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Research

Economic evaluation of delivering *Haemophilus influenzae* type b vaccine in routine immunization services in Kenya

Angela Oloo Akumu,^a Mike English,^a J Anthony G Scott^b & Ulla K Griffiths^c

Objective *Haemophilus influenzae* type b (Hib) vaccine was introduced into routine immunization services in Kenya in 2001. We aimed to estimate the cost-effectiveness of Hib vaccine delivery.

Methods A model was developed to follow the Kenyan 2004 birth cohort until death, with and without Hib vaccine. Incidence of invasive Hib disease was estimated at Kilifi District Hospital and in the surrounding demographic surveillance system in coastal Kenya. National Hib disease incidence was estimated by adjusting incidence observed by passive hospital surveillance using assumptions about access to care. Case fatality rates were also assumed dependent on access to care. A price of US\$ 3.65 per dose of pentavalent diphtheria-tetanus-pertussis-hep B-Hib vaccine was used. Multivariate Monte Carlo simulations were performed in order to assess the impact on the cost-effectiveness ratios of uncertainty in parameter values.

Findings The introduction of Hib vaccine reduced the estimated incidence of Hib meningitis per 100 000 children aged < 5 years from 71 to 8; of Hib non-meningitic invasive disease from 61 to 7; and of non-bacteraemic Hib pneumonia from 296 to 34. The costs per discounted disability adjusted life year (DALY) and per discounted death averted were US\$ 38 (95% confidence interval, CI: 26–63) and US\$ 1197 (95% CI: 814–2021) respectively. Most of the uncertainty in the results was due to uncertain access to care parameters. The break-even pentavalent vaccine price – where incremental Hib vaccination costs equal treatment costs averted from Hib disease – was US\$ 1.82 per dose.

Conclusion Hib vaccine is a highly cost-effective intervention in Kenya. It would be cost-saving if the vaccine price was below half of its present level.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Haemophilus influenzae type b (Hib) vaccine has been licensed for use in infants since 1991. Most industrialized countries introduced the vaccine quickly into routine infant immunization services. This was justified by observed annual incidence rates of Hib meningitis between 20 and 69 cases per 100 000 children under five years old.¹ Middle-income and developing countries have been hesitant to introduce the vaccine because of its relatively high price and the problem of establishing the Hib disease burden in areas with very little surveillance. However, since 2001 the GAVI Alliance (previously the Global Alliance for Vaccines and Immunization) has provided financial support for new and

underused vaccines in 72 low-income countries.² By July 2005, GAVI supported the introduction of Hib vaccine in 17 of these countries, usually delivered in combination with diphtheria-tetanus-pertussis (DTP) and hepatitis B vaccines as a pentavalent vaccine.²

Kenya was among the first nine countries to receive financial support from GAVI, and pentavalent vaccine was introduced nationwide in November 2001. GAVI's financial commitment for new vaccines in Kenya was US\$ 67.4 million over a five-year period,² after which it was anticipated that the vaccine price would decrease substantially – an expectation yet to be realized. Support was planned to end in 2006, but recently GAVI offered to extend assistance through 2006–2015

with country co-financing. GAVI's phase II strategy is that recipient countries make progressive increases to their contributions to vaccine costs so that they reach market prices by 2016.³ In 2007 the Kenyan Government agreed to co-finance the pentavalent vaccine with US\$ 0.38 per dose for the period 2006–2011 (letter from Minister of Health to GAVI, 18 April 2007). Hib vaccination is a new cost item in the Kenyan Government's health budget; therefore cost-effectiveness evidence is likely to be crucial when deciding on future financial support. The objective of this study was to estimate the incremental costs per case, death and DALY, averted by delivering Hib vaccine in routine infant immunization services in Kenya.

^a Kenya Medical Research Institute (KEMRI)/Wellcome Trust, Nairobi, Kenya.

^b KEMRI/Wellcome Trust, Kilifi, Kenya. Nuffield Department of Clinical Medicine, University of Oxford, England.

^c London School of Hygiene and Tropical Medicine, Health Policy Unit, Keppel Street, London WC1B 3DP, UK. Correspondence to Ulla K Griffiths (e-mail: ulla.griffiths@lshtm.ac.uk).

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Table 1. Parameters for estimating burden of Hib disease in Kenya before and after vaccine introduction

Parameter	Base case value	Range used in uncertainty analysis	Ref.
2004 birth cohort	1 322 000	–	24
Pentavalent & DTP+hep B vaccine coverage of 3rd dose	73%	70–75%	24
Types of Hib disease:			
Meningitis of total invasive Hib disease	54%	52–56%	11
Non-meningitic invasive disease of total invasive Hib disease	46%	–	11
Hib pneumonia:Hib meningitis cases	5:1	SD 0.5	5–7
Hib invasive disease hospital incidence:			
Before Hib vaccine introduction	66	49.6–81.6	11
After Hib vaccine introduction	7.60	1.6–22.3	11
Access to health care for children < 5 years with Hib disease:			
Hospital care	50%	30–70%	12,13
Outpatient care	25%	15–35%	12,13
No access to formal care	25%	15–35%	12,13
Case fatality rates for children < 5 years:			
Hib meningitis + hospital treatment	17%	7–44%	16,25
Hib meningitis & non-meningitis invasive Hib disease + outpatient treatment	63%	40–90%	26
Hib meningitis & Hib non-meningitis invasive disease + no biomedical treatment	97%	80–100%	Assumption
Non-meningitis invasive Hib disease + hospital treatment	26%	7–44%	9
Non-bacteraemic Hib pneumonia + hospital treatment	3.5%	2.5–4.5%	Assumption
Non-bacteraemic Hib pneumonia + outpatient treatment only	7%	2.5–10%	Assumption
Non-bacteraemic Hib pneumonia + no biomedical treatment	25%	15–35%	27

