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Economic evaluation of *Haemophilus influenzae* type b vaccination in Moscow, Russian Federation

A.E. Platonov [a,*], U.K. Griffiths [b], M.V. Voeykova [a], O.V. Platonova [a], I.L. Shakhanina [a,c], G.G. Chistyakova [c], S.E. Robertson [b], the Moscow Hib Study Team

[a] *Central Institute of Epidemiology, Novogireevskaya Street, 3a, Moscow 111123, Russian Federation*
[b] *Department of Immunization, Vaccines and Biologicals, World Health Organization CH1211, Geneva 27, Switzerland*
[c] *State Center for Sanitary and Epidemiological Control, Grafskii per, 5, Moscow, Russian Federation*

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Abstract

Objective: To estimate the cost-effectiveness of providing *Haemophilus influenzae* type b (Hib) vaccine to children in Moscow in routine immunization services.
Methods: The incidence of Hib meningitis among children aged <5 years in Moscow was obtained from a prospective surveillance study undertaken during October 1999–September 2001, with treatment cost data collected for all cases. Sequelae in surviving children were assessed in December 2002. The costs of Hib vaccination in Moscow were estimated assuming a vaccine price of US$5 per dose and the same four-dose schedule and 97% coverage as for diphtheria–tetanus–pertussis vaccine. The most uncertain variables were varied in a sensitivity analysis.
Results: The annual incidence of Hib meningitis was 5.7 per 100,000 children <5 years. The average treatment cost for an acute Hib meningitis case was US$1296. For a patient with sequelae, the average additional lifetime discounted treatment cost was US$15,820. The total annual cost of Hib vaccination of infants in Moscow was estimated as US$1.5 million per year. In the base case analysis, the cost-effectiveness ratios amount to US$77,503 per Hib meningitis case averted and US$10,842 per discounted disability adjusted life year averted. The break-even vaccine price, where the annual vaccination costs equal annual treatment costs averted, is only US$0.04 per dose in the base case scenario. If discounted indirect costs are included, the break-even vaccine price is US$0.5 per dose.
Conclusion: In Moscow, the incidence of Hib meningitis is low and the costs of hospitalization and subsequent medical treatment are relatively inexpensive. Given these factors, Hib vaccine at US$5 per dose would not be a cost-effective option in Moscow at the present time.

Keywords: *Haemophilus influenzae* type b vaccine; Economic evaluation; Meningitis; Russian Federation

1. Introduction

Conjugate *Haemophilus influenzae* type b (Hib) vaccines have been available since the early 1990s. Most industrialized countries quickly introduced Hib vaccine into their routine infant immunization services with the aim of preventing the well documented burden of invasive Hib disease. A total of 74 population-based studies conducted in industrialized countries in the pre-vaccine era found a mean annual incidence of 22 Hib meningitis cases per 100,000 children <5 years of age [1].

Developing countries and countries with economies in transition have been slow to introduce Hib vaccine. This is due to a variety of reasons, but the most important are the relatively high price of the vaccine and insufficient information on the disease burden caused by Hib. Of the 27 countries classified by the United Nations as having economies in transition [2], only Croatia, Czech Republic, Hungary, Latvia, Slovakia, and Slovenia have introduced Hib vaccine in their

* Corresponding author. Tel.: +7 095 305 5424; fax: +7 095 305 5423.
E-mail address: platonov@pcr.ru (A.E. Platonov).

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national immunization programme, based on data reported to the World Health Organization (WHO) as of October 2004.

In the Russian Federation, there has been interest in Hib as a cause of pediatric meningitis for many years [3–5]; however, previous studies were not population-based. According to these studies about 20% of bacterial meningitis among children <5 years of age in Moscow was due to Hib, with a 5–10% case–fatality rate. With technical and financial support from WHO, a prospective population-based surveillance study was carried out in Moscow during 1999–2001 to identify the incidence of Hib meningitis among children <5 years of age. Details on the surveillance aspects of this study have been reported elsewhere [6,7], as have other findings [8,9]. As part of the surveillance study, health care costs were collected from patients with Hib meningitis. In the present paper, the surveillance findings and the cost data have been incorporated into an economic evaluation of routine infant Hib vaccination. As the surveillance study was conducted in Moscow, we have limited the cost-effectiveness analysis to only include this city.

