Center for Vaccine Ethics and Policy
Symposium - Intended Consequences: ACIP and Vaccine Recommendations in the Healthcare Reform Era
19 January 2011
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Bibliography: Vaccines and Economic Evaluation – QALYs, CEAs and more….
January 2011

This bibliography was generated from the continuing *Vaccines: The Week in Review* from entries over the last 2-3 years http://centerforvaccineethicsandpolicy.wordpress.com/ It is not exhaustive. David R. Curry david.r.curry@centerforvaccineethicsandpolicy.org

Overviews

New England Journal of Medicine
October 14, 2010 Vol. 363 No. 16
Perspectives
Legislating against Use of Cost-Effectiveness Information
P.J. Neumann, M.C. Weinstein [free full-text]

The Patient-Centered Outcomes Research Institute . . . shall not develop or employ a dollars per quality adjusted life year (or similar measure that discounts the value of a life because of an individual's disability) as a threshold to establish what type of health care is cost effective or recommended. The Secretary shall not utilize such an adjusted life year (or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under title XVIII.
— The Patient Protection and Affordable Care Act1

In 1996, after 2 years of deliberation, the U.S. Panel on Cost-Effectiveness in Health and Medicine, composed of physicians, health economists, ethicists, and other health policy experts, recommended that cost-effectiveness analyses should use quality-adjusted life-years (QALYs) as a standard metric for identifying and assigning value to health outcomes.2 The recently enacted Patient Protection and Affordable Care Act (ACA) created a Patient-Centered Outcomes Research Institute (PCORI) to conduct comparative-effectiveness research (CER) but prohibited

this institute from developing or using cost-per-QALY thresholds. The two events serve as revealing bookends to a long-standing debate over the role and shape of cost-effectiveness analysis in U.S. health care.

QALYs provide a convenient yardstick for measuring and comparing health effects of varied interventions across diverse diseases and conditions. They represent the effects of a health intervention in terms of the gains or losses in time spent in a series of "quality-weighted" health states. QALYs are used in cost-effectiveness analyses (termed "cost-utility analyses" when QALYs are included) to inform resource-allocation decisions: the cost-per-QALY ratios of different interventions are compared in order to determine the most efficient ways of furnishing health benefits. In contrast, other health outcomes are generally expressed in disease-specific terms, such as incidence of cardiovascular events, cancer progression, intensity of pain, or loss of function. Though useful for measuring the effects of particular treatments, these outcomes do not permit comparisons among diseases and conditions or between treatment and prevention.[3] Researchers have published thousands of cost-utility studies in leading medical and health policy journals. Health policymakers around the world have used such analyses to inform clinical guidelines and reimbursement decisions. The U.S. government, through agencies such as the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, and the National Institutes of Health, has sponsored cost-utility analyses. Medical specialty societies have cited cost-utility studies in support of clinical guidelines.

The ACA specifically forbids the use of cost per QALY "as a threshold." The precise intent and consequences of this language are unclear. One might interpret it to mean that the PCORI, or its contractors or grantees, can still calculate cost-per-QALY ratios as long as they are not compared with a threshold (e.g., $100,000 per QALY) or used to make a recommendation based on such a threshold. Comparisons of cost-per-QALY ratios across interventions could still be useful to decision makers even without the invocation of an explicit threshold. However, the ACA suggests a broader ban on the use of cost-utility analyses — and this could have a chilling effect on the field.

The ACA's language might be seen as symptomatic of the legislation's aversion to policies that critics might see as enacting "big-government" health care or "death panels." It may reflect a certain xenophobia toward the kinds of approaches used in Britain, where the National Institute of Health and Clinical Excellence makes recommendations about technologies and services on the basis of cost-per-QALY thresholds. Reflecting this sentiment, the ACA creates a new CER institute that it labels "patient-centered" and states that the findings of PCORI-sponsored research cannot be construed as mandates for practice guidelines, coverage recommendations, payment, or policy recommendations.

The ban on using cost-per-QALY thresholds also seems to reflect long-standing concerns that the approach would discriminate on the basis of age and disability. The worry is that the metric unfairly favors younger and healthier populations that have more potential QALYs to gain. To be sure, there are legitimate debates about the role of QALYs as the sole benchmark of health gains for purposes of allocating society's resources. However, acknowledging the measure's limitations, panels in the United States and Britain and at the World Health Organization have found QALYs preferable to alternative measures of health improvement. QALYs simply give priority to interventions that offer the most health benefit in terms of measures people care about — more time spent in good health. In fact, populations with more impairment typically fare better in cost-effectiveness analyses, because they have more to gain from interventions; for example, it is generally less cost-effective to screen or treat healthier persons than persons who have poorer health at baseline or who are at greater risk for complications.

Moreover, a ban on valuing life extension presents its own ethical dilemmas. Taken literally, it means that spending resources to extend by a month the life of a 100-year-old person who is in a vegetative state cannot be valued differently from spending resources to extend the life of a child by many healthy years. Though the ACA may be seeking to avert discrimination, it instead helps to perpetuate the current system of implicit rationing and hidden biases.

The antagonism toward cost-per-QALY comparisons also suggests a bit of magical thinking — the notion that the country can avoid the difficult trade-offs that cost-utility analysis helps to illuminate. It pretends that we can avert our eyes from such choices, and it kicks the can of cost-consciousness farther down the road. It represents another example of our country's avoidance of unpleasant truths about our resource constraints. Although opportunities undoubtedly exist to eliminate health care waste, the best way to improve health and save money at the same time is often to redirect patient care resources from interventions with a high cost per QALY to those with a lower cost per QALY.4 At a time when health care costs loom as the greatest challenge facing our country's fiscal well-being, legislating against the use of the standard metric in the field of cost-effectiveness analysis is regrettable.

The ACA states that the PCORI is intended to assist patients, clinicians, purchasers, and policymakers. Yet a ban on cost-utility analysis would leave decision makers with less information with which to compare the relative effects of interventions across diseases. The ACA states that PCORI-produced CER is intended to inform, not mandate, decisions. Why, then, be so prescriptive about costs per QALY? Better to simply develop and disseminate the information and let decision makers choose whether or not to use it and in what settings. Decision makers could consider cost-per-QALY ratios alongside other criteria, such as the priority of an intervention for vulnerable populations and concerns about equity and fairness. How can our market-driven health system work efficiently if participants lack information about the relationship between the costs and benefits of health interventions?

