Assessment of vaccination policies from a health economic perspective: opportunities and emerging foci

Zeevat, Florian

DOI:
10.33612/diss.826151049

Chapter 3

Cost-Effectiveness of Meningococcal-B Vaccination in the Netherlands

Florian Zeevat & Joost J. M. Simons
Tjalke A. Westra
Jan C. Wilschut
Nina M. van Sorge
Cornelis Boersma
Maarten J. Postma

Submitted

Abstract

In the Netherlands, most cases of invasive meningococcal disease (IMD) are caused by meningococcal serogroup B (MenB). Here, we estimate the incremental cost-effectiveness ratio (ICER) of infant vaccination against MenB IMD with the four-component meningococcal B vac-cine (4CMenB), from a new analytical perspective using the Dynamic transmission-based Cost-Effectiveness (DyCE) model. A cost-effectiveness analysis of 4CMenB vaccination was per-formed, based on the average incidence of IMD from 2010 to 2019 in the Netherlands, using the DyCE model. Fifty cohorts of children were vaccinated and followed-up until the end of life. An optimized dosing schedule, new vaccine data (costs and effectiveness), and comprehensive cost estimates of the long-term effects of IMD were included. Various scenarios involving different numbers of cohorts and IMD incidence were explored. The ICER in the base case was estimated to be €105,525 per quality-adjusted life-year (QALY). This ICER is based on the list price of 4CMenB, of €78.50 per dose. By varying the incidence in scenarios, the ICER became more favorable, at €19,695 in the scenario with the highest incidence. Vaccination with 4CMenB is not cost-effective in the base case in the Netherlands, but could be cost-effective if alternative assumptions of an increased incidence in the future are considered.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has once more illustrated the enormous threat that infectious diseases can pose to our society and that vaccines remain the foremost approach to control this threat. While COVID-19 vaccines have necessarily been used to control the pandemic while it was ongoing, perhaps an even more important value of vaccines remains the prevention of infectious disease outbreaks.

Invasive meningococcal disease (IMD) is a severe infectious disease with an unpredictable nature, causing acute meningitis and sepsis, which are associated, for a high proportion of survivors (up to 51.6% of infants and more than 40% overall), with a range of long-term complications of varying severity, such as neurological deficits (for example, hearing loss and mental health problems) or the need for limb amputation. In Europe, most cases of IMD are caused by *Neisseria meningitidis* serogroup B (MenB)[44].

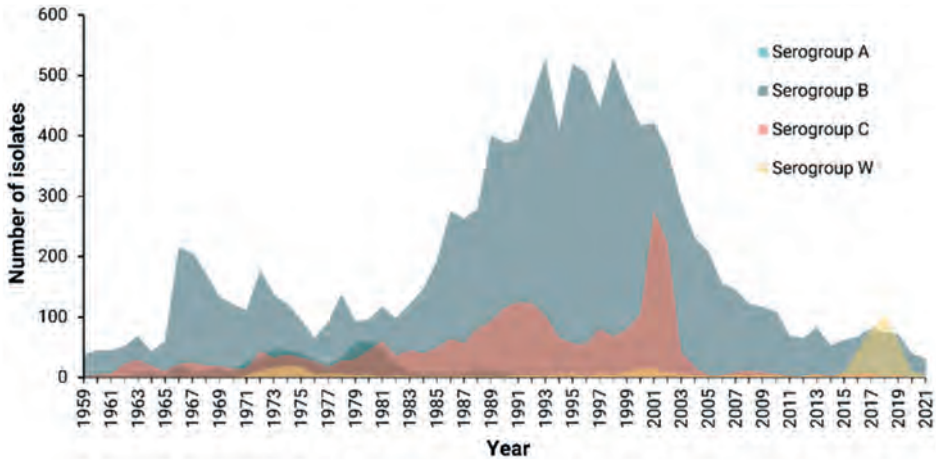

Figure 1. Historical numbers of invasive meningococcal disease cases in the Netherlands. 1959-2021, as reported by the Netherlands Reference Laboratory for Bacterial Meningitis (redrawn with permission). Adapted from the 2021 annual report of the Netherlands Reference Laboratory for Bacterial Meningitis57.

