The Economics of Immunization Policies

Click on title to access full text articles

1. **Developing a vaccination evaluation model to support evidence-based decision making on national immunization programs**

Vaccine, Volume 24, Issue 22, 29 May 2006, Pages 4769-4778

Tjeerd G. Kimman, Hein J. Boot, Guy A.M. Berbers, Patricia E. Vermeer-de Bondt, G. Ardine de Wit, Hester E. de Melker

**Keywords**
National immunization program; Vaccine-preventable disease; Vaccine; Pathogen; Disease; Cost-effectiveness; Vaccination

**Abstract**
Among all public health provisions national immunization programs (NIPs) are beyond doubt one of the most effective in reducing mortality, morbidity, and costs associated with major infectious diseases. To maintain their success, NIPs have to modernize in response to many new and old demands regarding efficacy, safety, availability of new vaccines, emerging and evolving pathogens, waning immunity, altered epidemiological situations, and the public's trust in the program. In this paper we present an evaluation model in the form of a checklist that may help in collecting relevant scientific information that is necessary for evaluation and decision making when considering changes in a NIP. Such a checklist points to relevant information on the vaccine-preventable disease, the pathogen causing it, the vaccine, and the cost-effectiveness ratio of the vaccine. However, the final judgment on a potential change in the NIP cannot be based on a simple algorithm, as the relevant information reflects factors of a very different kind and magnitude, to which different value judgments may be added, which may have certain degrees of uncertainty. Because any change in the NIP may be accompanied by more or less unforeseen changes in the vaccine's efficacy, evolutionary consequences, including the antigenic composition of the pathogen, and the vaccine's safety profile, an intensive surveillance program should accompany any NIP. Elements thereof include clinical–epidemiological surveillance, surveillance of vaccination coverage, immune surveillance, surveillance of microbial population dynamics, and surveillance of adverse events and safety issues. We emphasize that the decision to introduce a vaccine in the NIP should be taken as seriously, both scientifically and ethically, as the decision to withhold a vaccine from the NIP. In the latter case one might be responsible for vaccine-preventable disease and mortality.

2. **Developing a vaccination evaluation model to support evidence-based decision making on national immunization programs**

Vaccine, Volume 24, Issue 22, 29 May 2006, Pages 4769-4778

Tjeerd G. Kimman, Hein J. Boot, Guy A.M. Berbers, Patricia E. Vermeer-de Bondt, G. Ardine de Wit, Hester E. de Melker

**Keywords**
National immunization program; Vaccine-preventable disease; Vaccine; Pathogen; Disease; Cost-effectiveness; Vaccination

**Abstract**
Among all public health provisions national immunization programs (NIPs) are beyond doubt one of the most effective in reducing mortality, morbidity, and costs associated with major
infectious diseases. To maintain their success, NIPs have to modernize in response to many new and old demands regarding efficacy, safety, availability of new vaccines, emerging and evolving pathogens, waning immunity, altered epidemiological situations, and the public's trust in the program. In this paper we present an evaluation model in the form of a checklist that may help in collecting relevant scientific information that is necessary for evaluation and decision making when considering changes in a NIP. Such a checklist points to relevant information on the vaccine-preventable disease, the pathogen causing it, the vaccine, and the cost-effectiveness ratio of the vaccine. However, the final judgment on a potential change in the NIP cannot be based on a simple algorithm, as the relevant information reflects factors of a very different kind and magnitude, to which different value judgments may be added, which may have certain degrees of uncertainty. Because any change in the NIP may be accompanied by more or less unforeseen changes in the vaccine's efficacy, evolutionary consequences, including the antigenic composition of the pathogen, and the vaccine's safety profile, an intensive surveillance program should accompany any NIP. Elements thereof include clinical–epidemiological surveillance, surveillance of vaccination coverage, immune surveillance, surveillance of microbial population dynamics, and surveillance of adverse events and safety issues. We emphasize that the decision to introduce a vaccine in the NIP should be taken as seriously, both scientifically and ethically, as the decision to withhold a vaccine from the NIP. In the latter case one might be responsible for vaccine-preventable disease and mortality.

3. Using standardized tools to improve immunization costing data for program planning: The cost of the Colombian Expanded Program on Immunization

Vaccine, Volume 31, Supplement 3, 2 July 2013, Pages C72-C79

Carlos Castañeda-Orjuela, Martin Romero, Patricia Arce, Stephen Resch, Cara B. Janusz, Cristiana M. Toscano, Fernando De la Hoz-Restrepo

Keywords

Costs and cost analysis; Vaccines; Immunization programs

Abstract

Introduction The cost of Expanded Programs on Immunization (EPI) is an important aspect of the economic and financial analysis needed for planning purposes. Costs also are needed for cost-effectiveness analysis of introducing new vaccines. We describe a costing tool that improves the speed, accuracy, and availability of EPI costs that was piloted in Colombia.

Methods The ProVac CostVac Tool is a spreadsheet-based tool that estimates overall EPI costs considering program inputs (personnel, cold chain, vaccines, supplies, etc.) at three administrative levels (central, departmental, and municipal) and one service delivery level (health facilities). It uses various costing methods. The tool was evaluated through a pilot exercise in Colombia. In addition to the costs obtained from the central and intermediate administrative levels, a survey of 112 local health facilities was conducted to collect vaccination costs. Total cost of the EPI, cost per dose of vaccine delivered, and cost per fully vaccinated child with the recommended immunization schedule in Colombia in 2009 were estimated.

Results The ProVac CostVac Tool is a novel, user-friendly tool, which allows users to conduct an EPI costing study following guidelines for cost studies. The total costs of the Colombian EPI were estimated at US$ 107.8 million in 2009. The cost for a fully immunized child with the recommended schedule was estimated at US$ 153.62. Vaccines and vaccination supplies
accounted for 58% of total costs, personnel for 21%, cold chain for 18%, and transportation for 2%. Most EPI costs are incurred at the central level (62%). The major cost driver at the department and municipal levels is personnel costs.

Conclusion The ProVac CostVac Tool proved to be a comprehensive and useful tool that will allow researchers and health officials to estimate the actual cost for national immunization programs. The present analysis shows that personnel, cold chain, and transportation are important components of EPI and should be carefully estimated in the cost analysis, particularly when evaluating new vaccine introduction.

4. Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: A systematic review

Vaccine, Volume 31, Issue 1, 17 December 2012, Pages 96-108

Sachiko Ozawa, Andrew Mirelman, Meghan L. Stack, Damian G. Walker, Orin S. Levine

Keywords
Vaccine; Cost-effectiveness; Economic evaluation; DALY; Benefits; Systematic review

Abstract

Background Public health interventions that prevent mortality and morbidity have greatly increased over the past decade. Immunization is one of these preventive interventions, with a potential to bring economic benefits beyond just health benefits. While vaccines are considered to be a cost-effective public health intervention, implementation has become increasingly challenging. As vaccine costs rise and competing priorities increase, economic evidence is likely to play an increasingly important role in vaccination decisions.

Methods To assist policy decisions today and potential investments in the future, we provide a systematic review of the literature on the cost-effectiveness and economic benefits of vaccines in low- and middle-income countries from 2000 to 2010. The review identified 108 relevant articles from 51 countries spanning 23 vaccines from three major electronic databases (PubMed, Embase and Econlit).

Results Among the 44 articles that reported costs per disability-adjusted life year (DALY) averted, vaccines cost less than or equal to $100 per DALY averted in 23 articles (52%). Vaccines cost less than $500 per DALY averted in 34 articles (77%), and less than $1000 per DALY averted in 38 articles (86%) in one of the scenarios. 24 articles (22%) examined broad level economic benefits of vaccines such as greater future wage-earning capacity and cost savings from averting disease outbreaks. 60 articles (56%) gathered data from a primary source. There were little data on long-term and societal economic benefits such as morbidity-related productivity gains, averting catastrophic health expenditures, growth in gross domestic product (GDP), and economic implications of demographic changes resulting from vaccination.