DTP, diphtheria-tetanus-pertussis; hep B, hepatitis B; Hib, *Haemophilus influenzae* type b; SD, standard deviation.

Methods

A model was developed to follow the 2004 birth cohort until death. Two scenarios were constructed: one with Hib vaccine in routine immunization services and one without. Only immediate costs of care were estimated, excluding the costs of providing long-term care for patients with severe sequelae. The analysis was carried out from a public health provider perspective; costs incurred by households were not included. The 2004 average exchange rate of 79.49 Kenyan shillings to US\$ 1 was used in all calculations. All future costs and outcomes were discounted at 3% per year.

Hib disease incidence

Pneumonia is the most common manifestation of Hib disease in developing countries.⁴ Findings from Hib vaccine trials in the Gambia and Chile illustrate that reductions in radiologically proven pneumonia cases were approximately five times those in Hib meningitis cases.^{5–7} However, difficulties in establishing a definitive diagnosis of Hib disease in most parts of the world mean that the true disease burden remains largely unknown.^{4,8} Hib disease is divided into

three categories in this study: (a) Hib meningitis, (b) non-meningitic invasive Hib disease (mainly bacteraemic Hib pneumonia, but also severe sepsis with an unknown focus of infection), and (c) non-bacteraemic Hib pneumonia.

Age-specific incidences of category (a) and (b) before and after the introduction of Hib vaccine were estimated from hospital admission records at Kilifi District Hospital (KDH) between 2000 and 2005. KDH is a rural government-funded hospital with 42 paediatric beds and approximately 5000 paediatric admissions per year. A Kenya Medical Research Institute (KEMRI) centre at the hospital has been conducting research on common childhood illnesses since 1989. Data on paediatric invasive bacterial infections, including routine blood cultures on all children admitted to hospital, have been collected since 1998.⁹ Cases of Hib invasive disease were categorized as meningitis if a cerebrospinal fluid (CSF) specimen yielded a positive Hib culture, a positive Hib antigen test, or had an elevated CSF white cell count in the presence of a blood culture positive for Hib. If a positive blood culture was the only evidence of Hib disease, the case was

classified as non-meningitic invasive Hib disease.¹⁰ Detailed criteria for detecting meningitis cases, collecting specimens and laboratory processing at KDH have been published elsewhere.^{9,11}

Since 2000, KEMRI has conducted a demographic surveillance study (DSS) in an 891 km² area around the hospital: 25 000 households are visited and re-enumerated every six months. Hib cases admitted to KDH from within the DSS area were linked to age-specific population denominators to estimate annual incidence rates of invasive Hib disease detected by passive hospital surveillance.¹¹ The hospital incidence of Hib invasive disease per 100 000 children aged < 5 years was 66 (95% confidence interval, CI: 49.6–81.6) before the introduction of Hib vaccine (2000/2001) and 7.6 (95% CI: 1.6–22.3) three years after its introduction (2004/2005).¹¹ However, these estimates underestimate the true incidence, as a relatively large proportion of children in Kenya have limited access to health care and therefore would not be detected by hospital surveillance. Even within the Kilifi DSS, the area closest to the hospital, only one-third of childhood deaths occur in hospital, and one-third of children who die access only primary health-care fa-

Table 2. Model estimates of cases and deaths from Hib disease with and without Hib vaccine delivery in the 2004 Kenyan birth cohort

Age in years	Hib cases and deaths without Hib vaccine					Hib cases and deaths with Hib vaccine				
	Menin- gitis cases	Non- meningitic invasive cases	Non- bacteraemic pneumonia cases	Total cases	Total deaths	Menin- gitis cases	Non- meningitic invasive cases	Non- bacteraemic pneumonia cases	Total cases	Total deaths
0	2921	2488	12117	7526	3917	336	287	1395	2018	451
1	889	757	3688	5334	1192	102	87	425	614	137
2	452	385	1873	2709	605	52	44	216	312	70
3	198	168	819	1185	265	23	19	94	136	31
4	99	84	410	593	132	11	10	47	68	15
Total	4558	3883	18 907	27 347	6112	525	447	2177	3149	704

Hib, *Haemophilus influenzae* type b.

cilities during their terminal illness.^{12,13} These findings are consistent with data from rural communities elsewhere in Kenya.¹⁴ Based on these data, and adopting a conservative approach to take account of better access in urban communities, we estimated that 50% of Hib disease cases were detected by passive hospital-based surveillance. The true incidence of Hib invasive disease in children aged < 5 years was therefore calculated as twice that observed in the Kilifi study (Table 1).

