HEALTH POLICY AND PLANNING; 15(4): 408–416

The cost of integrating hepatitis B virus vaccine into national immunization programmes: a case study from Addis Ababa

WJ EDMUNDS,[1] A DEJENE,[2] Y MEKONNEN,[2] M HAILE,[3] W ALEMNU[4] AND DJ NOKES[1]
[1]Department of Biological Sciences, University of Warwick, Coventry, UK, [2]Ethiopian Health and Nutrition Research Institute, [3]Region 14 Health Bureau and [4]UNICEF, Addis Ababa, Ethiopia

National programmes of hepatitis B virus (HBV) vaccination are recommended by the World Health Organization for all countries. Countries suffering the highest burden of HBV disease are those most needy of universal vaccination, but are frequently of very low income and resources for health care are scarce. The introduction of HBV vaccination would inevitably stretch these resources further even with support of donor agencies. Thus an assessment of the cost-effectiveness of HBV vaccination is desirable to assist in decision making about resource allocation. We describe here a method for estimating the additional costs of introducing HBV vaccination into the Expanded Programme on Immunization (EPI) at a national level. Of fundamental importance is that this method enables costs to be assessed prior to the introduction of vaccination. We illustrate the method using a study carried out at the sub-national level, in the city of Addis Ababa, Ethiopia, but which can be expanded countrywide. The method, in brief, involved the use of a number of questionnaires which could be used to estimate the costs associated with the EPI programme from a large sample of the static clinics as well as from central sources. Since unit costs were collected along with the quantities of resources used and estimates of the capacity used for certain facilities (such as refrigerators), the additional cost of introducing HBV vaccine could be estimated largely by extrapolation of the resources used in vaccinating against diphtheria/pertussis/tetanus vaccine (which, similar to HBV vaccine, requires three doses).

The estimation of costs is only part of the information required to make decisions on resource allocation, and should be used in association with measures of the burden of disease due to the infection in the community and effectiveness of the control programme at reducing this burden. The prediction of the latter, based upon a sound epidemiological understanding of the infection, is the subject of a forthcoming paper.

Introduction

Whilst disease due to hepatitis B virus (HBV) occurs worldwide, its chronic manifestations of liver dysfunction are predominately a burden to countries with intermediate to high endemicity, where a significant fraction of the population are long-term carriers of the virus. In recognition of this the World Heath Organization's recommendation for introduction of HBV vaccine into all national immunization programmes gives priority to those countries with HBV carrier prevalence of 2% or greater (WHO 1991). In general these countries with the greatest burden of HBV disease are in the developing world, particularly sub-Saharan Africa and East Asia, with low gross domestic products and scarce resources for health care. The introduction of HBV vaccination would inevitably stretch these resources further, even with the support of donor agencies.

Under such circumstances, decisions of health resource allocation would benefit from information on both the potential effects on disease burden of introducing HBV vaccine, and the associated costs of introducing the vaccine into the schedule of the Expanded Programme on Immunization (EPI). Importantly, cost-effectiveness analysis should be used as an aid to decision making; in other words, in advance of introducing a vaccination programme. Unfortunately it is not straightforward to estimate the costs (and effectiveness) of a programme without having the programme in place. In this paper we present a questionnaire technique that can be used to estimate the costs of the EPI, and the additional costs of including HBV immunization, in a developing country. Estimation of the effectiveness of such a programme requires information to be gathered on the burden of disease in the population and the estimation of the effects of vaccination on the future incidence of infection. A later paper will describe how we can predict effectiveness and integrate this information with the costs to calculate the additional cost-effectiveness of HBV immunization.

For the purposes of demonstration, and as a pilot of the methods at the sub-national level, we present the results of using this questionnaire technique in Addis Ababa, the capital city of Ethiopia. This population was chosen as

representative of one for which the decision to include HBV vaccine into the EPI schedule is a real one, where disease due to HBV is known to be significant but scarcity of health resources demands careful assessment of any changes in expenditure.

Methods

HBV and the Expanded Programme on Immunization in Ethiopia

HBV infection is of intermediate-high endemicity in Ethiopia, with at least 70% of all individuals experiencing infection during their lives, and a prevalence of currently infected individuals (surface antigen, HBsAg, positive) of around 10% in adults (Tsega et al. 1986; Abebe et al. 1996). The significance of HBV infection to the disease burden of the population has not been thoroughly assessed. However, in Addis Ababa, liver dysfunction and carcinoma are described as one of the major causes of hospital admission (Tsega et al. 1986). Epidemiological studies suggest that horizontal infection predominates, starting from around 6 months and continuing throughout life (Tsega et al. 1986). Roughly 30% of children have evidence of past exposure by 15 years of age, indicating the importance of childhood transmission. In common with Africa as a region (Edmunds et al. 1996b), perinatal and vertical transmission of HBV appear to be of little significance. Women of childbearing age who are carriers of the virus tend not to be HBeAg positive (a marker of high infectivity) (Abebe et al. 1996) and are predominantly anti-HBe positive (Tsega et al. 1988), and carrier pregnant women followed up rarely pass on infection at birth (Tsega et al. 1988).