Conclusions This review documents the available evidence and shows that vaccination in low- and middle-income countries brings important economic benefits. The cost-effectiveness studies reviewed suggest to policy makers that vaccines are an efficient investment. This review further highlights key gaps in the available literature that would benefit from additional research, especially in the area of evaluating the broader economic benefits of vaccination in the developing world.
5. **Health economics of rotavirus immunization in Vietnam: Potentials for favorable cost-effectiveness in developing countries**

Vaccine, Volume 30, Issue 8, 14 February 2012, Pages 1521-1528

Hong-Anh T. Tu, Mark H. Rozenbaum, Peter C. Coyte, Shu Chuen Li, Herman J. Woerdenbag, Maarten J. Postma

**Keywords**
Rotavirus; Cost-effectiveness; Vaccination; Affordability

**Abstract**

*Introduction* Rotavirus is the most common cause of severe diarrhoea worldwide. Vietnam is situated in the region of high rotavirus infection incidence and eligible for financial support to introduce rotavirus vaccines into the Expanded Program of Immunization (EPI) from the GAVI. This study was designed to assess the cost-effectiveness of rotavirus immunization in Vietnam, explicitly the use of Rotateq® and to assess the affordability of implementing universal rotavirus immunization based on GAVI-subsidized vaccine price in the context of Vietnamese healthcare system for the next 5 years.

*Methodology* An age-structured cohort model was developed for the 2009 birth cohort in Vietnam. Two strategies were compared: one being the current situation without vaccination, and the other being mass universal rotavirus vaccination. The time horizon of the model was 5 years with time cycles of 1 month for children less than 1 year of age and annual analysis thereafter. Outcomes included mild, moderate, severe cases and death. Multiple outcomes per rotavirus infection are possible in the model. Monte Carlo simulations were used to examine the acceptability and affordability of the rotavirus vaccination. All costs were expressed in 2009 US$.

*Results* Rotavirus vaccination would not completely protect young children against rotavirus infection due to partial nature of vaccine immunity, however, would effectively reduce severe cases of rotavirus by roughly 55% during the first 5 years of life. Under GAVI-subsidized vaccine price (US$ 0.3/dose), the vaccine cost would amount to US$ 5.5 million per annum for 3-dose of the Rotateq® vaccine. In the base-case, the incremental cost per quality-adjusted-life-year (QALY) was US$ 665 from the health system perspective, much lower than per-capita GDP of ~US$ 1150 in 2009. Affordability results showed that at the GAVI-subsidized vaccine price, rotavirus vaccination could be affordable for Vietnamese health system.

*Conclusion* Rotavirus vaccination in Vietnam would be a cost-effective health intervention. Vaccination only becomes affordable if the country receives GAVI’s financial support due to the current high market vaccine price. Given the high mortality rate of under-five-year children, the results showed that rotavirus immunization is the “best hope” for prevention of rotavirus-related diarrhoeal disease in Vietnam. In the next five years, Vietnam is definitely in debt to financial support from international organizations in implementing rotavirus immunization. It is recommended that new rotavirus vaccine candidates be developed at cheaper price to speed up the introduction of rotavirus immunization in the developing world in general.
6. **Introducing new vaccines in developing countries.**

Sonali Kochhar, Barbara Rath, Lea D Seeber, Gabriella Rundblad, Ali Khamesipour, Mohammad Ali and The Vienna Vaccine Safety Initiative

**Keywords**

AEFI, developing countries, immunization, vaccines, vaccine introduction, vaccine safety

**Abstract**

Vaccines offer the most cost-effective approach to controlling infectious diseases. Access to vaccines remains unequal and suboptimal, particularly in poorer developing countries. Introduction of new vaccines and long-term sustainability of immunization programs will require proactive planning from conception to implementation. International and national coordination efforts as well as local and cultural factors need to be known and accounted for. Adequate infrastructure should be in place for the monitoring of disease burden, vaccine effectiveness and vaccine safety, based on the common terminology and international consensus. This overview paper aims to raise awareness of the importance of introduction efforts for vaccines of special relevance to resource-poor countries. The target audiences are those involved in immunization programs, from planning or oversight roles to frontline providers, as well as health care professionals.

7. **Cost-effectiveness of human papillomavirus vaccination in low and middle income countries: a systematic review.**

Vaccine, Volume 31, Issue 37, 20 August 2013, Pages 3786–3804

Michaela Fesenfeld, Raymond Hutubessy, Mark Jit

**Keywords**

Human papillomavirus; Developing countries; Cost-effectiveness; Vaccination; Cervical screening

**Abstract**

The World Health Organization recommends establishing that human papillomavirus vaccination is cost-effective before vaccine introduction. We searched Pubmed, Embase and the Cochrane Library to 1 April 2012 for economic evaluations of human papillomavirus vaccination in low and middle income countries. We found 25 articles, but almost all low income countries and many middle income countries lacked country-specific studies. Methods, assumptions and consequently results varied widely, even for studies conducted for the same country. Despite the heterogeneity, most studies conclude that vaccination is likely to be cost-effective and possibly even cost saving, particularly in settings without organized cervical screening programmes. However, study uncertainty could be reduced by clarity about vaccine prices and vaccine delivery costs. The review supports extending vaccination to low income settings where vaccine prices are competitive, donor funding is available, cervical cancer burden is high and screening options are limited.
8. **Influenza vaccines in low and middle income countries: a systematic review of economic evaluations.**


Jördis J. Ott, Janna Klein Breteler, John S. Tam, Raymond C.W. Hutubessy, Mark Jit, and Michiel R. de Boer

**Keywords**
cost analysis; developing countries; economic evaluation; influenza; systematic review; vaccines

**Abstract**

**Objectives** Economic evaluations on influenza vaccination from low resource settings are scarce and have not been evaluated using a systematic approach. Our objective was to conduct a systematic review on the value for money of influenza vaccination in low- and middle-income countries.

**Methods** PubMed and EMBASE were searched for economic evaluations published in any language between 1960 and 2011. Main outcome measures were costs per influenza outcome averted, costs per quality-adjusted life years gained or disability-adjusted life years averted, costs per benefit in monetary units or cost-benefit ratios.

**Results** Nine economic evaluations on seasonal influenza vaccine met the inclusion criteria. These were model- or randomized-controlled-trial (RCT)-based economic evaluations from middle-income countries. Influenza vaccination provided value for money for elderly, infants, adults and children with high-risk conditions. Vaccination was cost-effective and cost-saving for chronic obstructive pulmonary disease patients and in elderly above 65 from model-based evaluations, but conclusions from RCTs on elderly varied.

**Conclusion** Economic evaluations from middle income regions differed in population studied, outcomes and definitions used. Most findings are in line with evidence from high-income countries highlighting that influenza vaccine is likely to provide value for money. However, serious methodological limitations do not allow drawing conclusions on cost-effectiveness of influenza vaccination in middle income countries. Evidence on cost-effectiveness from low-income countries is lacking altogether, and more information is needed from full economic evaluations that are conducted in a standardized manner.

9. **Health economics of rubella: a systematic review to assess the value of rubella vaccination.**


Joseph B Babigumira, Ian Morgan, and Ann Levin

**Abstract**

**Background** Most cases of rubella and congenital rubella syndrome (CRS) occur in low- and middle-income countries. The World Health Organization (WHO) has recently recommended that countries accelerate the uptake of rubella vaccination and the GAVI Alliance is now supporting large scale measles-rubella vaccination campaigns. We performed a review of health
economic evaluations of rubella and CRS to identify gaps in the evidence base and suggest possible areas of future research to support the planned global expansion of rubella vaccination and efforts towards potential rubella elimination and eradication.

Methods We performed a systematic search of on-line databases and identified articles published between 1970 and 2012 on costs of rubella and CRS treatment and the costs, cost-effectiveness or cost-benefit of rubella vaccination. We reviewed the studies and categorized them by the income level of the countries in which they were performed, study design, and research question answered. We analyzed their methodology, data sources, and other details. We used these data to identify gaps in the evidence and to suggest possible future areas of scientific study.

Results We identified 27 studies: 11 cost analyses, 11 cost-benefit analyses, 4 cost-effectiveness analyses, and 1 cost-utility analysis. Of these, 20 studies were conducted in high-income countries, 5 in upper-middle income countries and two in lower-middle income countries. We did not find any studies conducted in low-income countries. CRS was estimated to cost (in 2012 US$) between $4,200 and $57,000 per case annually in middle-income countries and up to $140,000 over a lifetime in high-income countries. Rubella vaccination programs, including the vaccination of health workers, children, and women had favorable cost-effectiveness, cost-utility, or cost-benefit ratios in high- and middle-income countries.

Conclusions Treatment of CRS is costly and rubella vaccination programs are highly cost-effective. However, in order for research to support the global expansion of rubella vaccination and the drive towards rubella elimination and eradication, additional studies are required in low-income countries, to tackle methodological limitations, and to determine the most cost-effective programmatic strategies for increased rubella vaccine coverage.