Non-bacteraemic Hib pneumonia was not included in the surveillance at KDH as currently there is no diagnostic tool other than blood culture to determine accurately the etiology of pneumonia.⁸ The incidence of category (c) was therefore estimated from the 5:1 ratio between Hib meningitis and pneumonia referred to above. The incidence of disease category (b) was subtracted to avoid double-counting of bacteraemic pneumonia. Case fatality rates were varied according to the type of health care received, as summarized in Table 1.

Disability adjusted life years (DALYs) were estimated using the method recommended in the 1996 global burden of disease study.¹⁵ Age weighting was included. The disability weight is 0.616 for the acute phase of bacterial meningitis and 0.28 for an episode of non-meningitic invasive Hib disease and non-bacteraemic pneumonia.¹⁵ For survivors, we assumed that all episodes last one month. At KDH, 25% of Hib meningitis survivors suffer from clinically obvious significant neurological sequelae, predominantly motor deficits.¹⁶ Therefore, we applied the disability weight for motor deficits (0.334)

to meningitis sequelae and assumed that the sequelae last throughout the patients' lives. More minor sequelae (such as epilepsy) and even major non-motor sequelae (such as isolated sensorineural deafness) were not accounted for.

Vaccine delivery costs

The current costs of including pentavalent vaccine in the routine immunization schedule were compared to a hypothetical scenario using the diphtheria-tetanus-pertussis-hepatitis B combination without Hib vaccine. As all vaccines and injection equipment are procured through the United Nations Children's Fund (UNICEF), we used the 2004 vaccine and syringe prices of the UNICEF supply division.¹⁷ Other vaccine delivery costs, such as staff salaries and transport, were not included. These would not be affected markedly as there is no difference in the number of health service contacts for the two different types of vaccines. Ministry of Health staff members were interviewed in order to assess other costs related to vaccine introduction, such as enhanced surveillance and training activities.

Hib disease treatment costs

Hospital treatment costs were divided into patient-specific costs and costs per patient bed-day. Patient-specific costs of Hib meningitis and non-meningitic invasive Hib disease were estimated from patient records at KDH. We reviewed the hospital records of 31 children admitted in 2001 with proven invasive Hib disease (21 meningitis and 10 non-meningitic invasive disease) and extracted information on diagnostic tests, drugs administered and the length of

hospital stay. Data from the six children who died were included in the analysis. However, as KDH is a research setting, certain diagnostic tests and treatment procedures differ from standard Kenyan practices. To avoid inflating the national cost estimates we substituted KDH costs for third-generation cephalosporins, not currently recommended as first-line antibiotic therapy in Kenya, with costs for penicillin and chloramphenicol, and excluded blood culture costs. For non-bacteraemic Hib pneumonia, patient-specific data on resource usage were collected from a total of 76 pneumonia patient records at three district hospitals: Homa Bay, Kitui and Kerugoya.

Unit costs for drugs were collected largely from the Kenya Medical Supplies Agency (KEMSA). Costs per bed-day and per outpatient visit were taken from the WHO-CHOICE database.¹⁸ We used cost data for a secondary hospital, as we believe this provides the best average cost estimate for a national-level analysis. In 2004 values, the costs per bed-day and per outpatient visit were US\$ 6.57 and US\$ 1.92 respectively. The assumptions on access to care summarized in Table 1 were used to calculate treatment costs for the country as a whole.

Uncertainty and sensitivity analysis

We undertook a probabilistic multivariate analysis to assess the impact of uncertainty in parameter values. Prediction intervals around the mean cost-effectiveness ratios were derived from 50 000 Monte Carlo simulations by Crystal Ball software (Decisioneering, USA). For the disease burden parameters we assumed either triangular or normal

Table 3. Estimated annual cost (US\$) of vaccines and injection equipment in Kenyan public health sector with and without the pentavalent vaccine (2004)

Antigen	Dose per vial	Wastage (%)	Costs per dose (including freight)	No. of children reached	Total vaccine costs	Injection supply costs ^a	Total	% of total
Bacille Calmette–Guérin	20	70	0.10	1 150 140	372 645	86 133	458 778	3.2%
DTP+hep B+Hib (pentavalent)	2	15	3.70	965 060	12 618 727	305 519	12 924 246	89.6%
Measles	10	65	0.17	900 820	150 329	70 815	221 144	1.5%
Oral polio vaccine	20	10	0.11	965 060	468 118	–	468 118	3.2%
Tetanus toxoid	20	15	0.03	926 914	179 603	137 831	317 434	2.2%
Yellow fever	10	65	0.82	15 871	37 366	1 248	38 614	0.3%
Total costs with pentavalent vaccine	–	–	–	–	13 826 789	601 545	14 428 334	100%
DTP+hep B combination vaccine	10	35	1.23	965 060	5 497 279	210 468	5 707 747	–
Total costs with diphtheria-tetanus-pertussis-hep B instead of pentavalent vaccine	–	–	–	–	6 705 340	506 495	7 211 835	–
<i>Incremental costs of pentavalent vaccine compared with DTP+hep B</i>	–	–	–	–	7 121 448	95 050	7 216 499	–

DTP, diphtheria-tetanus-pertussis; hep B, hepatitis B; Hib, *Haemophilus influenzae* type b.