The EPI in Ethiopia was launched nation-wide in 1980 (Anon. 1995) with the aim of providing immunization services to all children under the age of 2 years. The target age range has, since 1986, changed to all infants under 1 year, with those between 1 and 2 years being immunized opportunistically. Within the programme, infants are currently offered four vaccines: DPT (diphtheria, pertussis, tetanus), measles, BCG and oral polio vaccine (OPV). In addition, all women of childbearing age, though particularly pregnant women, are targeted to receive two doses of tetanus toxoid (TT) vaccine in an attempt to reduce the transmission of neonatal tetanus.

In the light of the WHO recommendations and the epidemiological and medical picture, Ethiopia is a candidate for the introduction of HBV vaccination as part of the National EPI programme. By most economic indicators, such as gross national product (GNP) per capita, Ethiopia is one of the poorest countries in Africa, with limited resources for health care and disease prevention (World Bank 1993). At present HBV vaccine is not supplied as an EPI antigen by donor agencies (e.g. UNICEF). Universal infant vaccination integrated into the delivery of the three doses of DPT vaccine is indicated by the epidemiological picture (little perinatal, but significant childhood, transmission), and there is no infrastructure for vaccinating older age groups.

Gathering costs of the vaccination programme

What was measured, why and from what sources?

We required information by which to estimate the cost of including HBV vaccine into the current EPI schedule. In addition to this information (and to help facilitate accurate estimation of the extra cost of introducing HBV vaccination), we also estimated the cost of the current EPI schedule, which is also of intrinsic value to health authorities and funders. By estimating the costs of the various components of the EPI programme and the capacity of facilities used, it was possible to estimate the additional costs of introducing HBV vaccination into the EPI schedule.

Wherever possible we obtained unit costs as opposed to aggregate costs. That is, we identified the cost of each individual item of resource utilized to run the EPI programme. So, for example, rather than ask what was the annual cost to UNICEF for needles in Addis Ababa (aggregate cost), we obtained the price of a box of needles and information on how many of such boxes (units) were consumed. Proceeding in this way it was possible to estimate the additional inputs that would be required to include HBV immunization.

We took the perspective of the health care providers, hence the costs that we measured included those to the Ethiopian Ministry of Health, the Regional Health Authority (Region 14), donor agencies such as UNICEF and other non-governmental organizations (NGOs) involved in vaccine delivery (e.g. private health centres). We did not include costs to the patient, such as for travel. There is no widely available treatment for chronic hepatitis B and the other sequelae of HBV infection in Ethiopia, and if they are available, these treatment costs fall to the individual patient. Hence we did not estimate these costs.

Our sources of information were the Ministry of Health, Region 14 Health Authority, UNICEF and also the static clinics in the city that delivered the vaccines. Specifically, UNICEF in Addis Ababa provided information on unit costs of capital expenditure such as vehicles, cold storage and vaccines, salaries for outreach personnel, training and publicity costs; Region 14 gave information on quantities of vaccines and vaccine equipment distributed to the Zones (and thereby to the clinics), operating and maintenance costs of their central stores and EPI coverage rates; and the Ministry of Health gave information on the National Central Vaccine Stores and the quantity of vaccine supplied to the different regions (including Region 14). Static clinics were surveyed using a specially designed questionnaire (see below) to determine resource utilization in the form of cold storage, vehicles, cold boxes, labour time and status of capacity of the system (currently or anticipated with the introduction of HBV vaccine).

EPI programme structure in Region 14

Region 14 is the administrative region of Ethiopia that includes Addis Ababa and its immediate surroundings; it is a largely urban and peri-urban environment. At the time of the survey the population of Region 14 was estimated to be 2.4

million (about 4.6% of the population of Ethiopia). Vaccines are delivered in Region 14 via static clinics and outreach facilities. At the planning phase of the survey there were 45 static clinics in Region 14 (although shortly after this a total of five either stopped providing all the EPI antigens, or closed): 8 government hospitals; 16 government health centres; 2 private, or NGO, health centres; 9 government clinics; and 10 private and NGO clinics. The health centres and clinics are responsible for delivering vaccines to the outreach posts. These are usually local government (kebele) offices which are used for one or two days per month for vaccine delivery. The vaccine delivery teams, from the static sites, visit the outreach facilities according to a fixed schedule, and are paid a *per diem* from UNICEF for this activity, as well as receiving a travel allowance. At the time of the survey there were 95 outreach facilities in Region 14. The region is divided into six administrative zones. In each zone one of the governmental health centres acts as an administrative centre for the EPI and other activities.

Survey of static clinics by questionnaire

We used a block random sampling regime to sample half (20) of the operating static clinics in Region 14. The sample comprised three government run hospitals, eight government health centres, five government clinics, one private health centre and three private, or NGO, clinics. Only one vaccination facility (a private one) refused to respond to our questions and it was therefore substituted by another private clinic, selected at random.

The investigating team delivering the questionnaires consisted of two of us (YM and MH), and each clinic took roughly an hour and a half to sample (a total of $2 \times 20 \times 1.5$ h = 60 man hours). The data could therefore be collected at low cost.