10. Economics of vaccines revisited.


Maarten J. Postma*, Baudouin A. Standaert

Keywords

Cost-effectiveness; health economics; modeling; new approaches; perspectives

Abstract

Performing a total health economic analysis of a vaccine newly introduced into the market today is a challenge when using the conventional cost-effectiveness analysis we normally apply on pharmaceutical products. There are many reasons for that, such as: the uncertainty in the total benefit (direct and indirect) to be measured in a population when using a cohort model; (1) appropriate rules about discounting the long-term impact of vaccines are absent jeopardizing therefore their value at the initial investment; (2) the presence of opposite contexts when introducing the vaccine in developed vs. the developing world with high benefits, low initial health care investment for the latter vs. marginal benefit and high cost for the former; with a corresponding paradox for the vaccine becoming very cost-effective in low income countries but rather medium in middle low to high middle income countries; (3) and the type of trial assessment for the newer vaccines is now often performed with immunogenicity reaction instead of clinical endpoints which still leaves questions on their real impact and their head-to-
11. Economic analyses to support decisions about HPV vaccination in low- and middle-income countries: a consensus report and guide for analysts.


Mark Jit, Carol Levin, Marc Brisson, Ann Levin, Stephen Resch, Johannes Berkhof, Jane Kim and Raymond Hutubessy

Keywords
Human papillomavirus; vaccination; low- and middle-income countries; economic evaluation.

Abstract
Low- and middle-income countries need to consider economic issues such as cost-effectiveness, affordability and sustainability before introducing a program for human papillomavirus (HPV) vaccination. However, many such countries lack the technical capacity and data to conduct their own analyses. Analysts informing policy decisions should address the following questions: 1) Is an economic analysis needed? 2) Should analyses address costs, epidemiological outcomes, or both? 3) If costs are considered, what sort of analysis is needed? 4) If outcomes are considered, what sort of model should be used? 5) How complex should the analysis be? 6) How should uncertainty be captured? 7) How should model results be communicated? Selecting the appropriate analysis is essential to ensure that all the important features of the decision problem are correctly represented, but that the analyses are not more complex than necessary. This report describes the consensus of an expert group convened by the World Health Organization, prioritizing key issues to be addressed when considering economic analyses to support HPV vaccine introduction in these countries.

12. Health and economic outcomes of HPV 16,18 vaccination in 72 GAVI-eligible countries.


Sue J. Goldie, Meredith O'Shea, Nicole Gastineau Campos, Mireia Diaz, Steven Sweet, Sun-Young Kim

Keywords
HPV; Cost-effectiveness; GAVI

Abstract
The risk of dying from cervical cancer is disproportionately borne by women in developing countries. Two new vaccines are highly effective in preventing HPV 16,18 infection, responsible for approximately 70% of cervical cancer, in girls not previously infected. The GAVI Alliance (GAVI) provides technical assistance and financial support for immunization in the world's poorest countries. Using population-based and epidemiologic data for 72 GAVI-eligible countries we estimate averted cervical cancer cases and deaths, disability-adjusted years of life (DALYs) averted and incremental cost-effectiveness ratios ($/DALY averted) associated with HPV 16,18 vaccination of young adolescent girls. In addition to vaccine coverage and efficacy, relative and absolute cancer reduction depended on underlying incidence, proportion attributable to HPV...
types 16 and 18, population age-structure and competing mortality. With 70% coverage, mean reduction in the lifetime risk of cancer is below 40% in some countries (e.g., Nigeria, Ghana) and above 50% in others (e.g., India, Uganda, Kenya). At $10 per vaccinated girl (approximately $2 per dose assuming three doses, plus wastage, administration, program support) vaccination was cost-effective in all countries using a per capita GDP threshold; for 49 of 72 countries, the cost per DALY averted was less than $100 and for 59 countries, it was less than $200. Taking into account country-specific assumptions (per capita GNI, DPT3 coverage, percentage of girls who are enrolled in fifth grade) for the year of introduction, percent coverage achieved in the first year, and years to maximum coverage, a 10-year modeled scenario prevented the future deaths of approximately 2 million women vaccinated as adolescents. Despite favorable cost-effectiveness, assessment of financial costs raised concerns about affordability; as the cost per vaccinated girl was increased from $10 to $25 (approximately $2 to $5 per dose), the financial costs for the 10-year scenario increased from >US$ 900 million to US$ 2.25 billion. Provided high coverage of young adolescent girls is feasible, and vaccine costs are lowered, HPV 16,18 vaccination could be very cost-effective even in the poorest countries, and provide comparable value for resources to other new vaccines such as rotavirus.

13. Benefits, cost requirements and cost-effectiveness of the HPV16,18 vaccine for cervical cancer prevention in developing countries: policy implications


Sue J Goldie, Meredith O’She, Mirei Diaz, Sun-Young Kim

Keywords
Cervical cancer; human papillomavirus vaccine; cost-effectiveness; priority setting; health policy and programmes

Abstract
Approximately 70% of cases of cervical cancer worldwide are caused by genotypes 16 and 18 of human papillomavirus (HPV), which is sexually transmitted. With the availability of an effective vaccine against these HPV types, there is real hope for reducing the global burden of cervical cancer in developing countries. Stakeholders faced with decisions about where to invest money to improve health must consider the burden of disease caused by cervical cancer relative to other priorities and the comparative benefits of different interventions. We conducted a series of analyses to obtain information for agencies drafting immunisation policy recommendations, financing coordination mechanisms, and country decision-makers on the benefits, cost requirements and cost-effectiveness of the HPV16,18 vaccine. We found that making an HPV16,18 vaccine accessible to 70% of young adolescent girls in 72 of the poorest countries, China, Thailand, and all of Latin America and the Caribbean, could prevent the future deaths of more than four million women vaccinated over the next decade. Provided the cost per vaccinated girl is less than $10–$25, adolescent HPV16,18 vaccination would be cost-effective even in relatively poor countries. Concerns about financial costs and affordability highlight the need for lowering vaccine prices, cost-efficient mechanisms for delivery of vaccinations to adolescents, and creative sources of financing.

BMC Medicine 2011, 9:54

Mark Jit, Nadia Demarteau, Elamin Elbasha, Gary Ginsberg, Jane Kim, Naiyana Praditsitthikorn, Edina Sinanovic and Raymond Hutubessy

Abstract

Background The World Health Organization (WHO) recommends that the cost effectiveness of introducing human papillomavirus (HPV) vaccination is considered before such a strategy is implemented. However, developing countries often lack the technical capacity to perform and interpret results of economic appraisals of vaccines. To provide information about the feasibility of using such models in a developing country setting, we evaluated models of HPV vaccination in terms of their capacity, requirements, limitations and comparability.

Methods A literature review identified six HPV vaccination models suitable for low-income and middle-income country use and representative of the literature in terms of provenance and model structure. Each model was adapted by its developers using standardised data sets representative of two hypothetical developing countries (a low-income country with no screening and a middle-income country with limited screening). Model predictions before and after vaccination of adolescent girls were compared in terms of HPV prevalence and cervical cancer incidence, as was the incremental cost-effectiveness ratio of vaccination under different scenarios.

Results None of the models perfectly reproduced the standardised data set provided to the model developers. However, they agreed that large decreases in type 16/18 HPV prevalence and cervical cancer incidence are likely to occur following vaccination. Apart from the Thai model (in which vaccine and non-vaccine HPV types were combined), vaccine-type HPV prevalence dropped by 75% to 100%, and vaccine-type cervical cancer incidence dropped by 80% to 100% across the models (averaging over age groups). The most influential factors affecting cost effectiveness were the discount rate, duration of vaccine protection, vaccine price and HPV prevalence. Demographic change, access to treatment and data resolution were found to be key issues to consider for models in developing countries.

Conclusions The results indicated the usefulness of considering results from several models and sets of modelling assumptions in decision making. Modelling groups were prepared to share their models and expertise to work with stakeholders in developing countries.

15. Systematic review of studies on rotavirus disease cost-of-illness and productivity loss in Latin America and the Caribbean

Volume 31, Supplement 3, 2 July 2013, Pages C45–C57

Maíra Libertad Soligo Takemoto, Luciana Bahia, Cristiano M. Toscano, Denizar Vianna Araujo

Keywords

Rotavirus; Cost of illness; Systematic review; Latin America and Caribbean

Abstract
**Background** Rotavirus is the most common cause of severe acute diarrhea among children in both developed and developing countries. Vaccination can reduce the disease burden and its incorporation into health care systems should consider future costs and benefits.

