of interventions (case management, pneumonia-related vaccines, improved nutrition and reduced indoor air pollution from household solid fuels). We calculated health benefits (disability-adjusted life years, DALYs, averted) and intervention costs over a period of 10 years for 40 countries, accounting for 90% of pneumonia child deaths.

Findings Solid fuel use contributes 30% (90% confidence interval: 18–44) to the burden of childhood pneumonia. Efficacious community-based treatment, promotion of exclusive breastfeeding, zinc supplementation and *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* immunization through existing programmes showed cost-effectiveness ratios of 10–60 International dollars (I\$) per DALY in low-income countries and less than I\$ 120 per DALY in middle-income countries. Low-emission biomass stoves and cleaner fuels may be cost-effective in low-income regions. Facility-based treatment is potentially cost-effective, with ratios of I\$ 60–120 per DALY. The cost-effectiveness of community case management depends on home visit cost.

Conclusion Vaccines against Hib and *S. pneumoniae*, efficacious case management, breastfeeding promotion and zinc supplementation are cost-effective in reducing pneumonia mortality. Environmental and nutritional interventions reduce pneumonia and provide other benefits. These strategies combined may reduce total child mortality by 17%.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Progress in reducing mortality from pneumonia in children under 5 years of age has been relatively slow in many parts of the developing world, where about 155 million clinical pneumonia episodes and 2 million deaths occur annually. ^{1,2} Risk factors for pneumonia include stunting and underweight, ^{1,3,4} suboptimal breastfeeding, ^{5,6} lack of immunization ^{7,8} and indoor air pollution from household use of solid fuels. ⁹⁻¹² There is evidence that effective and appropriate management of clinical cases is possible ^{13,14} at health-care facilities ¹⁵ and in the community, ¹⁶ but this level of management is often lacking.

Efforts to control pneumonia are needed to meet Millennium Development Goal 4 (MDG 4), to reduce child mortality in the world by two-thirds by 2015. Toften, a package of priority interventions is developed to address MDG targets and reduce child mortality. Self-Re-20 Cost-effectiveness analysis has become vital in deciding what interventions to implement and scale up. Single-candidate interventions to reduce pneumonia have been evaluated in general economic terms, Self-1,18,22-24 but no comprehensive analysis has focused on pneumonia control.

Different interventions can affect incidence or case fatality, with differences noted across age groups. Population risk interventions can target specific subpopulations, while immu-

nization is intended for all infants. Preventive interventions of this kind may reduce the incidence of pneumonia, whereas case management influences case fatality after falling ill. Both types of interventions can reduce pneumonia mortality.

The aim of this study was to compare the impact of eight preventive and curative interventions at the population level ^{6,25–27} and to identify the intervention mixes that generate the highest possible level of child health at the lowest cost.

Methods

To estimate the population health effects and total costs of pneumonia interventions from a health-care perspective, we applied demographic life tables for the 40 countries with the highest mortality (list available at: http://oldwww.bmg.eur.nl/personal/niessen/Webtable%20Countries%20by%20Region. doc The tables were used to estimate the health effect of risk factors, as well as the reductions in incidence and case fatality in population cohorts, simultaneously and consistently.^{6,25–27} Detailed descriptions of concepts, methods, background papers, regional studies and data are available at: WHO-CHOICE (CHOosing Interventions that are Cost Effective) at: www.who.int/choice/en. Box 1 provides an overview of the approach.

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We considered the epidemiological characteristics and level of health care of each of the 40 countries, as well as the coverage levels of the expanded programme on immunization (EPI) and of facility-based case management. Due to the large uncertainties involved in the epidemiologic, effectiveness and cost estimates, we included a high and a low cost-effectiveness scenario for each mix of interventions.

Each country's life table provides summary estimates of how pneumonia affects mortality and morbidity, expressed in terms of disability-adjusted life years (DALYs) lost. The tables also provide estimates of the effect and cost of mixed health interventions, in United States dollars (US\$) for the year 2000, with a 3% discount rate according to health economics guidelines. We combined estimated health gains and costs per intervention to identify the sets of health interventions that maximized child health at different budget levels by providing the greatest health yield per dollar spent. The life tables were implemented in C++ (a general programming language) using M language (a language for working with data and building domain models). The script with M-equations is available at: http:// oldwww.bmg.eur.nl/persona/niessen/ GAPP_LOW.MPdf.pdf

Epidemiologic and demographic data

The life tables used in the model were based on the recently published WHO country data, which draw on reviews of incidence and mortality for childhood and neonatal pneumonia. Incidence estimates were taken from the epidemiological review. Consistent applied case-fatality rates were calculated by dividing annual incidence figures by annual mortality rates from the global burden of disease data set. ^{2,7}

Risk factor prevalence data were derived from the WHO Statistical Information System (WHOSIS), available at: http://www.who.int/whosis/en/index.html They included nonexclusive breastfeeding, undernutrition (defined as underweight for age, z < -2), measles immunization coverage and exposure to indoor air pollution in the population under 5 years of age. Relative risks of indoor air pollution by type of biomass fuel for pneumonia incidence were de-

Box 1. Stepwise description of impact assessment for comparatively analysing the costs and effects of interventions 6,25,26

- Construct epidemiologic disease model. Give a population-based description; establish how
 parameters of the disease model interact (i.e. relative risks, incidence, case-fatality ratio,
 neonatal and mortality rates, by age group and sex);
- 2. Review national data for year of study. Include population structure and absolute figures, births, pneumonia epidemiologic rates and intervention coverage;
- 3. Construct baseline epidemiological parameters. Reflect current population figures and epidemiologic rates, a situation of limited health care and the future United Nations demographic scenario;
- 4. Estimate effectiveness. Repeat analysis under Step 3 with changes to one or more key epidemiological parameters (incidence or case–fatality rate) as a result of intervention effectiveness; compute the total number of healthy life years gained (or of DALYs averted).
- 5. *Estimate costs*. Establish coverage and contact rates; apply unit costs and add programme costs by intervention mix.
- Generate a cost and effectiveness league table. Estimate the total costs and health benefits (DALYs averted) of single interventions and intervention mixes and establish a ranking table based on the cost-effectiveness ratio.

