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# Review of treatment cost protocol studies

## Report of a meeting
## Geneva, 11-12 December 2000

**DEPARTMENT OF VACCINES AND BIOLOGICALS**

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# Abbreviations

| | |
|---|---|
| ARI | acute respiratory infection |
| CVI | Children's Vaccine Initiative |
| DTP | diphtheria-tetanus-pertussis vaccine |
| EPI | Expanded Programme on Immunization |
| GCE | generalized cost-effectiveness |
| HepB | hepatitis B |
| Hib | *Haemophilus influenzae* type b |
| LSHTM | London School of Hygiene and Tropical Medicine |
| RSV | respiratory syncytial virus |
| RV | rotavirus |
| WHO | World Health Organization |

# Executive summary and conclusions

During 1999 the Children's Vaccine Initiative (CVI) supported the development and pilot testing of a protocol for estimation of the treatment costs for three vaccine preventable diseases: Meningitis, pneumonia and diarrhoea. The protocol has three main objectives: first, to determine the costs associated with the diseases in question; secondly, to describe demographic and clinical characteristics of patients as possible explanatory variables for differences in costs associated with the illnesses and thirdly, to assess the feasibility of applying a standardized costing protocol across different countries. The intended use of the results is to provide an estimate of potential costs averted due to the introduction of additional vaccines into routine childhood vaccination programmes: *Haemophilus influenzae* type b, pneumococcal conjugate, rotavirus and shigella vaccines.[1]

The protocol was developed by Dr Tessa Tantorras, WHO, Dr Gary Ginsberg, Ministry of Health, Israel, Mr Damian Walker, LSHTM and Dr Mark Miller, CVI. Three sites were selected for pilot testing of the protocol: the National Institute for Public Health, Cuernavaca, Mexico, the Foundation for the Advancement of Clinical Epidemiology, Manila, Philippines and the Centre for Community Medicine, New Delhi, India. The pilot studies began late 1999 and were scheduled to last approximately six months.

A meeting was organized in Geneva on 11-12 December 2000 to review the findings of the studies, to discuss how these should be used and published and to provide suggestions as to how the protocol could be improved for future use.

During the meeting a number of recommendations were made for changes to the protocol. It was agreed that all modules of the protocol should be revised based on the experiences of the pilot studies. It was furthermore recommended to add a standard software tool for data collection and analysis to the protocol, as well as providing a standard format for reporting of results.

It was agreed that it would be useful to publish the results of the three studies in a joint article. This paper should focus on the comparability of cost data between countries, thereby exploring whether global recommendations on treatment cost savings from introducing new vaccines can be made. It was also suggested that a paper on methods used in the studies be submitted for publication.

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[1] Only the *Haemophilus influenzae* type b vaccine is currently licensed. A 7 valent pneumococcal conjugate vaccine was recently licensed in the USA. 9 and 11 valent pneumococcal conjugate vaccines are currently in the phase III trial stage. Rotavirus and *Shigella* vaccines are still only in the early stages of development. A rotavirus vaccine was licensed in the USA in 1999, but it was relatively quickly withdrawn from the market due to possible links with intersusception.

# 1. Meeting objectives

Ms Ulla Kou reminded the participants that for a complete economic evaluation of a childhood vaccine the following cost data must be collected:

- Costs of vaccine and its administration.
- Costs of adverse events.
- Treatment costs averted from immunization.
- Time and other costs incurred by parents.

Very little evidence on treatment costs averted from immunization is available from developing countries. As a result, in many economic evaluations, this cost item is simply not included. Instead, conclusions are made based only on costs of the vaccine and its administration, as this is a relatively easy cost item to estimate. At the same time, some researchers question the importance of including these costs in the evaluations. The argument is that not much treatment is being carried out anyway in developing countries and the nominal value is therefore low. However, conclusions like these should not be made without evidence.

In response to the lack of data on treatment costs for vaccine preventable diseases, the Children's Vaccine Initiative (CVI) developed a protocol for collection of data for three vaccine preventable diseases: Meningitis, pneumonia and diarrhoea. The objective of the protocol is to determine the costs associated with these diseases in children below 5 years of age from the perspective of the health service as well as society. Research institutes in Mexico, the Philippines and India were chosen for pilot studies of the protocol.

The protocol is divided into six modules:

1) Direct hospital medical costs.
2) Direct health centre medical costs.
3) Out-of-pocket expenditures and productivity losses.
4) Hospital and health centre resources.
5) Follow-up visits after hospitalization.
6) Health seeking behaviour (this module has not yet been completed).

For a study using the protocol, data should be collected from a sample of health facilities:

- 10 public and 10 private urban primary physicians.
- 10 public and 10 private rural primary facilities.
- 4 secondary hospitals – urban, rural, public and private.
- 2 tertiary hospitals – 1 public and 1 private.

Using this sampling strategy, treatment costs of a total of 1700 patients with diagnosis of pneumonia, diarrhoea or meningitis should be estimated.

