Setting Priorities in Global Child Health Research Investments: Assessment of Principles and Practice

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This article reviews theoretical and practical approaches to priority setting in global child health research investments. It also provides an overview of previous attempts to develop appropriate tools and methodologies to define priorities in health research investments. A brief review of the most important theoretical concepts that should govern priority setting processes is undertaken, showing how different perspectives, such as medical, economical, legal, ethical, social, political, rational, philosophical, stakeholder driven, and others will necessarily conflict each other in determining priorities. We specially address present research agenda in glob-

al child health today and how it relates to United Nation's (UN) Millennium Development Goal 4, which is to reduce child mortality by two-thirds between 1990 and 2015. The outcomes of these former approaches are evaluated and their benefits and shortcomings presented. The case for a new methodology for setting priorities in health research investments is presented, as proposed by Child Health and Nutrition Research Initiative, and a need for its implementation in global child health is outlined. A transdisciplinary approach is needed to address all the perspectives from which investments into health research can be seen as priorities. This prioritization requires a process that is transparent, systematic, and that would take into account many perspectives and build on advantages of previous approaches.

Among the many challenges in global child health today, the main is that 10.6 million children younger than 5 years still die each year (1,2). In The World Health Report in 2002, the World Health Organization (WHO) identified the leading health risks in developing countries as underweight, unsafe sex, unsafe water, sanitation and hygiene, iron deficiency, and indoor smoke from solid fuels (3). Each of those risks heavily affects children in a more or less direct way. However, many health interventions that could reduce this burden are available. Globally, the coverage for most of those interventions is below 50%, and the children who do not receive them are usually also the poorest and those exposed to multiple risk factors listed above (4).

UN's Millennium Development Goal 4

At a turn of the Millennium, United Nations defined its 8 priorities for further development – "Millennium Development Goals" (5). One of these goals is to reduce child mortality by two-thirds between 1990 and 2015. Achieving this goal required a reliable assessment of the main causes of child deaths. In 2001, the WHO established the external Child Health Epidemiology Reference Group (CHERG) to develop estimates of the proportion of deaths attributable to each of the main causes in children under 5 years of age. This was needed as a starting point in further planning and setting priorities, because previous estimates varied widely with certain organizations or research groups overemphasizing the importance of some diseases (1). After reviewing all the available information, CHERG estimated that, over the period 2000-2003, six causes accounted for 73% of deaths in children younger than 5 years: pneumonia (19%), diarrhea (18%), malaria (8%), neonatal pneumonia or sepsis (10%), preterm delivery (10%), and asphyxia at birth (8%) (2,6). Undernutrition, as a major risk factor in children, was estimated to represent the underlying cause of 53% of all child deaths globally (5).

Jones et al (4) estimated that, if the existing interventions for which there is sufficient or limited evidence of the effect, and which are feasible for delivery at high coverage in low-income settings, were made available universally, a disproportionately high figure of 63% of child deaths would be prevented each year. Subsequently, Bryce et al (7) demonstrated that there were no financial obstacles to fund such an effort given the amount of funding available, but there is lack of knowledge on how to do it. Strategies are needed to reach the poor and deprived children and to sustain their coverage, and they need to be developed through further research.

Research agenda in global child health

Although the interventions and the financial resources needed to achieve Millennium Development Goal 4 seem available, more than half of the period (1990-2015) set by the UN has passed and mortality of children globally has not decreased enough. It is becoming apparent that the achievement of this goal may soon be out of reach. Why is this the case? One of the answers may lie in current practices in which funding priorities are being set in global child health research. Pneumonia and diarrhea, as an example, are jointly responsible for nearly 40% of all child deaths globally, which is about the same as the number of deaths from smoking, double the number of deaths from HIV/AIDS, and is 25 times the number of deaths from war globally (3). Interventions (antibiotics and oral rehydration therapy) have been developed and have been shown to be highly cost-effective in preventing deaths from both diseases in the mid 1980s (7), but this appears to be where research interest ended (Figure 1).