DALY, disability-adjusted life year.

rived from the Global Action Plan for Pneumonia (GAPP).^{9,10,28} Other relative risks for pneumonia incidence were obtained from the same review.¹

National statistics on neonatal, infant and child mortality for 2005 were obtained from the online database of the Institute for Health Metrics and Evaluation.⁷ The fractions of neonatal mortality attributable to pneumonia and sepsis were obtained from the *The Lancet* nutrition series.²⁰ Case-fatality ratios for children are specified by three age groups: neonatal period until 1 month of age, remainder of the first year (2–12 months of age) and 1–5 years.

The disability weight used to compute pneumonia morbidity for a disease episode lasting 2 weeks was 0.279.²⁹ DALYs were calculated by applying the region-specific disability weights for the general population by age and sex.³⁰ Country-level demographic data on population structure, birth rates and general mortality rates were obtained from official 2005 estimates by the Population Reference Bureau (available at: http://www.prb.org/Publications/Datasheets/2008/2008wpds.aspx).

Interventions, effectiveness and costs

In all scenarios we assumed a programme effectiveness time horizon of 10 years for all interventions, starting in 2005. After that, the new population cohorts resumed pre-intervention status, in line with the standardized cost-effectiveness approach of WHO-

CHOICE project.⁶ The calculations included the extra life-years lived by additional surviving children beyond the 10-year period, as well as the pneumonia incidence reduction from immunization until the last immunized age group reaches the age of 5 years (in 2020). We estimated total health effects over a period of 100 years to include all life-years gained beyond the 10-year time horizon, among all survivors. We calculated intervention costs in International dollars (I\$) to allow comparisons.

Table 1 shows the selected interventions and related input data for various scenarios. The subsections below describe the scenario assumptions by intervention category.

Reduction of indoor air pollution

The 90% confidence interval (CI) of the relative risk (RR) of pneumonia due to exposure to indoor air pollution was estimated to be 1.42 to 2.53.28 Two interventions for indoor air pollution were selected.^{9,28} The first was a switch at the household level to cleaner gaseous or liquid fuels (liquefied petroleum gas, kerosene or ethanol); the second was better combustion ventilation through high-quality and well-maintained biomass stoves. The health effect of intervening against this risk factor derives primarily from observational studies (including one unpublished randomized study of high-quality stoves). The GAPP reviews assumed that introducing cleaner fuel reduces pneumonia risk.^{9,28} Based on this assumption, changing to full-scale cleaner household fuel could

Table 1. Input data for pneumonia intervention effectiveness, estimated health care costs and literature sources, 2005

Code	Intervention	Effectiveness ^a low-high scenario range	Effect level	Source	Costs of intervention low-high scenario range	Source	
	Indoor air pollution						
E1	Liquid fuel stoves	RR-based exposure reduction [formula: $(1 - (1/RR_1)^b) - (1 - (1/RR_h)^c)$]	Incidence	9	I\$ 8.57–14.47 in AMR D ^d per household member, per year	23	
E2	Improved solid fuel stoves	RR-based exposure reduction 75% in specific settings	Incidence	9	I\$ 4.82–7.59 in AMR D ^d per household member, per year	23	
	Nutrition						
N1	Breastfeeding promotion	15–23% reduction in infants	Incidence	3,6	I\$ per child	WHO data set ^e	
N2	Zinc supplementation	14-25% (90% CI: 8-30) reduction	Incidence	3,6,30	I\$ per child	WHO data set ^e	
	Immunization						
l1	Pneumococcal conjugate	23–35% reduction	Incidence	8	I\$ 19–64 per immunized child	24	
12	Haemophilus influenzae type B	22–34% reduction	Incidence	8	I\$ 5.83–9.69 per immunized child	22	
	Case management						
C1	Community-based	34–50% (90% CI: 22–57) for neonatal pneumonia	Case fatality	13,16,31	1–2 visits of I\$ 2.13–9.40 per incident case	14	
C2	Facility-based	29–45% (90% CI: 20–49)	Case fatality	32	I\$ per child	WHO data set ^e	

AMR, WHO Region of the Americas; CI, confidence interval; I\$, International dollar; RR, relative risk (values from review).28

- ^a Age-specific reductions in exposure among all age groups under 5 years, unless otherwise indicated.
- $^{\mathrm{b}}$ RR, is the relative risk of pneumonia under low exposure (1.42 in this study).
- ^c RR, is the relative risk of pneumonia under high exposure (2.53 in this study).
- d High-tech and low-tech liquid fuel stoves were considered, as well as an improved stove for solid fuels.²³ For the latter, we assumed a 2-year (high-cost scenario) and a 4-year (low-cost scenario) average lifetime. Cost data are WHO-region specific.
- WHO-CHOICE (CHOosing Interventions that are Cost Effective) dataset for child survival interventions (http://www.who.int/choice/en), November 2007. Data are WHO-region specific.

lower pneumonia incidence by 50% (the attributable burden for indoor air pollution). However, high-quality, well-maintained stoves are not expected to prevent all exposure to indoor air pollution. In an earlier review and costeffectiveness study, a 75% reduction in exposure was assumed in a scenario of full coverage with good stoves.11 Given the high and low RRs linked to indoor air pollution under this scenario (equations in Table 1), the pneumonia incidence reduction would be 22.2% to 45.8%.28 The cost methodology and actual cost estimates are based on WHO reports 11,23 with a two- or fouryear stove lifetime.

Nutritional interventions

Selected nutritional interventions to reduce pneumonia were exclusive breast-feeding promotion up to 6 months of age^{6,18} and food supplementation with zinc.^{3,33} Region-specific cost estimates were based on those from the WHO-CHOICE programme.