The objectives of the meeting were identified as follows:

- To review results of the three pilot studies.
- To review the study process of the pilot studies.
- To suggest changes to the protocol and to the study process.
- To determine how to use the results of the pilot studies.
- To discuss how the protocol can be used in other ongoing work.
- To discuss how the protocol should be linked to burden studies so that cost-effectiveness estimates can be generated.

Following the presentation, it was agreed to change the session of the second day, with all the presentations on other related work being made in the morning and the afternoon being reserved for group work on recommendations for changes to be made to the protocol.

# 2. Findings from pilot studies

Investigators from the three study sites presented their preliminary results and commented on study methodology and constraints incurred during the data collection process.

## 2.1 Mexico

Dr Stefano Bertozzi presented the study from Mexico. He started by briefly explaining the structure of the health system in Mexico. There are four key providers of health services:

1) State Ministry of Health, including the Hospital del Nino (the national hospital).
2) Ministry of Health.
3) Social Security System.
4) Private sector providers.

Six hospitals and 22 clinics were included in the sample for the study. The best data on resource use and unit costs were found in Hospital del Nino where a highly developed cost accounting system is in place. This is in contrast to the social security system providers, who do not have transparent budgets and make use of an old-fashioned system that is not designed to improve management. For example, the same cost per laboratory test is being used across the whole country. However, for the study they had to make use of the unit costs provided to them by the social security system. Moreover the private sector in Mexico does not keep medical records and it was therefore not possible to estimate unit costs retrospectively for this sector. Instead, patient charges were used as an approximation. Dr Bertozzi argued that studies have indicated that patients' fees actually are quite similar to the real cost.

To get a sufficient number of cases of meningitis, case report forms from the last three years were used. To estimate the time spent with patients, interviews with doctors and nurses were conducted. Costs of drug wastage were included in the estimates.

Preliminary results of the study for pneumonia and diarrhoea are illustrated in the table below. Cost estimates for the meningitis cases are not yet complete.

**Table 2.1: Mean treatment costs per case in Mexico**

| | Pneumonia US$ | Diarrhoea US$ |
|---|---|---|
| Ambulatory care | 23.60 | 16.70 |
| Hospitalized care | 133.60 | 190.60 |

In ambulatory care the main cost driver is doctor's time for both pneumonia and diarrhoea. For hospitalized cases the main cost driver is laboratory tests.

## 2.2 India

Dr K. Anand presented the Indian study. While the overall methodology of the Indian study followed the underlying principles of the CVI protocol, the actual protocol was not used. For unknown logistical reasons the Indian study site never received the protocol and they therefore went ahead and produced their own assessment tool and questionnaires.

The study included a total of eight health facilities. At the primary and secondary level, one private facility and two public facilities were chosen. At the tertiary level, one private and one public facility were included in the study.

Data on indirect as well as direct costs were collected. Indirect costs were defined as transportation and lost wages of parents. Transport costs were based on actual costs as well as imputed costs based on distance and mode of transport. Wages lost were calculated as the monthly salary of the person, even if unemployed (the minimum wage was used). Direct costs were defined as consultation, investigations, drugs, and hospital stay costs. For the public sector, actual unit costs were calculated. For the private sector cost estimates were based on patient charges.

Some of the preliminary conclusions of the study are outlines in table 2.2.

**Table 2.2. Average total costs per case in India (indirect and direct costs)**

| Type of facility | ARI US$ | Diarrhoea US$ | Meningitis US$ |
|---|---|---|---|
| Primary level, public sector | 2.9 | 2.4 | NA |
| Primary level, private sector | 7.4 | 4 | NA |
| Secondary level, public sector, out patient | 3.1 | 2.2 | NA |
| Secondary level, private sector, out patient | 9.8 | 7.5 | NA |
| Secondary level, public sector, inpatient, | 58 | 37.3 | NA |
| Secondary level, private sector, inpatient | 216 | 133.4 | NA |
| Tertiary level, public sector, outpatient | NA | 11.6 | NA |
| Tertiary level, private sector, outpatient | 6.2 | 6.2 | NA |
| Tertiary level, public sector, inpatient | 155.3 | 163.8 | 449 |
| Tertiary level, private sector, inpatient | 142.4 | 87.3 | 217.6 |

The following were some of the data collection problems identified:

- There are biased results from tertiary care as all public tertiary hospitals in India are attached to a medical college and this is likely to inflate the costs.
- In the public sector, no isolation of specimens is done. This is done in the private sector, but not very carefully.

## 2.3 The Philippines

Dr Inday Dans presented the findings of the Philippines' study. This study followed the CVI protocol. However, for some reason, only the first three modules of the protocol were received in the first instance. When the fourth module was received recently, this data was as far as possible added to the study.

Prospective data collection was done from physicians' and caregivers' interviews. Retrospective data was obtained from chart reviews.

The health facility sample size is illustrated in table 2.3 below. The number of retrospective medical charts reviewed in each facility is included in bracket. A total of 454 charts were reviewed. 54 of these were meningitis cases. In general, the chart reviews were found to be much more complete than expected. In addition to the chart reviews, a total of 52 diarrhoea cases and 52 pneumonia cases were followed prospectively from all the eight types of providers and 20 physician interviews were done for diarrhoea as well as for pneumonia. Moreover, 11-12 physician interviews were carried out to gauge follow-up costs. For private hospitals, data on malnutrition were collected from a charity ward.