^a Injection supply costs consist of auto-disable syringes, reconstitution syringes and safety boxes.

distributions with ranges or standard deviations respectively (Table 1). Based on previous patterns¹⁹ and the analysis of patient records, a lognormal distribution was assumed for the treatment cost parameters.

One-way sensitivity analyses were undertaken to assess the importance of herd immunity and vaccine price. In the Gambia, invasive Hib disease has been eliminated among children aged < 5 years, despite the fact that the timing and coverage of Hib immunizations predict a direct vaccine protection of only 41%.²⁰ Most of the observed effectiveness is therefore attributable to indirect protection. We included a scenario of zero incidence of Hib disease to illustrate the potential long-term impact. The pentavalent vaccine price was varied to US\$ 3 per dose, representing an 18% decrease on the 2004 price. We also calculated the break-even price.

Results

Impact of Hib vaccine on disease incidence

Before the introduction of Hib vaccine, the annual incidence per 100 000 children aged < 5 was estimated at 71 for Hib meningitis, 61 for Hib non-meningitic invasive disease and 296 for non-bacteraemic Hib pneumonia. Three years after the introduction these incidence estimates were 88% lower at

8, 7 and 34 respectively. The estimated number of cases and deaths for the 2004 birth cohort with and without Hib vaccine are shown in Table 2. Without Hib vaccine we estimate that 27 347 children would experience Hib disease, resulting in 6112 deaths. With the introduction of the vaccine these numbers are reduced to 3149 cases and 704 deaths. Thus, over the first five years of life Hib vaccination is preventing 5408 deaths in the 2004 birth cohort (4% of under-five mortality). If children did not receive vaccine but all had access to hospital care at current Kenyan standards, the estimated number of deaths would decrease by 60%, resulting in 2164 deaths prevented by Hib vaccination.

Vaccine delivery costs

Costs of vaccine and injection equipment for the six different antigens currently included in the Kenyan immunization schedule are outlined in Table 3, together with the costs of a scenario using a diphtheria-tetanus-pertussis-hep B combination vaccine instead of pentavalent vaccine. The costs of pentavalent vaccine amount to 90% of total vaccine and injection equipment costs. GAVI supported the Kenyan Government with US\$ 100 000 to finance training and communication activities for introducing new vaccines. The health ministry did not introduce post-vaccine surveil-

lance for meningitis other than through the externally funded WHO-African Region Paediatric Bacterial Meningitis Surveillance Network, so we did not include additional surveillance costs.

Vaccine and injection equipment costs per fully immunized child are US\$ 14.95 for pentavalent vaccine and US\$ 7.47 for the diphtheria-tetanus-pertussis-hep B vaccine combination.

Treatment costs

The mean lengths of stay for meningitis, non-meningitic invasive disease and non-bacteraemic pneumonia patients were 11.7 (standard deviation, SD 6.5), 7.5 (SD 5.7) and 5.7 (SD 5.6) days respectively. The drug costs of Hib meningitis, non-meningitic invasive Hib disease and non-bacteraemic pneumonia were US\$ 10 (SD 8), US\$ 14 (SD 22) and US\$ 3 (SD 3) respectively. Mean total treatment costs were US\$ 132 for a case of Hib meningitis, US\$ 112 for non-meningitic invasive Hib disease and US\$ 48 for non-bacteraemic Hib pneumonia.

With current access to health-care services, total treatment costs saved due to Hib vaccination of the 2004 birth cohort amount to US\$ 871 539. This is 12% of Hib vaccine delivery costs. If all Kenyan children had access to hospital care, this figure would be US\$ 1 740 769, or 24% of Hib vaccine delivery costs.

Table 4. Incremental cost-effectiveness of Hib vaccine in Kenya: base case scenario (2004)

	Vaccine and injection equipment	Treatment costs (US\$)	Net costs (US\$)	Hib cases	Hib deaths	Disability adjusted life years (DALYs)	Costs (US\$) per case averted (95% CI)	Costs (US\$) per death averted (95% CI)	Costs (US\$) per DALY averted (95% CI)
Undiscounted results:									
No Hib vaccination	7 211 835	984 958	8 196 793	27 347	6 112	401 568	–	–	–
Hib vaccination	14 428 334	113 419	14 541 753	3 149	704	46 243	–	–	–
Increment	7 216 499	–871 539	6 344 960	24 198	5 408	355 325	262 (175–455)	1 173 (797–1982)	18 (12–30)
Discounted results (3%):									
No Hib vaccination	7 211 835	967 758	6 244 077	26 870	6 005	191 489	–	–	–
Hib vaccination	14 428 334	111 439	14 316 895	3 094	691	22 052	–	–	–
Increment	7 216 499	–56 319	6 360 180	23 775	5 314	169 438	268 (178–464)	1 197 (814–2021)	38 (26–63)

CI, confidence interval; Hib, *Haemophilus influenzae* type b.

