CHAPTER III

RESEARCH METHODOLOGY

This chapter presents the methodology adopted to carry out the current economic evaluation. The chapter opens with operational definitions used in this study and gives the conceptual framework of the study in the following section. Methods to calculate costs and effectiveness follow afterwards.

3.1 Research Design

This study followed cost-effectiveness analysis (CEA) model for the economic evaluation of two different VL case detection programs and the results were expressed in terms of 'cost per effectiveness' The period of the evaluation was 1998/99 (Nepalese fiscal year 2055/56).

3.2 Definitions

The operational definitions used in this study are given with some more explanations whenever it was thought appropriate.

Alternative A: Outreach Case Detection Program

A program in which health workers go to community and locate individuals who are currently ill with a clinical syndrome consistent with VL and perform simple diagnostic tests such as k39 dipstick. If tested positive, further confirmatory tests may be carried out, and treatment is given. This program is mobile/outreach in nature. This is also known as active case detection.

Alternative B: Health Facility based Case Detection Program

A health facility (hospital) based program in which individuals present to health facility on their own with some illness. If clinically found positive for VL, diagnostic tests such as aldehyde followed by bone marrow aspiration, are carried out and the treatment is given.

These two alternatives being considered are *separately* run programs. They are not *substitute* of each other. However, there may be a possibility in future that outreach program may be integrated with the health facility based program. It is very important to know the fundamental difference between these programs that might affect the respective effectiveness. The outreach program uses k39 dipstick test for diagnosis of VL while health facility based detection program uses aldehyde test followed by bone marrow aspiration. The former is of mobile in nature and the latter is static.

Case detected

A subject tested positive for visceral leishmaniasis by at least one of the following tests: 1) Serological test (direct agglutination test (DAT) or k39 antigen dipstick) or Aldehyde test 2) Parasitological test (bone marrow aspiration).

Clinically positive case

A subject with a history of fever for more than two weeks, and found to have enlarged spleen, liver and positive lymphnode on clinical exam.

Cost

Value of resources used to produce health effects. There are two major categories of costs: outlays costs and opportunity costs. An outlay cost is a past, present and future cash outflow (known as financial costs). Opportunity cost is the return that could be realized from best-forgone alternative use of a resource (sometimes known as economic cost also).

Death averted

An individual, who is detected as having VL, subsequently treated, and considered to have saved from dying due to the disease, with some specific probability.

Early case detected

A patient, not having a past history of VL, if presents with fever more than two weeks, may or may not have spleen/liver/limpsnode enlarged on clinical examination, and reported positive in serological test is an early case detected.

Effectiveness

Two kinds of effectiveness were considered- 1) number of cased detected, and 2)number of deaths averted. The intermediate outcome 'case detected' was the primary effectiveness measure. A '**case detected**' was defined as:

> "finding an individual who has not a past history of VL but presents with fever for more than two weeks, may or may not have spleen/liver/limpsnode enlarged on clinical examination, and reported positive for VL on serological test"

Since the rationale behind this research was to identify more cost-effective ways to detect more and more VL cases from the endemic areas, it was thought appropriate to consider that such an intermediate outcome as 'case detected' has some value and is capable of addressing the current research objectives.

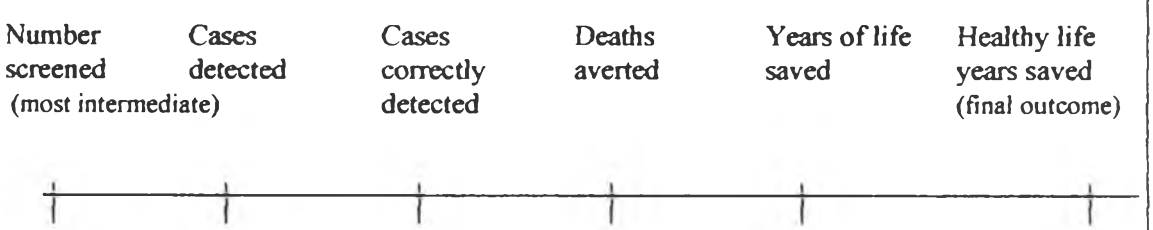
However, an attempt was made to move further in the outcome spectrum (see figure 3.1) and convert 'case detected' into 'death averted', since this measure has a direct link with the final outcome such as "healthy years of life saved", although in quantitative terms only. In that sense, this effectiveness measure has a "value" and provides a measure of health effects in more acceptable way than preliminary outcome such as "cases detected".