2. Methods

The costs and effects of the following two alternatives were compared in the economic evaluation: (1) status quo, where Hib vaccine is not delivered to infants as part of the routine childhood immunization services in Moscow, and (2) inclusion of Hib vaccine in the routine childhood immunization services in Moscow. The effect of the vaccine was estimated in terms of Hib meningitis cases, deaths and disability adjusted life years (DALYs) averted. This was done by multiplying the predicted annual number of cases, deaths, and DALYs by vaccine coverage and vaccine efficacy. Cost-effectiveness ratios were calculated by subtracting the predicted treatment cost savings from the costs of vaccine delivery and dividing this number by the effectiveness estimate. A societal viewpoint was taken in the analysis. The average 2001 exchange rate of 29.18 rubles to 1 US$ was used for all cost data [10]. Future values, such as treatment costs for sequelae, DALYs and productivity costs, were discounted by 3% per year as recommended in standard guidelines [11].

2.1. Estimating Hib meningitis disease burden

A prospective 2-year surveillance study was undertaken in Moscow from 1 October 1999 through 30 September 2001 following the WHO generic protocol for population-based surveillance of *H. influenzae* type b [12]. The study was reviewed and approved by the Ethical Committee of the Central Research Institute of Epidemiology, Moscow and the WHO Secretariat Committee for Research Involving Human Subjects, Geneva, Switzerland.

The Moscow population aged <5 years included 344,000 children at the time of the study. Prior to the study, public health regulations in Moscow were revised to require routine reporting of all cases of meningitis due to Hib (previously only meningitis due to *Neisseria meningitidis* had been officially reportable). Children with suspected meningitis were transported to hospital by ambulance free of charge. Inclusion of all possible cases of meningitis in children <5 years was ensured by active surveillance at the two main infectious disease hospitals (The First and Second Moscow Hospitals for Infectious Diseases) where patients with suspected meningitis are usually admitted, as well as at six pediatric hospitals (numbers 1, 2, 5, 7, 9, and 13), each of which reported at least seven pediatric meningitis admissions in the year prior to the study. Subsequent reviews of official data on hospital admissions for infectious diseases revealed that no other cases of meningitis in children <5 years of age were reported by any other hospital in Moscow during the study period.

Routine diagnostic procedures for children with meningitis include lumbar puncture with immediate transport of the cerebrospinal fluid (CSF) specimen to the laboratory. CSF specimens were cultured on chocolate agar supplemented with X and V factors using internationally recommended procedures [13], tested for Hib antigen by a commercial latex agglutination test, and sent to the Second Moscow Hospital for Infectious Diseases for polymerase chain reaction testing (PCR) [8]. Staff from the microbiology laboratories at all eight hospitals received training and were enrolled in a proficiency-testing scheme. As a result, 85% of suspected bacterial meningitis cases were laboratory confirmed with an organism identified. During the study international experts in epidemiology and microbiology visited all eight study hospitals and their laboratories to assess the completeness of case identification and the quality of the microbiological laboratory work. In addition, the WHO Collaborating Centre for *H. influenzae* at the Health Protection Agency, United Kingdom conducted blinded proficiency tests for the main laboratory and confirmed findings for a subset of the study samples.

The annual predicted number of Hib meningitis cases was estimated by dividing the number of cases found in the 2-year surveillance study by 2.

2.2. Vaccine coverage and costs of Hib vaccine delivery

In the base case scenario, it was assumed that Hib vaccine would be introduced into the infant immunization schedule at the same time as diphtheria–tetanus–pertussis (DTP) vaccine, e.g. at 3, 4, 5, and 18 months. While most other countries use Hib vaccine in a three-dose schedule, a four-dose schedule is part of the license for the Aventis-Pasteur Hib vaccine granted by the Russian Federation [14].

In Moscow, reported coverage of children with four doses of DTP vaccine has been >90% since 1995, DTP vaccine coverage was 95% for four doses and 97% for three doses in 2003. As the Hib vaccine would be given according to the same schedule as DTP vaccine, similar coverage rates were assumed.