As the country searches for ways to curb health care spending, consideration of the cost-effectiveness of health interventions will unavoidably be part of the health care debate, alongside considerations of possible payment- and delivery-system reforms. The use of explicit, standard metrics such as cost-per-QALY ratios has the advantage of transparency and can help direct our resources toward the greatest health gains. These kinds of analyses will therefore endure as a rough benchmark of value and as a normative guide to resource-allocation decisions. It would be unfortunate if the ACA created a barrier to their development and use.

Source Information

From the Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center (P.J.N.), and the Department of Health Policy and Management, Harvard School of Public Health (M.C.W.) — both in Boston.

Vaccine
Volume 27, Issue 43, Pages 5921-6102 (9 October 2009)
http://www.sciencedirect.com/science/journal/0264410X

Review

Decision support in vaccination policies

Pages 5923-5928

B. Piso, C. Wild

Abstract

Background

Looking across boarders reveals that the national immunization programs of various countries

differ in their vaccination schedules and decisions regarding the implementation and funding of new vaccines. The aim of this review is to identify decision aids and crucial criteria for a rational decision-making process on vaccine introduction and to develop a theoretical framework for decision-making based on available literature.
Methods
Systematic literature search supplemented by hand-search.
Results
We identified five published decision aids for vaccine introduction and program planning in industrialized countries. Their comparison revealed an overall similarity with some differences in the approach as well as criteria. Burden of disease and vaccine characteristics play a key role in all decision aids, but authors vary in their views on the significance of cost-effectiveness analyses. Other relevant factors that should be considered before vaccine introduction are discussed to highly differing extents. These factors include the immunization program itself as well as its conformity with other programs, its feasibility, acceptability, and equity, as well as ethical, legal and political considerations. Assuming that the most comprehensive framework possible will not provide a feasible tool for decision-makers, we suggest a stepwise procedure.
Conclusions
Though even the best rational approach and most comprehensive evaluation is limited by remaining uncertainties, frameworks provide at least a structured approach to evaluate the various aspects of vaccine implementation decision-making. This process is essential in making consistently sound decisions and will facilitate the public's confidence in the decision and its realization.

Pharmacoeconomics. 29(1):35-49, January 1, 2011.
Calibrating Models in Economic Evaluation: A Seven-Step Approach
Vanni, Tazio; Karnon, Jonathan; Madan, Jason; White, Richard G.; Edmunds, W. John; Foss, Anna M.; Legood, Rosa
Abstract:
In economic evaluation, mathematical models have a central role as a way of integrating all the relevant information about a disease and health interventions, in order to estimate costs and consequences over an extended time horizon. Models are based on scientific knowledge of disease (which is likely to change over time), simplifying assumptions and input parameters with different levels of uncertainty; therefore, it is sensible to explore the consistency of model predictions with observational data. Calibration is a useful tool for estimating uncertain parameters, as well as more accurately defining model uncertainty (particularly with respect to the representation of correlations between parameters). Calibration involves the comparison of model outputs (e.g. disease prevalence rates) with empirical data, leading to the identification of model parameter values that achieve a good fit.
This article provides guidance on the theoretical underpinnings of different calibration methods. The calibration process is divided into seven steps and different potential methods at each step are discussed, focusing on the particular features of disease models in economic evaluation. The seven steps are (i) Which parameters should be varied in the calibration process? (ii) Which calibration targets should be used? (iii) What measure of goodness of fit should be used? (iv) What parameter search strategy should be used? (v) What determines acceptable goodness-of-fit parameter sets (convergence criteria)? (vi) What determines the termination of the calibration process (stopping rule)? (vii) How should the model calibration results and economic parameters be integrated?

The lack of standards in calibrating disease models in economic evaluation can undermine the credibility of calibration methods. In order to avoid the scepticism regarding calibration, we ought to unify the way we approach the problems and report the methods used, and continue to investigate different methods.

Rotavirus Vaccines

Clinical Infectious Diseases
http://www.journals.uchicago.edu/toc/cid/current

Projected Impact and Cost-Effectiveness of a Rotavirus Vaccination Program in India, 2008

Douglas H. Esposito, Jacqueline E. Tate, Gagandeep Kang and Umesh D. Parashar

Abstract

Background. To assess the value of rotavirus vaccination in India, we determined the potential impact and cost-effectiveness of a national rotavirus vaccination program.

Methods. We compared the national rotavirus disease and cost burden with and without a vaccination program and assessed the cost-effectiveness of vaccination. Model inputs included measures of disease and cost burden, vaccine performance, and vaccination coverage and cost. We measured the annual number of health-related events and treatment costs averted, as well as the cost-effectiveness in US dollars per disability-adjusted life-year (DALY) and cost per death averted. One-way sensitivity analyses were performed by individually varying each model input.

Results. With use of a vaccine that has an estimated effectiveness of 50%, a rotavirus vaccination program in India would prevent approx 44,000 deaths, 293,000 hospitalizations, and 328,000 outpatient visits annually, which would avert $20.6 million in medical treatment costs. Vaccination would be cost-saving at the GAVI Alliance price of $0.15 per dose. At $1.00 per dose, a vaccination program would cost $49.8 million, which would result in an expenditure of $21.41 per DALY averted or $662.94 per life saved. Even at $7.00 per dose, vaccination would be highly cost-effective. In sensitivity analyses, varying efficacy against severe rotavirus disease and vaccine price had the greatest impact on cost-effectiveness.

Conclusions. A national rotavirus vaccination program in India would prevent substantial rotavirus morbidity and mortality and would be highly cost-effective at a range of vaccine prices. Public health officials can use this locally derived data to evaluate how this highly cost-effective intervention might fit into India's long-term health care goals.

Clinical Infectious Diseases
http://www.journals.uchicago.edu/toc/cid/current

EDITORIAL COMMENTARY: Reaching MDG 4 in India: A Role for Rotavirus Vaccine?