**Objectives** To systematically review studies on costs due to rotavirus infection in Latin America and Caribbean (LAC) region, considering their methods and results.

**Methods** A search of relevant databases including the Cochrane Central Register of Controlled Trials, Embase, MEDLINE via PubMed, the Latin American and Caribbean Health Sciences Literature database (LILACS), and the Brazilian Thesis Databank was performed. Inclusion criteria for studies were: (a) economic evaluation or cost-of-illness studies; (b) conducted in the LAC region; (c) assess economic burden of rotavirus disease or the economic impact of rotavirus vaccination programs. Two authors independently screened the studies for eligibility.

**Results** Of 444 studies initially retrieved, 21 met the eligibility criteria and were included (14 cost-effectiveness analyses of vaccination programs and 7 cost-of-illness studies). Direct medical costs were assessed in all 21 studies, but only 10 also investigated indirect and non-medical direct costs. The most commonly observed methods for cost estimation were retrospective database analysis and hospital-based surveillance study. Only one study was a household-based survey. A wide cost range was identified (e.g., inpatient care US$79.91 to US$858.40 and outpatient care US$13.06 to US$64.10), depending on the methods, study perspective, and type of costs included.

**Conclusion** Rotavirus-associated costs were assessed in 21 studies across the Latin America and Caribbean region. The majority of studies were made alongside economic evaluations of vaccination programs. Methods are broadly different among studies but administrative databases seem to be the most employed source of data.

16. **Screening, prevention and treatment of cervical cancer—A global and regional generalized cost-effectiveness analysis**

Volume 27, Issue 43, 9 October 2009, Pages 6060–6079

Gary Michael Ginsberg, Tessa Tan-Torres Edejer, Jeremy A. Lauer, Cecilia Sepulveda

**Keywords**

Cervical cancer; Cost-utility analysis; Screening; Vaccination

**Abstract**

The paper calculates regional generalized cost-effectiveness estimates of screening, prevention, treatment and combined interventions for cervical cancer.

Using standardised WHO-CHOICE methodology, a cervical cancer model was employed to provide estimates of screening, vaccination and treatment effectiveness. Intervention effectiveness was determined via a population state-transition model (PopMod) that simulates the evolution of a sub-regional population accounting for births, deaths and disease epidemiology. Economic costs of procedures and treatment were estimated, including programme overhead and training costs.
In regions characterized by high income, low mortality and high existing treatment coverage, the addition of any screening programme to the current high treatment levels is very cost-effective. However, based on projections of the future price per dose (representing the economic costs of the vaccination excluding monopolistic rents and vaccine development cost) vaccination is the most cost-effective intervention.

In regions characterized by low income, low mortality and existing treatment coverage around 50%, expanding treatment with or without combining it with screening appears to be cost-effective or very cost-effective. Abandoning treatment in favour of screening in a no-treatment scenario would not be cost-effective. Vaccination is usually the most cost-effective intervention. Penta or tri-annual PAP smears appear to be cost-effective, though when combined with HPV-DNA testing they are not cost-effective.

In regions characterized by low income, high mortality and low treatment levels, expanding treatment with or without adding screening would be very cost-effective. A one-off vaccination plus expanding treatment was usually very cost-effective. One-off PAP or VIA screening at age 40 are more cost-effective than other interventions though less effective overall.

From a cost-effectiveness perspective, consideration should be given to implementing vaccination (depending on cost per dose and longevity of efficacy) and screening programmes on a worldwide basis to reduce the burden of disease from cervical cancer. Treatment should also be increased where coverage is low.

17. **Benefits, cost requirements and cost-effectiveness of the HPV16,18 vaccine for cervical cancer prevention in developing countries: policy implications**


Sue J Goldie, Meredith O'Sea, Mireia Diaz, Sun-Young Kim

**Keywords**

cervical cancer; human papillomavirus vaccine; cost-effectiveness; priority setting; health policy and programmes

**Abstract**

Approximately 70% of cases of cervical cancer worldwide are caused by genotypes 16 and 18 of human papillomavirus (HPV), which is sexually transmitted. With the availability of an effective vaccine against these HPV types, there is real hope for reducing the global burden of cervical cancer in developing countries. Stakeholders faced with decisions about where to invest money to improve health must consider the burden of disease caused by cervical cancer relative to other priorities and the comparative benefits of different interventions. We conducted a series of analyses to obtain information for agencies drafting immunisation policy recommendations, financing coordination mechanisms, and country decision-makers on the benefits, cost requirements and cost-effectiveness of the HPV16,18 vaccine. We found that making an HPV16,18 vaccine accessible to 70% of young adolescent girls in 72 of the poorest countries, China, Thailand, and all of Latin America and the Caribbean, could prevent the future deaths of more than four million women vaccinated over the next decade. Provided the cost per vaccinated girl is less than $10–$25, adolescent HPV16,18 vaccination would be cost-effective even in relatively poor countries. Concerns about financial costs and affordability highlight the need for lowering vaccine prices, cost-efficient mechanisms for delivery of vaccinations to
adolescents, and creative sources of financing.

18. The decision making process on new vaccines introduction in South Africa

Vaccine, Volume 30, Supplement 3, 7 September 2012, Pages C9–C13

Ntombenhle Judith Ngcobo, Neil A. Cameron

Keywords

New vaccines; Introduction; Decision making; Cost-effectiveness; Immunisation policy

Abstract

South Africa has a functional decision making process for the introduction of new vaccines; with an established National Immunisation Technical Advisory Group (NITAG), referred to as National Advisory Group on Immunisation (NAGI). South Africa has played a leadership role in the African continent with introduction of new vaccines, which dates back to 1995 with the introduction of hepatitis B, followed by the Haemophilus influenzae type b in 1999 and recently the national roll out of the pneumococcal conjugate and rotavirus vaccines in 2009.

NAGI has the responsibility to deliberate on key policy issues as part of the process for decision making on the introduction of new vaccines. In developing recommendations NAGI considers: disease burden, cost effectiveness, and the impact on the Expanded Programme on Immunisation (EPI). Although guidance and recommendations from WHO are considered, the decision to introduce a new vaccine in South Africa is based on local data. NAGI recommendations are presented to the National Department of Health (NDOH). The NDOH pursues the matter further through the involvement of provinces. When an agreement has been reached to accept the NAGI recommendations, the NDOH seeks funding from the Ministry of Finance (MOF). Once funds are available, the new vaccines are implemented by the immunisation programme.

Although there is an established functional system for decision making in South Africa, some areas need to be addressed. A system should be developed to allow the NDOH, NAGI and the MOF to engage in the deliberations on financial and economic impact of new vaccines. It is further recommended that a committee be established that will assess the programmatic issues to weigh the potential benefits of a new vaccine. Furthermore, political commitment should support the immunisation programme and strengthen it so that it can make an impact in the achievement of the Millennium Development Goal no. 4 of reducing child mortality.


Stahl HC, Butenschoen VM, Tran HT, Gozzer E, Skewes R, Mahendradhata Y, Runge-Ranzinger S, Kroeger A, Farlow A.

Keywords
Dengue outbreaks; Dengue surveillance; Cost of dengue outbreaks

Abstract

Background Dengue disease surveillance and vector surveillance are presumed to detect dengue outbreaks at an early stage and to save – through early response activities – resources, and reduce the social and economic impact of outbreaks on individuals, health systems and economies. The aim of this study is to unveil evidence on the cost of dengue outbreaks.

Methods Economic evidence on dengue outbreaks was gathered by conducting a literature review and collecting information on the costs of recent dengue outbreaks in 4 countries: Peru, Dominican Republic, Vietnam, and Indonesia. The literature review distinguished between costs of dengue illness including cost of dengue outbreaks, cost of interventions and cost-effectiveness of interventions.

Results Seventeen publications on cost of dengue showed a large range of costs from 0.2 Million US$ in Venezuela to 135.2 Million US$ in Brazil. However, these figures were not standardized to make them comparable. Furthermore, dengue outbreak costs are calculated differently across the publications, and cost of dengue illness is used interchangeably with cost of dengue outbreaks. Only one paper from Australia analysed the resources saved through active dengue surveillance. Costs of vector control interventions have been reported in 4 studies, indicating that the costs of such interventions are lower than those of actual outbreaks. Nine papers focused on the cost-effectiveness of dengue vaccines or dengue vector control; they do not provide any direct information on cost of dengue outbreaks, but their modelling methodologies could guide future research on cost-effectiveness of national surveillance systems.