There is considerably less interest in research on how to implement these interventions in the context of health services in countries with limited resources. Implementation research is not ranked highly by the scientific community or by most funding agencies. As it is rarely considered a research priority, research on new interventions far exceeds that on delivery. A vaccine against measles has been available for decades and it is highly cost-effective and deliverable, but even in this case only about 50% of world's children have been vaccinated (4).

Research funding for global child health currently favors opening new frontiers with their attractive promises over realizing the full public health impact of the interventions which led from past advances in knowledge (8-11). Even if work on new research avenues
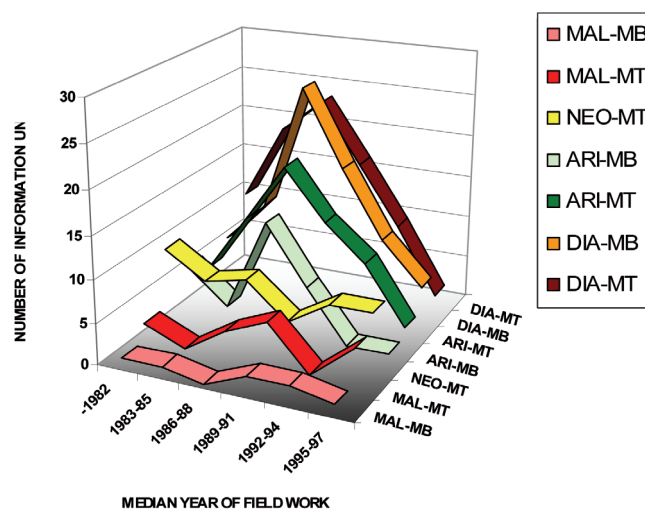

Figure 1. Number of papers with policy-relevant information on epidemiology of specific childhood illnesses in developing countries identified by Child Health Epidemiology Reference Group shows depleting interest in diseases that continue to kill most children. MAL – malaria; NEO – neonatal causes; ARI – acute respiratory infections; DIA – diarrhea; MB – morbidity; MT – mortality (7).

proves successful, the beneficiaries are only those who can afford the results of the research success. This further increases already unacceptable levels of inequity. The methodology for setting investment priorities is needed which could carefully balance between long-term investments and supporting research on better use of the existing knowledge (12-15).

Instruments (domains) of health research

Current areas of progress in health research can be classified into four large (and to some extent overlapping) categories from the perspective of their potential to reduce persisting mortality and morbidity burden (16). Assessment of existing and averted disease burden can be achieved through epidemiological research. Further reduction of disease burden can then be achieved through health policy and systems research, research to improve existing interventions, and research for development of new health interventions. The key challenge in setting investment priorities for

health research is to find the right balance of investments into those 4 different "instruments" of health research. The aim should be to achieve maximum gains in disease burden reduction with improved health information, efficiency of health systems, and deliverability of available interventions, while still supporting long-term strategic investments into new interventions with large potential to remove the existing disease burden.

A history of priority setting in global health research investments

1990 - Commission on Health Research for Development

The Commission is usually referred to as the first truly significant international initiative aimed toward systematic approach to setting priorities in global health research. It reviewed global health needs and priorities for health research and identified great inequity in the allocation of research funds globally – the "10/90" gap, where less than 10% of global health research funds is devoted to 90% of the world's health problems. This led to subsequent promotion of the concept of Essential National Health Research (ENHR), in which countries take responsibilities to delineate a research agenda by themselves (17).

1944 – Ad Hoc Committee (AHC) on Health Research Relating to Future Intervention Options

The second major initiative in similar direction came from the World Health Organization (WHO), when the Ad Hoc Committee on Health Research Relating to Future Intervention Options (AHC) was formed. The Committee's mandate was to address: 1) priorities for health research and development, 2) prospects for funding, and 3) institutional changes that might enhance the output of ongoing research and development investments at the time. In 1996, Ad Hoc Committee pre-

sented a report "Investing in Health Research and Development," that recommended policies for investments into research and development of particular relevance to poor nations (16). Ad Hoc Committee is also credited with conceptual framework showing the relationship between different "instruments" of health research and their potential to reduce different components of disease burden, as presented in the previous section (16).