### Table 2.3. Facilities included in the Philippines' study and number of charts reviewed in each (in bracket)

| | Urban | | Rural | |
|---|---|---|---|---|
| Health facility | Public | Private | Public | Private |
| Hospital | Philippine General Hospital (PGH)<br><br>(40 D, 40 P, 25 M) | St. Lucas Medical Centre (SLMC)<br><br>(40 D, 41 P, 15 M) | Bataan Provincial Hospital (BPH)<br><br>4(0 D, 40 P, 14 M) | Bataan Doctor's Hospital (BDH)<br><br>(39 D, 37 P) |
| Primary care centre | 5 health centres<br><br>(10 D, 9 P) | 5 private medical doctors<br><br>(10 D, 10 P) | 5 health centres<br><br>(12 D, 12 P) | 5 private medical doctors<br><br>(10 D, 10 P) |

D = Diarrhoea, P = Pneumonia, M= Meningitis

Considerable problems were incurred when collecting financial data from private health facilities. These providers were reluctant to collaborate in terms of providing the data and the fees paid by the patient for treatment were therefore used as an approximation for real costs.

Table 2.4 illustrates mean direct medical costs per patient as collected from charts from the four hospitals included in the study.

### Table 2.4: Mean direct medical costs per patient in the Philippines (in US$)

| | Diarrhoea | Pneumonia | Meningitis |
|---|---|---|---|
| PGH | 66 | 209 | 809 |
| SLMC | 719 | 1011 | 4155 |
| BPH | 72 | 118 | 373 |
| BDH | 128 | 165 | NA |
| Urban private medical doctor | 9 | 30 | NA |
| Rural private medical doctor | 7 | 24 | NA |
| Urban public health centre | 3 | 6 | NA |
| Rural public health centre | 3 | 9 | NA |

The following are some of the key results from the study:

- Hotel stay is the cost driver for direct medical costs for hospitalized pneumonia, diarrhoea and meningitis cases (>50%).
- For outpatient diarrhoea cases, consultation fees are the cost driver. For pneumonia, the cost of drugs used is the main determinant.
- For out-of-pocket expenditures, cost drivers are the costs of drugs, medical consults and hospital/clinic stay.

- Productivity loss is biggest among hospitalized diarrhoea cases, mostly from private hospitals.
- Cost differences may be attributed to: a) variable physicians' practices b) unit cost difference of resources c) co-morbidity d) socioeconomic status and e) difference in productivity loss.
- Direct medical costs using chart reviews approximated the value from physicians' interviews for diarrhoea cases, but not for pneumonia.
- Private urban centres are the most expensive per bed day.
- Treatment of pneumonia is on average more expensive than diarrhoea.
- Public hospitals are only carrying out 10% of the diagnostic tests carried out by private practitioners.

Key data collection problems identified were as follows:

- It would be desirable to collect case definitions as not all cases are vaccine preventable. However, it is generally not possible to obtain the case definition. For example, only one rotavirus case was identified.
- There is an urgent need to revisit the case definition of pneumonia.
- Random sampling of centres is difficult due to the logistics involved.
- Annual financial reports of private hospitals are confidential.
- Many of the questionnaires in the protocol are unclear.

For future studies it is very important to ensure quality control of data collectors.

# 3. Discussion on study results

Following the presentations, problems incurred during the data collection process and alternatives for how the results should be used were discussed.

The three sites had the following comments to make on the usefulness of the protocol and on problems experienced during the data collection process and analysis:

## 3.1 Mexico

1) How can the case definition and etiologic agent be determined?
2) How can we identify the real burden of disease on a national level? For policy-makers it is crucial to come up with a state average cost.
3) Minimum acceptable defaults should be included, for instance for laboratory and x-ray costs. Perhaps just one laboratory could be costed and this figure could be used in all settings?
4) We should define where the major variations come from and thereby use the time during the study in the most cost-effective way.
5) Where are the greatest sources of uncertainty?
6) How to include pre and post-institutional costs?

The concerns of the investigators were discussed. There was general agreement that it is a problem that the protocol does not give realistic guidance on how to sample institutions. The sample is absolutely crucial as the type of institution could be the factor that makes the biggest difference in average costs.

Is a static model appropriate? When including outcomes, might a dynamic approach be more appropriate?

Is it a problem that the protocol does not give guidance on how to determine the antigen?

Discussions also took place on how governments could use the results in their countries. From the Philippines it was argued that especially at institutional level managers are very interested in using the results, in particular as a basis to set prices. However, the costing part is not enough for overall advice at a national level. It has to be included in a cost-effectiveness analysis. In India, this type of information is not readily available and the cost information is therefore useful on its own. For instance, cost per bed day is a very useful measure for the health care institution.

It is more doubtful if policy-makers would use the information to introduce new vaccines. In Mexico, the cost information is also especially useful at institutional level. At national level, vaccines are relatively "easily" being introduced in Mexico.