Immunizations

The scenarios included two vaccines as potential interventions to reduce pneumonia risk. The measles vaccine was not included, since its already high coverage in most of the 40 countries studied would have made its effect on pneumonia mortality difficult to quantify. The population effectiveness of immunization depends on the level of protection against the bacteria (Hib and pneumococcus), but even more on the actual attributable contribution of these bacteria to the pneumonia burden. Hib and pneumococcus may account for more than half of pneumonia mortality in children.¹⁷ The relative importance of these bacteria as causes of pneumonia in different settings is unknown, but the similarity of the trial results suggests that major differences between populations do not exist. The effectiveness range given by the high and low country scenarios takes into account the variety of agents (Table 1). The joint effect of the two vaccination

programmes targeting two different microorganisms was assumed to be additive. The cost estimates were based on earlier economic evaluations.^{22,24} Implementation was assumed to occur within existing immunization programmes and infrastructure.

Pneumonia case management

Two delivery strategies were chosen to treat children with pneumonia: a facility-based approach, 15 and a communitylevel approach in which children were diagnosed and treated by community health workers.16 The estimated reduction of pneumonia mortality through pneumonia case management was based on two reviews. 13,16 These reported an efficacious (i.e. under ideal circumstances) reduction of 42% (90% CI: 22-57) in neonatal pneumonia mortality and of 36% (90% CI: 20-49) in child pneumonia mortality, confirmed by a review of management by community health workers.³¹ We subtracted these expected reductions from the

Table 2. Population using solid fuels, and PAR for pneumonia mortality among children < 5 years of age, by WHO subregions, 2005

WHO	Population	Population using s	olid fuels	PAR ^b (%)	PAR ^b (%)	PAR ^b (%) (based on RR ^c = 2.53)	
subregion ^a		No.	%	(based on RR° = 1.80)	(based on $RR^c = 1.42$)		
AFR D	304 199 839	211 063 296	69	36	23	51	
AFR E	338 409 271	273 010 077	81	39	25	55	
AMR A	325 897 888	18 074 771	6	4	2	8	
AMR B	435 563 238	57 197 830	13	10	5	17	
AMR D	70 637 557	28 599 404	40	24	15	38	
EMR B	137 098 168	11 394 365	8	6	3	11	
EMR D	346 537 669	175 005 075	51	29	17	44	
EUR A	413 765 659	21 062 657	5	4	2	7	
EUR B	218 138 441	55 160 415	25	17	10	28	
EUR C	242 471 330	19 684 368	8	6	3	11	
SEAR B	290 459 728	208 138 629	72	36	23	52	
SEAR D	1 246 955 684	951 016 609	76	38	24	54	
WPR A	154 258 746	7 898 007	5	4	2	7	
WPR B	1 532 885 216	1 137 968 143	74	37	24	53	
Residual	11 915 069	2 770 500	23	16	9	26	
World	6 069 193 503	3 178 044 147	52	30	18	44	

CI, confidence interval; PAR, population-attributable risk; RR, relative risk.

country-specific, age-specific case fatality rates, while we included the uncertainty range based on the CI. In severe cases (8.6% of all incident cases), we assumed a case fatality reduction of 51%.32 The cost data of case-management strategies at the facility level are from the WHO-CHOICE programme and updates by WHO's Child and Adolescent Health Department.^{21,32} The community-based cost estimates are from the Disease Control Priorities in Developing Countries (DCP2) project.¹⁴ We varied the number of budgeted visits by a village agent to children treated for pneumonia by one (low-cost scenario) to two times (highcost scenario).14,31

Results

Table 2 shows the regional aggregate results on the effect of using solid fuels on pneumonia mortality in children. Table 3 shows the potential impact of pneumonia interventions on total mortality among children under 5, and Table 4 lists the cost-effectiveness ratios. In each table, all eight intervention options are grouped into the four intervention areas described above (indoor air pollution, undernutrition,

Table 3. High and low estimates of child mortality reduction for two pneumonia intervention packages for 40 countries clustered by WHO subregion

WHO	C1, N1, N2, I	I, I2 package	E1, C1, N1+2, l1+2 package			
subregion ^a	High	Low ^b	High⁵	Low ^b		
AFR D	10.7	7.8	12.9	9.5		
AFR E	14.7	10.8	17.3	13.2		
AMR B	8.6	6.3	9.8	7.3		
AMR D	8.6	6.3	9.8	7.3		
EMR D	14.4	10.5	17.0	12.7		
SEAR B	7.1	5.2	8.2	6.2		
SEAR D	8.5	6.1	10.3	7.5		
WPR B	9.1	6.7	10.3	7.9		

C1, case management community-based; E1, use of cleaner liquid fuels; I1, pneumococcal vaccine; I2, *Haemophilus influenza* type B vaccine; N1, breastfeeding promotion; N2, zinc supplementation.

immunization and case management). In the country profiles, further expansion of pneumonia programmes is considered, alongside existing vaccination programmes and curative services.

The attributable pneumonia burden due to indoor air pollution by

WHO region was based on the countryspecific exposure estimates from the WHOSIS database. The two countries with the largest populations – China and India – showed a high level (> 70%) of solid fuel use. The attributable burden for indoor air pollution in world

^a AFR, WHO African Region; AMR, WHO Region of the Americas; EMR, WHO Eastern Mediterranean Region; EUR, WHO European Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region. WHO regions are subdivided based on child and adult mortality: A, very low child and very low adult mortality; B, low child and low adult mortality; C, low child and high adult mortality; D, high child and high adult mortality; E, high child and very high adult mortality. A list of countries in WHO subregions is available at: http://www.who.int/choice/demography/regions

b Based on $[P \times (RR - 1)] / [(P \times (RR - 1) + 1]$ where P is risk prevalence and RR is the relative risk related to the exposure to solid fuel use. 2.25 The calculations include 90% Cls for the RR of pneumonia (based on the aggregate of 40 high-burden countries).

^c The RR value range is based on the systematic review.²⁸

^a AFR, WHO African Region; AMR, WHO Region of the Americas; EMR, WHO Eastern Mediterranean Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region. WHO regions are subdivided based on child and adult mortality: A, very low child and very low adult mortality; B, low child and low adult mortality; C, low child and high adult mortality; D, high child and high adult mortality. A list of countries in WHO subregions is available at: http://www.who.int/choice/demography/regions

b The low and high figures are based on the low and high scenario input values in Table 1.