1998 – Global Forum for Health Research

In 1998, the Global Forum for Health Research (GFHR) began its operations with the main focus on helping to correct this "10/90" gap. It had been holding annual conferences at which ideas and strategies for correcting the "10/90 gap" were exchanged. Working as a consultant for Global Forum for Health Research, Hyder wrote a report on priority investments in research and development ("best buys") identified by Ad Hoc Committee (16). Through structured interviews and comprehensive review of the literature, and a number of other methods that took into account issues such as dynamic nature of "best buys," time factor, baseline status, and research intensity, 17 research and development priorities were identified and classified as either "Strategic research," "Package development and evaluation," and "New tool or intervention development."

Examples of "Strategic research options" were "Sequencing genomes of major pathogens responsible for disease burden" or "Investigating factors influencing the development of anti-microbial resistance" (16). Examples of "Package development and evaluation" were "Evaluating and refining the package for the Integrated Management of Childhood Illness" and "Developing, evaluating and refining the Mother-Baby package for pregnancy, delivery and neonatal care" (16). Finally, the examples of proposed "New

tool or intervention development" research options were "Evaluating the efficacy and dosage of candidate rotavirus vaccine in low-income countries," "Evaluating the efficacy of candidate conjugate pneumococcal vaccine and conducting trials in low-income countries," "Developing malaria vaccine," and "Developing HIV vaccine" (16).

2000 – Council on Health Research and Development (COHRED)

In October 2000, an International conference on health research and development was held in Bangkok, Thailand. The conference was chaired by an international organizing committee formed by the representatives of the WHO, The World Bank, Global Forum for Health Research, and the Council on Health Research and Development. COHRED reviewed experiences and lessons from developing countries (10). The issues addressed were systematically categorized into the processes and methods for priority setting, assessing the results of Essential National Health Research strategy, defining who sets priorities and how to get participants involved, the potential functions, roles, and responsibilities of various stakeholders, information and criteria for setting priorities, strategies for implementation, and indicators for evaluation (10).

2003 – "The Grand Challenges", World Economic Forum, Davos, Switzerland

The next major global initiative emerged at the World Economic Forum, held in Davos, Switzerland, in January 2003. Bill and Melinda Gates Foundation (BMGF) announced the release of US$ 200 million to support the initiative of "The Grand Challenges" in global health research. This was based on a model formulated by the mathematician David Hilbert, who defined ultimate problems in mathematics and prizes were then offered to any-

one who would succeed in solving them. This initiative resulted in more focused research by scientists in mathematics and resulted in major progress in the field at the time (11).

The identification of "Grand Challenges" was achieved with financial support from BMGF and the National Institutes of Health. It gathered a scientific board of 20 scientists and public health experts from 13 countries (including some developing countries), while the scientific community supplied ideas for challenges. "Grand Challenge" was described as "...a call for a specific scientific or technological innovation that would remove a critical barrier to solving an important health problem in the developing world with a high likelihood of global impact and feasibility" (11). More than 1000 submissions were received from scientists and institutions in 75 countries, and scientific board reached the decision on declaring 14 submissions as "Grand Challenges" (11). Grants of up to a total of $20 million were then made available by Bill and Melinda Gates Foundation to remove these major obstacles to progress against diseases that disproportionately affect the developing world (11). All of the identified "Grand Challenges" fell into 7 broad categories, as follows: "Improving childhood vaccines," "Creating new vaccines," "Controlling insects that transmit agents of disease," "Improving nutrition to promote health," "Improving drug treatment of infectious diseases," "Curing latent and chronic infections," and "Measuring disease and health status accurately and economically in poor countries" (11).

