

University of Groningen

Pharmacoeconomics in infectious disease

Bos, Jasper Marnix

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2004

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Bos, J. M. (2004). *Pharmacoeconomics in infectious disease: the evaluation of prevention programmes*. s.n.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

SUMMARY

In this thesis, applications and limitations of pharmacoeconomics in the evaluation of prevention strategies are discussed. In part 1, some of the current methodological issues are discussed. Part 2 shows some current applications of pharmacoeconomics in the field of vaccine preventable diseases, while part 3 evaluates some of the aspects of HIV prevention.

Chapter 2 elaborates on the development of models to assess the future impact of vaccination strategies. It is noted that often not only progression of disease and associated costs are important, but also the transmission of the causing agent in the target population should be considered. A distinction can be made between models that incorporate the external effects of reducing transmission of disease, (dynamic transmission models) and models that do not incorporate this externality (static models). Static models are by far the most widely used in economic evaluations. However, a dynamic transmission model should be considered when the force of infection is likely to be altered due to the intervention. This occurs when the intervention affects the transmission of the causing agent. Such models have some downsides, in being more complex and the necessity of detailed insights in the transmission dynamics of the disease. Especially the latter will not always be available, forcing the analyst to use simpler models instead. Nevertheless, both the analyst and policy makers should be aware of the limitations of those models, such as the fact that a dynamic model can account for the effects of shifts in age-specific incidence, the occurrence of herd immunity and the consequences of less than optimal vaccination rates.

The use of cost-effectiveness analysis for rational decision-making requires an implicit valuation of what is considered cost-effective. In the literature, values for such a single threshold value for the willingness to pay per QALY have been proposed. Large differences exist in the cost-effectiveness ratio of implemented interventions in the field of blood safety when compared to vaccination. This seems to contradict the existence of a single threshold as the decision rule in cost-effectiveness analysis. In chapter 3, factors influencing the cost-effectiveness threshold are identified and the implications of using thresholds for cost-effectiveness in the decision-making process are discussed. The use of a single threshold value for cost-effectiveness analysis ignores the reality of a fixed budget, where additional funding must come from cuts in other programs. This may thus cause expenditures for health care to rise. Also, in this chapter we argue that the willingness to pay per QALY is depended on the context and should not be generalized. In conclusion, the use of a threshold value for cost-effectiveness as the decision rule could have serious implications and is based on political considerations and not necessarily supported by science.

One of the most influential factors in the evaluation of preventive interventions with future health benefits is the valuing of future health benefits. One of the findings in chapter 4 is the fact that these decisions affect the results of prevention studies to the greatest extent, and completely inverse the study results in some instances. In this chapter, an overview is presented of the main current views on the valuation of future health gains. Two areas of controversy are identified, namely the use of similar or differential discount rates for health and money; and the choice of the underlying discounting model. A number of convincing arguments are found that contradict the current practice of discounting health and money at the social rate of time preference.

In chapter 5, an alternative framework for the measurement of health gains of preventive interventions is developed. It is argued that denominators such as life years gained or QALYs are only indirect and partial measures of the effects of a preventive intervention. The actual effect of the intervention could be measured as a reduction of the risk of exposure in a given period of time. This risk reduction will not always coincide with the timing of the impact on (quality-adjusted) life years gained (i.e. at risk exposure, e.g. preventing chronic disease with an asymptomatic stage). In chapter 5, we thus show that truly acknowledging the origin of health benefits could have implications for the discounting procedure. As an alternative, a discounting procedure is presented that adequately focuses on the reduction of risk. This chapter also discusses the associated potential implications for public health policy and discuss how the effects of the intervention can be additionally corrected for societal preferences.

In the second part of this thesis, applications of pharmacoeconomic evaluation are presented. In chapter 6, the impact of influenza vaccination of all elderly in The Netherlands is projected from the healthcare perspective. The modelling framework for the economic evaluation linked epidemiological aspects of influenza (e.g. incidence, mortality, years of life lost) to vaccination coverage and healthcare resource use. The cost-effectiveness ratio was estimated at €1820 per life year gained. Subgroup analysis demonstrated that the programme had a more favourable cost-effectiveness among the chronically ill elderly population (cost-saving) than among the rest of the elderly population (€6900 per life-year gained). Influenza vaccination has a favourable cost-effectiveness ratio compared to other implemented Dutch programmes in the prevention of infectious diseases.

In chapter 7, the future impact of vaccinating infants with meningococcal B vaccine is estimated by applying decision-analysis. In this simulation model, vaccination would prevent 19 deaths and 8 cases with severe long-term sequelae per year, rendering 526 QALYs per year. The program costs of meningococcal vaccination are estimated at €8,267,300, resulting in a cost-effectiveness ratio of €15,720 per QALY. At this baseline value, meningococcal B vaccination of infants in The Netherlands might be a potential cost-effective intervention.