## 3.2 India

1) For selection of health facilities it is very difficult to follow the requirements of the protocol. For example, in India there are no secondary hospitals in rural areas.
2) During a six months study period it is not possible to get the required number of cases of meningitis as this disease is relatively rare.
3) The definition of pneumonia needs to be revisited.
4) HIV testing is not done and can be due to ethical reasons not related to the patient.
5) It is not possible to review medical records in private facilities.
6) Medical records cannot be collected retrospectively in outpatient facilities.
7) For the costing of drugs, generic names are not used in India. It is therefore very difficult to get the exact cost of the drugs, as prices are very variable (on this comment, Dr Dans noted that in the Philippines an average price of all brands was used to estimate the unit cost).
8) It was difficult to estimate overhead costs for hospitals.
9) In physician interviews it is easy to get a selection bias due to rejection of participation of many physicians.
10) The consultation fee can be difficult to obtain.
11) Follow-up costs could be difficult to obtain from physicians as the patient might go somewhere else.
12) How should the valuation of the caregiver be estimated? Can the minimum wage be used?

## 3.3 The Philippines

1) Without a case definition it is a concern how the results can be used in a cost-effectiveness study for a vaccine. How will the burden of the vaccine-preventable illnesses be generated?
2) It was difficult to quantify resources based on chart reviews. It was especially difficult to estimate the quantities of drugs, including wastage of vials.
3) Only an abridged version of the protocol was initially received from the CVI. The longer version which was later received is preferred.
4) It is important to include quality control for the investigators, both on chart reviews and on physician interviews.
5) Due to logistical problems it is difficult to do a random sampling of facilities. The criteria of 2% death rate, stated in the protocol could not be met in the Philippines.
6) The questionnaires provided were in many cases confusing.

# 4. Ongoing work related to the protocol

Four presentations were made on on-going work related to the protocol. The aim of the session was to identify useful links between these projects and the protocol.

## 4.1 WHO generalized cost-effectiveness approach

Mr Hutubessy summarized work on WHO generalized cost-effectiveness (GCE) approach which is being spearheaded by the Department of Evidence for Health Policy.

The objective of GCE is to provide policy-makers with evidence necessary to review existing resource allocation decisions (mix of current "interventions") and choose appropriate new or expanded interventions should more resources become available. The requirement for GCE is evidence on the costs and health impacts of a wide range of new and existing interventions, at different levels of coverage. The goal is to provide evidence for a large number of interventions at a regional level thereby finding a balance between being locally applicable and providing information useful to decision-makers in many settings (generalizable). A simple decision rule is being designed in terms of generalized league tables at regional level.

The GCE approach compares interventions to the "null" of stopping all interventions against that disease/condition or cluster of conditions. It thereby allows assessment of what is currently done and possible alternatives. For measurement of effectiveness an assessment of outcomes without current interventions is required. One is thus considering each outcome with each possible intervention in turn and in combination, e.g. case management alone, vaccine alone and vaccine with treatment of remaining cases.

The GCE approach is described in Murray C.J.L., Evans D.B., Acharya A. & Baltussen R.M.P.M. "Development of WHO Guidelines on Generalized Cost-Effectiveness Analysis", *Health Economics* 9 (3): 235-51, 2000. The paper can also be downloaded from the internet on: www.who.int/evidence (GPE discussion paper No.4).

## 4.2 LSHTM project

Mr Damian Walker presented the outline of a DFID-funded project which will soon begin at the London School of Hygiene and Tropical Medicine (LSHTM). The title of the project is “Modelling the impact and incremental cost-effectiveness of introducing vaccines against hepatitis B (HepB), *Haemophilus influenzae* type b (Hib) and rotavirus (RV) into routine infant immunization programmes in Bangladesh and Peru”. The research team is comprised of:

- LSHTM: Dr Felicity Cutts, Dr Julia Fox-Rushby, Dr Colin Sanderson and Mr Damian Walker.
- International Centre for Diarrhoeal Disease Research, Bangladesh: Dr SM Akramuzzamman and Dr Disha Ali.
- Instituto de Investigación Nutricional, Peru: Dr Claudio Lanata and Dr Mary Penny.
- National Institutes of Health, USA: Dr Mark Miller.

A decision-analytic framework will be used to assess the incremental cost-effectiveness of introducing vaccines against HepB, Hib, and RV. Fieldwork will be conducted in Bangladesh and Peru in order to evaluate the incremental net costs from a societal perspective of introducing infant vaccination against additional vaccines. Standard EPI/WHO costing guidelines will be used to determine the costs of each country’s EPI, and the incremental costs of introducing HepB, Hib and RV vaccines at various coverage levels, through different distribution mechanisms and with given equity-driven policies will be estimated. A standardized human capital, incidence-based cost-of-illness approach will be developed to estimate the direct (medical and non-medical) and indirect costs of the diseases. Markov models will estimate the disease burden in terms of the number of deaths and disability-adjusted life years (DALYs) due to HepB, Hib and RV.