Table 4. High and low cost-effectiveness estimates (I\$ per DALY averted) of single interventions to reduce pneumonia mortality, for 40 countries clustered by WHO subregion

WHO subre- gion ^a	E1		E2		N1		N2		11		12		C1		C2	
	Low ^b	High⁵	Low ^b	High⁵	Low ^b	High⁵	Low ^b	High⁵	Low ^b	High	Low ^b	High	Low ^b	High⁵	High	High
SEAR B	1567	8918	930	3312	177	242	66	105	238	1292	159	407	90	274	780	1011
SEAR D	808	2149	448	1647	67	90	25	40	109	593	115	293	69	210	277	357
WPR B	3200	17 823	1382	5612	299	407	86	137	266	1447	238	610	112	343	678	879
AFR D	107	356	72	243	49	66	12	19	44	241	27	69	21	65	62	81
AFR E	232	780	139	498	35	48	12	19	45	244	46	120	35	107	64	83
EMR D	135	837	86	296	47	63	16	26	50	273	35	89	66	203	71	92
AMR D	467	1572	343	1097	218	295	18	28	223	1207	96	245	108	330	492	635
AMR B	1226	3936	1420	3812	261	356	17	27	243	1324	130	335	56	172	489	637

C1, case management community-based; C2, case management facility-based; DALY, disability-adjusted life year; E1, use of cleaner liquid fuels; E2, solid fuel stoves; I1, pneumococcal vaccine; I2, *Haemophilus influenza* type B vaccine; I\$, International dollar; N1, breast feeding promotion; N2, zinc supplementation.

regions varied from 10% to 38%, with a limited uncertainty range. The contribution of indoor air pollution to the global burden of childhood pneumonia is large (30%; CI: 18–44). Table 3 provides the aggregated results by WHO region of health gains for two intervention packages in the high-burden countries.

Table 5, which illustrates the possibilities for country-level policy-making, presents two country profiles with combinations of eight intervention scenarios. Both single (Table 4) and combined interventions (Table 5) show low-cost outcomes between I\$ 10 and I\$ 60 per DALY averted for interventions in the WHO Africa D and E subregions, and in the WHO Eastern Mediterranean D subregion. In other regions, effective options were immunization, nutritional interventions and community-based case management. A listing of WHO epidemiological subregions is available at: http://www. who.int/choice/demography/regions Many mixes of interventions fell in the cost range of I\$ 60 to I\$ 120 per DALY averted; others were less cost-effective in light of the general country income level. In some poorer regions, the two indoor air pollution interventions showed the same cost-effective levels as other interventions. In general, the indoor air pollution interventions appear to be less cost-effective than other interventions for reducing pneumonia mortality. The maximum potential reduction in child mortality, given

existing infrastructures and including indoor air pollution interventions, appears to be about 13–17%. Thus, most of the child pneumonia mortality could be avoided if all interventions were implemented.

Discussion

Population-based preventive measures and expanding community-based case management appear to be the most effective options for reducing pneumonia mortality. Adding these measures to existing facility-based case management would increase the efficiency of health system as a whole. When outreach expansion is limited and infrastructure is lacking, immunization is costly. Where measles vaccination coverage is already high, both types of pneumonia vaccine are attractive options. The estimates on immunization depend strongly on the price per dose. Expanded case management, combined with expanded use of new vaccines, would increase system efficiency further. Adding new vaccines and expanding immunization coverage, nutritional interventions and community case management lead to relatively cost-effective pneumonia packages, as compared with facility-based management alone, because the latter was more costly in all scenarios.

Additionally, we found that health risk reduction through nutritional and immunization intervention programmes increases the cost-effectiveness of programmes for case management of childhood illnesses. The region and country league tables present the additional cost-effective options of expanded community case management and improved neonatal management.

The cost-effectiveness results showed the efficiency of implementing interventions alongside an existing health care structure, in comparison with a baseline situation. Presenting the results in this way provides policymakers with a general impression of the impact of an intervention; it also makes it possible to compare the efficiency of existing and new packages and possible ways to improve the allocation of funds. For example, in a country such as Guatemala, the most attractive additional options would be zinc supplementation combined with community case management. If these interventions were introduced simultaneously with the available environmental interventions, the additional cost of the package per DALY would increase. When environmental interventions are introduced wherever other interventions are already in place, the extra health benefits are limited and the additional cost per DALY (i.e. marginal cost-effectiveness) can be high. For example, in a country such as Nigeria, which has some infrastructure but no proven options to reduce indoor air pollution, including up-scaling community case management, along with preventive programmes, would increase the cost-effectiveness of implementing a pneumonia control package.

^a AFR, WHO African Region; AMR, WHO Region of the Americas; EMR, WHO Eastern Mediterranean Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region. WHO regions are subdivided based on child and adult mortality: A, very low child and very low adult mortality; B, low child and low adult mortality; C, low child and high adult mortality; D, high child and high adult mortality; E, high child and very high adult mortality. A list of countries in WHO subregions is available at: http://www.who.int/choice/demography/regions

^b The low and high cost-effectiveness figures are based on the low and high scenario input values in Table 1.