The country case studies – conducted in very different geographic and health system settings - unveiled rough estimates for 2011 outbreak costs of: 12 million US$ in Vietnam, 6.75 million US$ in Indonesia, 4.5 million US$ in Peru and 2.8 million US$ in Dominican Republic (all in 2012 US$). The proportions of the different cost components (vector control; surveillance; information, education and communication; direct medical and indirect costs), as percentage of total costs, differed across the respective countries. Resources used for dengue disease control and treatment were country specific.

Conclusions The evidence so far collected, further confirms the methodological challenges in this field: 1) to define technically dengue outbreaks (what do we measure?) and 2) to measure accurately the costs in prospective field studies (how do we measure?). Currently, consensus on the technical definition of an outbreak is sought through the International Research Consortium on Dengue Risk Assessment, Management and Surveillance (IDAMS). Best practice guidelines should be further developed, also to improve the quality and comparability of cost study findings. Modelling the costs of dengue outbreaks and validating these models through field studies should guide further research.

20. The role of health economic analyses in vaccine decision making.


Black S.

Keywords

Cost-effectiveness; Vaccine policy
Abstract

Beginning in the 20th century with the consideration of the seven-valent pneumococcal conjugate vaccine in the US, the cost effectiveness became a topic of discussion when this vaccine was being considered for universal use by the US Advisory Committee on Immunization practices (ACIP). In 2008, the ACIP began using formal criteria for the presentation of such data and their inclusion in ACIP discussions. More recently, the US Institute of Medicine has recommended that health economic considerations play a primary role in the prioritization of future vaccine for development. However, such analyses can be biased towards vaccines that provide economic benefit rather than those that reduce severe morbidity and mortality. This is because the economic impact of minor common events that result in medical utilization or time lost from work for parents can outweigh the economic impact of severe morbidity and mortality. Thus diseases with a low mortality and morbidity but with a common clinical manifestation such as the common cold could be prioritized over vaccines against diseases such as meningococcal sepsis where the morbidity and mortality associated with each case is very high, but there is no associated common clinical syndrome. Thus the use of cost effectiveness analyses as a ‘gating criteria’ to decide which vaccines should be developed or routinely used runs the risk of transforming vaccines into primarily a tool for achieving cost savings within the health care system rather than a public health intervention targeting human suffering, death and disability. It is the purpose of this article to review the framework under which health economic evaluations can be undertaken, to review the experience with and reliability of such analyses, and to discuss the potential negative implications of the use of health economic analyses as a primary decision making tool.


Hum Vaccin Immuno. 2014 Jul 7;10(11).

Geynisman DM, Chien CR, Smieliauskas F, Shen C, Tina Shih YC.

Keywords

Cancer; cancer immunotherapy; cancer vaccines; cost; cost-effectiveness, economics; immunotherapy; monoclonal antibodies

Abstract

Background Cancer immunotherapy is a rapidly growing field in oncology. One attractive feature of cancer immunotherapy is the purported combination of minimal toxicity and durable responses. However such treatments are often very expensive. Given the wide-spread concern over rising health care costs, it is important for all stakeholders to be well-informed on the cost and cost-effectiveness of cancer immunotherapies. Methods We performed a comprehensive literature review of cost and cost-effectiveness research on therapeutic cancer vaccines and monoclonal antibodies, to better understand the economic impacts of these treatments. We summarized our literature searches into three tables by types of papers: systematic review of economic studies of a specific agent, cost and cost-effectiveness analysis. Results Our review showed that out of the 16 immunotherapy agents approved, nine had relevant published economic studies. Five out of the nine studied immunotherapy agents had been covered in systematic reviews. Among those, only one (rituximab for non-Hodgkin lymphoma) was found to be cost-effective. Of the four immunotherapy drugs not covered in systematic reviews
(alemtuzumab, ipilimumab, sipuleucel-T, ofatumumab), high incremental cost-effectiveness ratio (ICER) was reported for each. Conclusion Many immunotherapies have not had economic evaluations, and those that have been studied show high ICERs or frank lack of cost-effectiveness. One major hurdle in improving the cost-effectiveness of cancer immunotherapies is to identify predictive biomarkers for selecting appropriate patients as recipients of these expensive therapies. We discuss the implications surrounding the economic factors involved in cancer immunotherapies and suggest that further research on cost and cost-effectiveness of newer cancer vaccines and immunotherapies are warranted as this is a rapidly growing field with many new drugs on the horizon.

22. **EPIVAC International Conference on Financial Sustainability of Immunization Programs in sub-Saharan Africa, February 16-18, 2012, Ouidah, Benin.**


Drach M, Le Gargasson JB, Mathonnat J, Da Silva A, Kaddar M, Colombini A.

**Keywords**

Africa; Budgetary burden; Financial sustainability; Financing paradigms; Immunization programs

**Abstract**

The introduction of new vaccines with much higher prices than traditional vaccines results in increasing budgetary pressure on immunization programs in GAVI-eligible countries, increasing the need to ensure their financial sustainability. In this context, the third EPIVAC (Epidemiology and Vaccinology) technical conference was held from February 16 to 18, 2012 at the Regional Institute of Public Health in Ouidah, Benin. Managers of ministries of health and finance from 11 West African countries (GAVI eligible countries), as well as former EPIVAC students and European experts, shared their knowledge and best practices on immunization financing at district and country level. The conference concluded by stressing five major priorities for the financial sustainability of national immunization programs (NIPs) in GAVI-eligible countries. - Strengthen public financing by increasing resources and fiscal space, improving budget processes, increasing contribution of local governments and strengthen efficiency of budget spending. - Promote equitable community financing which was recognized as a significant and essential contribution to the continuity of EPI operations. - Widen private funding by exploring prospects offered by sponsorship through foundations dedicated to immunization and by corporate social responsibility programs. - Contain the potential crowding-out effect of GAVI co-financing and ensure that decisions on new vaccine introductions are evidence-based. - Seek out innovative financing mechanisms such as taxes on food products or a national solidarity fund.

23. **Systematic review of studies evaluating the broader economic impact of vaccination in low and middle income countries.**


Deogaonkar R, Hutubessy R, van der Putten I, Evers S, Jit M.

**Abstract**
**Background** Most health economic evaluations of childhood vaccination only capture the health and short-term economic benefits. Measuring broader, long-term effects of vaccination on productivity and externalities could provide a more complete picture of the value of vaccines.

**Method** MEDLINE, EconLit and NHS-EED databases were searched for articles published between January 1990 and July 2011, which captured broader economic benefits of vaccines in low and middle income countries. Studies were included if they captured at least one of the following categories on broader economic impact: outcome-related productivity gains, behaviour-related productivity gains, ecological externalities, equity gains, financial sustainability gains or macroeconomic benefits.

**Results** Twenty-six relevant studies were found, including observational studies, economic models and contingent valuation studies. Of the identified broader impacts, outcome-related productivity gains and ecological externalities were most commonly accounted for. No studies captured behaviour-related productivity gains or macroeconomic effects. There was some evidence to show that vaccinated children 8-14 years of age benefit from increased cognitive ability. Productivity loss due to morbidity and mortality was generally measured using the human capital approach. When included, herd immunity effects were functions of coverage rates or based on reduction in disease outcomes. External effects of vaccines were observed in terms of equitable health outcomes and contribution towards synergistic and financially sustainable healthcare programs.

**Conclusion** Despite substantial variation in the methods of measurement and outcomes used, the inclusion of broader economic impact was found to improve the attractiveness of vaccination. Further research is needed on how different tools and techniques can be used in combination to capture the broader impact of vaccination in a way that is consistent with other health economic evaluations. In addition, more country level evidence is needed from low and middle income countries to justify future investments in vaccines and immunization programs. Finally, the proposed broader economic impact framework may contribute towards better communication of the economic arguments surrounding vaccine uptake, leading to investments in immunization by stakeholders outside of the traditional health care sector such as ministries of finance and national treasuries.

24. **Health and economic impact of rotavirus vaccination in GAVI-eligible countries.**


Kim SY1, Sweet S, Slichter D, Goldie SJ.

**Abstract**

**Background** Rotavirus infection is responsible for about 500,000 deaths annually, and the disease burden is disproportionately borne by children in low-income countries. Recently the World Health Organization (WHO) has released a global recommendation that all countries include infant rotavirus vaccination in their national immunization programs. Our objective was to provide information on the expected health, economic and financial consequences of rotavirus vaccines in the 72 GAVI support-eligible countries.