The questionnaire developed to assess the quantity of inputs used by individual static clinics, and their capacity to sustain increased load of vaccination, was adapted from Robertson et al. (1992) and Hall et al. (1993), and closely follows the WHO guidelines for costing the EPI (WHO EPI/GEN/79/5). At each of the static clinics surveyed a series of questions were asked on the capital and recurrent costs of the EPI programme, both at the static site and at their outreach sites. Additionally, a series of questions were asked to gather information on the additional resource use for HBV immunization. For instance, if a clinic stored its vaccines in a refrigerator (which they all did) then we would ask how many refrigerators would be needed if they were required to give HBV vaccine. To help, we informed the respondent that HBV vaccine required three doses like DPT. The response was checked for internal consistency by assessing the capacity of the refrigerator. A similar set of questions was used to gather information on recurrent costs such as labour. We asked the respondents to estimate how much of their time they spent on administering DPT vaccine. If they were unsure we first asked if they gave the usual 10 doses in the EPI schedule (measles, BCG, 2× TT, 3× DPT and 3× OPV), to which all replied in the affirmative. Secondly, we asked whether it was reasonable to assume that they spent approximately 30% of the time they spend on the EPI programme on DPT related activities (as DPT takes up 3 out of 10 of the doses given). Finally, we asked how much extra time it would take to vaccinate against HBV (which would require an extra 3 doses). Separate questionnaires were used to obtain information from the National Central Vaccine Stores and Region 14 Health Authority.

Proceeding in this way we obtained estimates of (1) the resource use for the EPI programme in Addis Ababa, and (2) the additional costs of vaccination against HBV, even though HBV vaccination was not in the EPI schedule at the time of the survey. A copy of the questionnaires can be obtained from the authors on request.

Other data collection

The number of doses of vaccines received by Region 14 were obtained for the period July 1995 to June 1996 from central sources (both Region 14 and the National Central Vaccine Stores – any inconsistencies were investigated further). The number of children immunized was obtained from Region 14 Health Bureau (tally sheets of the number of vaccinations are kept by the clinics and sent to Region 14). Operating costs of the outreach facilities (labour, and the fuel and maintenance of the vehicles) and training and publicity costs for the entire EPI programme were obtained from UNICEF. In these instances the aggregate data were easier to collect and more reliable than the individual clinic data.

Analyzing the cost data

As stated earlier, unit costs were obtained from the main providers (UNICEF and Region 14 Health Authority). We used current prices as a proxy for economic costs. All prices were expressed in US dollars. If the current price of an item was not available, we inflated the price to the current price using the US consumer price index (2.6% in 1994 and 2.8% in 1995). The exchange rate was taken as 1 US dollar = 6.34 Ethiopian birr, which was current at the time of the study (June 1996). The discount rate (which was used to annuitize capital costs) was taken as 6%, the difference between the interest rate (7%) and the rate of inflation (1%).

Assumptions used when calculating costs

Overhead costs are the costs of resources shared between the programme being studied and other programmes. There is no standard technique employed for dealing with these costs (Drummond et al. 1987), hence we dealt with them in two separate ways. First, we performed an incremental analysis. That is, we asked how many units of the shared facility would still be required if there was no EPI programme. This gives us an estimate of the additional cost of the EPI programme over the costs of the other activities. So, for instance, if a clinic used its vehicle for delivering vaccines and for ambulance services, then we asked if the vehicle would still be required if there was no EPI programme. Clearly, under most circumstances the respondent would answer that it was and so the additional cost of the EPI programme would be zero. There is, however, a drawback in using this technique in that if we had been analyzing the incremental cost of the ambulance service over the

EPI programme then we might have found that the additional cost of this service was zero. In order to avoid this path dependency problem we also estimated the fraction of the facility that was used for EPI, then by multiplying this by the unit cost of the facility we obtained an estimate of the cost of the facility to the EPI programme. This technique is often termed direct allocation (Drummond et al. 1987). In the analysis that follows we took the direct allocation technique as our base case assumption for the costs and used the incremental analysis as providing an estimate of the minimum cost of the EPI programme. All costs of the HBV immunization programme were considered incremental to the costs of the EPI.

We assumed that all capital costs (except buildings and vehicles) had a life-span of 10 years with no resale value. We assumed that vehicles had a life-span of 5 years with no resale value. Using a discount rate of 6% per annum we converted these capital costs to annual costs following standard procedures (Drummond et al. 1987). For buildings we asked the respondents to estimate a market rent and the proportion of the building used for EPI activities. For outreach facilities we assumed that the cost of the buildings to the EPI programme was zero, as they are only used for one or two days a month for this activity. We assumed that the inclusion of HBV vaccine would not require more building space. Start up costs (including extra-ordinary publicity and extra-ordinary training) were estimated from the costs associated with the recent polio campaign and were treated in the same fashion as capital costs (that is every 10 years they would need to be 'replaced').