Edmund Anthony S. Nelson and Damian G. Walker

Clin Infect Dis. (2011) 52(2): 178-179 doi:10.1093/cid/ciq095

Abstract

A new health intervention can be either more or less expensive than existing intervention(s) (usually more). It can also be more or less effective (again, usually more). Thus, improving the health of a population usually costs more money (for governments, taxpayers, and/or individuals). Occasionally, the situation arises when a new and better intervention costs less and is cost-saving. In this case, the decision should be to introduce the intervention, and a failure to do so would require a very detailed explanation.

The economic evaluation by Esposito et al of the introduction of rotavirus vaccine to India's National Immunization Programme reports that if the Government of India applies to the GAVI Alliance and is approved to receive funds to support its introduction, it could pay the heavily

discounted copay price of US$ .15 per dose (US$ .30 for a 2-dose course); at such a price per dose, it would be in the fortunate position of saving both lives and money. Of importance, however, the contribution of the Government of India to the cost of the vaccine would be expected to steadily increase over time until the full cost was borne by the government; thus, the potential cost-saving scenario would not last forever. Nevertheless, even at higher prices, purchasing the rotavirus vaccine would be considered to still be a very sound investment. What is the likely eventual …

Vaccine
http://www.sciencedirect.com/science/journal/0264410X
Volume 28, Issue 47 pp. 7453-7576 (3 November 2010)
Letters to the Editor
An update to "The cost-effectiveness of rotavirus vaccination: Comparative analyses for five European countries and transferability in Europe"
Pages 7457-7459
Mark Jit, Marie-Josée J. Mangen, Hugues Melliez, Yazdan Yazdanpanah, Joke Bilcke, Heini Salo, W. John Edmunds, Philippe Beutels
Abstract
A cost-effectiveness analysis of rotavirus vaccination in Belgium, England and Wales, Finland, France and the Netherlands published in 2009 was updated based on recent studies on rotavirus burden of disease and vaccine efficacy. All the qualitative conclusions in the previous study were found to remain valid. Vaccination remains cost-effective in Finland only when using plausible tender prices.

Vaccine
Volume 27, Issue 29, Pages 3801-3926 (12 June 2009)
http://www.sciencedirect.com/science/journal/0264410X
An economic analysis of rotavirus vaccination in Italy
Pages 3904-3911
Maria Daniela Giammanco, Maria Anna Coniglio, Sarina Pignato, Giuseppe Giammanco
Abstract
We have evaluated health and economic benefits of a universal infant vaccination with two rotavirus vaccines registered in Italy, on the bases of the burden of rotavirus gastroenteritis (RVGE) in a birth cohort of 520,000 Italian infants followed until 5 years of age. Estimates from published and unpublished sources of disease burden, costs, vaccine coverage, efficacy trials of both vaccines, and price were used to estimate cost-effectiveness from the perspectives of the Italian National Health Service (NHS) and society. According to our estimates, a universal rotavirus vaccination program would avoid 10,679 hospitalizations, 39,202 emergency visits, and 44,223 at home visits. At €65.6 per vaccination courses, the program would cost €30,700,800 and realize a net loss of €9,057,928 from the Italian NHS perspective. On the contrary, the program would provide a net savings of €24,324,198 from the societal perspective. From the Italian NHS perspective, the break-even price per vaccination course should be reduced at least to €46.25 to achieve a zero cost-effectiveness ratio.

Vaccine
Volume 27, Issue 44, Pages 6103-6268 (19 October 2009)
http://www.sciencedirect.com/science/journal/0264410X

The cost-effectiveness of rotavirus vaccination: Comparative analyses for five European countries and transferability in Europe

Mark Jit, Joke Bilcke, Marie-Josée J. Mangen, Heini Salo, Hugues Melliez, W. John Edmunds, Yazdanpanah Yazdan, Philippe Beutels

Abstract

Cost-effectiveness analyses are usually not directly comparable between countries because of differences in analytical and modelling assumptions. We investigated the cost-effectiveness of rotavirus vaccination in five European Union countries (Belgium, England and Wales, Finland, France and the Netherlands) using a single model, burden of disease estimates supplied by national public health agencies and a subset of common assumptions. Under base case assumptions (vaccination with Rotarix®, 3% discount rate, health care provider perspective, no herd immunity and quality of life of one caregiver affected by a rotavirus episode) and a cost-effectiveness threshold of €30,000, vaccination is likely to be cost effective in Finland only. However, single changes to assumptions may make it cost effective in Belgium and the Netherlands. The estimated threshold price per dose for Rotarix® (excluding administration costs) to be cost effective was €41 in Belgium, €28 in England and Wales, €51 in Finland, €36 in France and €46 in the Netherlands.

Vaccine
Volume 27, Issue 33, Pages 4381-4550 (16 July 2009)
http://www.sciencedirect.com/science/journal/0264410X

Cost-effectiveness of infant vaccination with RIX4414 (Rotarix™) in the UK

Pages 4520-4528

A. Martin, A. Batty, J.A. Roberts, B. Standaert

Abstract

This study estimated the cost-effectiveness of infant rotavirus vaccination with Rotarix™ in the UK, taking into account community rotavirus infections that do not present to the healthcare system. A Markov model compared the costs and outcomes of vaccination versus no vaccination in a hypothetical birth cohort of children followed over a lifetime, from a societal perspective and the perspective of the National Health Service (NHS). The model estimated costs and quality-adjusted life-years (QALYs) lost due to death, hospitalisation, general practitioner (GP) consultation, emergency attendance and calls to NHS Direct for rotavirus infection in children aged <5 years. Time lost from work and parents' travel costs were also included in the societal perspective. The base case cost-effectiveness ratio for vaccination compared with no vaccination was £23,298/QALY from the NHS perspective and £11,459 from the societal perspective. In sensitivity analysis, the most important parameters were hospitalisation cost and number of GP consultations. Addition of Rotarix™ to the paediatric vaccination schedule would be a cost-effective policy option in the UK at the threshold range (£20,000–30,000/QALY) currently adopted by the National Institute for Health and Clinical Excellence.