Transition probabilities will be estimated by reviewing published and unpublished studies and epidemiological data from each country. The impact of each vaccine will be modelled in terms of the number of deaths and DALYs averted. Incremental net costs of introducing each vaccine will be estimated, these being the incremental costs of introducing the vaccines, minus the costs of averted disease and productivity losses due to disease. The estimated impact of each vaccine will be combined with the net incremental cost to obtain estimates of cost-effectiveness. Sensitivity analyses will assess the robustness of the results to changes in economic and epidemiological data. This study will provide guidance to policy-makers in Bangladesh, Peru and the international community as to whether these vaccines should be introduced. Furthermore, the project will explore a method for evaluating the generalizability of the cost-effectiveness of each vaccine in different settings.

## 4.3 Cost-effectiveness studies alongside pneumococcal vaccine trials

Ms Ulla Kou summarized work being undertaken to set up cost-effectiveness studies alongside ongoing and planned pneumococcal vaccine trials. At present the following trials are either planning or undertaking cost-effectiveness studies (vaccine manufacturers in bracket):

- South Africa (Wyeth Lederle)
- The Gambia (Wyeth Lederle)
- Philippines (Aventis Pasteur)
- Chile (Aventis Pasteur)
- Israel (Aventis Pasteur)
- Costa Rica (Smith Kline Beecham)

The rationale for carrying out a cost-effectiveness study alongside the pneumococcal vaccine trials is:

- It is a great opportunity to collect patient specific prospective resource utilization data.
- It is the only way to identify treatment costs of pneumococcal vaccine-preventable diseases (otitis media, pneumonia and invasive disease). In a non-trial setting this is not feasible as the pneumococcal bacteria is difficult to isolate.
- It is possible to do statistical analysis of two independent groups.

The rationale for standardizing the methodologies used in the different clinical trials is:

- To get more robust results.
- To make valid comparisons between settings.
- To facilitate generalization of results to non-trial settings.
- To learn from each other's experiences and agree on the most appropriate approach for collection and analysis of resource utilization data.

The overall methodology for cost-effectiveness analysis at the trials consists of comparing the two independent groups: the vaccinated group (v) and the placebo group (p). The incremental cost-effectiveness ratio is defined as: $(C_v - C_p) / (E_v - E_p)$, where C = costs and E = an outcome measure.

Outcome measures vary according to the trial. While some of the trials look mainly at otitis media and invasive disease, others focus on radiological proven pneumonia, mild pneumonia and death.

WHO is funding the cost-effectiveness study alongside the South African trial. It is a one year study (the last year of the trial) starting from February 2001. Resource use data will be collected from all trial-enrolled patients admitted to the Chris Hani Baragwanath Hospital in Soweto. It is estimated that data will be collected from approximately 2000 patients. Three nurses will be employed full time to collect the data and a health economist will estimate unit costs, overhead costs, etc. as well as doing the overall analysis.

The recommended methodology for the studies closely follows the CVI protocol. The main difference is that while the CVI protocol is concerned with retrospective patient-specific data, the trials will mainly collect prospective, patient-specific data.

Some of the unresolved methodological questions of the cost-effectiveness studies are:

- The sample size: do we collect resource use data from all trial patients or only from those with pneumococcal related diseases?
- What should the overall sample size be to avoid under-powering?
- Are end-points from the clinical trial sufficient for the cost-effectiveness analysis?

Dr Marilla Lucero presented the cost-effectiveness study that is being designed for the Philippines pneumococcal trial in the island of Bohol. The trial is testing an 11-valent pneumococcal conjugate vaccine (11-Pnc) produced by Aventis Pasteur. The funding agencies of the trial are the European Union, the Finnish Government, the Bill and Melinda Gates' Children's Vaccine Programme, the Finnish Academy, the Philippine Government and the Bohol Provincial Health Office.

During the trial the study vaccine and a placebo will be given to children at the age of 6, 10 and 14 weeks, which is the regular EPI schedule for DTP. The follow-up of clinical endpoints and serious adverse events will continue until the child is two years old. The primary endpoint is community-acquired x-ray positive pneumonia. Secondary endpoints are community-acquired pneumonia requiring hospitalization, community-acquired pneumonia not requiring hospitalization and culture-proven type-specific invasive pneumococcal disease. The tertiary endpoints are correlates of protection, RSV and mixed viral-bacterial pneumonia.

The trial site is situated in 6 municipalities of Bohol, which in total have 48 health centres. The total population is 147 200 and the annual birth cohort is 3585. The trial started in July 2000 and is planned to continue until May 2005. It is expected that 12 190 children will be enrolled into the trial during the four years of study.

It is proposed that a cost-effectiveness study taking a societal perspective is carried out alongside the clinical trial. This study will compare the following two interventions:

- EPI vaccines plus *Haemophilus influenzae* tybe b conjugate vaccine (Hib).
- EPI vaccines, Hib vaccine and 11 Pnc.