We estimated the additional labour cost of introducing HBV vaccine in a similar way to that for capital items such as refrigerators (see above). We asked respondents to estimate what fraction of their EPI time was spent on DPT, and what extra fraction would be spent on HBV. Most respondents stated that it would take an extra 30% of their EPI time to vaccinate against HBV. This would only represent an extra cost if the vaccinators were working at maximum capacity so that individuals would have to be paid for overtime work or more individuals would need to be employed. It is unlikely that this is the case and so this estimate is likely to be an overestimate of the true incremental labour cost of HBV immunization, i.e. an upper limit to the estimated labour cost. This is varied as part of a sensitivity analysis.

A number of costs were omitted from the analysis as they were deemed too time consuming to estimate and were thought to be of minor significance. These costs included the cost of renting kebele offices for two afternoons a month, furniture in the individual clinics, electricity, stationary and so on.

Data storage and analysis

The data were entered onto an Excel spreadsheet (Version 7.0, Microsoft®). The costs of the sample were then extrapolated to give the total for the whole programme in Region 14 by doubling all costs except those of the central vaccine stores, central administration and the operating costs of the outreach clinics (which were derived from central sources). Wastage rates were calculated as the difference between the number of vials delivered to the zones and the number of vials used divided by the number of vials delivered and expressed as a percentage; that is, the proportion of vials donated which are not used in a given year. Note that calculation of the wastage rate using the difference between the doses used and doses delivered would result in somewhat higher estimates as all the vaccines come in multi-dose vials. Note also that vaccines could be used in the following year just as vaccines from the previous year could be used in the current year. Assuming that the carry-over rate is roughly equal from year to year then these cancel out. However, there is one caveat: a polio campaign had been implemented in the year prior to the survey. Some vaccine was left over and used in the routine programme (the exact amount being impossible to estimate).

Results

Estimated costs

Table 1 presents a summary of the estimated costs of the EPI programme and the estimated additional costs of HBV immunization in Region 14 subdivided by the category of resource input (the raw data are available from the authors on request).

Cost of the current EPI schedule

Table 1 reveals a number of interesting points. First, about 45% of the costs fall to Region 14 health authority (buildings, excluding the central vaccine store, and labour); the remainder of the programme is externally funded (almost exclusively by UNICEF). Secondly, non-recurrent costs make up 29% of the total costs. The majority of these costs are attributed to buildings; only 5% of the non-recurrent costs are attributed to vehicles. This reflects the fact that all the vehicles are used for a number of different programmes and are, in general, just used to pick up vaccines from the Central Stores, or the Zone once a month or so. The proportion of EPI costs attributable to buildings is higher than in comparable studies, whereas the proportion of costs attributable to transport is somewhat lower (see, for example, Creese 1986; Robertson et al. 1992), which is probably a reflection of the predominantly urban environment of Region 14.

Recurrent costs make up the bulk of the remaining costs: 25% on labour, 28% on vaccines and a further 8% on maintenance and fuel. The proportion of costs attributable to vaccines was higher in this study than in other comparable studies [28% compared with between 3 and 16% (Creese 1986; Robertson et al. 1992)]. This may simply reflect that transport and labour costs were generally lower in this study, therefore the proportion attributable to vaccines would be higher. The use of auto-destruct syringes (at a cost of US$0.085 each) would increase the cost of vaccine supplies by approximately US$1400 per year (excluding the additional disposal costs).

The cost of the outreach programme was estimated to be 7.5% of the total. However, this is an underestimation as, due to accounting procedures, vaccines and vaccine supplies used in the outreach clinics are attributed to the static facilities. The bulk of the cost of the outreach programme is attributed

Table 1. The costs of the EPI programme and the estimated additional cost of HBV immunization in Addis Ababa health region[a]

	Cost of EPI programme		Additional cost of HBV programme	
	US$	% of total	US$	% of total
Non-recurrent costs				
Transport	12 967	5.0	0	0.0
Buildings	52 528	20.3	579	0.5
Cold chain	8 296	3.2	488	0.4
Other capital costs	1 554	0.6	185	0.2
Extra-ordinary publicity & training	49	0.0	264	0.2
Sub-total	*75 394*	*29.1*	*3 095*	*1.4*
Recurrent costs				
Labour	65 231	25.2	19 593	17.7
Vaccines	72 468	28.0	87 500	79.0
Vaccine supplies	2 047	0.8	877	0.8
Maintenance & operating costs	20 202	7.8	0	0.0
Routine publicity & training	1 956	0.8	196	0.2
Other recurrent costs	1 999	0.8	855	0.8
Sub-total	*163 903*	*63.3*	*109 021*	*98.4*
Outreach				
Capital items	3 448	1.3	243	0.2
Per diems & mobility allowance	13 610	5.3	0	0.0
Fuel allowance	2 484	1.0	0	0.0
Sub-total	*19 542*	*7.5*	*243*	*0.2*
Total cost	258 839	100	110 780	100