Hep B Vaccine

Vaccine
Volume 29, Issue 3 pp. 363-612 (10 January 2011)

Economic evaluation of infant and adolescent hepatitis B vaccination in the UK

Original Research Article
Pages 466-475

M. Ruby Siddiqui, Nigel Gay, W. John Edmunds, Mary Ramsay

Abstract
A Markov model of hepatitis B virus (HBV) disease progression in the UK estimated that 81% of predicted HBV-associated morbidity and mortality could be prevented by universal infant vaccination at a cost of approximately £260,000 per QALY gained.
Universal adolescent vaccination would be less effective (45% prevented) and less cost-effective (£493,000 per QALY gained). Higher HBV incidence rates in males and intermediate/high risk ethnic populations meant it was approximately 3 times more cost-effective to vaccinate these groups. At current vaccine costs a selective infant vaccination programme, based on vaccinating intermediate/high risk ethnic populations would not be considered cost effective.
The threshold cost per vaccinated child at which the programme would be considered cost-effective was investigated. Universal infant vaccination would be cost-effective if the average cost of vaccinating each child against HBV, including vaccine and administration costs of all doses, was less than £4.09. Given the low cost of vaccination required to make a universal programme cost-effective the most feasible policy in the UK would be to use a suitably priced combined vaccine that included the other antigens in the current infant vaccination schedule.

HPV Vaccine

The Lancet Infectious Disease
Dec 2010 Volume 10 Number 12 Pages 813 – 892
http://www.thelancet.com/journals/laninf/issue/current
Articles
Targeted human papillomavirus vaccination of men who have sex with men in the USA: a cost-effectiveness modelling analysis
Jane J Kim
Summary
Background
A vaccine targeting human papillomavirus (HPV) types 16 and 18, which are associated with 80% of anal cancers, is efficacious in men. High-risk populations such as men who have sex with men (MSM) might especially benefit from vaccination. I aimed to estimate the cost-effectiveness of HPV vaccination of MSM in the USA.
Methods
I constructed decision-analytic models to estimate the direct health and economic outcomes of HPV vaccination (against types 6, 11, 16, and 18) for prevention of HPV-related anal cancer and genital warts. The model parameters that were varied were age at vaccination (12 years, 20 years, and 26 years), previous exposure to vaccine-targeted HPV types, and prevalence of HIV-1. I used the models to conduct sensitivity analyses, including duration of vaccine protection, vaccine cost, and burden of anal cancer and genital warts.
Findings
In a scenario of HPV vaccination of MSM at 12 years of age without previous exposure to HPV, compared with no vaccination, vaccination cost US$15 290 per quality-adjusted life-year gained. In scenarios where MSM are vaccinated at 20 years or 26 years of age, after exposure to HPV infections, the cost-effectiveness ratios worsened, but were less than $50 000 per quality-adjusted life-year under most scenarios. For example, HPV vaccination of MSM at 26 years cost $37 830 per quality-adjusted life-year when previous exposure to all vaccine-targeted HPV types was assumed to be 50%. Outcomes were most sensitive to variations in anal cancer incidence, duration of vaccine protection, and HIV prevalence in MSM.
Interpretation
HPV vaccination of MSM is likely to be a cost-effective intervention for the prevention of genital warts and anal cancer.
Funding
US National Cancer Institute.

Ann Intern Med; October 20, 2009: 151:538-545;
Cost-Effectiveness of Human Papillomavirus Vaccination and Cervical Cancer Screening in Women Older Than 30 Years in the United States
Jane J. Kim, PhD; Jesse Ortendahl, BS; and Sue J. Goldie, MD, MPH
Abstract
Background: Women older than 30 years are the main beneficiaries of improved cervical cancer screening with human papillomavirus (HPV) DNA testing. The role of vaccination against HPV types 16 and 18, which is recommended routinely for preadolescent girls, is unclear in this age group.

Objective: To assess the health and economic outcomes of HPV vaccination in older U.S. women.
Design: Cost-effectiveness analysis with an empirically calibrated model.
Data Sources: Published literature.
Target Population: U.S. women aged 35 to 45 years.
Time Horizon: Lifetime.
Perspective: Societal.
Intervention: HPV vaccination added to screening strategies that differ by test (cytology or HPV DNA testing), frequency, and start age versus screening alone.
Outcome Measures: Incremental cost-effectiveness ratios (2006 U.S. dollars per quality-adjusted life-year [QALY] gained).
Results of Base-Case Analysis: In the context of annual or biennial screening, HPV vaccination of women aged 35 to 45 years ranged from $116 950 to $272 350 per QALY for cytology with HPV DNA testing for triage of equivocal results and from $193 690 to $381 590 per QALY for combined cytology and HPV DNA testing, depending on age and screening frequency.
Results of Sensitivity Analysis: The probability of HPV vaccination being cost-effective for women aged 35 to 45 years was 0% with annual or biennial screening and less than 5% with triennial screening, at thresholds considered good value for money.
Limitation: The natural history of the disease and the efficacy of the vaccine in older women are uncertain.
Conclusion: Given currently available information, the effectiveness of HPV vaccination for women older than 30 years who are screened seems to be small. Compared with current screening that uses sensitive HPV DNA testing, HPV vaccination is associated with less attractive cost-effectiveness ratios in this population than those for other, well-accepted interventions in the United States.
Primary Funding Source: National Cancer Institute, Centers for Disease Control and Prevention, and the American Cancer Society.

Vaccine
Volume 27, Issue 44, Pages 6103-6268 (19 October 2009)
http://www.sciencedirect.com/science/journal/0264410X

The potential cost-effectiveness of adding a human papillomavirus vaccine to the cervical cancer screening programme in South Africa

Edina Sinanovic, Jennifer Moodley, Mark A. Barone, Sumaya Mall, Susan Cleary, Jane Harries

Abstract
This study was designed to answer the question of whether a cervical cancer prevention programme that incorporates a human papillomavirus (HPV) vaccine is potentially more cost-effective than the current strategy of screening alone in South Africa. We developed a static Markov state transition model to describe the screening and management of cervical cancer within the South African context. The incremental cost-effectiveness ratio of adding HPV vaccination to the screening programme ranged from US $1078 to 1460 per quality-adjusted life year (QALY) gained and US$3320–4495 per life year saved, mainly depending on whether the study was viewed from a health service or a societal perspective. Using discounted costs and benefits, the threshold analysis indicated that a vaccine price reduction of 60% or more would make the vaccine plus screening strategy more cost-effective than the screening only approach. To address the issue of affordability and cost-effectiveness, the pharmaceutical companies need to make a commitment to price reductions.