Treatment cost data from the management of different clinical outcomes will be collected from hospitals as well as from health centres. Direct medical costs include hotel, diagnostics and drugs. In addition, productivity losses of parents of sick children will be estimated. To simplify the data collection it has been decided not to include follow-up and transport costs. The economic outcomes will be cost per episode of pneumonia, sepsis and meningitis prevented, cost per life year saved and cost per life saved.

## 4.4 Generic protocol to measure the burden of pneumonia and pneumococcal disease in children

Dr Orin Levine stressed the need for ongoing collaboration between researchers on cost-effectiveness analysis and researchers concerned with disease burden. It is crucial that their case-definitions relate to one another. If case definitions differ between cost-effectiveness work and disease burden estimates, this will provide biased results, as treatment costs estimates will not reflect the disease burden that is being accounted for.

# 5. Recommendations

During the first part of the afternoon of the second day, participants were divided into three groups. Two groups were asked to provide recommendations for changes to the different modules of the protocol and one group was asked to come up with suggestions for how the results of the three pilot sites can be published in a joint article. The composition of the three groups is outlined in Annex 3.

## 5.1 Recommendations on changes to the protocol

### *Module 1*

Module 1 is concerned with identification and measurement of direct medical costs during hospitalization of patients with specific diagnosis. The group had the following recommendations for amendments to this module:

1) Case definition: for retrospective and prospective review of charts, the WHO case definition is acceptable. However, for pneumonia the issue of wheezing needs to be addressed.
2) Data on antibiotic resistance is difficult to collect but, if available, it should be collected.
3) When selecting hospitals according to the sampling criteria stated in the module, it is very difficult to find a hospital that is not affiliated with a medical school and at the same time has an occupancy rate of 80-85%. The recommendation is that there should not be a need to specify an occupancy rate in the sample criteria. Furthermore, there should not be a need to specify a death rate criteria nor an upper limit of number of beds. This constrains the representation of the sample.
4) Some representative private institutions are unwilling to participate and that the protocol should state what should be done about this. Is it valid only to include willing unrepresentative facilities?
5) A list of required data should be submitted prior to data collection at the hospital. This will make it easier for the institution to decide whether they want to participate and whether they are able to provide the data.
6) It might be a good idea to recommend a “feasibility study” of the institution before starting. This could be done by briefly reviewing patient charts prior to data collection to ascertain the quality, but this depends on choice of institutions.
7) Co-morbidity is a problem for the qualitative analysis as this leads to insufficient power to perform statistical analyses.

8) It would be a good idea to design a standard data entry system where co-morbidities are coded and classified according to the severity of co-morbidity. Instructions to the system and a standard data entry scheme should be made. In this way, categories of drugs etc. can be collapsed for data entry.

9) The definition of malnourished children needs to be standardized. An index of weight and age could be used (weight is easier to use than height). Perhaps a separate questionnaire should collect age and weight (and perhaps height?).

10) The quantity of pharmaceuticals used needs to be standardized for data collection. For this, nursing practices with respect to wastage should be identified so that better estimates can be obtained. This can perhaps be done through a short interview.

11) The distinction of labour time and intensity is an issue. Is length of stay a good proxy for the intensity of care?

12) Analysis of data should not be included in the early modules. There is need for a separate module on data analysis and presentation. A unit cost menu should be developed for all resources and modules 1 and 2 should only focus on the identification and measurement of resource use, not their valuation.

13) A common database with analysis performed on common software is recommended.

### *Module 2*

Module 2 is concerned with the identification, measurement and valuation of direct medical costs at primary care level. The following recommendations were made by the group:

1) The possibility of doing a random sampling of institutions should be considered.

2) If there is a lack of medical records for quality control when data is collected retrospectively, it is recommended that a small prospective study be carried out for two weeks. Furthermore, the practitioner observations should be increased from 5 to 10 instead of only 5.

3) A question about the type of medical training received by the doctor should be considered. It is implicit in module 2 that we are dealing with medical doctors, but this is not necessarily the case.

4) Subjective case definitions will have to remain, but this is a major problem with the questionnaire.

5) Do we need estimates from the practitioners about the duration of consultations? What is the purpose of this?

6) The same issues as in module 1 arise with regard to the quantities of resources consumed. It is recommended to collapse some of the categories, e.g. oral rehydration salts (ORS), antibiotics, cough prep, anti-motility, others.

7) Provision of a scenario of illness and asking practitioners to describe the process of treatment is recommended.

8) It would be a good idea to include a community study to collect information on out of pocket expenditures – see Indian study for information

9) There is no obvious need for questions related to the maximum number of tests performed.
10) Asking practitioners for their consultation fees is a problem.