Streptococcus pneumoniae is one of the main causes of meningitis, bacteremia, pneumonia and otitis media. In chapter 8, epidemiological impact and cost-effectiveness analysis of vaccinating infants in the Netherlands with a 7-valent conjugated pneumococcal vaccine is estimated using decision analysis. A model is used to simulate vaccination of all. Introduction of the vaccine would prevent 48 cases of meningitis and 88 cases of pneumococcal bacteremia per year. Additionally, 3411 cases of pneumococcal pneumonia and 42,695 cases of otitis media would be prevented. This translates into 382 quality adjusted life years gained or 329 discounted life years gained, or. With a vaccine price of €40 per dose, base case cost-effectiveness is €71,250 per QALY. The model is sensitive to changes in incidence of disease and vaccine price. The introduction of this vaccine for infants will lead to large reductions in morbidity and mortality. However, compared to other interventions in the Netherlands, the cost-effectiveness ratio at the baseline level is relatively unfavourable.

Pharmacoeconomic evaluations can be performed at many stages in the development of a new pharmaceutical or intervention. An example of the pre-marketing use of pharmacoeconomics to assess the impact is given in chapter 9. In this chapter, cost-effectiveness analysis is used to project the vaccine parameters, economic consequences and market size associated with HIV-1 vaccination of infants in sub-Saharan Africa through the Expanded Program on Immunisation (EPI).

This analysis is performed as a means of providing incentives for the research for an effective HIV vaccine. It is concluded that if technological and financial problems associated with the development and distribution of an HIV vaccine can be solved, HIV vaccination in Africa could be potentially cost-effective from a healthcare provider's perspective. Since the vaccine needs to be accessible to low-income countries, vaccine prices should be low. Given the costs of R&D needed to develop such a vaccine (mean cost per NCE: >\$80 million), these results illustrate the need for additional funding of R&D. This would be necessary to provide the necessary incentives for research.

In part 3 of this thesis, some aspects of HIV prevention are evaluated. In chapter 10, the cost-effectiveness of universal HIV screening of attenders of clinics for sexually transmitted diseases is discussed. A Bernoulli model for the secondary transmission of HIV is presented that links epidemiological data on infection with HIV and other STD in patients attending a STD-clinic in Amsterdam from 1991 to 1997. The number of secondary HIV infections caused by attenders of the STD-clinic can be calculated using this model. Combined with data on the health and monetary benefits of averting HIV infection and costs of HIV-screening, the cost-effectiveness of HIV-screening of attenders of the STD-clinic was assessed. An increased risk for HIV infection was found in STD clinic attenders infected with another STD (Odds ratio: 2.07). The risk differed for specific STDs, highest odds ratios were found for syphilis and gonorrhoea. Screening of all attenders was estimated at net costs of €82,550 per secondary infection averted. The cost-effectiveness ratio range between €680 and €9340 per life year gained, depending on the value of key parameters used in the model.

Amsterdam has a relatively high prevalence of HIV and results obtained in chapter 10 therefore may not be transferable to lower HIV prevalence settings, such as the rest of The Netherlands. In chapter 11, the cost-effectiveness of this intervention was investigated for lower prevalence settings. Data was used from the STD-clinic in Rotterdam, the Netherlands, a city with a relatively low HIV prevalence. Our results for the Netherlands may indicate the effects of HIV screening of attenders of STD-clinics in other regions of countries with a low-level HIV epidemic. For this analysis, we linked a Bernoulli model, estimating the probability of secondary infection by an asymptomatic HIV-infected patient, to epidemiological data on the prevalence of HIV in a STD-clinic in Rotterdam from 1995 to 1998. With screening of all attenders of the EMCR STD-clinic, 8.4 cases of HIV-infection are prevented, at a cost of €98,860 per secondary infection averted. The results display a favourable economic profile. Routine HIV screening in STD-clinics should be considered as a highly cost-effective prevention measure even in countries with a low HIV prevalence.

In chapter 12 of this thesis, the pharmacoeconomic profile of highly active antiretroviral therapies (HAART) in HIV/AIDS is evaluated. An overview of the studies that have been published is presented as well as the most important outcomes and methodological issues. The articles studied in this review provide a clear indication about the pharmacoeconomic effects of the different antiretroviral therapies on health economics and patient outcomes. The use of HAART (highly active antiretroviral therapy) is associated with a large increase in costs for pharmaceuticals, which are in many studies offset by a large decline in opportunistic infections and related hospitalisations. From a pharmacoeconomic viewpoint, HAART is preferable above dual NRTI and single NRTI use.

Chapter 13 lists the main findings of this thesis, ranging from methodological issues such as the choice of the cost-effectiveness model or the valuing of future health benefits, to practical applications. The increasing importance of pharmacoeconomic evaluations for policy-making is noted and some limitations are discussed. The importance of other factors, such as ethical and political, is stressed as drivers for the decision-making process.