Cost-effectiveness

In the base case scenario the costs per discounted case, death and DALY averted were US\$ 268, US\$ 1197 and US\$ 38 respectively (Table 4).

Uncertainty and sensitivity analysis

The 95% prediction interval of certainty for the cost per discounted DALY and death averted were US\$ 26–63 and US\$ 814–2021 respectively (Table 4). Hence, if the Kenyan Government considers an investment that costs US\$ 63 per discounted DALY averted to be cost-effective, Hib vaccine can be considered cost-effective with 97.5% certainty.

Fig. 1 illustrates which parameters contribute to most of the uncertainty in the cost-effectiveness ratios. Of the 27 variables with a distribution and an uncertainty range in the analysis, five caused 96% of the variability in the costs per discounted DALY averted estimate. Three of these are access to care parameters. Since the access to hospital care parameter affects the disease incidence and the case fatality rates, uncertainty in this parameter causes 44% of the uncertainty. Hence, more knowledge about access to care is required in order to obtain a more precise cost-effectiveness estimate.

Assuming that herd immunity would lead to the elimination of Hib disease, the cost-effectiveness ratio decreases to US\$ 1041, US\$ 233 and US\$ 33 per discounted death, case and DALY averted, respectively. With a pentavalent vaccine price of US\$ 3 per dose, the incremental costs per discounted death

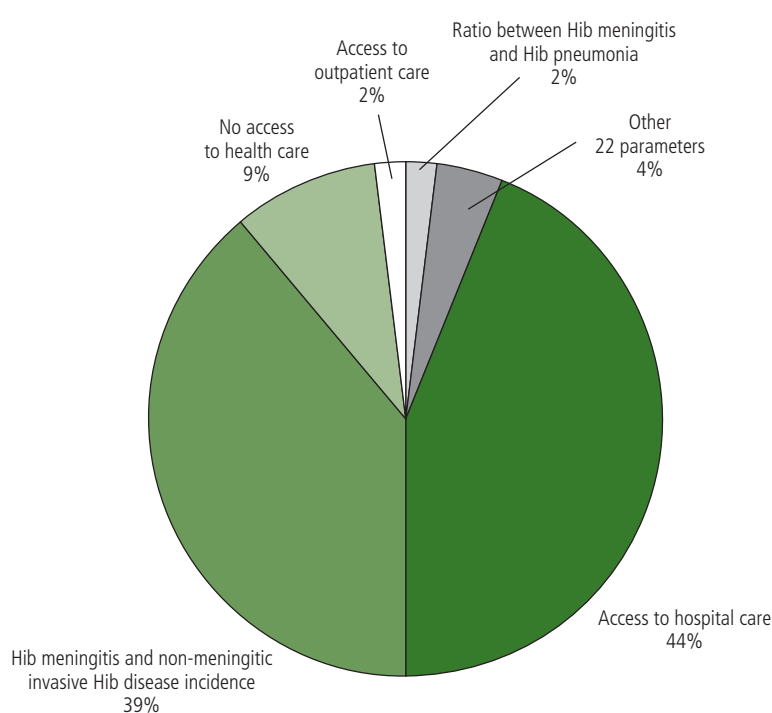
and DALY averted are US\$ 774 and US\$ 24 respectively. The break-even pentavalent vaccine price per dose, where incremental Hib vaccination costs equal averted treatment costs for Hib disease, is US\$ 1.82. Hence, a price lower than this for Hib vaccination provides government health sector savings.

Discussion

The most pressing question faced by health policy-makers in Kenya is whether Hib vaccine is a priority deserv-

ing public funds. The decision should be based on the affordability and estimated cost-effectiveness of the vaccine. We have found that the costs per discounted DALY averted are in the range of US\$ 26–63 at the current vaccine price. By all generally used benchmarks, this is considered a highly cost-effective intervention. WHO suggests that an intervention may be considered very cost-effective if the costs per discounted DALY averted are less than the country's per-capita GDP.²¹ Hib vaccination easily

Fig. 1. Percentage contribution to variance of uncertain parameters included in the analysis for costs per discounted DALY averted



falls below this benchmark – the per capita GDP was US\$ 481 in 2004.

A cost-effectiveness analysis is relative in the sense that one intervention can only be considered cost-effective in relation to another. However, there is little cost-effectiveness information on other interventions in Kenya for comparison. The cost-effectiveness of Hib vaccine is comparable to preventive interventions against malaria, such as bednets (US\$ 4–85 per discounted DALY)²² and to some tuberculosis control strategies (US\$ 13–496 per discounted DALY).²³

Our estimates of Hib disease incidence, with and without vaccine, are derived from a study monitoring its decline in a largely rural district. The only plausible explanation for this is the provision of Hib vaccine as part of the government's routine immunization programme.¹¹ The vaccine's impact was measured from a hospital setting; low levels of access to care produce an underestimate of the true disease burden. By adjusting the hospital incidence estimates for access to care, we generated a considerably higher vaccine impact. We

believe our estimate of the proportion of children having access to inpatient care (50%) is conservative given the available data.¹⁴ There are several other reasons why the cost-effectiveness results are likely to be underestimates. First, the case fatality rate attributed to inpatient Hib meningitis (17%) is considerably lower than the average reported for sub-Saharan Africa (27.6%).¹ Second, we account only for serious motor sequelae in children with meningitis and not those with other invasive Hib disease. Third, the cost-effectiveness estimates include only the provider's perspective and do not take into account costs borne by households.