**Methods** We synthesized population-level data from various sources (primarily from global-level
databases) for the 72 countries eligible for the support by the GAVI Alliance (GAVI-eligible countries) in order to estimate the health and economic impact associated with rotavirus vaccination programs. The primary outcome measure was incremental cost (in 2005 international dollars [I$]) per disability-adjusted life year (DALY) averted. We also projected the expected reduction in rotavirus disease burden and financial resources required associated with a variety of scale-up scenarios.

**Results** Under the base-case assumptions (70% coverage), vaccinating one single birth cohort would prevent about 55% of rotavirus associated deaths in the 72 GAVI-eligible countries. Assuming I$25 per vaccinated child (approximately $5 per dose), the number of countries with the incremental cost per DALY averted less than I$200 was 47. Using the WHO's cost-effectiveness threshold based on per capita GDP, the vaccines were considered cost-effective in 68 of the 72 countries (approximately 94%). A 10-year routine rotavirus vaccination would prevent 0.9-2.8 million rotavirus associated deaths among children under age 5 in the poorest parts of the world, depending on vaccine scale-up scenarios. Over the same intervention period, rotavirus vaccination programs would also prevent 4.5-13.3 million estimated cases of hospitalization and 41-107 million cases of outpatient clinic visits in the same population.

**Conclusions** Our findings suggest that rotavirus vaccination would be considered a worthwhile investment for improving general development as well as childhood health level in most low-income countries, with a favourable cost-effectiveness profile even under a vaccine price ($1.5-$5.0 per dose) higher than those of traditional childhood vaccines.

25. **The decision to vaccinate a child: an economic perspective from southern Malawi.**


Holte JH, Mæstad O, Jani JV.

**Abstract**

The dynamics of childhood vaccination uptake in developing countries are unclear. Numerous studies document the relationship between vaccination coverage and access, socio economic and demographic factors. However, there is less knowledge about the relationship between vaccination coverage and carers’ motivation and willingness to seek childhood vaccinations. The aim of this paper is to introduce a framework for studying demand for childhood vaccination and to examine the coherence between theoretical predictions and empirical findings in a rural area in Malawi. We interviewed 635 carers with children aged 18-59 months. About 96 percent of the respondents reported to have fully vaccinated their youngest eligible child for all routine vaccinations scheduled in the Expanded Program on Immunization. This paper concludes that easy access to vaccination services cannot explain why demand is high. Many carers had to travel long distances to reach vaccination delivery points and a considerable share of the respondents scored waiting and travelling time as long. Results from the present study, in combination with theoretical predictions, suggest that a high level of trust in distributors of information and vaccines may be an essential explanatory factor for why carers seek immunization for their children, even in the presence of considerable costs. Trust may be an
important explanatory factor as it can be seen to generate positive perceived benefits.

26. **Systematic review of economic evaluations of preparedness strategies and interventions against influenza pandemics.**


**Abstract**

**Background** Although public health guidelines have implications for resource allocation, these issues were not explicitly considered in previous WHO pandemic preparedness and response guidance. In order to ensure a thorough and informed revision of this guidance following the H1N1 2009 pandemic, a systematic review of published and unpublished economic evaluations of preparedness strategies and interventions against influenza pandemics was conducted.

**Methods** The search was performed in September 2011 using 10 electronic databases, 2 internet search engines, reference list screening, cited reference searching, and direct communication with relevant authors. Full and partial economic evaluations considering both costs and outcomes were included. Conversely, reviews, editorials, and studies on economic impact or complications were excluded. Studies were selected by 2 independent reviewers.

**Results** 44 studies were included. Although most complied with the cost effectiveness guidelines, the quality of evidence was limited. However, the data sources used were of higher quality in economic evaluations conducted after the 2009 H1N1 pandemic. Vaccination and drug regimens were varied. Pharmaceutical plus non-pharmaceutical interventions are relatively cost effective in comparison to vaccines and/or antivirals alone. Pharmaceutical interventions vary from cost saving to high cost effectiveness ratios. According to ceiling thresholds (Gross National Income per capita), the reduction of non-essential contacts and the use of pharmaceutical prophylaxis plus the closure of schools are amongst the cost effective strategies for all countries. However, quarantine for household contacts is not cost effective even for low and middle income countries.

**Conclusion** The available evidence is generally inconclusive regarding the cost effectiveness of preparedness strategies and interventions against influenza pandemics. Studies on their effectiveness and cost effectiveness should be readily implemented in forthcoming events that also involve the developing world. Guidelines for assessing the impact of disease and interventions should be drawn up to facilitate these studies.

27. **Benefits of catch-up in vaccination against human papillomavirus in medium- and low-income countries.**


Baussano I, Lazzarato F, Ronco G, Dillner J, Franceschi S.

**Abstract**
Human papillomavirus (HPV) vaccination of a birth cohort of girls in the 9-13 age range is recommended as a priority, but decreases in HPV vaccine cost may make catch-up of a few additional cohorts more attractive not only in high-income countries. We assessed the reduction in HPV16 and 18 infections that could be achieved in a medium- (Poland) and a low-income (Guinea) country by adding one-time catch-up of 12- to 19-year-old girls to the vaccination of 11-year-old girls. According to our ad hoc adapted dynamic model of HPV infection transmission, the addition of catch-up was estimated to bring forward the 50% reduction of HPV16/18 prevalence due to vaccination in women \( \leq 35 \) by as much as 5 years. Catch-up of 12- to 15-year olds reduced the cumulative probability of HPV16/18 infections by age 35 in the relevant cohorts by about 30% in both countries. Catch-up of 16- to 19-year-old girls added little. Regardless of the chosen catch-up strategy, 16 to 20% of HPV16/18 prevention from vaccination was attributable to herd immunity. Assuming a sufficiently low vaccine cost, the addition of a catch-up round is, therefore, worth considering in medium/low-income countries to extend vaccine benefits to less young adolescent girls whose future access to cervical screening is uncertain.

28. **Projected health and economic impact of rotavirus vaccination in GAVI-eligible countries: 2011-2030.**


Atherly DE, Lewis KD, Tate J, Parashar UD, Rheingans RD.

**Keywords**

Rotavirus vaccines; Cost-effectiveness; Health impact

**Abstract**

Rotavirus is the leading cause of diarrheal disease in children under 5 years of age. It is responsible for more than 450,000 deaths each year, with more than 90% of these deaths occurring in low-resource countries eligible for support by the GAVI Alliance. Significant efforts made by the Alliance and its partners are providing countries with the opportunity to introduce rotavirus vaccines into their national immunization programs, to help prevent childhood illness and death. We projected the cost-effectiveness and health impact of rotavirus vaccines in GAVI-eligible countries, to assist decision makers in prioritizing resources to achieve the greatest health benefits for their populations. A decision-analytic model was used to project the health outcomes and direct costs of a birth cohort in the target population, with and without a rotavirus vaccine. Current data on disease burden, vaccine efficacy, immunization rates, and costs were used in the model. Vaccination in GAVI-eligible countries would prevent 2.46 million childhood deaths and 83 million disability-adjusted life years (DALYs) from 2011 to 2030, with annual reductions of 180,000 childhood deaths at peak vaccine uptake. The cost per DALY averted is $42 for all GAVI countries combined, over the entire period. Rotavirus vaccination would be considered very cost-effective for the entire cohort of GAVI countries, and in each country individually, as cost-effectiveness ratios are less than the gross domestic product (GDP) per capita. Vaccination is most cost-effective and has the greatest impact in regions with high rotavirus mortality. Rotavirus vaccination in GAVI-eligible countries is very cost-effective and is projected to substantially reduce childhood mortality in this population.

29. **Health economics of rotavirus immunization in Vietnam: potentials for favorable cost-**

**effectiveness in developing countries.**


Tu HA, Rozenbaum MH, Coyte PC, Li SC, Woerdenbag HJ, Postma MJ.

**Abstract**

**Introduction** Rotavirus is the most common cause of severe diarrhoea worldwide. Vietnam is situated in the region of high rotavirus infection incidence and eligible for financial support to introduce rotavirus vaccines into the Expanded Program of Immunization (EPI) from the GAVI. This study was designed to assess the cost-effectiveness of rotavirus immunization in Vietnam, explicitly the use of Rotateq® and to assess the affordability of implementing universal rotavirus immunization based on GAVI-subsidized vaccine price in the context of Vietnamese healthcare system for the next 5 years.

