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Short communication

Health impact and cost-effectiveness of introducing the vaccine (Bexsero) against MenB disease into the Brazilian immunization programme

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ABSTRACT

Invasive meningococcal disease (IMD) is associated with a high mortality and severe sequelae. The aim of the present study was to evaluate the potential cost-effectiveness of the Bexsero vaccine in Brazil. We used a cohort model to compare routine vaccination against MenB disease with no vaccination. Epidemiological and cost estimates were obtained from the Brazilian Health Information System. The cost per disability-adjusted life year (DALY) averted and incremental cost-effectiveness ratio (ICER) was estimated assuming a 3-dose vaccination schedule, at R$90 (£ 20.50) per vaccine dose, 82.0% vaccine efficacy against MenB disease and a vaccine uptake of 90.0%. We estimated that 1,527 MenB cases would be prevented and 78 deaths averted. This strategy would cost R$ 762,381, 000 (£ 174,059,503) with a R$ 4,364,280 (£ 996,410) reduction in disease treatment costs. However, at an ICER of 372,256 (£ 84,990) per DALY averted, a vaccination programme is unlikely to be cost-effective.

1. Introduction

Neisseria meningitidis remains an important cause of bacterial meningitis in all ages and is a major public health problem [1]. Invasive meningococcal disease (IMD) may become rapidly life-threatening, often within hours and may cause neurological and other disabling sequelae [2]. In Brazil, *N. meningitidis* is the main etiological agent of meningitis in children above the age of 3 months and in young adults; since the 1970s IMD is predominantly caused by serogroups B and C [3,4]. Between 1990 and 2001, the annual incidence rate was approximately 1–3 cases per 100,000 population. A significant shift from serogroup B to serogroup C was observed from 2002 onwards, when serogroup C became the most frequent. Notification rates of IMD as high as 7.0/100,000 population were reported for children under two years old during 2009 and 2010 [5,6].

Vaccination is considered the best strategy for IMD control [7]. In May 2015, Bexsero, a new protein-based vaccine designed to offer widespread protection against group B disease, was licenced in Brazil. This vaccine has not yet been included in the National Immunization Program (NIP). Since 2005, health technology assessments and economic evaluation studies have been requested to assist decision-making for the introduction of new vaccines into the NIP in Brazil [8]. Here, we aimed to evaluate the potential health impact and cost-effectiveness of the introduction of Bexsero vaccine into Brazil's NIP for children younger than 1 year of age.

2. Methods

The IMD incidence rate was calculated based on the number of confirmed cases of the disease reported in 2014 from the National Information System for Notifiable Diseases (*Sistema de Informação de Agravos de Notificação*, SINAN), which registers data from both public and private health services. IMD notification is mandatory in Brazil, but the serogroup is not identified in a large proportion of cases. For the purposes of this study we assumed that the distribution of serogroups in these unidentified cases would be proportional to that observed in identified cases and thus inflated our serogroup-specific estimates.

Age-specific incidence were calculated using population estimates for Brazil. The under-one-year-old population and 1–4 years olds were based on the Live Birth Information System *(Sistema de Informacões sobre Nascidos Vivos*, SINASC). Data for individuals age 5–75 years olds were obtained from National Survey of

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Household Samples (*Pesquisa Nacional por Amostra de Domicílios*, PNAD). The life expectancy at birth was based on Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística*, IBGE).

We also determined that survivors of IMD could have neurological sequelae, amputation, skin disorders or no sequelae. The proportion of survivors with sequelae was estimated from a global systematic review as 7.2% [9]. The DALY weight for survivors with sequelae was 0.26. Case-fatality rates by age groups were calculated based on confirmed cases and deaths reported to SINAN. Costs for IMD treatment were based on Department of the Unified Health System (*Departamento de Informática do Sistema Único de Saúde*, DATASUS) and costs for hospital admissions in the public sector were obtained from the Hospital Information System (*Sistema de Informação Hospitalar*). In the absence of national data, the vaccine cost per dose was assumed to be R$ 90.00 (£ 20.5) and administration cost per dose was assumed to be R$ 3.57 (£ 0.81) based on literature [10]. An 3-dose vaccine immunization schedule at 2, 4 and 12 months was considered as reported in other studies [11,12].