The "17 Best Buys" and the "14 Grand Challenges" addressed very similar problems and some of them entirely overlapped. The key difference was that the "17 Best Buys" were generally very specific technologies or interventions already under a certain degree of development and targeted at specific diseases, while the "Grand Challenges" were more

broadly and generally defined and could impact several diseases and conditions.

2004 – Combined Approach Matrix, Global Forum for Health Research

To improve the process in which the respected scientists discuss and decide on funding priorities based on their own views and knowledge, Global Forum for Health Research developed a useful tool, the "Combined Approach Matrix" (CAM). The tool has proven to be highly useful for systematic classification, organization, and presentation of the large body of information that is needed at different stages of priority setting process, so that the decisions made by the members of decision-making committees could be based on all relevant and available information, rather than their own personal knowledge and judgment.

CAM incorporates "economic" dimension of priority setting process along one axis, and "institutional" dimension along the other, thus covering the information on the determinants of health at the population level. Components of "economic dimension" are "disease burden," its "determinants," "present level of knowledge," "cost and effectiveness," and "resource flows." Components of "institutional dimension" are "the individual, household and community," "health ministry and other health institutions," "sectors other than health," and "macro-economic policies." CAM can be applied at the level of disease, risk factor, group or condition, and also at local, national, or international level (18).

2007 – Research challenges to improve maternal and child survival

Over the past several years, *The Lancet* journal bravely engaged into advocacy of international health issues through publication of several series of papers focusing on main priority areas in international health. Recently, *The Lancet* expanded this effort through conducting a Delphi process similar to the one that had led to the "Grand Challenges" among a wide range of academics and professionals who had experience in developing countries (19). The coordinators of the process ranked by their perceived importance a limited number of very general and broad research themes in child health, maternal health, health systems, and community development (19).

Assessment of the outcomes of previous attempts to define priorities in health research investments

All the initiatives from the past aiming to set priorities in health research investments resulted in apparent benefits and successes. The benefits were that discussions over these issues were taking place and highlighted many important factors relevant to setting health research priorities. The successes were that a more specific research focus was agreed, which then attracted attention of many researchers groups. The investments began to follow the specified goals. Such situation was more favorable than having no priorities, when each research group followed its own path.

However, the past approaches were also not free from certain shortcomings. Identified interventions and research questions that were outlined as the priorities were not compiled in a truly systematic way, using scientifically convincing conceptual framework and objective and repeatable methods, but rather through consensus reached by panels of experts. This often made it difficult to present the identified priorities to wider audiences as legitimate and fair, as the decisions could be seen as driven by research interest bias of individual experts.

Also, the claim of "best buys" was not supported by scientific and repeatable arguments. The "best buys" were not consistent or infor-

mative with respect to their potential for targeted disease burden reduction. The category of "package development" represented a mix of health policy and systems research options and options to improve the existing interventions. Similarly, some items among the "best buys" listed as "new tools or interventions" were clearly research options addressing the improvement of efficacy, affordability, deliverability, or sustainability of existing interventions. More fundamentally, the claim that the proposed items are indeed "best buys" was not convincingly demonstrated in a scientifically based, repeatable manner.

The decision-making process leading to the concept of "Grand Challenges," although better designed, informed, explained, and documented, had a somewhat biased focus from the start. The whole process was designed so that it largely promoted very difficult upstream technology developments. Among the "challenges," there is hardly any that addressed the improvement of efficacy, effectiveness, deliverability, affordability, and sustainability of the existing interventions, so that these important instruments of health research were nearly ignored. This is particularly unfortunate, because one of motivations behind the "Grand Challenges" initiative was to promote equity. Equity, however, is best promoted through delivery of the already existing and effective interventions to all children.

One of the conclusions of the recent Lancet's Child Survival series was a concern that global child health is perhaps losing its focus (4,8). Amid the large number of new interventions advertised and validated, levels of attention and effort directed at new, complex, and expensive interventions seem to be receiving higher profile and funding priority than the efforts to save millions of children by applying insecticide-treated materials, oral rehydration therapy, or promoting breastfeeding, all at a tiny fraction of costs of the former (4).