A **'death averted'** was defined as:

> "an individual who is detected as having VL, subsequently treated, and considered to have saved from dying due to the disease, with some specific probability".

The probability in the above definition is the survival rate of cases detected as having VL and subsequently given the treatment for the disease. This is further discussed on the section on outcome measurement below.

Figure 3.1 Outcome spectrum for the case detection program



It is, however, important to note that efficacy and effectiveness of the drug together with patients' compliance might substantially affect the outcome of the treatment by any program. There might also be several other factors such as diagnostic test's characteristics and coverage of the programs, etc. Thus, the definition given above might not reflect the true deaths averted by a program, but might give, under some assumptions, a rough idea about how many deaths might have been averted by a specific program.

Health effect

Effect of intervention (alternatives) in terms of number of VL case detected at the early stage of the disease as defined above.

Patient's cost

Value of resources consumed by a VL case for treatment. This also includes the value of potential loss of earnings due to this disease.

Provider's cost

Value of resources consumed by health facilities or intervention programs to deliver services relevant to VL to individuals

Serological test

A Direct Agglutination Test (DAT) or k39 antigen dipstick test or Aldehyde test used to diagnose VL.

Treatment of VL

Treatment of a case with first line drug sodium antimony gluconate, and if not responding well to it, treated with amphotericin B under medical supervision

3.3 Viewpoint for the Analysis

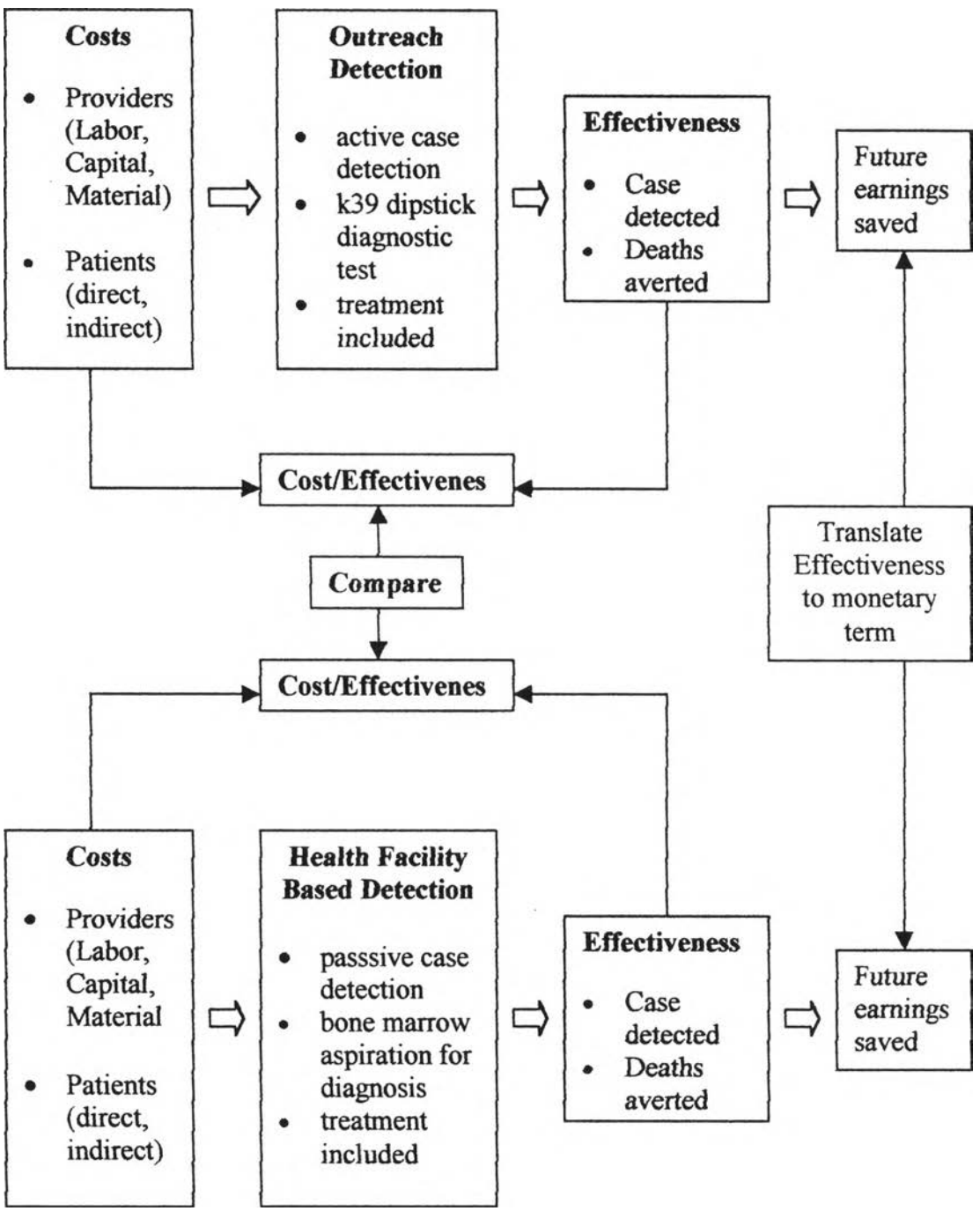
This study was carried out from the viewpoint of **providers** and **patients**, since the answers to the current research questions were deemed more important to the providers. A broader perspective (that of the society) could not be considered here due to some practical difficulty in obtaining all relevant data needed to have societal point of view within the time frame given to complete this research.