Vaccine
Volume 27, Issue 36, Pages 4875-5026 (6 August 2009)
http://www.sciencedirect.com/science/journal/0264410X

Cost-effectiveness of prophylactic vaccination against human papillomavirus 16/18 for the prevention of cervical cancer: Adaptation of an existing cohort model to the situation in the Netherlands

Pages 4776-4783

R.M. Rogoza, T.A. Westra, N. Ferko, J.J. Tamminga, M.F. Drummond, T. Daemen, J.C. Wilschut, M.J. Postma

Abstract

Cervical cancer is one of the most prevalent cancers among women worldwide. Implementation of an HPV-vaccination strategy targeting the major oncogenic types 16 and 18 that cause cervical cancer is generally expected to significantly reduce the burden of cervical cancer disease. Here we estimate the costs, savings and health gains with the addition of HPV-16/18 vaccination to the already existing Dutch screening programme. In the base-case analysis, it was estimated that implementation of an HPV-16/18 vaccine would result in an incremental cost-effectiveness ratio (ICER) of €22,700 per life-year gained (LYG). In sensitivity analysis, the robustness of our finding of favourable cost-effectiveness was established. The ICER appeared sensitive to the vaccine price, discount rate and duration of vaccine-induced protection. From our results, it validly follows that immunization of 12-year-old Dutch girls against HPV-16/18 infection is a cost-effective strategy for protecting against cervical cancer.

Vaccine
Volume 27, Issue 44, Pages 6103-6268 (19 October 2009)
http://www.sciencedirect.com/science/journal/0264410X

The potential cost-effectiveness of adding a human papillomavirus vaccine to the cervical cancer screening programme in South Africa

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Abstract

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Vaccine
Volume 27, Issue 37, Pages 5027-5170 (13 August 2009)
http://www.sciencedirect.com/science/journal/0264410X

Cost-effectiveness analysis of human papillomavirus-vaccination programs to prevent cervical cancer in Austria

Pages 5133-5141
Ingrid Zechmeister, Birgitte Freiesleben de Blasio, Geoff Garnett, Aileen Rae Neilson, Uwe Siebert
Abstract
Objective
The study predicts long-term cervical cancer related population health and economic effects of introducing the HPV-vaccination for 12-year-old girls (and boys) in addition to current screening compared with screening only.
Method
Health effects are predicted by a dynamic transmission model. Model results are used to calculate incremental cost-effectiveness ratios (ICER) in € per life year gained (LYG) for a time-horizon between 2008 and 2060 from a public payer and a societal perspective.
Results
Vaccination of girls results a discounted ICER of € 64,000/LYG and € 50,000/LYG from a payer's and societal perspectives respectively. The additional vaccination of boys increases the ICER to € 311,000 and € 299,000/LYG respectively. Results were most sensitive to vaccination price, discount rate and time-horizon.
Conclusion
HPV-vaccination for girls should be cost-effective when adopting a longer time-horizon and a societal perspective. Applying a shorter time frame and a payer's perspective or vaccinating boys may not be cost-effective without reducing the vaccine price.

Vaccine
Volume 28, Issue 42 pp. 6809-6942 (4 October 2010)
http://www.sciencedirect.com/science/journal/0264410X
Impact of vaccinating boys and men against HPV in the United States
Original Research Article
Pages 6858-6867
Elamin H. Elbasha, Erik J. Dasbach
Abstract
We assessed the public health impact and value of vaccinating boys and men with the quadrivalent HPV vaccine in the United States. We used mathematical population models, accounting for both the direct and indirect protective effects of vaccination. Inputs for the models were obtained from public data sources, published literature, and analyses of clinical trial data. Compared with a program of vaccinating girls and women only, including boys and men 9–26 years of age would further decrease the cumulative mean number of genital wart cases, cervical intraepithelial neoplasia 2/3 cases, cancer cases, and cancer deaths by 5,146,000, 708,000, 116,000, and 40,000, respectively, within 100 years. The mean cost-effectiveness ratio (2008 US $) of this strategy was $25,700 (range: 13,600–48,800) per QALY gained if vaccination protects against all HPV 6/11/16/18-associated diseases, and $69,000 (range: 37,700–152,300)/QALY if it only protects against diseases currently in the vaccine indication. Vaccinating boys and men age 9–26 against all HPV 6/11/16/18-associated diseases provides substantial public health benefits and is cost-effective at commonly cited thresholds.

Pneumococcal Vaccine

Vaccine
http://www.sciencedirect.com/science/journal/0264410X
Volume 28, Issue 48 pp. 7577-7712 (10 November 2010)
Regular Papers
Cost-effectiveness of dual influenza and pneumococcal vaccination in 50-year-olds
Original Research Article
Pages 7620-7625
Kenneth J. Smith, Bruce Y. Lee, Mary Patricia Nowalk, Mahlon Raymund, Richard K. Zimmerman
Abstract
Influenza vaccination is now recommended for all ages; CDC pneumococcal polysaccharide vaccination (PPV) recommendations are comorbidity-based in nonelderly patients. We constructed a Markov model to estimate the cost-effectiveness of dual influenza and pneumococcal vaccination in 50-year-olds. Patients were followed for 10 years, with differing time horizons examined in sensitivity analyses. With 100% vaccine uptake, dual vaccination cost $37,700/QALY gained compared to a CDC recommendation strategy; with observed vaccine uptake, dual vaccination cost $5,300/QALY. Results were sensitive to shorter time horizons, favoring CDC recommendations. We found dual vaccination of all 50-year-olds economically reasonable. Shorter duration models may not fully account for PPV effectiveness.