**Methodology** An age-structured cohort model was developed for the 2009 birth cohort in Vietnam. Two strategies were compared: one being the current situation without vaccination, and the other being mass universal rotavirus vaccination. The time horizon of the model was 5 years with time cycles of 1 month for children less than 1 year of age and annual analysis thereafter. Outcomes included mild, moderate, severe cases and death. Multiple outcomes per rotavirus infection are possible in the model. Monte Carlo simulations were used to examine the acceptability and affordability of the rotavirus vaccination. All costs were expressed in 2009 US$.

**Results** Rotavirus vaccination would not completely protect young children against rotavirus infection due to partial nature of vaccine immunity, however, would effectively reduce severe cases of rotavirus by roughly 55% during the first 5 years of life. Under GAVI-subsidized vaccine price (US$ 0.3/dose), the vaccine cost would amount to US$ 5.5 million per annum for 3-dose of the Rotateq® vaccine. In the base-case, the incremental cost per quality-adjusted-life-year (QALY) was US$ 665 from the health system perspective, much lower than per-capita GDP of ~US$ 1150 in 2009. Affordability results showed that at the GAVI-subsidized vaccine price, rotavirus vaccination could be affordable for Vietnamese health system.

**Conclusion** Rotavirus vaccination in Vietnam would be a cost-effective health intervention. Vaccination only becomes affordable if the country receives GAVI’s financial support due to the current high market vaccine price. Given the high mortality rate of under-five-year children, the results showed that rotavirus immunization is the "best hope" for prevention of rotavirus-related diarrhoeal disease in Vietnam. In the next five years, Vietnam is definitely in debt to financial support from international organizations in implementing rotavirus immunization. It is recommended that new rotavirus vaccine candidates be developed at cheaper price to speed up the introduction of rotavirus immunization in the developing world in general.

30. **Comparative review of three cost-effectiveness models for rotavirus vaccines in national immunization programs; a generic approach applied to various regions in the world.**


Postma MJ, Jit M, Rozenbaum MH, Standaert B, Tu HA, Hutubessy RC.

**Abstract**
**Background** This study aims to critically review available cost-effectiveness models for rotavirus vaccination, compare their designs using a standardized approach and compare similarities and differences in cost-effectiveness outcomes using a uniform set of input parameters.

**Methods** We identified various models used to estimate the cost-effectiveness of rotavirus vaccination. From these, results using a standardized dataset for four regions in the world could be obtained for three specific applications.

**Results** Despite differences in the approaches and individual constituting elements including costs, QALYs Quality Adjusted Life Years and deaths, cost-effectiveness results of the models were quite similar. Differences between the models on the individual components of cost-effectiveness could be related to some specific features of the respective models. Sensitivity analysis revealed that cost-effectiveness of rotavirus vaccination is highly sensitive to vaccine prices, rotavirus-associated mortality and discount rates, in particular that for QALYs.

**Conclusions** The comparative approach followed here is helpful in understanding the various models selected and will thus benefit (low-income) countries in designing their own cost-effectiveness analyses using new or adapted existing models. Potential users of the models in low and middle income countries need to consider results from existing studies and reviews. There will be a need for contextualization including the use of country specific data inputs. However, given that the underlying biological and epidemiological mechanisms do not change between countries, users are likely to be able to adapt existing model designs rather than developing completely new approaches. Also, the communication established between the individual researchers involved in the three models is helpful in the further development of these individual models. Therefore, we recommend that this kind of comparative study be extended to other areas of vaccination and even other infectious disease interventions.

**31. Using cost-effectiveness analysis to support research and development portfolio prioritization for product innovations in measles vaccination.**


Garrison LP Jr, Bauch CT, Bresnahan BW, Hazlet TK, Kadiyala S, Veenstra DL

**Abstract**

**Background** Several potential measles vaccine innovations are in development to address the shortcomings of the current vaccine. Funders need to prioritize their scarce research and development resources. This article demonstrates the usefulness of cost-effectiveness analysis to support these decisions.

**Methods** This study had 4 major components: (1) identifying potential innovations, (2) developing transmission models to assess mortality and morbidity impacts, (3) estimating the unit cost impacts, and (4) assessing aggregate cost-effectiveness in United Nations Children’s Fund countries through 2049.

**Results** Four promising technologies were evaluated: aerosol delivery, needle-free injection, inhalable dry powder, and early administration DNA vaccine. They are projected to have a small absolute impact in terms of reducing the number of measles cases in most scenarios because of already improving vaccine coverage. Three are projected to reduce unit cost per dose by $0.024 to $0.170 and would improve overall cost-effectiveness. Each will require additional investments to reach the market. Over the next 40 years, the aggregate cost savings could be substantial,
ranging from $98.4 million to $689.4 million.

Conclusions Cost-effectiveness analysis can help to inform research and development portfolio prioritization decisions. Three new measles vaccination technologies under development hold promise to be cost-saving from a global perspective over the long-term, even after considering additional investment costs.

32. Rotavirus vaccination: cost-effectiveness and impact on child mortality in developing countries.

Atherly D, Dreibelbis R, Parashar UD, Levin C, Wecker J, Rheingans RD.

Abstract

Background Rotavirus is the leading cause of severe gastroenteritis in children <5 years of age and is responsible for >500,000 deaths annually; approximately 85% of this burden is in low-income countries eligible for financial support from the GAVI Alliance. We projected the uptake, health impact, and cost-effectiveness of introducing rotavirus vaccination in GAVI-eligible countries to help policy makers in prioritizing resources to gain the greatest health improvements for their constituencies.

Methods A demand forecast model was used to predict adoption of rotavirus vaccine in the poorest countries in the world. We then modeled health outcomes and direct costs of a hypothetical birth cohort in the target population for scenarios with and without a rotavirus vaccine with use of data on health outcomes of rotavirus infection, vaccine effectiveness, and immunization rates.

Results Vaccination would prevent 2.4 million rotavirus deaths and >82 million disability-adjusted life-years (DALYs) in 64 of the 72 GAVI-eligible countries introducing vaccine from 2007 through 2025. The cost per DALY averted decreases over time, from a high of US$450 per DALY averted in the first year to a sustained low of $30 per DALY during 2017-2025, with a cumulative figure of $43 per DALY averted during 2008-2025. By applying the baseline scenario with an initial vaccine price of $7 per dose for a 2-dose vaccine, with a gradual decrease beginning in 2012 and stabilizing at $1.25 per dose by 2017, vaccination was very cost-effective in all GAVI-eligible countries with use of each country’s gross domestic product per DALY averted as a threshold.

Conclusions Introduction of rotavirus vaccines into the world’s poorest countries is very cost-effective and is projected to substantially reduce childhood mortality.

33. Economic issues in vaccination against highly pathogenic avian influenza in developing countries.

McLeod A, Rushton J, Riviere-Cinnamond A, Brandenburg B, Hinrichs J, Loth L.

Abstract
We consider the use of vaccination against highly pathogenic avian influenza (HPAI) in three contexts: as part of a stamping-out programme, as a government-led action for disease prevention and as private insurance by farmers. Poultry systems in developing countries cover all four of the poultry sectors defined by FAO and the OIE, each with particular economic aspects that might motivate farmers to take part in vaccination programmes or to initiate and finance them. Outbreaks in flocks of different types have different potential impacts in terms of disease spread and economic effects, which influence the potential benefits of vaccination as a means to prevent or control outbreaks. We use data from three countries to illustrate the costs of vaccination and discuss measures of cost-effectiveness and ways to improve it. We also consider the question of funding sources and their impact on the sustainability of vaccination programmes.

34. **Economics of polio vaccination in the post-eradication era: should OPV-using countries adopt IPV?**


Khan MM.

**Keywords**

Post-certification era; Polio immunisation; Vaccination costs

**Abstract**

The continued use of oral polio vaccine (OPV) poses a threat to polio virus eradication. Stopping all polio vaccination in the post-certification era is no longer considered to be a practical option. Policy makers agree that OPV use must stop immediately after certification. Therefore, the pragmatic alternative is for the OPV-using countries to switch to IPV. This study estimates the cost of switching to IPV, and the cost-effectiveness of this switch. Using data on the number of polio cases and the number of unvaccinated children in different countries of the world, the risks of polio and polio outbreaks have been calculated. The current cost of routine and intensive OPV immunisation is about US $2143 million in the 148 OPV-using countries. Routine use of IPV in these countries should cost US $1246 million. If the current costs of routine and intensive polio immunisation are considered, adopting IPV to replace OPV will not increase the total global cost. Even if the cost of intensive polio immunisation is ignored, cost-effectiveness ratio of adopting IPV remains less than the average GNI per capita of OPV-using countries. The incremental cost of adopting IPV to replace OPV is relatively low, about US $1 per child per year, and most countries should be able to afford this additional cost.