Table 5. Impact of pneumonia interventions: population costs and health effects of intervention mixes, ranked by costeffectiveness ratio

Scenario	(Cost (I\$)		npact s averted)	Cost-effectiveness (I\$ per DALY averted)		
	Low ^a	High ^a	Low ^a	High ^a	Low	High	
Guatemala							
N2	3 388 548	3 388 755	94 708	168 753	20	36	
C1 + N2	14 456 120	22 847 770	153 759	248 160	58	149	
N2 + I2	22 947 950	35 885 920	197 545	310 204	74	182	
C1 + N2 + I2	32 557 260	51 380 010	247 505	370 709	88	208	
12	19 556 400	32 489 570	117 737	181 722	108	276	
C1 + I2	30 645 650	52 833 210	175 482	261 407	117	301	
C1	12 771 920	25 549 410	68 752	105 082	122	372	
N2 + I1 + I2	69 744 980	202 430 400	304 660	455 961	153	664	
C1 + N2 + I1 + I2	77 836 540	213 846 400	345 132	496 946	157	620	
C1 + I1 + I2	75 686 320	214 000 500	286 650	422 480	179	747	
11 + 12	66 348 560	199 012 700	239 878	368 496	180	830	
N1 + N2 + I1 + I2	92 885 300	225 585 800	339 382	489 399	190	665	
C1 + N1 + N2 + I1 + I2	100 765 800	236 592 300	376 289	525 116	190	629	
N1	23 128 920	23 129 580	61 849	94 573	245	374	
1 	46 777 990	166 457 900	122 548	187 061	250	1 358	
E2 + N1 + N2	102 294 300	145 676 800	223 486	369 041	277	652	
E2 + N1 + N2 + I1 + I2	168 673 800	344 773 400	391 775	557 602	302	880	
E1 + N2 + I1 + I2	207 344 100	429 838 300	380 875	559 431	371	1 129	
E2	75 765 250	119 135 400	96 467	196 759	385	1 235	
C1 + N1 + N2 + E1 + I1 + I2	236 928 300	459 878 300	439 383	602 671	393	1 047	
l1 + C2	105 490 400	225 193 400	183 402	266 837	395	1 228	
E1 + N1 + N2 + I1 + I2	230 488 000	452 992 500	409 236	580 330	397	1 107	
E1	137 565 200	227 326 900	128 460	262 222	525	1 770	
C2	58 702 570	58 704 310	72 978	106 185	553	804	
Nigeria							
N2	128 164 700	128 202 800	3 762 062	6 731 571	19	34	
C1	168 511 300	337 498 200	5 526 855	8 480 821	20	61	
C1 + N2	274 758 000	387 071 600	8 583 929	13 260 480	21	45	
C1 + I2	258 060 800	471 722 200	7 368 852	11 046 040	23	64	
C1 + N2 + I2	365 650 800	528 628 400	10 237 650	15 369 100	24	52	
N2 + I2	227 851 200	293 837 000	5 713 960	9 466 567	24	51	
12	99 643 700	165 537 400	2 173 602	3 366 076	30	76	
C1 + N2 + I1 + I2	608 643 400	1 401 358 000	11 960 940	17 543 130		117	
					35		
C1 + 1 + 2	499 627 700	1 336 704 000	9 288 789	13 691 530	36	144	
N2 + I1 + I2	479 963 200	1 191 108 000	7 748 521	12 287 710	39	154	
C1 + N1 + N2 + I1 + I2	831 553 600	1 618 765 000	12 606 920	18 236 400	46	128	
11 + 12	351 680 200	1 062 450 000	4 450 029	6 849 750	51	239	
N1 + N2 + I1 + I2	706 739 500	1 418 207 000	8 546 800	13 268 470	53	166	
E2 + N1 + N2	1 019 693 000	1 444 036 000	8 300 044	14 377 170	71	174	
11	251 974 300	896 624 000	2 263 079	3 465 493	73	396	
E2 + N1 + N2 + I1 + I2	1 371 835 000	2 507 878 000	11 689 880	18 402 300	75	215	
E2	664 495 100	1 088 280 000	4 275 433	8 763 258	76	255	
E1 + N2 + I1 + I2	1 800 313 000	3 322 043 000	12 097 260	19 531 300	92	275	
C1 + N1 + N2 + E1 + I1 + I2	2 127 876 000	3 669 423 000	16 001 450	23 081 510	92	229	
C2	804 987 900	805 210 800	5 870 092	8 570 428	94	137	
l1 + C2	1 057 172 000	1 702 514 000	7 765 486	11 202 330	94	219	
E1 + N1 + N2 + I1 + I2	2 027 254 000	3 549 299 000	12 738 820	20 116 860	101	279	
E1	1 319 492 000	2 128 944 000	5 706 202	11 697 470	113	373	
N1	226 542 300	226 555 500	1 067 216	1 642 060	138	212	

C1, case management community-based; C2, case management facility-based; DALY, disability-adjusted life year; E1, use of cleaner liquid fuels; E2, use of solid fuel stoves; I1, pneumococcal vaccine; I2, *Haemophilus influenza* type B vaccine; I\$, International dollar; N1, breastfeeding promotion; N2, zinc supplementation.

^a The low and high cost-effectiveness figures are based on the low and high scenario input values in Table 1.

Data are limited in almost all countries. Detailed data on pneumonia deaths are lacking, and communitybased data on clinical episodes are sparse.1 Research is needed to better diagnose pneumonia and identify it as the cause of death. Our results are therefore difficult to validate beyond the recent reviews presented, whose quality determines the results of the economic impact evaluation. We were unable to distinguish between studies that reported intervention efficacy and those that reported community effectiveness. We attempted to consider this issue and other sources of uncertainty in our high and low effectiveness and cost scenarios; however, better data on community effectiveness and associated costs are needed. New preventive interventions may lead to net cost savings by preventing costly disease. However, we did not take into account potential savings due to cost offsets, lower use of health services and averted loss of workdays due to fewer illness episodes. Our results are thus conservative.

A point of debate is the cost of investing in cleaner fuels, whose cost per DALY averted is higher than that of other options. The results are not directly comparable, however, because the cost of cleaner fuels is offset by other societal benefits, such as time saved looking for firewood or other biomass fuels. If only the additional implementation efforts in an already existing health sector setting are considered and the extra costs of clean fuels are ignored, the cost-effectiveness ratio

is lower. Uncertainty also surrounds the effectiveness and cost of community case management programmes. These are likely to be directly correlated with the quality improvements and the additional cost per village of visits by a village agent. These variables make it difficult to draw definite conclusions from the economic evaluation of these interventions. Still, our studies have identified three potentially valuable interventions to improve child survival: nutritional interventions, immunization and low-cost, effective case management. Innovative use of vaccines, focusing on the highest at-risk groups, could amplify the impact.