[a] Overhead costs are allocated by the direct method (see text for details). Non-recurrent costs (with the exception of building costs, but including the costs of the cold and freezer rooms at the central vaccines stores) are annuitized by standard techniques; for buildings the estimated rental value was taken. Cold chain includes the cost of refrigerators, freezers, coldboxes, icepacks, thermometers and vaccine carriers. Other capital costs include sterilizers, stoves and the computer at the Region 14 headquarters. Labour costs exclude the *per diem* allowances for outreach clinics; these are listed separately. Vaccine supplies include needles and syringes. Maintenance and operating costs includes maintenance of vehicles, fuel allowances for the static clinics and maintenance of refrigerators and buildings. Other recurrent costs include computer disks, vaccination cards and disposal of syringes and needles. The additional cost of labour for HBV vaccination assumes that the vaccine teams are currently working at maximum capacity (see text for details). The unit cost of HBV vaccine is taken to be US$0.5 per dose. The number of HBV doses given is assumed to be equal to the number of doses of DPT given (see Table 2). The additional number of needles and syringes is estimated to be 3/7ths extra (as HBV requires 3 doses, and there are 7 injected doses at present in the EPI).

to the *per diems* and mobility allowances paid to the vaccine teams.

The results presented in Table 1 are derived from using the direct allocation method for overhead costs. When an incremental analysis was performed, i.e. we asked if the facility would still be needed if the EPI was not in place, the annuitized capital costs were found to equal US$11 097 (75% due to cold chain costs).

Costs associated with introducing HBV vaccine

The estimated non-recurrent costs of introducing HBV immunization into the EPI (Table 1) are exceptionally low (only an additional US$3095 per annum, 1.4% of the total estimated cost). This is largely because the capital equipment is not being used at maximum capacity, therefore HBV vaccine can be integrated into the EPI with little additional cost. For instance, the average used capacity of the refrigerators was 53.5%, the cold boxes 57.6% and the vaccine carriers 52.3%. Nevertheless, the possibility remains that some respondents gave strategic answers and so underestimated their capital requirements for HBV vaccine to facilitate the introduction of HBV vaccine into the EPI. We attempted to control for this by estimating the maximum capacity of the facility used under the current schedule in each of the clinics. If we assume that if the used capacity of the facility was 75% or greater then the clinic would need an additional facility, then the total non-recurrent costs of introducing HBV vaccine would be US$4725 per annum, and the total additional cost of HBV immunization would be US$115 017 per annum.

Seventy-nine percent of the cost of introducing HBV vaccine into the EPI schedule is estimated to be due to the cost of the vaccine (at an assumed cost of US$0.5 per dose). Hence the cost of a HBV immunization programme would be most sensitive to this variable. If HBV vaccine could be procured at US$0.25 per dose, for instance, then the estimated total annual cost of introducing HBV vaccine would be reduced to US$67 030, but would be US$198 280 if the vaccine could only be procured at US$1 per dose (see Table 3).

The majority of the remaining estimated costs of HBV vaccination in Addis Ababa is that for labour. This is, at least in part, because we assume that the individuals working in the vaccination clinics are doing so at maximum capacity, i.e. they could not vaccinate another child without having to stay late, or without extra manpower. This is probably not the case. Most clinics vaccinated in the mornings and used the afternoons for preparation and sterilization. In many instances it would not be necessary to employ more staff or to pay for overtime work. Therefore this figure is likely to represent an overestimate of the true additional labour cost of HBV vaccination. If we assume that the additional labour cost would be zero, then the total cost of introducing HBV vaccination would be US$91 187 per annum at a unit cost of US$0.5 per dose. Utilizing the figures shown in Table 2 for the numbers of DPT doses given, and assuming that the number of HBV doses given would be the same, we derive a cost per HBV dose of US$0.78 if the additional labour costs are zero, or US$0.94 if they are as shown in Table 1, at a unit price of US$0.5 per vaccine dose.

EPI coverage rates and cost per dose

Table 2 shows the number of doses given and the number of individuals fully vaccinated over the period June 1995 to July 1996. There were 52 589 infants eligible for vaccination, approximately 60% of which were fully vaccinated with all the standard EPI antigens (data provided by Region 14 Health Authority).

The average cost per infant dose in the EPI schedule in Region 14 can be calculated as US$0.72 (including those infants who did not receive a full course).

Estimated cost of HBV vaccine

Table 3 shows the estimated cost of HBV vaccination at various assumed prices of HBV vaccine. Utilizing data from Region 14 Health Authority on the number of doses of DPT given during the study period (July 1995–June 1996), the average (additional) cost per HBV dose can be estimated to be US$0.94, assuming that the number of doses of HBV given would be similar and a price of US$0.5 per HBV dose (Table 3).

Cost of introducing a combined HBV/DPT vaccine

If HBV vaccine were to be given in a combined preparation with DPT, the administrative costs can be estimated to be only US$264 per annum (for extra-ordinary publicity and training only). Assuming that the combined preparation is equally as effective as the separate vaccines, and that the vaccination teams are currently working at maximum capacity (thus there would be extra labour costs of HBV vaccination), then if the combined preparation can be procured for less than US$0.77 per dose, it will be more cost-effective than giving the two vaccines separately (at an assumed cost of HBV vaccine of US$0.5 per dose). If, however, the extra labour costs of HBV vaccine are zero, a combined vaccine would need to be procured for less than US$0.64 per dose for it to be more cost-effective than the two vaccines separately.