3.4 Conceptual Framework

Ideally, cost-benefit analysis (CBA) model should be followed in order to carry out any economic evaluation of alternative interventions in which "an attempt is made to quantify total costs and total benefits into monetary value" (Fowler and Austoker, 1997). Economic theory also "favors measuring costs and benefits in monetary terms because it avoids the problem of measuring and valuing non-monetary benefits" (Raftery, 1998). However, the usefulness of CBA to evaluate health care programs can be troublesome because of the need to place values on human life, increased longevity, and improvements in health status. Moreover, when a program has widespread benefits that are largely in the form of intangibles, as in the case of early case detection, cost effectiveness analysis (CEA) represents a more modest approach to program evaluation (Folland, 1997). Subscribing to these points, it is thought that difficulties may arise in the current study while valuing all benefits of the alternative programs in monetary terms because there might be several benefits in terms of externalities and intangibles. Further, since the primary viewpoint of this study was that of the provider and both alternative programs have common objectives (i.e. to detect cases), it was deemed appropriate to consider CEA model, for evaluation of alternative programs in question.

The CEA framework in such a case would require a comparison of the resource costs (inputs) and effectiveness (outputs or consequences) of alternative health interventions (Drummond, 1997). The resource costs (inputs) would include the costs of resources used by health sector to provide intervention (direct cost to provider) and the costs of resources used by patients to gain access to and participate in this intervention (direct costs to patients). Moreover, indirect costs to patients (lost work time to receive intervention) would also be included. Different levels of effectiveness measure such as cases detected and deaths averted would be used. As the study focused on the need to detect cases early, the effectiveness measure like 'cases detected' would have a value in itself, and therefore, could be considered as the consequence in CEA. An attempt would also be made to convert 'cases detected' into higher level of effectiveness measure such as 'deaths averted' and also to value 'deaths averted' into monetary term. Figure 3.2 on the next page presents the concept.

Fig 3.2 Conceptual Framework for the Study



The research design is Cost-Effectiveness Analysis (CEA), where similar outcomes are assessed using a ratio expressed in terms of cost per effectiveness. The outcomes are measured in natural health units such as 'cases detected' and 'deaths averted'.