In the base case we estimated that the vaccine had 82% vaccine efficacy against MenB disease (all strains) and that vaccine uptake was 90.0%. [12]. The average duration of protection was assumed to be 3 years [13]. We used a cohort model to compare routine vaccination against MenB disease with no vaccination. We conducted a cost–effectiveness analysis (CEA). The analysis was performed using Microsoft Excel (2016) and is expressed in terms of Incremental Cost Effectiveness Ratio (ICER) per DALY averted. According to the Ministry of Health guidelines a 5% wastage rate was included [10]. We examined the sensitivity of our results to changes in key parameters using one-way sensitivity analyses on vaccine duration, vaccine coverage and vaccine price. In addition, we developed a 'most favourable' scenario where we considered the longest duration and lowest vaccine price. Adverse events following immunization (AEFI) were not considered in the model [14].

3. Results

The health and economic outcomes of introducing the Bexsero vaccine into the Brazilian NIP are presented in Table 1. A universal infant MenB vaccination program would prevent some 1,527 IMD cases, 78 deaths and 7,792 DALYs in one birth cohort, assuming 3 years of protection. This strategy would cost R$ 762,381,000 (£ 174,060,000) with a corresponding R$ 4,364,280 (£ 996,410) reduction in disease treatment costs. This results in an ICER of R$ 372,256 (£ 84,990) per DALY averted. We explored the change in cost-effectiveness according to different durations of vaccine protection. Extending the duration to 5 years, would prevent 2,728 IMD cases and 136 deaths. This also improved the ICER to R$ 236,325 (£ 53,955) for 5 years protection.

Bexsero was designed to provide protection against MenB, however, it has been reported that it does appear to also induce protection on non-B serogroups [15]. We explored this, when considering protection against all serogroups (all other parameters at base case value), vaccination would prevent 3,034 IMD cases and 146 deaths

Table 1
Epidemiological impact and cost-effectiveness of Bexsero vaccination in Brazil assuming coverage 74% of circulating meningococcal strain and 82% vaccine efficacy against disease.

Parameters	No vaccination[a]	MenB vaccination programme (duration of protection)		
		3 years	5 years	10 years
Cases	4,987	3,460	2,259	1,908
Deaths	302	224	166	148
Total DALYs				
Undiscounted	21,671	7,792	12,871	14,497
Discounted at 5%	4,678	2,048	3,218	3,561
Total IMD costs (R$)				
Undiscounted	10,607,965	4,180,826	6,626,384	7,334,192
Discounted at 5%	8,302,570	4,364,280	6,251,090	6,722,816
ICER (R$/DALY averted)				
Undiscounted		97,309	58,719	52,083
Discount at 5%		370,219	234,823	212,042

MenB, meningococcal group B disease; ICER, incremental cost-effectiveness ratio; DALY, disability-adjusted life year; [a]no vaccination was estimated considering MenB incidence. The costs were estimated in Brazilian Reais.

Table 2
Epidemiological impact and cost-effectiveness of Bexsero vaccination in Brazil when considering protection against all serogroups assuming coverage 74% of circulating meningococcal strain and 82% vaccine efficacy against disease.

Parameters	No vaccination[a]	Vaccination programme (duration of protection)		
		3 years	5 years	10 years
Cases	17,714	14,679	11,723	9,355
Deaths	1,634	1,487	1,289	1,190
Total DALYs				
Undiscounted	80,746	14,955	27,110	36,636
Discounted at 5%	13,254	3,720	6,056	8,056
Total IMD costs (R$)				
Undiscounted	33,552,672	8,608,849	14,301,930	19,061,344
Discounted at 5%	21,308,897	9,351,953	13,224,568	16,390,690
ICER (R$/DALY averted)				
Undiscounted		50,403	27,593	20,289
Discount at 5%		202,606	123,534	92,267

ICER, incremental cost-effectiveness ratio; DALY, disability-adjusted life year; [a]no vaccination was estimated considering meningococcal disease (all serogroups) incidence. The costs were estimated in Brazilian Reais.

assuming 3 years protection and 5,991 IMD cases and 345 deaths assuming 5 years (Table 2).