Combined Approach Matrix was launched, aiming to ensure that decision-makers are better informed about these facts and realities when making their decisions (18). However, the CAM also has its shortcomings. Although it is an extremely helpful tool for gathering and organizing information needed for priority setting process, it does not in itself represent an algorithm for making the decisions on the priorities by ranking or separating the competing investment options. Therefore, in the absence of reliable information, which is usually very scarce for developing countries, most of the decisions will still be based on discussions and agreements within the panels of experts. The recent effort by *The Lancet* made a step further in specifying broad research avenues that should be considered priorities, but did very little to point to more specific research programs or research questions which should be initiated or addressed urgently (19).

Need for systematic methodology for priority setting in global child health research investments

Today, investments into health research on new interventions far exceed those on delivery in spite of the evidence that emphasizes large potential contribution of the latter to mortality burden reduction (4,8). The dominant model of research priority setting is driven by criteria such as interests of different advocacy groups, media exposure, interests of donors, individual biases of the members of policy-making panels, attractiveness of research results, novelty of proposed research and potential for publication in high-impact journals. We are concerned that continuing application of these criteria in decisions over investments into health research is resulting in gross under-achievement of potential disease burden reduction and is actually generating further health inequity. Even when new

research avenues succeed in the development of new interventions, the initial beneficiaries usually are those who can afford the results. More complete coverage of the population in need often lags decades behind (20).

The current model of research priority setting is a closed circle set to increasingly favor basic research and generate ever-increasing inequity. A major underlying problem is lack of clear criteria and principles that would guide health research investments based on a vision of what the endpoints of such investments should be. If we can agree that the ultimate endpoint of any health research should be reduction of disease burden and improvement of health, then some of the criteria needed for prioritization of investments should include: 1) usefulness of the proposed research in terms of its potential to lead to development of new or improved health interventions, 2) true effectiveness of those interventions, 3) their deliverability, affordability, and sustainability in the context of interest, and 4) their maximum potential to reduce persisting disease burden in an equitable way.

In addition, there is growing need to make decisions on research priorities not only globally, but also at lower levels – regional, national, and local community levels, and at single health facilities. Because of this, a methodology proposed to assist in health research priority setting should ideally have a form of an algorithm, that would be able to rank the priorities in very specific research programs or questions in a given setting (global, regional, national, and local) and for a given disease, risk factor, or a set of diseases and risk factors. Such methodology should also be simple enough for application, so that it could gain popularity among the users. It should provide simple, intuitive, and easily understandable answers, so that they could be presented to policy-makers from different

regions of the world and be understood in the similar way. The methodology should be able to incorporate the available information relevant to priority setting (such as that compiled by Combined Approach Matrix).

The future application of this new methodology in the area of child health would greatly benefit from a particularly favorable knowledge base, represented in recently defined global burden of disease and death in children based on collective review of over 17 000 sources and references published over the past two decades, that was performed by WHO Child Health Epidemiology Reference Group (CHERG) (2,7,21-25). It would also have a solid base for comparatively evaluating the competing interventions, through the recently completed "Disease Control Priorities Project II" (26).

Designing a new methodology respecting the principles of fair and legitimate priority setting

There are several fundamental principles that need to be respected in order to develop, promote, and implement priority setting methodology that would have a chance to become widely accepted and used. To begin with, Daniels and Sabin (27) defined two main principles that must underlie any process of setting priorities – legitimacy and fairness. Legitimacy can only be insured by involving a large and diverse range of stakeholders from different regions and with different backgrounds into development of such methodology.