### *Module 3*

Module 3 is concerned with out-of-pocket expenditures including direct medical and non-medical costs and productivity losses. The group made the following recommendations to this module:

1) An interviewers manual for standardization of the training should be included. Interview instructions should be made in bold with each question.
2) A standard inputting database structure and software should be included with the protocol.
3) The questions should be re-organized: first, all the demographic questions (caregiver as well as for patient), next direct medical costs (potential "double counters") such as drugs and doctor's fees, and finally extra expenses (transport, toys, food etc).
4) It would be useful to check with the Evidence and Information for Policy cluster in WHO whether they have standard questionnaires for demographics.
5) It should be stated in the questionnaire when repeat interviews should start.
6) Change the name "sex" to gender.
7) A patient's or caregiver's name should never be entered in a database.
8) Data management specialists should be involved in designing the forms.
9) Standard coding system should be used. For instance Female O and males 1.
10) Question 3 should be "how old are you AND what year were you born (in the analysis, the current year minus the year the person were born should be used).
11) Change parent to "mother" and "father". Add grandparents.
12) Question no. 5: Years of schooling. Relevant categories should be added such as what level of schooling did you complete? For instance, completed primary, secondary or university.
13) It should be added whether the person works full time or part time.
14) Questions 7, 8 and 9 go together. From question 7, the interviewer would know the kilometres. Perhaps leave out the question on kilometres.
15) Question 10, 11, 12, 13 are targeted at different times. Perhaps just say "repeat". In the beginning of the questionnaire it should be indicated whether this is a repeat visit and, if so, the interviewer should go straight to question X.
16) In question 11, add how the person usually gets to the hospital (only ask this question once and use this figure for all visits).
17) In questions 12 and 13 there is a number problem.
18) In question 14, it should be possible to enter what type of "kind" is paid.
19) In question 15, it should be emphasized that this is only since the last interview or since admission.

20) Question 17 should be deleted.

21) Question 18 should be moved to the section on transport. Frequency of travel should be added to the transport section. "How many times have you gone back and forth"?

22) Question 19 should be changed to "how many hours have you spent caring for the child"?

23) Question 21 should be moved forward.

24) Question 30 is an interesting question, but not directly related to the CE analysis.

25) Question 31 should only refer to before admission. Furthermore, a heading should be added to questions about alternative healers.

26) It is questionable whether the question on salary should be moved up or kept at the end.

27) In the table, the last column should be deleted as no analysis is recommended in the interview.

### *Module 4*

Module 4 is concerned with costing of the health facility. The following recommendations were made to this module:

1) It should be stated that this information should be collected in the beginning of the study as it is important to get the process started right away. It can take quite a long time to cost the facility if data need to be collected from different sources.

2) The protocol should be divided into two parts: one for hospitals and one for health centres. Since some questions are only related to hospitals, this will make it more user-friendly. In the protocol it should be assumed that hospitals have a budget, but health centres have not.

3) It might be necessary to divide the costing exercise of the hospitals into a intensive care unit and normal wards.

4) For capital costs the 5% discount rate might have to be changed. It is not likely to be feasible to use the same discount rate in all settings. The formula for the discount rate should be entered in the software.

5) The official recommended life span for buildings should be double-checked.

6) In the table a column should be added for the number of full time equivalent staff.

7) Cost of diagnostics: for private hospitals, use the average fee. For public hospitals, do costing exercise.

8) For pharmaceutical costs in private hospitals it is also recommended to use the fee.

9) The section on "fee equal to price" should be deleted.

10) The table on "locally purchased or imported" should be deleted.

### *Module 5*

Module 5 is concerned with the determination of costs at follow-up after hospitalization. The following recommendations were made:

1) It is not recommended that the physician questionnaire be self-administered.
2) The questionnaire should be changed so that more than three follow-up visits are available for meningitis.
3) Questions 23-29 should be deleted.
4) Question 19 should be made semi-closed with categories.
5) Question 20 should only be asked once (on the first visit). Therefore, this question should be moved to the top of the questionnaire.

## Other recommendations

During the meeting a number of other recommendations were made:

1) It would be very useful to standardize the format for presentation of results of the studies. This should include statistical analysis of the data.
2) It is important to decide what type of costs can be easily adjusted to other countries. Some cost items are more locally defined than others.
3) There should be a division between shared costs and specific costs as well as between traded and non-traded goods.
4) It is crucial to find a solution to determining the case definition so that the costs attributable to vaccine-preventable diseases can be determined.
5) It is a problem for the studies that different physicians have different case definitions for the same patient.
6) Recommendations should be made on how to calculate wastage of drugs to be included in the costs.
7) In most private hospitals financial data is confidential. It is therefore recommended that fees charged to patients are used as an approximation for costs. This should be stated in the protocol.
8) It should be explained in the protocol that unit cost data collected from one facility can often be applied to others as well.
9) Recommendations on how to value lost productivity should be made in the protocol.
10) The main sources of variation in resource utilization data should be investigated and explained in the protocol to guide the intensity of future data collection.
11) It should be investigated how costs can be related to sources of care assessed so that a national estimate can be generated.
12) The statistical distribution of costs should be assessed.
13) It is questionable whether static models can be used for dynamic situations.

The meeting participants agreed that the results of the pilot studies have national as well as international use.

At national level, the following assessments can be made:

1) The relation of treatment costs to quality of care.
2) As an input to a cost-effectiveness analysis of a vaccine (if data on etiology is collected as well).
3) Institutional use for price setting or management.
4) Generally, the cost of health care is not very well known, so the data could be useful for researchers as well as policy-makers.
5) Analysis of variability of costs.