Cost-effectiveness

A common measure of the cost-effectiveness of immunization programmes is the cost per fully vaccinated child, FVC (Creese 1986; Shepard et al. 1989; Robertson et al. 1992). This is calculated as the annual cost of the EPI programme (excluding the cost of TT) divided by the number of infants who receive a full course of vaccinations in a year (Shepard et al. 1989; Robertson et al. 1992). The estimated annual cost of the EPI programme excluding TT (overhead costs were attributed to TT by direct allocation) was US$247 060, and the cost per fully vaccinated child was US$7.83 (as 31 553 infants were fully vaccinated – data from Region 14 Health Authority).

Discussion

A central problem in estimating the cost-effectiveness of a proposed intervention is that the costs of the programme (as well as the health benefits) cannot be accurately estimated until the programme is under way. If the cost-effectiveness analysis is to be used as an aid to the decision-making process (i.e. whether to implement the programme or not), then the costs and health benefits must be estimated indirectly (as we have attempted here) or extrapolated from other areas where the proposed programme has already been implemented. We show here how a questionnaire can be used to estimate the cost of integrating HBV vaccine into the existing vaccination

Table 2. The number of doses provided by Region 14 during July 1995–June 1996 and the number and % of children fully immunized[a] for each of the vaccines

	Price per vial (US$)	Doses per vial	Vials delivered to zones	Vials used (opened)	Cost (US$)	Fully vaccinated per Ag.	% fully vaccinated	Wastage rate (%)
OPV	1	10	14 500	11 000	14 500	37 390	71.1	24.1
DPT	0.9	10	17 500	17 000	15 750	37 391	71.1	2.9
Measles	1.6	10	9 500	9 000	15 200	33 131	63.0	5.3
BCG	1.45	20	10 564	5 200	15 317.8	40 493	77.0	50.8
TT	0.6	10	19 500	14 500	11 700	32 436		25.6
Total					72 467.8			

[a] Fully immunized: received three doses of OPV and DPT and one dose of measles and BCG.

Table 3. The estimated additional annual cost of HBV vaccine, the total additional annual cost of the HBV vaccination programme (which includes labour etc.) and the average cost per HBV dose given using various assumptions about the unit price per dose of HBV vaccine (all costs in US$)[a]

Unit cost of HBV vaccine	Annual cost of HBV vaccine	Total annual cost of HBV vaccination programme	Average cost per HBV dose given
1	175 000	198 280	1.69
0.5	87 500	110 780	0.94
0.25	43 750	67 030	0.57
0.1	17 500	40 780	0.35

[a] The number of doses given was taken to equal the number of doses of DPT given in Region 14 during July 1995–June 1996 (117 326 doses in total), not the total number of doses used by Region 14 (175 000). Thus these estimates include wastage.

programme in Addis Ababa, based largely on the current resource use associated with DPT vaccination.

The questionnaire approach seemed particularly suited to accurately estimate the additional capital costs of HBV vaccination as it was possible to check for inaccurate or strategic answers by assessing the capacity of the facility used. For instance, if a refrigerator was currently being used at close to its maximum capacity, we could assume that the clinic would need an additional facility to store HBV vaccine, even if the respondents replied that they would not. Applying this check increased the estimated annual capital cost of introducing HBV vaccine by US$1600. Indeed, it is noteworthy that the additional annual capital costs of HBV vaccination were estimated to be very low, largely because the facilities were, in general, not used at close to their maximum capacity.

Where the technique is probably least accurate is in estimating the additional labour costs of HBV vaccination. The way the questions were framed ('How much extra time would you need to vaccinate against HBV?', and respondents were helped by asking how much time they currently spent on DPT) led most respondents to suggest that they would have to spend roughly 30% extra time vaccinating. While this may be true, the vaccination teams did not spend all their time vaccinating – they tended to vaccinate in the morning and spend the afternoon on administrative duties or preparing for the next day. Hence it seems likely that there would, in practice, be very little additional labour costs associated with HBV vaccination. One way we could have avoided this problem would have been to ask how many extra *people* would be required if the clinic were to introduce HBV vaccine, and how many would be needed if there were no EPI. Indeed, as labour is not entirely divisible (individuals come in integer units) this approach may also have yielded more appropriate results. However, it was thought that these questions were unlikely to lead to accurate or reliable answers, and might endanger the rest of the survey. The adopted approach (asking individuals how much time they spent on DPT and how much extra they would spend on HBV vaccination) is likely to give an upper limit to the extra labour costs of introducing HBV vaccination into the EPI schedule, i.e. this approach is likely to overestimate the cost per immunized child (and underestimate the cost-effectiveness of the programme).

Notwithstanding the difficulties associated with accurately assessing the additional labour costs likely to be associated with the introduction of HBV vaccination, we feel that this questionnaire technique is worth applying in other field conditions because data can be collected at low cost, and with minimal disruption to the clinics concerned (it took roughly 90 minutes to sample each clinic).