Respecting the principle of fairness is an equally difficult, but in many ways even more complex problem. There are different perspectives from which prioritizing between two or more competing options for health research investments can be made (eg, medical, economical, legal, ethical, social, political, rational, philosophical, stakeholder driven, and

others). Even if each process from each single perspective was driven through "perfect" decisions, the outcomes will necessarily conflict each other. Therefore, developing methods for setting priorities fairly will be a highly complex and multidimensional process that will require wide agreement of numerous experts from different disciplines working collaboratively to produce such methods.

A standard multidisciplinary approach, where researchers work in parallel from their respective disciplinary bases to address a common problem (as has been usually done in the past), would not have a capacity to address this particular problem. A transdisciplinary approach, where researchers of different backgrounds work jointly, using shared conceptual frameworks to draw together disciplinary specific knowledge and address common problems, will be significantly more likely to meet the target (28). Encouraging steps in providing theoretical guidelines for achieving success in transdisciplinary priority setting were made by Gibson et al (29), who managed to merge ethics principles on how priority-setting should be made ("Accountability for reasonableness, A4R") with empirical observations on how priority setting is made in absence of any guidelines ("The diamond model") into a single model. Their further collaboration with leading representatives of economy-based model of priority setting ("Program budgeting and marginal analysis") resulted in the development of a joint model that incorporates principles and knowledge from all three disciplines – theory of ethics, theory of economy, and qualitative assessment of how model-free priority setting is made in practice – into a satisfactory general model (30). The task for Child Health and Nutrition Research Initiative (CHNRI) experts will be to collaborate with those experts and continue to expand their work by incorporating the principles from medical

dimension (eg, public health reasoning), social dimension (eg, concern about equity), and public opinion dimension (eg, respecting stakeholders' views) into an even more general transdisciplinary framework that could be useful in setting health research priorities at all levels. It would also remain open to emerging ideas, such as recently presented decision theory and "value of information" concept (31).

Conclusion

The dominant model of priority setting in health research investments today continues to result in gross under-achievement of potential disease burden reduction among world's children and is actually generating further health inequity. There is growing need for a sound and informed process to make decisions on health research priorities, both globally and at lower levels – regional, national, and local community levels, and at single health facilities. A methodology in a form of algorithm that would enable this and that would be simple and practical enough to gain wider acceptance is much needed. In the series of papers that will follow this assessment of the past approaches, Child Health and Nutrition Research Initiative will propose a methodology for prioritization in global and national child health and nutrition research that attempts to satisfy most of those requirements. The proposed methodology will not seek to replace the existing methodologies, but will attempt to build upon their experiences, supplement them with input of knowledge and concepts from new and different perspectives, and seek to bring them all together and enhance transdisciplinary approach.

References

1 Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet. 2003;361:2226-34. Medline:12842379

2 Bryce J, Boschi-Pinto C, Shibuya K, Black RE; WHO Child Health Epidemiology Reference Group. WHO estimates of the causes of death in children. Lancet. 2005;365:1147-52. Medline:15794969

3 World Health Organization. The World Health Report 2002. Geneva: WHO; 2002.

4 Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS; Bellagio Child Survival Study Group. How many child deaths can we prevent this year? Lancet. 2003;362:65-71. Medline:12853204

5 Millennium Project. Available from: *http://www.unmillenniumproject.org/goals/index.htm*. Accessed: October 20, 2006.

6 Bryce J, Victora CG; Conference Organizing Group. Child survival: countdown to 2015. Lancet. 2005;365:2153-4. Medline:15978906

7 Rudan I, Lawn J, Cousens S, Rowe AK, Boschi-Pinto C, Tomaskovic L, et al. Gaps in policy-relevant information on burden of disease in children: a systematic review. Lancet. 2005;365:2031-40. Medline:15950717

8 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. Medline:15978927

9 Global Forum for Health Research. The 10/90 report on health research, 1999. Geneva: GFHR; 1999.

10 The Working Group on Priority Setting. Priority setting for health research: lessons from developing countries. Health Policy Plan. 2000;15:130-6. Medline:10837035

11 Varmus H, Klausner R, Zerhouni E, Acharya T, Daar AS, Singer PA. Grand challenges in global health. Science. 2003;302:398-9. Medline:14563993

12 Rudan I, El Arifeen S, Black RE. A systematic methodology for setting priorities in child health research investments. In: Child Health and Nutrition Research Initiative (CHNRI). A new approach for systematic priority setting in child health research investments. Dhaka: CHNRI; 2006.