National priorities

Donors and national agencies involved in child survival programmes need to select those that maximize child health after considering existing mortality levels, infrastructure and funds available.³⁴ The present study, focused on children, offers policy-makers a range of potential pneumonia interventions and estimates of the money they require.³⁵

Internationally, there is agreement on using disease-burden estimates and data on the cost-effectiveness of interventions to select priority areas. New insights should be applied in real-life country settings to find local solutions and implement appropriate options. Country programme managers need more specific information on the effects and costs of child programmes so they can weigh them against other

criteria, such as equity and other societal benefits.^{35–37}

We included in our scenarios only interventions for which effectiveness data were available. Due to a lack of data we could not examine the management of severe malnutrition through improved complementary feeding or strong community programmes. Malnutrition is a major risk factor for severe pneumonia, 1 yet no adequate study of the preventive effectiveness of such programmes has been performed.

The links between evidence and policy tend to be weak because national policies are the outcome of complicated processes among parties with different interests. 36,37 Impact analysis strengthens the selection of optimum child packages, and this paper shows how policy in this area can be more evidence based.

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Résumé

Evaluation comparative des impacts des interventions contre la pneumonie chez l'enfant

Objectif Comparer les rapports coût/efficacité d'interventions pour diminuer la mortalité par pneumonie à travers la réduction des risques, la vaccination et la prise en charge des cas.

Méthodes Nous avons utilisé des estimations établies par l'OMS pour la charge de pneumonies par pays et les coûts des interventions afin d'analyser les estimations du risque de pneumonie chez les enfants de moins de 5 ans et l'efficacité d'un certain nombre d'interventions (prise en charge des cas, vaccinations en rapport avec la pneumonie, amélioration de la nutrition et réduction de la pollution de l'air intérieur due aux combustibles solides ménagers). Nous avons calculé les bénéfices pour la santé [années de vie corrigées de l'incapacité (DALY) évitées] et les coûts des interventions sur une période de 10 ans pour 40 pays totalisant 90 % des décès d'enfants par pneumonie.

Résultats L'utilisation de combustibles fossiles contribue pour

30 % (intervalle de confiance à 95 % : 18-44) à la charge de pneumonie infantile. Le traitement efficace au niveau communautaire, la promotion de l'allaitement exclusif, la supplémentation en zinc et les vaccinations contre *Haemophilus influenzae* type B (Hib) et *Streptocccus pneumoniae* par le biais des programmes existants ont présenté des rapports coût/efficacité de \$ int. 10 à \$ int. 60 par DALY dans les pays à faible revenu et inférieurs à \$ int. 120 par DALY dans les pays à revenu moyen. L'utilisation de fourneaux à biomasse à faible émission et de combustibles plus propres pourrait offrir un rapport coût/efficacité satisfaisant dans les régions à faible revenu. Le traitement en établissement de soins pourrait également fournir un bon rapport coût/efficacité, situé entre \$ int. 60 et 120 par DALY. Le rapport coût/efficacité de la prise en charge des cas au niveau communautaire dépend du coût des visites à domicile.

Conclusion La vaccination contre Hib et *S. pneumoniae*, la prise en charge efficace des cas, la promotion de l'allaitement maternel et la supplémentation en zinc sont des interventions présentant un bon rapport coût/efficacité dans la réduction de la mortalité

par pneumonie. Les interventions d'ordre environnemental et nutritionnel font régresser la pneumonie et procurent d'autres bénéfices. La combinaison de ces stratégies peut permettre une réduction globale de la mortalité infantile de 17 %.

Resumen

Evaluación comparativa del impacto de las intervenciones contra la neumonía en la niñez

Objetivo Comparar la costoeficacia de las intervenciones tendentes a reducir la mortalidad por neumonía mediante la reducción del riesgo, la inmunización y el manejo de casos.

Métodos Partiendo de estimaciones de la carga de neumonía por países y del costo de las intervenciones según la OMS, se analizaron las estimaciones del riesgo de neumonía entre los menores de 5 años y la eficacia de las intervenciones (manejo de casos, vacunas relacionadas con la neumonía, mejoras de la nutrición y reducción de la contaminación del aire en locales cerrados por combustibles sólidos domésticos). Calculamos los beneficios para la salud (años de vida ajustados en función de la discapacidad -AVAD- evitados) y el costo de las intervenciones a lo largo de 10 años para 40 países, abarcando el 90% de las defunciones por neumonía en la niñez.

Resultados El uso de combustibles sólidos contribuye en un 30% (intervalo de confianza del 90%: 18–44) a la carga de neumonía en la niñez. Un tratamiento comunitario eficaz, la promoción de la lactancia natural como alimentación exclusiva, la administración de suplementos de zinc y la inmunización contra *Haemophilus*

influenzae tipo b (Hib) y Streptococcus pneumoniae a través de los programas existentes mostraron unas relaciones costo-eficacia de 10–60 dólares internacionales (I\$) por AVAD en los países de ingresos bajos, y de menos de I\$ 120 por AVAD en los países de ingresos medios. Las estufas de biomasa de baja emisión y unos combustibles más limpios pueden ser costoeficaces en las regiones de ingresos bajos. La administración de tratamiento en servicios de salud es una opción potencialmente costoeficaz, pues supone I\$ 60–120 por AVAD. La relación costo-eficacia del manejo de casos comunitario depende del costo de las visitas domiciliarias.

Conclusión La vacunación contra Hib y *S. pneumoniae*, el manejo eficaz de los casos, la promoción de la lactancia natural y la administración de suplementos de zinc son medidas costoeficaces contra la mortalidad en la niñez. Las intervenciones ambientales y nutricionales reducen la neumonía y reportan también otros beneficios. La combinación de estas estrategias puede reducir en total la mortalidad en la niñez en un 17%.