Figure 1, which shows the incidence of serotype-specific IMD in the Netherlands, illustrates the unpredictable nature of IMD[57]. Notably, there is a generally low incidence of meningococcal serogroup A (MenA) in the Netherlands. A vaccination program against meningococcal serogroup C (MenC) was initiated in the Netherlands in 2001 following an outbreak. Figure 1 also shows a more recent outbreak, of meningococcal serogroup W (MenW), which has been countered by switching from the monovalent MenC vaccine to the quadrivalent, meningococcal types A, C, W, and Y (MenACWY) vaccine in children and introducing MenACWY vaccination in adolescents in 2017[44,57,95]. Figure 1 further shows that levels of MenB disease were relatively high in the 1990s but have drastically decreased since then. In the past two years particularly, the number of MenB cases has

been low as a result of the COVID-19-related countermeasures that prevented the spread of many other infectious diseases in addition to COVID-19[57,96]. These data highlight the unpredictable nature of this infectious disease and the potential risk of increasing incidence in the (near) future, both as a result of natural fluctuations and in relation to a potential rebound effect following the removal of all COVID-19 countermeasures. This risk is especially likely for MenB as the other serotypes are currently covered by vaccination programs.

Some countries, for example the United Kingdom, have included MenB vaccination in their national immunization programs since 2015. The Netherlands, among some other European countries, has not yet introduced MenB vaccination, partly due to assumed unfavorable cost-effectiveness[44,48].

Previously, a cost-effectiveness analysis of the implementation of the four-component meningococcal B vaccine (4CMenB) was performed for the specific situation in the Netherlands[48]. However, this analysis needs to be updated based on newly available data.

New (long-term) effectiveness and safety data have been published, for example from England, Italy and Portugal[47,97–99]. In addition, more insights have been gained into the long-term burden and cost of MenB IMD in the Netherlands to patients and more broadly[100]. A recent cost-of-illness study analyzed the economic burden of IMD, including acute infection and its associated sequelae (e.g., hearing loss, neurological disabilities, limb amputation, epilepsies, skin scarring, renal disease, blindness/severe visual impairment, and psychological impairments)[100].

Previous cost-effectiveness analyses were based on single-cohort models[44,48], whereas vaccination programs are inevitably not implemented for one cohort only. Therefore, multi-cohort models are more appropriate to reflect incremental cost-effectiveness ratios (ICERs) and provide an improved estimate of the impact of 4CMenB vaccination on potential herd immunity, cross-protection against other serotypes, and of the desired impact of differential discounting. Concerning the last of these, the Netherlands implemented differential discounting (4% for costs and savings and 1.5% for quality-adjusted life-years (QALYs)), to prevent undervaluation of QALYs for future cohorts to be vaccinated[54].

A study by Pouwels *et al.* (2013) served as a starting point for our updated analysis[48]. As already mentioned, this previous analysis was performed with a single-cohort model, based on scarce resource use and cost data available at the time, no spillover effect, a schedule requiring four doses, and a (then hypothetical) per-dose price of €40. The base-case ICER was estimated to be €243,778 per QALY gained, using epidemiological data from the early 21st century (Figure 1)[57]. Notably, if the epidemiological data of the late 20th century (1985-2000) were used (Figure 1), the ICER would have improved to €85,931 per QALY gained.

Given the severity of MenB infections, €80,000 per QALY was previously defined as the threshold to be applied in the Netherlands[101,102], illustrating that an upsurge in incidence could bring the ICER close to acceptable levels, even in an analysis that did not fully reflect the potential value of MenB vaccination.

The present study aims to provide estimates in terms of costs per QALY gained, derived from a new analytical approach using the Dynamic transmission-based Cost-Effectiveness (DyCE) model with the latest data and following Dutch health-economic guidelines.

Materials and Methods

A comprehensive cost-effectiveness analysis of the broad-ranging disease burden of MenB IMD in the Netherlands was performed using the DyCE model. This model, recently developed and applied in England and Germany, has been used to assess the cost-effectiveness of implementing an infant vaccination program with the recombinant meningococcal serogroup B (4CMenB) vaccine[51,103]. The DyCE model is a dynamic, transmission-based cost-effectiveness model consisting of a dynamic transmission model (DTM) to simulate the transmission of the disease carriage and an economic decision tree to simulate the long-term effects of the infection and its sequelae. In the base case of our updated analysis, the average number of infections in the second decade of the 21st century was used (Figure 1), derived from data collated by the Netherlands Reference Laboratory for Bacterial Meningitis (NRLBM) that were based on isolates submitted by Dutch hospitals.

In our updated analysis, using the DyCE model, we applied the updated resource use, burden of sequelae (physical and neurological, excluding mental), and cost estimates[100]; a three-dose schedule; 50 vaccinated cohorts (followed until end of life); and slightly higher estimates of vaccine effectiveness and duration of protection[97–99]. Comparable to the analyses in Germany and England, health spillover effects from the affected children to their parents were included in the QALY estimates. Additionally, sensitivity analyses were conducted to investigate increased incidence (outbreaks) and reduced/increased numbers of cohorts included in the model. An overview of the key parameters for the model is shown in the Supplementary Materials.