Many people in low-income countries consider Hib disease to be relatively uncommon and expensive to prevent. Our findings indicate that while the burden of disease is smaller than for diseases such as malaria, so too is the investment required to prevent the disease. Thus, Hib vaccine is as cost-effective as any other priority intervention: each life saved requires an investment similar to that required for impregnated bednets

to prevent malaria. This analysis should encourage action in countries that have delayed introducing the vaccine into their immunization schedule because the costs did not appear to be matched by the benefits. The findings indicate to manufacturers and donors that a small decrease in vaccine price markedly improves its cost-effectiveness and that pentavalent vaccine would be affordable by all if its price was halved. ■

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Competing interests: None declared.

Résumé

Evaluation économique de la délivrance du vaccin contre *Haemophilus influenzae* type b par les services de vaccination systématique du Kenya

Objectif La vaccination contre *Haemophilus influenzae* type b (Hib) a été intégrée au programme de vaccinations systématiques kenyan en 2001. Nous nous sommes efforcés d'estimer le rapport coût/efficacité de la délivrance de ce vaccin.

Méthodes Un modèle a été mis au point pour suivre jusqu'à leur mort une cohorte d'enfants nés en 2004, vaccinés ou non contre le virus Hib. L'incidence des infections à Hib invasives a été estimée à l'hôpital de district de Kilifi et par le biais du système de surveillance démographique environnante de la région côtière du Kenya. L'incidence nationale des affections à Hib a été estimée à partir d'ajustements sur l'incidence observée par la surveillance passive dans les hôpitaux et d'hypothèses concernant l'accès aux soins. Les taux de létalité ont également été supposés comme dépendants de l'accès aux soins. L'étude s'est basée sur un prix d'US\$ 3,65 par dose pour le vaccin pentavalent DTCP + Hib. L'influence sur les rapports coût/efficacité des incertitudes sur les paramètres a été évaluée par des simulations multivariées de type Monte Carlo.

Résultats Chez les enfants de moins de 5 ans, l'introduction du

vaccin anti-Hib a permis de réduire l'incidence de la méningite à Hib de 71 à 8 cas pour 100 000, celle des affections invasives non méningées de 61 à 7 cas pour 100 000 et celle des pneumonies à Hib non bactériennes de 296 à 34 cas pour 100 000. Les économies réalisées grâce au nombre d'années de vie corrigées de l'incapacité (DALY) épargnées et aux décès évités s'élèvent respectivement à US\$ 38 [intervalle de confiance à 95% (IC) : 26-63] et à US\$ 1 197 [intervalle de confiance à 95% (IC) : 814-2021]. La plus grande part de l'incertitude sur les résultats est imputable aux difficultés d'évaluation des paramètres relatifs aux soins. Le seuil de rentabilité du vaccin pentavalent (prix pour lequel l'économie sur les dépenses entraînées par les infections à Hib compense l'augmentation des coûts de vaccination) est d'US\$ 1,82 par dose.

Conclusion La vaccination contre le virus Hib constitue une intervention hautement efficace dans le cas du Kenya. Elle permettrait une économie si le prix du vaccin était inférieur de 50% au moins à son niveau actuel.

Resumen

Evaluación económica de la administración de la vacuna contra *Haemophilus influenzae* tipo b en los servicios de inmunización sistemática de Kenya

Objetivo Estimar la costoeficacia de la administración de la vacuna contra *Haemophilus influenzae* tipo b (Hib), que se introdujo en los servicios de inmunización sistemática de Kenya en 2001.

Métodos Se elaboró un modelo para seguir la evolución de la cohorte de nacimiento de 2004 hasta el momento de la defunción, con y sin vacuna anti-Hib. Se estimó la incidencia de la enfermedad invasiva por Hib en el Hospital de Distrito de Kilifi

y en el sistema circundante de vigilancia demográfica de la costa de Kenya. La incidencia nacional de enfermedad por Hib se estimó ajustando la incidencia observada mediante vigilancia pasiva en los hospitales, asumiendo algunas premisas sobre el acceso a la atención. Se asumió que las tasas de letalidad también dependían del acceso a la asistencia. Fijando en US\$ 3,65 el precio de la dosis de vacuna pentavalente contra difteria-tétanos-tos ferina-hep B-Hib, se realizaron simulaciones multifactoriales con el método de Monte Carlo para determinar el impacto de la incertidumbre de los parámetros en los valores de la costo-eficacia.