Vaccine
Volume 28, Issue 48 pp. 7577-7712 (10 November 2010)
Public health and economic impact of the 13-valent pneumococcal conjugate vaccine (PCV13) in the United States
Original Research Article
Pages 7634-7643
Jaime L. Rubin, Lisa J. McGarry, David R. Strutton, Keith P. Klugman, Stephen I. Pelton, Kristen E. Gilmore, Milton C. Weinstein
Abstract
The 7-valent pneumococcal conjugate vaccine (PCV7) has dramatically decreased pneumococcal disease incidence, and the 13-valent vaccine (PCV13) protects against 6 additional Streptococcus pneumoniae serotypes. A decision-analytic model was constructed to evaluate the impact of infant vaccination with PCV13 versus PCV7 on pneumococcal disease incidence and mortality as well as the incremental benefit of a serotype catch-up program. PCV13 effectiveness was extrapolated from observed PCV7 data, using assumptions regarding serotype prevalence and PCV13 protection against additional serotypes. The model predicts that PCV13 is more effective and cost saving compared with PCV7, preventing 106,000 invasive pneumococcal disease (IPD) cases and 2.9 million pneumonia cases, and saving $11.6 billion over a 10-year period. The serotype catch-up program would prevent an additional 12,600 IPD cases and 404,000 pneumonia cases, and save an additional $737 million compared with no catch-up program.

Vaccine
Volume 27, Issue 24, Pages 3127-3238 (21 May 2009)
http://www.sciencedirect.com/science/journal/0264410X
Age, revaccination, and tolerance effects on pneumococcal vaccination strategies in the elderly: A cost-effectiveness analysis
Pages 3159-3164
Kenneth J. Smith, Richard K. Zimmerman, Mary Patricia Nowalk, Mark S. Roberts
Abstract
Optimal pneumococcal polysaccharide vaccination (PPV) policy is unknown for cohorts aged ≥65 years. Using a Markov model, we estimated the cost-effectiveness of single- and multiple-dose PPV strategies in 65-, 75-, and 80-year-old cohorts. PPV at age 65 cost $26,100 per QALY (quality adjusted life years) gained. Vaccination at ages 75 and 80 cost $71,300–75,800 per QALY; revaccination strategies cost more. When prior vaccination and loss of vaccine effectiveness due to tolerance are assumed, cost-effectiveness ratios increase substantially. Single-dose PPV is worth considering in patients aged 65–80 from clinical and economic standpoints. Revaccination strategies for the elderly are less cost-effective, particularly when prior vaccination and vaccine tolerance are considered.

Vaccine
Volume 27, Issue 50, Pages 6967-7138 (23 November 2009)
http://www.sciencedirect.com/science/journal/0264410X
Cost-effectiveness of a 3-dose pneumococcal conjugate vaccine program in the province of Quebec, Canada
Béatrice Poirier, Philippe De Wals, Geneviève Petit, Lonny J. Erickson, Jacques Pépin
Abstract
In the province of Quebec, Canada, the pneumococcal 7-valent conjugate vaccine (PCV-7) was licensed in 2001 and a publicly funded program was implemented in 2004, recommending 3 doses for healthy children. An economic analysis was performed both from a health care and societal perspective. Outcomes possibly prevented by PCV-7 and observed in 2006–2007 were compared to expected frequencies based on rates measured before PCV-7 use. Annual program costs were close to $21 M for the health system and $23 M for society. Approximately 20 000 infections were prevented annually and estimated economic benefits were $5 M for the health system and $23 M for society, using a 3% per annum discounting rate. The incremental cost-effectiveness ratio was $18 000 per QALY gained for the health system and the program was close to the break-even threshold in a societal perspective.

Vaccine
Volume 27, Issue 36, Pages 4875-5026 (6 August 2009)
http://www.sciencedirect.com/science/journal/0264410X
Cost-effectiveness of pneumococcal polysaccharide vaccination in adults: A systematic review of conclusions and assumptions
Pages 4891-4904
Isla Ogilvie, Antoine El Khoury, Yadong Cui, Erik Dasbach, John D. Grabenstein, Mireille Goetghebeur
Abstract
Streptococcus pneumoniae infections in adults are associated with substantial morbidity, mortality, and costs. A literature review was conducted to identify strengths and limitations of the cost-effectiveness of pneumococcal polysaccharide vaccine studies. A comparative analysis

of the impact of model parameters on cost-effectiveness ratios was complemented by systematic assessment of the studies. We identified 11 economic evaluations of pneumococcal polysaccharide vaccine (PPV-23) in adults. In general, all 11 studies found that vaccination with PPV-23 is a cost-effective, and in some cases a cost-saving strategy for the prevention of invasive pneumococcal disease (IPD). The systematic assessment indicated that the results of the cost-effectiveness studies of PPV-23 are influenced by the values applied to vaccine efficacy, IPD incidence and case-fatality.

Vaccine
Volume 28, Issue 12, Pages 2361-2472 (11 March 2010)
http://www.sciencedirect.com/science/journal/0264410X
Short Communication
Huge impact of assumptions on indirect effects on the cost-effectiveness of routine infant vaccination with 7-valent conjugate vaccine (Prevnar)
Pages 2367-2369
Mark H. Rozenbaum, Albert Jan van Hoek, Eelko Hak, Maarten J. Postma
Abstract
Several recently published European cost-effectiveness studies on the 7-valent pneumococcal conjugate vaccine (PCV-7: Prevnar®) have included net-indirect vaccine benefits for non-vaccine protected groups into their studies, which might be too optimistic an approach given recent data. Net-indirect effects result from herd protection minus serotype replacement effects. In this study we analyze the impact of net-indirect effects in non-vaccine protected groups of 5 years of age and older with updated assumptions regarding epidemiologic data and health care unit costs. Without net-indirect benefits for non-vaccine protected groups included the cost-effectiveness ratio is estimated at €72,360 per QALY. In order to obtain cost-effectiveness ratios below the threshold of €50,000 per QALY – which is in the middle of the range that is often referred to in the Netherlands – the net-indirect protective effect should at least be 16% of which has been observed in the USA after the introduction of PCV-7.

Vaccine
Volume 28, Issue 7, Pages 1661-1892 (17 February 2010)
http://www.sciencedirect.com/science/journal/0264410X
Cost-effectiveness of the CRM-based 7-valent pneumococcal conjugated vaccine (PCV7) in Argentina
Pages 2302-2310
Norberto D. Giglio, Alejandro D. Cane, Paula Micone, Angela Gentile
Abstract
Due to the region's own conditions, universal vaccination with pneumococcal conjugate heptavalent vaccine (PCV-7) in Latin American countries is still controversial.
Objective
To compare projected economic costs and health benefits associated with pneumococcal conjugate heptavalent vaccine as a routine immunization in healthy children in Argentina.
Design
A decision analytic model of Markov simulated lifetime evolution of a birth cohort (n 696,451) was developed and compared costs and health benefits of pneumococcal disease in the presence and absence of vaccination.

