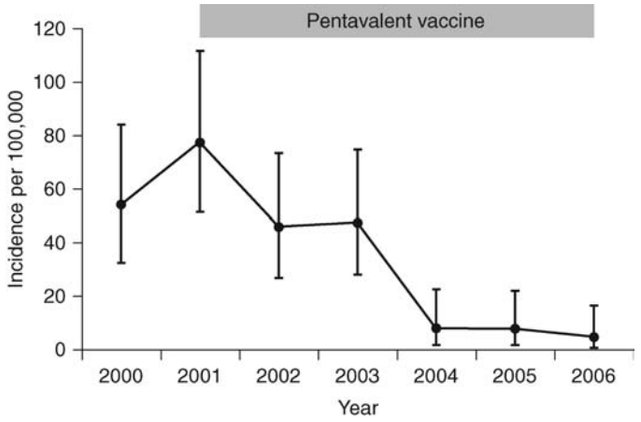

Figure 2 Invasive Hib disease in children aged less than five years in Kilifi DSS.

Hib disease in children aged less than five years in Kenya in that year. In contrast to The Gambia, where a significant drop in incidence of Hib disease was recorded two years after introduction of the vaccination program, incidence of Hib disease did not decrease significantly in Kenya until the third year after vaccine introduction. As in The Gambia, there was no catch-up campaign of older children when Hib vaccine was introduced into Kenya's EPI. It is important to take vaccination schedule and years of surveillance before and after introduction of vaccination into consideration when evaluating the impact of routine use of a new vaccine in a developing country setting.

Other Developing Countries

In Malawi, routine immunization with Hib vaccine was introduced into EPI in a pentavalent formulation in January 2002. The vaccination schedule consisted of three doses given to infants at ages 6, 10, and 14 weeks. A booster dose was not given. Surveillance was undertaken with a focus on meningitis using the AFRO-PBM database, and was located at Blantyre district covering a population of about 1 million. A case-control method was used to estimate vaccine effectiveness using children hospitalized with *Streptococcus pneumoniae* meningitis as controls. The frequency of Hib meningitis admissions began to decrease only one month after vaccine introduction. Nine months after introduction, the number of Hib meningitis cases had dropped to only two to three per month from a baseline of 12 or more. Cases of Hib meningitis occurred only in children who were not fully vaccinated. The frequency of presentations of pneumococcal meningitis remained constant indicating that the observed results were not due to declining laboratory performance. Additionally, Hib disease decreased in older, unvaccinated children after the first year of the program, which is suggestive of an indirect effect of vaccination. High vaccine effectiveness for Hib meningitis was demonstrated among children aged less than five years (94%; 95% CI, 70–99%). This occurred despite limited health care resources and a high burden of HIV infection (40). At least 14% of children with Hib meningitis were coinfected with HIV in the study population.

Serotype Replacement Disease

Serotype replacement disease, which is well documented following introduction of conjugate pneumococcal vaccine in the United States (47), has not been observed following Hib vaccine introduction in developing countries. Early reports from the National Public Health surveillance in Brazil suggested an increase in the annual incidence of *H. influenzae* type a meningitis in the first year after vaccine introduction from 0.01 to 0.14/100,000 total population (48). In the subsequent three years, the incidence returned to pre-vaccine levels, and the transient increase is probably best explained by heightened surveillance in the aftermath of the vaccine introduction.

Herd Protection Effect

Hib conjugate vaccines reduce asymptomatic nasopharyngeal carriage of Hib in vaccinated children, leading to a reduction in transmission with subsequent herd protection effect. In The Gambia, Hib disease was eliminated in the community at a point when, based on coverage estimates, only 41% of potential cases would have been protected by the direct effects of immunization (42). Although two doses were required for the direct protection of children in the Gambia study, most received their second dose too late to benefit from direct protection. The latter doses may be required to achieve and maintain the high levels of antibodies required for protection against Hib carriage. Nasopharyngeal carriage studies may therefore be helpful in surveillance programs to observe indirect vaccine effect after Hib vaccine introduction.

COST-EFFECTIVENESS OF CONJUGATE Hib VACCINES IN DEVELOPING COUNTRIES

An assessment of the costs and benefits of introducing new vaccines is critical in the developing world, where many competing initiatives vie for spending from very limited health budgets. In March 2007, GAVI detailed the second phase of vaccine support for 72 eligible developing countries—those with a gross domestic product per capita of less than $1000 in the year 2005. Developing countries will be required to co-pay for vaccine at a subsidized price, and the level of co-payment is decreased for each new vaccine introduced. Assuming that conjugate Hib vaccine is the first new vaccine (usually in a formulation with DPT and hepatitis B vaccines), countries introducing this vaccine will be asked to contribute $0.30/dose. The questions that drive present cost-effectiveness analyses are therefore, (*i*) What is the ratio of vaccine introduction costs to the sum of treatment (and societal) costs that would be averted by vaccine introduction? (*ii*) On the assumption that countries will eventually have to sustain their health services independently and pay the full economic price for vaccine, what happens to the cost-benefit ratio as the cost per dose increases from its presently subsidized level?

The first approach to these questions from Africa was a cost-benefit study from South Africa in 1995 (49). The authors used an estimate of the incidence of invasive Hib disease, 133 cases/100,000 children aged less than five years, which is comparable with several other centers in Africa. They converted the value of a life into monetary terms to quantify the benefits of the vaccine program. Despite assuming a vaccine price of US$14 per dose, the authors concluded that conjugate Hib vaccine was cost saving from a societal perspective. Three studies from newly industrializing countries, Chile, Malaysia,