3.5 Selection of research setting

This study was carried out in one district of Nepal (Siraha). The selection of this district was purposive. A research on VL was underway in this district (Joshi, 1999), and it was both easy and less costly to carry out this study by combining it with the ongoing project. The district is known to have kala-azar epidemic for a long time. The district has 497,816 population at risk of the visceral leishmaniasis. The incidence rate in the district 1997 was 46.60 with case fatality rate of 3.88 per cent. (MOH, 1997), one of the highest rates in twelve VL endemic districts.

The total area of the district is 1188 square kilometer and is located in the eastern development region with Dhanusha on the west and Bihar state of India in the south with tropical and sub-tropical climate. The total population of the district is 532,587 with annual growth rate of 2.05 and literacy rate of 6 years and above is 32 per cent. The number of males is 273043 and that of females is 259545, out of which 130751 males and 41712 females are economically active. Majority of the active population is involved in farming and fishing works. The total number of village development committees (VDCs) in this district is 109 (Nepal District Profile, 1992).

3.6 Study Population, Sampling and Inclusion Criteria

For program evaluation, Siraha District Hopital was chosen for health facility based case detection program, which has all the facility for VL case diagnosis and treatment. For the outreach program, the recently concluded Kala-azar Project (Joshi, 1999) was evaluated. Both programs detected and treated VL cases in Siraha district and thus served a better comparison, as the setting and population were the same for both programs. A patient diagnosed as VL case by outreach program may receive the services at the hospital also. No such cases were included in this study.

For estimation of patient costs, all *known* VL patients diagnosed clinically at hospitals in these districts in the year 1998-99 formed the sampling frame for alternative 'B' (health facility based detection). The sampling frame was prepared using the information

available through VL registries of the Siraha District Hospital A total of **22** VL cased detected and treated by the hospital were traced in the villages they lived in and necessary information was collected as per the guidelines given in the following sub-sections.

For alternative 'A' (outreach detection), the study population was defined as individuals who were currently ill with a clinical syndrome consistent with VL in this district. All these specified cases formed the sampling frame for alternative 'A'. A total of **28** such cases were interviewed

3.7 Study instruments

Data on provider's costs in both alternatives were collected from the accounts of respective programs, using a structured record form designed before fieldwork started. The epidemiological data and patient specific clinical data were collected from the database available at these programs' office.

Patient specific other relevant data needed to estimate both direct and indirect costs were collected by using a structured interview. These included: (1) patients characteristics (2) information on direct expenses (3) information related to indirect costs (4) time taken to recover from the disease (also see Appendix A). The probability data required to feed into the cost and effectiveness formulae were estimated using past data, where appropriate, together with experts' opinion. The following table summarizes data requirement, their source and study instruments.

Table 3.1 Summary of data requirement and their source

Data requirement	Study instruments	Source
1. **Costs to providers**	Accounts record	Secondary
2. **Clinical data** No. of cases, patient history, tests performed, results of tests, diagnosis, treatment, clinical outcome of treatment, etc.	Program's database	Secondary
3. **Other patient specific data** Patient characteristics, information related to direct and indirect costs, time taken to recover, etc	Structured interview	Primary
4. **Probability**	Past epidemiological information / estimates	Secondary

3.8 Validity and Reliability

Two medical field workers and a vector control assistant were hired and trained properly to interview the cases in February 2000. A sample of questionnaire filled by these workers was verified by the Investigator during the fieldwork to ensure precision of data collection.

The Investigator himself collected the costs data from the programs using a pre-determined information schedule. Standard costing methods, as suggested by Drummond (1997) were used in the estimates. Collection of estimated data were verified again to ensure the quality of information being reported.

3.9 Data collection and analysis

Data were collected as discussed below. Analysis of providers' costs was done using Microsoft Excel 97 software while patients' data was entered and analyzed on EPI INFO software version 6.04 with Year 2000 upgrade (CDC, Atlanta, 1997).