35. **Estimating the economic value to societies of the impact of health research: a critical review.**


Buxton M, Hanney S, Jones T.

**Keywords**

Health services research/economics; Cost-benefit analysis; Delivery of health care/economics; Cost savings; Longevity; Economic development; Review literature (source: MeSH, NLM).

**Abstract**
Estimating the economic value to societies of health research is a complex but essential step in establishing and justifying appropriate levels of investment in research. The practical difficulties encountered include: identifying and valuing the relevant research inputs (when many pieces of research may contribute to a clinical advance); accurately ascribing the impact of the research; and appropriately valuing the attributed economic impact. In this review, relevant studies identified from the literature were grouped into four categories on the basis of the methods used to value the benefits of research. The first category consists of studies that value the direct cost savings that could arise from research leading either to new, less-costly treatments or to developments such as vaccines that reduce the number of patients needing treatment. The second category comprises studies that consider the value to the economy of a healthy workforce. According to this "human capital" approach, indirect cost savings arise when better health leads to the avoidance of lost production. The third category includes studies that examine gains to the economy in terms of product development, consequent employment and sales. The studies placed in the fourth category measure the intrinsic value to society of the health gain, by placing a monetary value on a life. The review did not identify any consistency of methodology, but the fourth approach has most promise as a measure of social value. Many of the studies reviewed come from industrialized nations and a proposal is made by the present reviewers for an international initiative, covering developed and developing countries, to undertake further methodological analysis and testing.


Lu C, Michaud CM, Gakidou E, Khan K, Murray CJ.

Abstract

Background The Global Alliance for Vaccines and Immunisation (GAVI) was created in 1999 to enable even the poorest countries to provide vaccines to all children. We aimed to assess the effect of GAVI on combined diphtheria, tetanus, and pertussis vaccine (DTP3) coverage.

Methods We examined the relation between DTP3 coverage for GAVI recipient countries from 1995 to 2004 and immunisation services support (ISS) and non-ISS expenditure per surviving child, controlling for income per head and local political governance variables. We analysed DTP3 coverage reported by governments and estimated by WHO/UNICEF. We also investigated the effect of GAVI on country reporting behaviour.

Results In countries with DTP3 coverage of 65% or less at baseline, ISS spending per surviving child had a significant positive effect on DTP3 coverage \( (p=0.0005) \). This effect was not present in countries with DTP3 coverage of 65-80% or 80% or more at baseline. If ISS expenditure only is assessed, the estimated cost per additional child immunised in countries with baseline coverage of 65% or less is US$14 and if ISS and non-ISS expenditures are included the cost per child is almost $20.

Interpretation The success of ISS funding in countries with baseline DTP3 coverage of 65% or less provides evidence that a public-private partnership can work to reverse a negative trend in global health and that performance-related disbursement can work in some settings. Because ISS funding seems to have no effect in countries with baseline coverage greater than 65%, GAVI should consider redistributing its resources to countries with the lowest coverage.
37. Impact of BRICS’ investment in vaccine development on the global vaccine market.


Kaddar M, Milstien J, Schmitt S.

Abstract

Brazil, the Russian Federation, India, China and South Africa – the countries known as BRICS – have made considerable progress in vaccine production, regulation and development over the past 20 years. In 1993, all five countries were producing vaccines but the processes used were outdated and non-standardized, there was little relevant research and there was negligible international recognition of the products. By 2014, all five countries had strong initiatives for the development of vaccine technology and had greatly improved their national regulatory capacity. South Africa was then the only BRICS country that was not completely producing vaccines. South Africa is now in the process of re-establishing its own vaccine production and passing beyond the stage of simply importing, formulating and filling vaccine bulks. Changes in the public sector’s price per dose of selected vaccines, the global market share represented by products from specific manufacturers, and the attractiveness, for multinational companies, of partnership and investment opportunities in BRICS companies have all been analysed. The results indicate that the BRICS countries have had a major impact on vaccine price and availability, with much of that impact attributable to the output of Indian vaccine manufacturers. China is expected to have a greater impact soon, given the anticipated development of Chinese vaccine manufacturers in the near future. BRICS’ accomplishments in the field of vaccine development are expected to reshape the global vaccine market and accelerate access to vaccines in the developing world. The challenge is to turn these expectations into strategic actions and practical outcomes.

38. New vaccine adoption in lower-middle-income countries.


Makinen M, Kaddar M, Molldrem V, Wilson L.

Abstract

Objectives Lower-middle-income countries (LMICs) are lagging behind both high-income and low-income countries in new vaccine adoption. Our study involved the following objectives: (1) understand the decision-making processes of LMICs on new vaccine adoption, (2) identify the factors influencing LMIC decisions, (3) obtain the views of vaccine manufacturers about LMIC markets for new vaccines, and (4) make recommendations concerning how to speed up and improve decision making, including proposing mechanisms for implementation of the recommendations.

Methods Collect and analyse qualitative data from participants in decision making in 15 case study countries [12 LMICs and three upper-middle-income countries (UMICs)] and
multinational and developing country vaccine manufacturers.

Findings Interviews of actors in decision making indicate that the aspects deemed most important for adoption are: World Health Organization (WHO) recommendations, the existence of local epidemiological data and a set of factors comprising affordability, cost-effectiveness and overall cost of the new vaccine for the programme. National Immunization Technical Advisory Groups (NITAG) have a key role in advising decision-makers, although their resources and capacity vary.

Country decision-makers and manufacturers both see advantages in pooled procurement mechanisms for vaccine purchasing. Recommendations for countries and the international community involve assisting with making epidemiological data and vaccine market information accessible to countries, building and reinforcing related analysis capacity, and assisting with purchasing mechanisms and practices such as pooled procurement.

39. Role of the private sector in the provision of immunization services in low- and middle-income countries.


Levin A, Kaddar M.

Abstract

The authors conducted a literature review on the role of the private sector in low- and middle-income countries. The review indicated that relatively few studies have researched the role of the private sector in immunization service delivery in these countries. The studies suggest that the private sector is playing different roles and functions according to economic development levels, the governance structure and the general presence of the private sector in the health sector. In some countries, generally low-income countries, the private for-profit sector is contributing to immunization service delivery and helping to improve access to traditional EPI vaccines. In other countries, particularly middle-income countries, the private for-profit sector often acts to facilitate early adoption of new vaccines and technologies before introduction and generalization by the public sector.

The not-for-profit sector plays an important role in extending access to traditional EPI vaccines, particularly in low-income countries. Not-for-profit facilities are situated in rural as well as urban areas and are more likely to be coordinated with public services than the private for-profit sector. Although numerous studies on non-governmental organizations (NGOs) suggest that the extent of NGO provision of immunization services in low- and middle-income countries is substantial, the contribution of this sector is poorly documented, leading to a lack of recognition of its role at national and global levels.

Studies on quality of immunization service provision at private health facilities suggest that it is sometimes inadequate and needs to be monitored. Although some articles on public–private collaboration exist, little was found on the extent to which governments are effectively interacting with and regulating the private sector.

The review revealed many geographical and thematic gaps in the literature on the role and regulation of the private sector in the delivery of immunization services in low- and middle-income countries.
Changes in population health status are known to influence government fiscal transfers both in terms of lost tax revenue and increased expenditure for health and social services. To estimate the fiscal impact of changes in morbidity and mortality attributed to rotavirus immunisation, we developed a government perspective model to estimate discounted net tax revenue for Ghana and Vietnam. The model derived the impact of rotavirus morbidity and mortality on lifetime productive capacity and related tax transfers, and demand for government transfers in relation to education and healthcare in immunised and non-immunised cohorts. The discounted age-specific net tax revenue was derived by deducting transfers from gross taxes and discounting for time preference. In Ghana, taking into account immunisation costs, tax and transfers, the estimated net discounted tax for the immunised cohort was estimated to generate $2.6 billion in net taxes up to age 65. In Vietnam, the net revenue attributed to the immunised cohort reached $55.17 billion suggesting an incremental benefit of approximately $29 million. We posit that the government perspective fiscal framework described here is a valid approach for estimating how governments benefit from investments in immunisation that can be considered supplementary to conventional cost-effectiveness approaches for defining value.