We used a simple summary measure for estimating the cost-effectiveness of the EPI programme, that is, the cost per fully vaccinated child. Clearly, a more appropriate measure would be the cost per life-year gained or cost per disability adjusted life-year (DALY) gained, as these statistics give a measure of the cost per health gain derived from the EPI programme. However, the effort required to estimate the health gained for the EPI programme would be prohibitive, since we would need to project how many life-years are likely to be gained from each of the antigens given in the EPI programme, as well as adjust for health related quality of life and the timing of the health gains (discounting). Our estimates of the cost per fully vaccinated child (US$7.84) in the EPI programme in Region 14 compare favourably with estimates of other routine EPI programmes (Creese 1986), for instance US$7.14 in The Gambia (excluding yellow fever and HBV; Robertson et al. 1992) and US$6.08 for the routine programme in Ecuador (Shepard et al. 1989) (both of these latter estimates are expressed here in 1996 prices, assuming a 3% inflation rate). It is, however, unlikely that the EPI programme is as cost-effective in other areas of Ethiopia as Region 14 is predominantly urban and able to achieve higher levels of coverage than many other regions (Tesfaye et al. 1997).

We estimated that between 3 and 51% of the vaccines were wasted (depending on the antigen). Since vaccines make up the largest proportion (28%) of the costs of the EPI programme (Table 1), the cost, and therefore cost-effectiveness, of the programme is particularly sensitive to this variable. Thus, reducing the wastage rate would clearly improve the efficiency of the EPI programme, though it should not be done at the expense of increasing the likelihood of missed opportunities, or encouraging the use of out of date vaccines.

Although the cost of introducing HBV vaccine into the EPI programme is estimated to be considerable (roughly 40% extra using our base case assumptions), the cost per dose of

HBV vaccine is estimated to be low compared with The Gambia: US$0.94 compared with US$1.67 in The Gambia (in 1996 prices at 3% inflation; Hall et al. 1993). Note that although our study used output measures such as cost per dose or cost per fully vaccinated child, it is still possible to extrapolate the cost-effectiveness of HBV immunization in terms of outcome measures such as life years gained relative to The Gambia. Prior to immunization the prevalence of carriage in The Gambia was approximately 15% (Vall Mayans et al. 1990; Whittle et al. 1990; Edmunds et al. 1996a); in Region 14 the prevalence of carriage is roughly 7% (Abebe et al. 1996). Assuming that the prevalence of HBV-associated disease roughly correlates with the prevalence of carriage, then the per person risk of HBV-associated disease in The Gambia will be roughly twice that in Region 14. But the cost per dose of HBV vaccine in Addis Ababa is estimated here to be little more than half the cost per dose in The Gambia. This implies that HBV vaccination in Region 14 is likely to be similarly cost-effective as in The Gambia, i.e. highly cost-effective (Hall et al. 1993).

The majority of the cost of introducing HBV vaccine into the programme is attributable to the cost of the vaccine (even using our base case assumption regarding labour, the cost of the vaccine is still estimated to make up 79% of the cost of introducing HBV vaccine). The primary reason for this is that the equipment used in the current EPI programme is not being used at or near maximum capacity, thus very little extra capital expenditure would be needed if HBV vaccine were to be introduced. The implications of this are that the cost-effectiveness of HBV vaccine will be most sensitive to the cost of the vaccine. Ensuring that the vaccine can be procured at minimum cost should be a priority consideration.

It is unlikely that a combined DPT/HBV vaccine can be procured for less than US$0.77 per dose. Assuming that HBV vaccine can be procured at US$0.50 per dose, then it is unlikely that a combined DPT/HBV vaccine will be more cost-effective to introduce than the separate preparations. The potential of a future combined DPT/HBV vaccine should not be used to delay the introduction of HBV vaccination in Addis Ababa.

References

Abebe A, Messele T, Dejene A, Enquselassie F, Tsegaye E, Cutts F, Nokes DJ. 1996. Seroepidemiological study of hepatitis B virus in Addis Ababa, Ethiopia: transmission and control. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **90**: 461.

Anon. 1995. *Report of a joint national review of the Expanded Programme on Immunization (EPI)*. Addis Ababa: Family Health Department, Ethiopian Ministry of Health.

Creese AL. 1986. Cost effectiveness of potential immunization interventions against diarrhoeal disease. *Social Science and Medicine* **23**: 231–40.

Drummond MF, Stoddart GL, Torrance GW. 1987. *Methods for the economic evaluation of health care programmes*. Oxford: Oxford University Press.

Edmunds WJ, Medley GF, Nokes DJ. 1996a. The transmission dynamics and control of hepatitis B virus in The Gambia. *Statistics in Medicine* **15**: 2215–33.

Edmunds WJ, Medley GF, Nokes DJ, O'Callaghan CJ, Whittle HC, Hall AJ. 1996b. Epidemiological patterns of hepatitis B virus (HBV) in highly endemic areas. *Epidemiology and Infection* **117**: 313–25.

Hall AJ, Robertson RL, Crivelli PE, Lowe Y, Inskip H, Snow SK, Whittle H. 1993. Cost-effectiveness of hepatitis B vaccine in The Gambia. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **87**: 333–6.