ملخص

التقييم المقارن لتأثير الخاصة بالالتهاب الرئوي لدى الأطفال

الهدف: مقارنة مردودية التدخلات الرامية إلى خفض معدلات وفيات الالتهاب الرئوي لدى الأطفال من خلال تقليل عوامل الاختطار والتمنيع وتدبر الحالات.

الطريقة: استخدم الباحثون تقديرات العبء الناجم عن الالتهاب الرئوي والخاص بكل بلد وتكاليف التدخلات التي تكبدتها منظمة الصحة العالمية لمراجعة تقديرات اختطار الالتهاب الرئوي لدى الأطفال دون سن الخامسة من العمر وكفاءة التدخلات (تدبير الحالات واللقاحات المتعلقة بالالتهاب الرئوي وتحسين التغذية وتقليل تلوث الهواء داخل المنازل والناجم عن استخدام الوقود الصلب فيها). وقد حسبت الفوائد الصحية (بسنوات العمر المصححة باحتساب مدد العجز التي أمكن تفاديها)، وتكاليف التدخلات على مدى 10 سنوات في 40 بلداً تحدث فيها 90% من وفيات الأطفال بالالتهاب الرئوي.

الموجودات: يساهم استخدام الوقود الصلب في 30% من عبء الالتهاب الرئوي لدى الأطفال (بفاصلة ثقة 90% إذ تراوحت بين 18 و44). وقد أظهرت كل من المعالجة الفعالة المرتكزة على المجتمع، وتعزيز الاقتصار على الرضاعة من الثدي، وتقديم مكملات غذائية من الزنك، والتمنيع بلقاح المستدمية

النزلية من النمط B والعقديات الرئوية عبر البرامج القائمة، أظهرت مردودية عالية بلغت 01-60 دولاراً دولياً لكل سنة من سنوات العمر المصححة باحتساب مدد العجز في البلدان المنخفضة الدخل، وأقل من 021 دولاراً أمريكياً لكل سنة من سنوات العمر المصححة باحتساب مدد العجز في البلدان المتوسطة الدخل. وقد يكون للمواقد التي تنتج انبعاثات ضئيلة من الكتلة الحيوية وللوقود النظيف مردودية عالية في المناطق المنخفضة الدخل ويمكن أن تكون المعالجة في المرافق الصحية عالية المردودية حيث يمكن أن تتراوح معدلاتها بين 03 و021 دولاراً دولياً لكل سنة من سنوات العمر المصححة باحتساب مدد العجز. وتعتمد مردودية تدبير الحالات في المجتمع على تكاليف الزيارات المنزلية.

H الاستنتاج: يعد كلً من التلقيح ضد المستدميات النزلية من النمط والعقديات الرئوية، وتعزيز الرضاعة من الثدي وتقديم مكملات غذائية من الزنك تدخلات عالية المردود لخفض معدلات الوفيات الناجمة عن الالتهاب الرئوي. وتقلل التدخلات البيئية والتغذوية من الالتهاب الرئوي وتقدم منافع أخرى، وقد تخفض هذه الاستراتيجيات عند تطبيقها مجتمعة مجمل معدلات وفيات الأطفال عقدار 17%.

References

- Rudan I, Boschi-Pinto C, Wardlaw T, Johansson E, Biloglav Z, Mulholland K, et al. The epidemiology and etiology of childhood pneumonia. *Bull World Health Organ* 2008;86:408-16. doi:10.2471/BLT.07.048769 PMID:18545744
- Lopez AD, Mathews CD, Ezzati M, Jamison DT, Murray CJL. Global burden of disease and risk factors. Washington, DC: The World Bank; 2006.
- Roth DE, Caulfield LE, Ezzati M, Black RE. Acute lower respiratory infections in childhood: opportunities for reducing the global burden through nutritional interventions. *Bull World Health Organ* 2008;86:356-64. doi:10.2471/ BLT.07.049114 PMID:18545738
- Gakidou E, Oza S, Vidal Fuertes C, Li AY, Lee DK, Sousa A, et al. Improving child survival through environmental and nutritional interventions: the importance of targeting interventions toward the poor. *JAMA* 2007;298:1876-87. doi:10.1001/jama.298.16.1876 PMID:17954539
- Victora CG, Kirkwood BR, Ashworth A, Black RE, Rogers S, Sazawal S, et al. Potential interventions for the prevention of childhood pneumonia in developing countries: improving nutrition. *Am J Clin Nutr* 1999;70:309-20. PMID:10479192
- Edejer TT, Aikins M, Black RE, Wolfson L, Hutubessy R, Evans DB. Cost effectiveness analysis of strategies for child health in developing countries. BMJ 2005;331:1177. doi:10.1136/bmj.38652.550278.7C PMID:16282378
- Murray CJ, Laakso T, Shibuya K, Hill K, Lopez AD. Can we achieve Millennium Development Goal 4? New analysis of country trends and forecasts of under-5 mortality to 2015. *Lancet* 2007;370:1040-54. doi:10.1016/S0140-6736(07)61478-0 PMID:17889243
- 8. Madhi SA, Levine OS, Hajjeh R, Mansoor OD, Cherian T. Vaccines to prevent pneumonia and improve child survival. *Bull World Health Organ* 2008;86:365-72. doi:10.2471/BLT.07.044503 PMID:18545739
- Bruce N, Rehfuess E, Mehta S, Hutton S, Smith K. Indoor air pollution. In: Jamison DT, Breman GJ, Measham AR (eds). *Disease control priorities in developing countries*. 2nd ed. Washington, DC: The World Bank and Oxford University Press; 2006. pp. 793-815.
- Smith KR, Mehta S, Maeusezahl-Fuez M. Indoor air pollution from household use of solid fuels. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva: World Health Organization; 2004. pp. 1436-93.
- Mehta S, Shahpar C. The health benefits of interventions to reduce indoor air pollution from solid fuel use: a cost-effectiveness analysis. *Energy Sustain Develop* 2004;8:353-9.
- Bailis R, Ezzati M, Kammen DM. Mortality and greenhouse gas impacts of biomass and petroleum energy futures in Africa. *Science* 2005;308:98-103. doi:10.1126/science.1106881 PMID:15802601
- Sazawal S, Black RE. Pneumonia Case Management Trials Group. Effect
 of pneumonia case management on mortality in neonates, infants, and
 preschool children: a meta-analysis of community-based trials. *Lancet Infect Dis* 2003;3:547-56. doi:10.1016/S1473-3099(03)00737-0
 PMID:12954560
- Simoes EAF, Cherian T, Chow J, Shahid–Salles SA, Laxminarayan R, Jacob John T. Acute respiratory infections in children. In: Jamison DT, Breman GJ, Measham AR (eds). *Disease control priorities in developing countries*. 2nd ed. Washington, DC: The World Bank; 2006.
- Graham SM, English M, Hazir T, Enarson P, Duke T. Challenges to improving case management of childhood pneumonia at health facilities in resourcelimited settings. *Bull World Health Organ* 2008;86:349-55. doi:10.2471/ BLT.07.048512 PMID:18545737
- Marsh DR, Gilroy KE, Weerdt van de R, Wansi E, Qazi S. Community-based treatment of pneumonia – at a tipping point? *Bull World Health Organ* 2008;86:381-9. doi:10.2471/BLT.07.048462 PMID:18545741
- Mulholland K. Childhood pneumonia mortality a permanent global emergency. *Lancet* 2007;370:285-9. doi:10.1016/S0140-6736(07)61130-1 PMID:17658399
- Adam T, Lim SS, Mehta S, Bhutta ZA, Fogstad H, Mathai M, et al. Cost effectiveness analysis of strategies for maternal and neonatal health in developing countries. *BMJ* 2005;331:1107. doi:10.1136/bmj.331.7525.1107 PMID:16282407
- Bryce J, Victora CG, Habicht JP, Black RE, Scherpbier RW. Programmatic pathways to child survival: results of a multi-country evaluation of Integrated Management of Childhood Illness. *Health Policy Plan* 2005;20:15-17. doi:10.1093/heapol/czi055