Main outcome measures
Cost per life year (LY) gained, reduce in diseases burden and costs of vaccination.
Results
From the society's perspective, the incremental cost per LY gained was US$ 5599.42 and the purchase of the 4 doses of vaccine for the entire cohort with a cost of US$ 26.5 dose requires an investment of US$ 73,823,806.00.
The model estimated that vaccination reduce the number of death by 159 cases of meningitis, 756 cases of bacteriemias 4594 cases of pneumonias about 84,769 cases of otitis media and 20 meningitis sequelae.
The value of the cost per LY gained was considerably modified by the variation in the cost of the vaccine dose, efficacy/effectiveness of the vaccine for pneumonia the mortality from pneumonia and herd immunity.
Conclusions
Our analysis predicted that routine vaccination of healthy infants <2 years could prevent an important number of pneumococcal infectious and reduce related mortality and morbidity. This strategic could be highly cost-effective in Argentina.

Vaccine
Volume 27, Issue 47, Pages 6481-6650 (5 November 2009)
Cost-effectiveness of pneumococcal conjugate vaccine: An update after 7 years of use in the United States
G. Thomas Ray, Stephen I. Pelton, Keith P. Klugman, David R. Strutton, Matthew R. Moore
Abstract
Seven-valent pneumococcal conjugate vaccine (PCV7) has been in routine use in the United States since 2000 and data have indicated direct and indirect effects of the vaccine. We simulated the effects of PCV7 on children vaccinated during 2000–2006, incorporating direct and indirect effects on incidence of invasive pneumococcal disease (IPD), hospitalized pneumonia and otitis media. Before accounting for indirect effects, PCV7 cost $201,000 per life-year saved. After incorporating indirect effects on IPD, cost per life-year saved was $10,400. The presence of modest additional indirect effects against hospitalized pneumonia and otitis media in children may have resulted in overall cost savings.

Vaccine
Volume 27, Issue 24, Pages 3127-3238 (21 May 2009)
http://www.sciencedirect.com/science/journal/0264410X
Age, revaccination, and tolerance effects on pneumococcal vaccination strategies in the elderly: A cost-effectiveness analysis
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Optimal pneumococcal polysaccharide vaccination (PPV) policy is unknown for cohorts aged ≥65 years. Using a Markov model, we estimated the cost-effectiveness of single- and multiple-dose PPV strategies in 65-, 75-, and 80-year-old cohorts. PPV at age 65 cost $26,100 per QALY (quality adjusted life years) gained. Vaccination at ages 75 and 80 cost $71,300–75,800 per QALY; revaccination strategies cost more. When prior vaccination and loss of vaccine effectiveness due to tolerance are assumed, cost-effectiveness ratios increase substantially. Single-dose PPV is

worth considering in patients aged 65–80 from clinical and economic standpoints. Revaccination strategies for the elderly are less cost-effective, particularly when prior vaccination and vaccine tolerance are considered.

Influenza Vaccines

Vaccine
Volume 28, Issue 12, Pages 2361-2472 (11 March 2010)
http://www.sciencedirect.com/science/journal/0264410X
Regular Papers
Vaccination against pandemic influenza A/H1N1v in England: A real-time economic evaluation
Pages 2370-2384
Marc Baguelin, Albert Jan Van Hoek, Mark Jit, Stefan Flasche, Peter J. White, W. John Edmunds
Abstract
Decisions on how to mitigate an evolving pandemic are technically challenging. We present a real-time assessment of the effectiveness and cost-effectiveness of alternative influenza A/H1N1v vaccination strategies. A transmission dynamic model was fitted to the estimated number of cases in real-time, and used to generate plausible autumn scenarios under different vaccination options. The proportion of these cases by age and risk group leading to primary care consultations, National Pandemic Flu Service consultations, emergency attendances, hospitalisations, intensive care and death was then estimated using existing data from the pandemic. The real-time model suggests that the epidemic will peak in early November, with the peak height being similar in magnitude to the summer wave. Vaccination of the high-risk groups is estimated to prevent about 45 deaths (80% credibility interval 26–67), and save around 2900 QALYs (80% credibility interval 1600–4500). Such a programme is very likely to be cost-effective if the cost of vaccine purchase itself is treated as a sunk cost. Extending vaccination to low-risk individuals is expected to result in more modest gains in deaths and QALYs averted. Extending vaccination to school-age children would be the most cost-effective extension. The early availability of vaccines is crucial in determining the impact of such extensions. There have been a considerable number of cases of H1N1v in England, and so the benefits of vaccination to mitigate the ongoing autumn wave are limited. However, certain groups appear to be at significantly higher risk of complications and deaths, and so it appears both effective and cost-effective to vaccinate them. The United Kingdom was the first country to have a major epidemic in Europe. In countries where the epidemic is not so far advanced vaccination of children may be cost-effective. Similar, detailed, real-time modelling and economic studies could help to clarify the situation.

Cholera Vaccine

Vaccine
Volume 27, Issue 23, Pages 3013-3126 (18 May 2009)
http://www.sciencedirect.com/science/journal/0264410X

Cost–benefit comparisons of investments in improved water supply and cholera vaccination programs

Pages 3109-3120

Marc Jeuland, Dale Whittington

Abstract

This paper presents the first cost–benefit comparison of improved water supply investments and cholera vaccination programs. Specifically, we compare two water supply interventions – deep wells with public hand pumps and biosand filters (an in-house, point-of-use water treatment technology) – with two types of cholera immunization programs with new-generation vaccines – general community-based and targeted and school-based programs. In addition to these four stand-alone investments, we also analyze five combinations of water and vaccine interventions: (1) borehole + hand pump and community-based cholera vaccination, (2) borehole + hand pump and school-based cholera vaccination, (3) biosand filter and community-based cholera vaccination, (4) biosand filter and school-based cholera vaccination, and (5) biosand filter and borehole + hand pump. Using recent data applicable to developing country locations for parameters such as disease incidence, the effectiveness of vaccine and water supply interventions against diarrheal diseases, and the value of a statistical life, we construct cost–benefit models for evaluating these interventions. We then employ probabilistic sensitivity analysis to estimate a frequency distribution of benefit–cost ratios for all four interventions, given a wide variety of possible parameter combinations.