When we evaluated the cost of the vaccine at R$ 45.00 (£ 10.20) per dose (i.e. 50% lower) and at 3 years of protection the ICER remained high R$ 191,190 (£ 43,650) per DALY averted. Considering that vaccination could only be considered cost-effective ICER at 3 × gross domestic product (GDP) per capita (2016 Brazilian GDP per capita: R$ 30,407) [10], this suggests an upper price limit of only R$ 19.00 (£4.30) per dose (with 3 years protection), although this rises to R$ 37.00 (£8.40) for 10 years of protection.

4. Discussion

In this study, we used data obtained from the SINAN database to evaluate the cost-effectiveness of introducing a universal childhood immunization with Bexsero into the Brazilian NIP. Our findings suggest that a routine immunization program is expected to prevent 1,527 invasive MenB cases and 78 deaths over 3 years with at a net cost of R$ 762,381,000 (£ 174,059,503). There is no official willingness-to-pay threshold for Brazil, nevertheless, with an ICER of R$ 372,256 (£ 84,990) per DALY averted, it is highly unlikely that vaccination with Bexsero would be cost-effective, (particularly when considering a threshold ICER of between 1 × and 3 × the GDP per capita), as recommended by the World Health Organization (WHO) [16]. The ICERs remained high even when we increased the duration of protection up to 10 years. This is because the risk of IMD declines with age over the first 10 years of life.

The United Kingdom became the first country to routinely offer Bexsero vaccination to infants in 2015. Moreover, several countries are considering the introduction of this vaccine for universal immunisation. In general, our findings are consistent with previous studies. Economic evaluations of Bexsero have been published for Germany (ICER of € 2,015,300 per QALY), Netherlands (ICER of € 243,778 per QALY), Canada (ICER of C$4,756,189 per QALY), Italy (ICER of €376,042 per QALY), Belgium (ICER of € 422,700 per QALY) and France (ICER of € 380,973 per QALY). These studies concluded that Bexsero would not be cost-effective even when considering herd immunity effects, increasing invasive MenB disease incidence, lower discount rates and increased duration of protection [13,14,17–19]. However, an Italian study reported that routine vaccination is advisable (ICER of € 109,762 per QALY) when the official data on disease incidence were considered compared to an ICER of € 26,599 per QALY avoided if estimated data were considered [20].

It is important to emphasize that our analysis was carried out from the healthcare payer's perspective and that indirect costs (e.g., caregiver productivity losses and transportations cost) were not evaluated. Nevertheless, our findings are consistent with other studies from a societal perspective [14,19]. Additionally, in this analysis we considered that the Bexsero would be administered simultaneously with other vaccines already included in the NIP, thus the costs of additional visits were not included in the analysis.

One of the main strengths of this study is that we used the latest available data for MenB incidence and treatment cost in Brazil. Additionally, to our knowledge this is the first study to consider Bexsero cost-effectiveness in a lower or middle-income country (LMIC). However, some limitations of this study should be considered. Firstly, we did not correct for any herd immunity effects in our analysis, even though a study of a MenC vaccination program reported that herd protection is an important variable for vaccine effectiveness [21] However, the impact of Bexsero on carriage and its ability to generate herd immunity remains unknown [17]. In addition, only the sequelae-specific procedure costs were included as the costs for long-term for neurological sequelae and rehabilitation are not available in Brazil. Ignoring the impact of herd immunity and the associated costs for long-term sequelae could underestimate the positive effect of the vaccination programme. However, considering an ICER of R$ 372,256 (£ 84,990) these limitations are unlikely to have influenced the results to such an extent that Bexsero could be considered cost-effective.

5. Conclusion

This is the first study on the cost-effectiveness of Bexsero vaccination against invasive MenB disease in a lower or middle-income country. While there are uncertainties about some vaccine parameters, Bexsero, as priced for high income countries, would not represent a cost-effective intervention. Further work should investigate the utility of Bexsero in outbreak situations.

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Author contributions

Conceptualization: MMS, AJAM, CLT. Drafting the manuscript: MMS, CLT. Data collection: MMS. Statistical Data analysis: MMS, CLT. Interpretation of the results: MMS, CLT. Wrote the paper and preparation of the manuscript: MMS, CLT. Review and editing: MMS. AJAM, CLT. All authors approved the final version of the manuscript.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [CTL reports receiving consulting payments from GSK (2018) and an honorarium from Sanofi-Pasteur (2015)].

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