Finally, it should be noted that for the current analysis, herd immunity effects and potential protective effects against other serotypes were excluded.

Results, Discussion, and Conclusion

The cost-effectiveness of vaccination with the 4CMenM vaccine in the base case in the Netherlands was estimated at €105,525 per QALY gained, based on the current 4CMenB list price of €78.50, 50 cohorts vaccinated, and the average incidence of IMD in the Netherlands during the period 2010 to 2019 (approximately 80 cases per year). The ICER was calculated using the total QALYs gained (9,299) and the total discounted incremental costs including productivity losses (€981,240,557). When mental health sequelae were excluded, the ICER became less favorable (€131,940). Changing the number of cohorts in the model to 100 and 1 cohorts resulted in ICERs of €80,185 and €137,531, respectively.

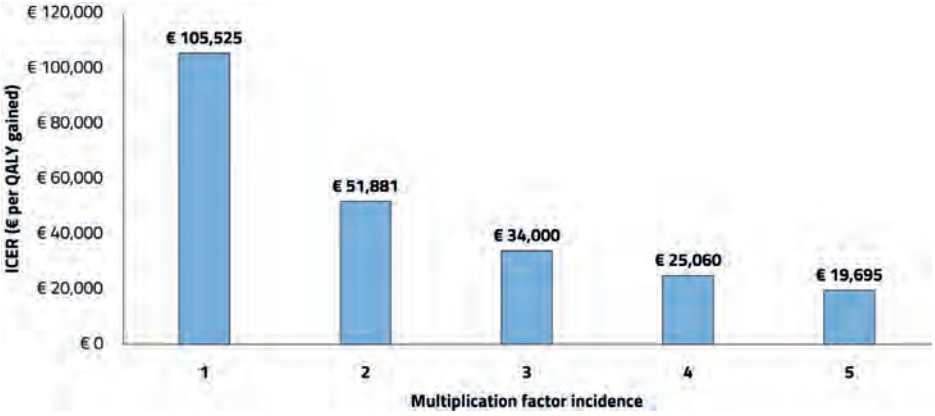

Figure 2. ICER analysis of vaccination with the four-component meningococcal vaccine (4CMenB) in the Netherlands by incidence. The incidence is presented on the x-axis as the multiplier on the average MenB base-case incidence from 2009 to 2019. This figure is based on the DyCE model running 50 cohorts. Note: DyCE, Dynamic Cost-Effectiveness model; ICER, incremental cost-effectiveness ratio; MenB, meningococcal serogroup B; QALY, quality-adjusted life-year.

Figure 2 shows all five scenarios of the cost-effectiveness analysis for incidence (base-case incidence multiplied by 2, 3, 4, or 5) with 50 cohorts included in the model. These analyses illustrate the potential to reduce the ICER to levels of less than €80,000 per QALY gained, if the incidence increases to the levels seen between 1990 and 1999 (×5) or 2000 and 2009 (×3). In total, four out of the five scenarios assessed showed an ICER of less than €80,000 per QALY gained.

The follow-up of one cohort in our analysis is comparable to the previous analysis in which a single-cohort model was used. The previous analysis by Pouwels *et al.* (2013) estimated an ICER of €243,778 per QALY gained with a lower vaccine price (€40.00 compared with €78.50) and higher incidence rates (approximately 435 cases on average in the period 1990 to 1993 compared with 85 cases on average in the period 2010 to 2019)[48].

It is important to assess the potential impact of any increasing incidence (or outbreak) of MenB IMD, especially as the recent COVID-19 counter-measurements are being lifted. This unpredictability could be partly countered by early implementation of vaccination. When we applied a multiplication factor of 5 to the base-case incidence (referring to an outbreak setting, comparable to 1990–1999), the ICER decreased from €105,525 to €19,695 (see Figure 2). Doubling the incidence leads to the outcome being cost-effective, with an ICER of €51,881. This difference in outcome is due to the optimized dosing schedule, new vaccine data, and more comprehensive cost- and disease-burden estimates of the long-term effects of IMD.

For 4CMenB, the National Health Care Institute of the Netherlands ("Zorginstituut Nederland") and the Health Council (HC) have indicated that, due to the severity of MenB-induced disease, the appropriate cost-effectiveness threshold to be applied is €80,000 per QALY gained[101,102]. Here, we showed that most of the ICER values found in different scenarios are below this threshold. Only the scenario with the current historically low incidence is just above the cost-effectiveness threshold.

In conclusion, when assuming different scenarios with a potential elevated incidence of IMD to account for future outbreaks, vaccination against MenB with the 4CMenB vaccine may well represent a cost-effective intervention in the Netherlands, even though such an approach is not cost-effective in the current base case with a historically low incidence.