Our results demonstrate that there are many plausible conditions in developing countries under which these interventions will be attractive, but that the two improved water supply interventions and the targeted cholera vaccination program are much more likely to yield attractive cost–benefit outcomes than a community-based vaccination program. We show that implementing community-based cholera vaccination programs after borehole + hand pump or biosand filters have already been installed will rarely be justified. This is especially true when the biosand filters are already in place, because these achieve substantial cholera risk reductions on their own. On the other hand, implementing school-based cholera vaccination programs after the installation of boreholes with hand pump is more likely to be economically attractive. Also, if policymakers were to first invest in cholera vaccinations, then subsequently investing in water interventions is still likely to yield positive economic outcomes. This is because point-of-use water treatment delivers health benefits other than reduced cholera, and deep boreholes + hand pumps often yield non-health benefits such as time savings.

Anthrax Vaccine

Ann Intern Med April 19, 2005 142:601-610

Cost-Effectiveness of Defending against Bioterrorism: A Comparison of Vaccination and Antibiotic Prophylaxis against Anthrax

Robert A. Fowler, Gillian D. Sanders, Dena M. Bravata, Bahman Nouri, Jason M. Gastwirth, Dane Peterson, Allison G. Broker, Alan M. Garber, and Douglas K. Owens

Abstract

Background: Weaponized Bacillus anthracis is one of the few biological agents that can cause death and disease in sufficient numbers to devastate an urban setting.

Objective: To evaluate the cost-effectiveness of strategies for prophylaxis and treatment of an aerosolized B. anthracis bioterror attack.

Design: Decision analytic model.

Data Sources: We derived probabilities of anthrax exposure, vaccine and treatment characteristics, and their costs and associated clinical outcomes from the medical literature and bioterrorism-preparedness experts.

Target Population: Persons living and working in a large metropolitan U.S. city.

Time Horizon: Patient lifetime.

Perspective: Societal.

Intervention: We evaluated 4 post-attack strategies: no prophylaxis, vaccination alone, antibiotic prophylaxis alone, or vaccination and antibiotic prophylaxis, as well as preattack vaccination versus no vaccination.

Outcome Measures: Costs, quality-adjusted life-years, life-years, and incremental cost-effectiveness.

Results of Base-Case Analysis: If an aerosolized B. anthracis bioweapon attack occurs, postexposure prophylactic vaccination and antibiotic therapy for those potentially exposed is the most effective (0.33 life-year gained per person) and least costly ($355 saved per person) strategy, as compared with vaccination alone. At low baseline probabilities of attack and exposure, mass previous vaccination of a metropolitan population is more costly ($815 million for a city of 5 million people) and not more effective than no vaccination.

Results of Sensitivity Analysis: If prophylactic antibiotics cannot be promptly distributed after exposure, previous vaccination may become cost-effective.

Limitations: The probability of exposure and disease critically depends on the probability and mechanism of bioweapon release.

Conclusions: In the event of an aerosolized B. anthracis bioweapon attack over an unvaccinated metropolitan U.S. population, postattack prophylactic vaccination and antibiotic therapy is the most effective and least expensive strategy.

Additional Articles

Journal of Infectious Diseases
15 October 2009 Volume 200, Number 8
http://www.journals.uchicago.edu/toc/jid/current
Major Articles and Brief Reports: Bacteria
Cost-Effectiveness of a Potential Prophylactic Helicobacter pylori Vaccine in the United States
Marcia F. T. Rupnow, Alicia H. Chang, Ross D. Shachter, Douglas K. Owens, and Julie Parsonnet
Background.Helicobacter pylori vaccines are under development to prevent infection. We quantified the cost-effectiveness of such a vaccine in the United States, using a dynamic transmission model.
Methods.We compartmentalized the population by age, infection status, and clinical disease state and measured effectiveness in quality-adjusted life years (QALYs). We simulated no intervention, vaccination of infants, and vaccination of school-age children. Variables included costs of vaccine, vaccine administration, and gastric cancer treatment (in 2007 US dollars), vaccine efficacy, quality adjustment due to gastric cancer, and discount rate. We evaluated possible outcomes for periods of 10–75 years.
Results.H. pylori vaccination of infants would cost $2.9 billion over 10 years; savings from cancer prevention would be realized decades later. Over a long time horizon (75 years), incremental costs of H. pylori vaccination would be $1.8 billion, and incremental QALYs would be 0.5 million, yielding a cost-effectiveness ratio of $3871/QALY. With school-age vaccination, the cost-effectiveness ratio would be $22,137/QALY. With time limited to <40 years, the cost-effectiveness ratio exceeded $50,000/QALY.
Conclusion.When evaluated with a time horizon beyond 40 years, the use of a prophylactic H. pylori vaccine was cost-effective in the United States, especially with infant vaccination.

Vaccine
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http://www.sciencedirect.com/science/journal/0264410X
A cost–effectiveness analysis of Japanese encephalitis vaccine in Cambodia
Sok Touch, Chutima Suraratdecha, Chham Samnang, Seng Heng, Lauren Gazley, Chea Huch, Ly Sovann, Chab Seak Chhay, Sann Chan Soeung
Abstract
This study aimed to evaluate the cost and effectiveness of introducing a live, attenuated vaccine (SA 14-14-2) against Japanese encephalitis (JE) into the immunization program. The study demonstrated that SA 14-14-2 immunization is cost–effective in controlling JE in Cambodia compared to no vaccination. Averting one disability-adjusted life year, from a societal perspective, through the introduction of SA 14-14-2 through routine immunization, or a combination of routine immunization plus a campaign targeting children 1–5 or 1–10 years of age, costs US$22, US$34 and US$53, respectively. Sensitivity analyses confirmed that there was a high probability of SA 14-14-2 immunization being cost–effective under conditions of uncertainty.