Resultados La introducción de la vacuna anti-Hib redujo la incidencia estimada de meningitis por Hib por 100 000 niños menores de 5 años de 71 a 8; de enfermedad invasiva no meningítica por Hib, de 61 a 7; y de neumonía por Hib no

bacteriémica, de 296 a 34. Los costos por AVAD (año de vida ajustado en función de la discapacidad) descontado evitado y por muerte descontada evitada fueron de US\$ 38 (intervalo de confianza (IC) del 95%: 26-63) y US\$ 1197 (IC95%: 814-2021), respectivamente. La mayor parte de la incertidumbre de los resultados se debió a la incertidumbre de los parámetros relativos al acceso a la atención. El umbral de rentabilidad de la vacuna pentavalente -punto de equivalencia del incremento de los costos de la vacunación anti-Hib y de los costos evitados en concepto de tratamiento de la enfermedad por Hib- fue de US\$ 1,82 por dosis.

Conclusión La vacunación contra Hib es una intervención altamente costoeficaz en Kenya, y permitiría hacer economías si la vacuna costara menos de la mitad de lo que cuesta ahora.

ملخص

التقييم الاقتصادي لإعطاء لقاح النمط البائي للمستدمية النزلية في خدمات التمنيع الروتيني في كينيا

معدلات الحدوث المقدرة لالتهاب السحايا بالمستدمية النزلية من النمط البائي لدى كل مئة ألف من الأطفال دون سن الخامسة من 71 إلى 8، وخفض معدلات الحدوث المقدرة للأمراض الغازية غير السحائية الناجمة عن النمط البائي من المستدمية النزلية من 61 إلى 7، وخفض معدلات الحدوث المقدرة للالتهاب الرئوي بالنمط البائي من المستدمية النزلية غير المصحوب بتجرثم الدم من 296 إلى 34. وقد كانت تكاليف سنوات العمر المصححة باحتساب مدد العجز التي أمكن إنقاذها 38 دولاراً أمريكياً (بفاصل ثقة 95% إذ تراوحت القيم المقاسة بين 26 و63)، وتكاليف الوفيات التي أمكن تفاديها 1197 دولاراً أمريكياً (بفاصل ثقة 95% إذ تراوحت القيم المقاسة بين 814 و2021). وقد كان معظم الارتياح في النتائج ناجماً عن الارتياح في متباينات إتاحة الرعاية الصحية. إن نقطة التعادل في سعر اللقاح الخماسي التكافؤ والتي يتساوى فيها التكاليف المترتبة للقاح النمط البائي للمستدمية النزلية مع التكاليف التي أمكن تفاديها لمعالجة الأمراض الناجمة عن النمط البائي للمستدمية النزلية كانت 1.82 دولاراً أمريكياً لكل جرعة. الاستنتاج: إن لقاح النمط البائي للمستدمية النزلية من التدخلات الرقيقة الفعالية لقاء التكلفة في كينيا. وسيكون موقراً للتكاليف إذا كانت أسعار اللقاح أقل من نصف المستوى الذي عليه في الوقت الحاضر.

الهدف: لقد أدخل لقاح النمط البائي للمستدمية النزلية ضمن خدمات التمنيع الروتيني في كينيا منذ عام 2001. وهدفنا في هذه الدراسة هو تقييم الفعالية لقاء تكلفة إعطاء هذا اللقاح. الطريقة: أعدنا نموذجاً لمتابعة أتراب الولادة لعام 2004 حتى وفاتهم، وهم مجموعة تلقت اللقاح ومجموعة أخرى لم تتلقاه، وقدّرنا معدل حدوث الأمراض الغازية الناجمة عن النمط البائي للمستدمية النزلية في مستشفيات مقاطعة كيليفي وفي نظام التصد الجغرافي للمناطق المحيطة بها في السواحل الكينية. وقدّرنا معدل حدوث الأمراض الناجمة عن النمط البائي للمستدمية النزلية على المستوى الوطني بتصحيح المعدل الذي لاحظناه عن طريق التصد في المستشفيات وبالاستفادة من معلومات حول إتاحة الرعاية الصحية. كما قدرنا معدلات وفيات الحالات اعتماداً على إتاحة الرعاية الصحية. واستخدمنا سعراً مقداره 3.65 دولاراً أمريكياً للقاح الخماسي التكافؤ الذي يتضمن لقاحات الخناق (الدفتريا) والكزاز (التيتانوس) والشاهوق (السعال الديكي) والنمط البائي للمستدمية النزلية. وأجرينا مجموعة محاكاة مونت كارلو المتعددة المتغيرات لتقييم أثر اللقاح على نسب الفعالية لقاء التكلفة بقيم من الارتياح للمتباينات المستخدمة. الموجودات: لقد أدى إدخال لقاح النمط البائي للمستدمية النزلية إلى خفض