13 Rudan I, El Arifeen S, Black RE, Campbell H. Childhood pneumonia and diarrhoea: setting our priorities right. Lancet Infect Dis. 2007;7:56-61. Medline:17182344

14 Tomlinson M, Chopra M, Sanders D, Bradshaw D, Hendricks M, Greenfield D, et al. Setting Priorities in Child Health Research Investments for South Africa. PLoS Med. 2007;4:e259. Medline:17760497

15 Nuyens Y. Setting priorities for health research: lessons from low- and middle-income countries. Bull World Health Organ. 2007;85:319-21. Medline:17546314

16 Hyder A. Research and development in priority investments ("best buys") identified by the Ad Hoc Committee on Health Research Relating to Future Intervention Options 1996-1998. Progress Report. Geneva: Global Forum for Health Research; 1998.

17 Commission on Health Research for Development. Health research: essential link to equity in development. Geneva: CHRD; 1990.

18 Ghaffar A, de Francisco A, Matlin S, editors. The combined approach matrix: a priority-setting tool for health research. Geneva: Global Forum for Health Research; 2004.

19 Costello A, Filippi V, Kubba T, Horton R. Research challenges to improve maternal and child survival. Lancet. 2007; 369:1240-3. Medline:17434384

20 Victora CG, Hanson K, Bryce J, Vaughan JP. Achieving universal coverage with health interventions. Lancet. 2004;364:1541-8. Medline:15500901

21 Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. Lancet Infect Dis. 2002;2:25-32. Medline:11892493

22 Rudan I, Tomaskovic L, Boschi-Pinto C, Campbell H; WHO Child Health Epidemiology Reference Group. Global estimate of the incidence of clinical pneumonia among children under five years of age. Bull World Health Organ. 2004;82:895-903. Medline:15654403

23 Boschi-Pinto C, Tomaskovic L. Methods and assumptions for diarrhoea mortality estimates. Available from: *http://www.who.int/child-adolescent-health/New_Publications/CHILD_HEALTH/EPI/CHERG_Diarrhoea_Mortality.pdf*. Accessed October 20, 2006.

24 Rowe AK, Rowe SY, Snow RW, Korenromp EL, Schellenberg JR, Stein C, et al. The burden of malaria mortality among African children in the year 2000. Int J Epidemiol. 2006;35:691-704. Medline:16507643

25 Lawn JE, Cousens S, Zupan J; Lancet Neonatal Survival Steering Team. 4 million neonatal deaths: when? Where? Why? Lancet. 2005;365:891-900. Medline:15752534

26 Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al. Disease control priorities in developing countries. 2nd ed. Washington (DC): Oxford University Press and The World Bank; 2006.

27 Daniels J, Sabin JE. Setting limits fairly: can we learn to share medical resources? Oxford: Oxford University Press; 2002.

28 Gibson JL, Martin DK, Singer PA. Priority setting for new technologies in medicine: a transdisciplinary study. BMC Health Serv Res. 2002;2:14. Medline:12126482

29 Gibson JL, Martin DK, Singer PA. Setting priorities in health care organizations: criteria, processes, and parameters of success. BMC Health Serv Res. 2004;4:25. Medline:15355544

30 Gibson J, Mitton C, Martin D, Donaldson C, Singer P. Ethics and economics: does programme budgeting and marginal analysis contribute to fair priority setting? J Health Serv Res Policy. 2006;11:32-7. Medline:16378530

31 Claxton K, Ginnelly L, Sculpher M, Philips Z, Palmer S. A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme. Health Technol Assess. 2004;8:1-103. Medline:15248937