Robertson RL, Hall AJ, Crivelli PE, Lowe Y, Inskip HM, Snow SK. 1992. Cost-effectiveness of immunizations: The Gambia revisited. *Health Policy and Planning* **7**: 111–22.

Shepard DS, Robertson RL, Cameron CSM et al. 1989. Cost-effectiveness of routine and campaign vaccination strategies in Ecuador. *Bulletin of the World Health Organization* **67**: 649–62.

Tesfaye F, Enquselassie F, Ali K, Andom G. 1997. EPI coverage in Adami-Tullu Woreda. *Ethiopian Journal of Health Development* **11**: 109–13.

Tsega E, Mengesha B, Hansson B, Lindberg J, Nordenfelt E. 1986. Hepatitis A, B, and Delta infection in Ethiopia: a serological survey with demographic data. *American Journal of Epidemiology* **123**: 344–50.

Tsega E, Tsega M, Mengesha B, Nordenfelt E, Hansson B, Lindberg J. 1988. Transmission of hepatitis B virus infection in Ethiopia with emphasis on the importance of vertical transmission. *International Journal of Epidemiology* **17**: 874–9.

Vall Mayans M, Hall AJ, Inskip HM et al. 1990. Risk factors for the transmission of hepatitis B virus to Gambian children. *Lancet* **336**: 1107–9.

Whittle H, Inskip H, Bradley AK et al. 1990. The pattern of childhood hepatitis B infection in two Gambian villages. *Journal of Infectious Diseases* **161**: 1112–5.

WHO. 1991. Hepatitis B vaccine. *Weekly Epidemiological Record* **3**: 11.

World Bank. 1993. *World Development Report 1993: Investing in health*. Oxford: Oxford University Press.

Acknowledgements

We thank Region 14 Health Authority, UNICEF, the Ethiopian Ministry of Health, and the participants in the survey without whose help and support this study would not have been possible. We also thank Steve Hilton for help with the questionnaire and study design. We are grateful for funds from the University of Warwick's Research and Training Development Fund for financial support. WJE is in receipt of a Wellcome Health Services Research Fellowship (grant number 040952). DJN is a Royal Society University Research Fellow.

Biographies

W. John Edmunds, BSc, MSc, Ph.D., has a Ph.D. in modelling the transmission dynamics of hepatitis B virus from Imperial College London and a masters in Health Economics from the University of York. His main area of interest is the use of transmission dynamic models in the economic evaluation of vaccination programmes. After a Wellcome post-doctoral Fellowship at the University of Warwick he is now working at the Communicable Disease Surveillance Centre in London.

Amare Dejene, BSc, MSc, MPH, graduated with a BSc in Statistics from Addis Ababa University, followed by an MSc in Medical Statistics at the London School of Hygiene and Tropical Medicine and an MPH in the School of Public Health in Brussels. He has published papers in the fields of reproductive health, information systems and harmful traditional practices. He has participated in international research projects into the epidemiology of measles, rubella and hepatitis. He is currently a Senior Researcher working in the Ethiopian Health and Nutrition Research Institute (EHNRI).

Yared Mekonnen, BSc, MSc, received a BSc in Statistics from Addis Ababa University, followed by an MSc in Demography from the

same university. He is presently an Associate Researcher in the Department of Epidemiology and Biostatistics at EHNRI. He has published a number of articles on population health related issues.

Moges Haile is a public health nurse responsible for the daily running of the EPI programme in Region 14, Addis Ababa, Ethiopia.

Wondimagegnehu Alemu, MD, MPD, TM, graduated from the Medical Faculty of Addis Ababa University in 1983 and began his career as a practising physician and Medical Director of a rural hospital in Eastern Ethiopia. He later became the National EPI Manager. He earned a masters in Public Health and Tropical Medicine in 1991 from Tulane School of Public Health and Tropical Medicine. From 1991–94 he worked at the Ministry of Health. From 1994–97, he worked for UNICEF Addis Ababa Office. Currently, he is acting Head of the Integrated Disease Surveillance Program of Communicable Diseases Prevention and Control, WHO/AFRO. He is one of the founding members of the Ethiopian Public Health Association and has served on the Editorial board of the Ethiopian Health Development Journal.

D. James Nokes, BSc, Ph.D., trained as a Zoologist at Imperial College London, followed by a Ph.D. in infectious disease epidemiology (rubella seroepidemiology and control) at Imperial and University College Hospital. Subsequent post-doctoral Fellowships held at London, Oxford and Warwick Universities, all relate to understanding the patterns of microparasitic infections in human populations both in the developed and developing world (most field work in Ethiopia). Currently a Royal Society University Research Fellow at Warwick University, with particular interest in developing the use of salivary antibody surveillance techniques in epidemiological research and the mathematical modelling of vaccination programmes.

Correspondence: Dr WJ Edmunds, Immunisation Division, PHLS CDSC, 61 Colindale Avenue, London NW9 5EQ, UK. Email: jedmunds@phls.nhs.uk