At international level, the following analysis can be made:

1) Global recommendations for the introduction of new vaccines.
2) Generalized cost-effectiveness analysis studies.
3) Extrapolation to other countries. (For this use, adjustments should be made to the protocol.

## 5.2 Publication of results in a joint article

During the meeting it was agreed that the results of the three pilot studies were comparable and that it would be useful and interesting to publish these in a joint article. The best approach to achieve this would be to design a joint reporting format for the studies. The working group looking at this issue recommended that an Excel table should be prepared for the three sites to fill in. The following information should be collected from this table:

1) Direct medical costs including sample size, median, range, mean and standard deviation.
2) Transport costs, including sample size, median, range, mean and standard deviation.
3) Productivity losses, including sample size, median, range, mean and standard deviation.
4) Total costs, estimated by the mean cost of all components.
5) Direct medical costs divided into items: medicines, diagnostics, special services and hotel.
6) Costs of drug utilization.
7) Costs of diagnostic tests.
8) Costs of inpatient stay in hospital.
9) Costs of outpatient visits specified.
10) Costs of productivity losses specified.
11) Sampling profiles for data on diarrhoea, pneumonia and meningitis.
12) Clinical profiles.

## 5.3 Completion of pilot studies and second version of protocol

It was agreed that the following products should be delivered for completion of the pilot studies:

1) Each site should deliver data for use in a joint article. WHO will prepare standard forms for the sites to fill in their data. Stefano Bertozzi and Mark Miller will be responsible for drafting the joint article.
2) Each site must prepare a report with their findings and send to the WHO. This will release the final payment.
3) The three investigators are encouraged to submit an article for publication in a journal, but this is not obligatory.

Additional work needed to complete the protocol:

1) The protocol should be amended according to the recommendations made during the meeting. Damian Walker and Ulla Kou will be responsible for this.
2) A paper on methods should be submitted for publication. Damian Walker and Ulla Kou will be responsible for coordinating this.

# Annex 1: List of participants

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## WHO headquarters

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Mr Raymond Hutubessy, GPE/EIP
Dr Tessa Tan-Torres Edejer, GPE/EIP

**Family and Community Health (FCH) cluster**
**Department of Child and Adolescent Health & Development (CAH)**

Dr Shamin Qazi, CAH

* Invited but unable to attend

# Annex 2: Agenda

### Monday 11 December 2000

| | |
|---|---|
| **08:30 - 09:00** | **Registration** |
| **09:00 - 09:15** | Opening |
| | Welcoming comments (D. Evans) |
| | Nomination of Chair (M. Miller) and Rapporteur (U. Kou) |
| **09:15 - 09:30** | Review of meeting objectives (U. Kou) |
| **09:30 - 10:15** | Findings from pilot studies |
| | The Philippines (L. Dans) |
| ***10:15 – 10:45*** | ***Coffee break*** |
| **10:45 - 11:30** | Mexico (S. Bertozzi and V. Granados) |
| **11:30 - 12:15** | India (K. Anand) |
| ***12:30 - 14:00*** | ***Lunch break*** |
| **14:00 - 15:30** | Discussions on interpretations of results: |
| | What problems have the three pilot studies encountered during the data collection and the data analysis? |
| | What are the solutions to these problems? |
| ***15:30 - 16:00*** | ***Coffee break*** |
| **16:00 - 17:00** | Discussion on overall study findings: |
| | • How comparable are the study results?<br>• What is the robustness of the results?<br>• How should the results be used?<br>• Should the results be published in a joint article? |
| **17:00** | **Closing** |

## Tuesday 12 December 2000

**Chair: J. Fox-Rushby, Rapporteur: U. Kou**

| | |
|---|---|
| **09:00 - 10:30** | Discussion on advantages and weaknesses of the protocol:<br>• How should the protocol be improved?<br>• What are the next steps? |
| ***10:30 - 11:00*** | ***Coffee break*** |
| **11:00 - 12:30** | Ongoing work relating to the protocol:<br>LSHTM project (D. Walker) |
| **12:30 - 13:00** | Who generalized cost-effectiveness approach<br>(R. Hutubessy and T. Tan Torres) |
| ***13:00 - 14:00*** | ***Lunch break*** |
| **14:00 - 14:30** | Cost-effectiveness studies alongside pneumococcal<br>vaccine trials (M. Lucero And U. Kou) |
| **14:30 -15:00** | Generic protocol to measure the burden of pneumonia<br>and pneumococcal disease in children (O. Levine) |
| ***15:00 - 15:45*** | ***Coffee break*** |
| **15:45 - 17:00** | Recommendations |
| **17:00** | **Closing of meeting** |

# Annex 3: Groups

Meeting participants were divided into the following groups to work on recommendations for changes to the protocol and framework for a joint article:

| Group 1: | Group 2: | Group 3: |
| --- | --- | --- |
| K. Anand | L. Dans | S. Bertozzi |
| D. Walker | G. Ginsberg | J. Fox-Rushby |
| V. Granados | U. Kou | T. Tantorres |
| M. Lucero | R. Hutubessy | M. Miller |
| | C. Nelson | |