- Bryce J, Black RE, Walker N, Bhutta ZA, Lawn JE, Steketee RW. Can the world afford to save the lives of 6 million children each year? *Lancet* 2005;365:2193-200. doi:10.1016/S0140-6736(05)66777-3 PMID:15078927
- Johns B, Sigurbjörnsdóttir K, Fogstad H, Zupan J, Mathai M, Tan-Torres Edejer T. Estimated global resources needed to attain universal coverage of maternal and newborn health services. *Bull World Health Organ* 2007;85:256-63. doi:10.2471/BLT.06.032037 PMID:17546306
- Akumu AO, English M, Scott JA, Griffiths UK. Economic evaluation of delivering *Haemophilus influenzae* type b vaccine in routine immunization services in Kenya. *Bull World Health Organ* 2007;85:511-8. doi:10.2471/ BLT.06.034686 PMID:17768499
- 23. Hutton G, Rehfuess E, Tediosi F, Weiss S. *Evaluation of the costs and benefits of household energy and health interventions.* Geneva: World Health Organization; 2006.
- Sinha A, Levine O, Knoll MD, Muhib F, Lieu TA. Cost-effectiveness of pneumococcal conjugate vaccination in the prevention of child mortality: an international economic analysis. *Lancet* 2007;369:389-96. doi:10.1016/ S0140-6736(07)60195-0 PMID:17276779
- Weinstein MC, Stason WB. Foundations of cost-effectiveness analysis for health and medical practices. N Engl J Med 1977;296:716-21. PMID: 402576
- Niessen LW. Roads to health multi-state modelling of population health and resource use. Amsterdam: Dutch University Press and Barnes and Noble; 2002
- Baltussen R, Brouwer W, Niessen L. Cost-effectiveness analysis for priority setting in health: penny-wise but pound-foolish. *Int J Technol Assess Health Care* 2005;21:532-4. doi:10.1017/S0266462305050750 PMID:16262980
- Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ* 2008;86:390-8. doi:10.2471/BLT.07.044529 PMID:18545742
- Murray CJL, Lopez AD. The global burden of disease. Cambridge, MA: Harvard University Press; 1996 (Global Burden of Disease and Injury Series).
- Ustün TB, Rehm J, Chatterji S, Saxena S, Trotter R, Room R, et al. WHO/NIH Joint Project CAR Study Group. Multiple-informant ranking of the disabling effects of different health conditions in 14 countries. *Lancet* 1999;354:111-5. doi:10.1016/S0140-6736(98)07507-2 PMID:10408486
- Lehmann U, Sanders D. The state of the evidence on programmes, activities, costs and impact on health outcomes of using community health workers.
 Geneva: World Health Organization; 2007.
- Qazi SA, Rehman GN, Khan MA. Standard management of acute respiratory infections in a children's hospital in Pakistan: impact on antibiotic use and case fatality. *Bull World Health Organ* 1996;74:501-7. PMID:9002330
- Black RE, Allen LH, Bhutta ZA, Caulfield LE, de Onis M, Ezzati M, et al., Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet* 2008;371:243-60. doi:10.1016/S0140-6736(07)61690-0 PMID:18207566
- Stenberg K, Johns B, Scherpbier RW, Edejer TT. A financial road map to scaling up essential child health interventions in 75 countries. *Bull World Health Organ* 2007;85:305-14. doi:10.2471/BLT.06.032052 PMID:17546312
- Laterveer L, Niessen LW, Yadcek A. Progress in poverty reduction strategies. Health Policy Plan 2003;18:138-45. doi:10.1093/heapol/czg018 PMID:12740318
- Baltussen R, ten Asbroek AH, Koolman X, Shrestha N, Bhattarai P, Niessen LW. Priority setting using multiple criteria: should a lung health programme be implemented in Nepal? *Health Policy Plan* 2007;22:178-85. doi:10.1093/heapol/czm010 PMID:17412742
- Niessen LW, Grijseels EWM, Rutten FFH. The evidence-based approach in health policy and health care delivery. Soc Sci Med 2000;51:859-69. doi:10.1016/S0277-9536(00)00066-6 PMID:10972430