References

- Bennett JV, Platonov AE, Slack MPE, Mala P, Burton AH, Roberson SE. *Haemophilus influenzae* type b (Hib) meningitis in the pre-vaccine era: a global review of incidence, age distributions, and case-fatality rates. Geneva: WHO; 2002.
- Estimated five-year commitment in US\$ to 72 countries (July 2005). Geneva: Global Alliance for Vaccines and Immunization; 2005. Available at: www.vaccinealliance.org/support_to_country/country_status/index.php
- Bridge financing investment case. Geneva: GAVI; 2005.
- Peltola H. Worldwide *Haemophilus influenzae* type b disease at the beginning of the 21st century: global analysis of the disease burden 25 years after the use of the polysaccharide vaccine and a decade after the advent of conjugates. *Clin Microbiol Rev* 2000;13:302-17.
- Mulholland K, Hilton S, Adegbola R, Usen S, Oparaugo A, Omosigbo C, et al. Randomised trial of *Haemophilus influenzae* type-b tetanus protein conjugate vaccine [corrected] for prevention of pneumonia and meningitis in Gambian infants. *Lancet* 1997;349:1191-7.
- Levine OS, Lagos R, Munoz A, Villaroel J, Alvarez AM, Abrego P, et al. Defining the burden of pneumonia in children preventable by vaccination against *Haemophilus influenzae* type b. *Pediatr Infect Dis J* 1999;18:1060-4.
- Mulholland K, Levine O, Nohynek H, Greenwood BM. Evaluation of vaccines for the prevention of pneumonia in children in developing countries. *Epidemiol Rev* 1999;21:43-55.
- Cherian T. Describing the epidemiology and aetiology of bacterial pneumonia in children: an unresolved problem. *J Health Popul Nutr* 2005;23:1-5.
- Berkley JA, Lowe BS, Mwangi I, Williams T, Bauni E, Mwarumba S, et al. Bacteremia among children admitted to a rural hospital in Kenya. *N Engl J Med* 2005;352:39-47.
- Berkley JA, Maitland K, Mwangi I, Ngetsa C, Mwarumba S, Lowe BS, et al. Use of clinical syndromes to target antibiotic prescribing in seriously ill children in malaria endemic area: observational study. *BMJ* 2005;330:995.
- Cowgill KD, Ndiritu M, Nyiro J, Slack MP, Chipchatsi S, Ismail A, et al. Effectiveness of *Haemophilus influenzae* type b conjugate vaccine introduction into routine childhood immunization in Kenya. *JAMA* 2006;296:671-8.
- Snow RW, Schellenberg JR, Forster D, Mung'ala VO, Marsh K. Factors influencing admission to hospital during terminal childhood illnesses in Kenya. *Int J Epidemiol* 1994;23:1013-9.
- Brent AJ, Ahmed I, Ndiritu M, Lewa P, Ngetsa C, Lowe B, et al. Incidence of clinically significant bacteraemia in children who present to hospital in Kenya: community-based observational study. *Lancet* 2006;367:482-8.
- Garg R, Omwomo W, Witte JM, Lee LA, Deming MS. Care seeking during fatal childhood illnesses: Siaya District, Kenya, 1998. *Am J Public Health* 2001;91:1611-3.

15. Murray CJL, Lopez ADE. *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020*. Boston: Harvard School of Public Health; 1996.
16. Mwangi I, Berkley J, Lowe B, Peshu N, Marsh K, Newton CR. Acute bacterial meningitis in children admitted to a rural Kenyan hospital: increasing antibiotic resistance and outcome. *Pediatr Infect Dis J* 2002;21:1042-8.
17. *2004 vaccine projections: quantities and pricing*. Available at: http://www.unicef.org/supply/files/UNICEF_-_procuring_supplies_for_children_-_GAVI.pdf
18. Adam T, Evans DB, Murray CJ. Econometric estimation of country-specific hospital costs. *Cost Eff Resour Alloc* 2003;1:3.
19. Heyse JF, Cook JR, Carides GW. Statistical considerations in analysing health care resource utilization and cost data. In: Drummond M, McGuire A, editors. *Economic evaluation in health care: merging theory with practice*. Oxford: Oxford University Press; 2001.
20. Adegbola RA, Secka O, Lahai G, Lloyd-Evans N, Njie A, Usen S, et al. Elimination of Haemophilus influenzae type b (Hib) disease from the Gambia after the introduction of routine immunisation with a Hib conjugate vaccine: a prospective study. *Lancet* 2005;366:144-50.
21. *Threshold values for intervention cost-effectiveness by region*. Available at: www.who.int/choice/costs/CER_levels/en/indexhtml
22. Goodman CA, Coleman PG, Mills AJ. Cost-effectiveness of malaria control in sub-Saharan Africa. *Lancet* 1999;354:378-85.
23. Currie CS, Floyd K, Williams BG, Dye C. Cost, affordability and cost-effectiveness of strategies to control tuberculosis in countries with high HIV prevalence. *BMC Public Health* 2005;5:130.
24. *WHO vaccine preventable diseases monitoring system. 2005 global summary*. Geneva: WHO; 2005 (WHO/IVB/2005).
25. Molyneux E, Walsh A, Phiri A, Molyneux M. Acute bacterial meningitis in children admitted to the Queen Elizabeth Central Hospital, Blantyre, Malawi, in 1996-97. *Trop Med Int Health*. 1998 Aug; 3(8):610-18.
26. Snow RW, Mung'ala VO, Foster D, Marsh K. The role of the district hospital in child survival at the Kenyan Coast. *Afr J Health Sci* 1994;1:71-5.
27. Kohn J, Weiner S. Pneumonia in children: a survey of one thousand cases with attempted follow-up. *Am J Dis Child* 1936;51:1095-100.