3.9.1 Costs Data

The following criteria were developed for identifying, measuring and valuing costs.

Table 3.2 Identification, measurement and valuation of costs

Resource use	How to measure	Basis of valuation
Health providers' costs		
Staffing (direct)	Time (hours)	Salary/Wage rate
Capital (direct)	Units/amounts consumed	Market prices (conversion costs) (Annualized)
Consumables (direct)	Units/amounts consumed	Market prices
Overheads (allocated)	Units/amount consumed	Market prices
	Time (hours)	Wage rates/Salary
Patients' costs		
Direct	Units/amounts consumed	Market prices/Actual expenses
Indirect (time lost from work)	Time (Hours/days/weeks/years)	Wage rate/salary or other labor costs

Note: This table is adapted from Donaldson and Shackley (1997).

The overhead allocation criteria to calculate full costs were determined as follows:

Table 3.3 Criteria for allocation of overhead costs

Type of service	Allocation criteria
Space for clinic and/or office	Square meter
	(Square meter taken up by program divided by square meter taken by all clinics) X building cost (depreciated)
Utility services (Cleaning, Heating, Lighting, etc.)	Space (square meter)
	(Square meter taken up by program divided by square meter taken by all clinics) X departmental cost
Laundry	Number of requisitions
	(Number of requisitions made by program divided by total number of requisitions by all clinics) X departmental cost
Administration	Number of cases
	(Number of cases registered to the program divided by total number of cases registered at all clinics) X departmental cost

Note: This table is adapted from Donaldson and Shackley (1997).

However, there were a number of difficulties encountered while allocating costs to the program. These difficulties and how they were solved are widely discussed in Chapter IV while describing about the results.

3.9.2 Considerations of costs of false negatives and false positives

The costs of false positives and false negatives are other components of total costs incurred to any health care program that uses diagnostic tests, as no diagnostic test is perfectly sensitive and specific. That is, all diagnostic tests are likely to give false positives and false negatives. Following considerations were given for these costs.

Cost of false negative

There are mainly two types of costs involved in false negative cases. 1) costs of probable deaths due to missing out of true cases, and 2) future costs arisen from the missed cases probability of spreading the disease in the community. Both cases are not considered here, assuming that the probability of the diagnostic test giving false negative results is

negligible, and the costs would therefore be negligible (based on a review of performance of screening tests and having sought expert's opinion). Another reason for excluding these costs was the study's narrower perspective.

Cost of false positive

The cost of false positives is basically the unnecessary costs paid for the treatment of wrongly diagnosed cases. Other intangible costs may include pain and suffering of individuals due to the belief that they have disease. For the similar reasons as above, these costs were also not considered in this study.

Total costs

Addition of all relevant costs discussed so far gave the total costs of case detection. They are expressed in terms of Rupees, 1999 prices.

3.10 Outcome measurement and valuation

Measurement of Effectiveness

The primary effectiveness (i.e. 'cases detected') was measured by **counting the number** of individuals who fell on the following criteria:

> "not having a past history of VL but presents with fever for more than two weeks, may or may not have spleen/liver/limpsnode enlarged on clinical examination, and reported positive for VL on serological test"

The next level of effectiveness i.e. 'deaths averted", will be measured using the following formula:

$$\textbf{No. of deaths averted} = N_{dt} \times (1-p_0)$$

Where, N_{dt} = Number of cases detected and treated

p_0 = Probability that a case dies due to VL even after treatment

Underlying assumption of this formula:

1. Not all cases that are detected as having VL and consequently given treatment for the disease will survive. If p_0 is the probability that a VL case will die even after treatment, $1-p_0$ will give the survival rate of patients undergoing treatment for VL.
2. The number of deaths and disability among these detected cases by a cause other than VL is assumed to be zero.
3. Detection of a VL cases and subsequent treatment to them is assumed to provide these cases with a chance to survive, given that the supply of other interventions (which might also contribute to aversion of deaths among these cases) do not remain limited.
4. The formula incorporates only quantitative aspect (number of deaths averted), not health related quality of life years among averted deaths, assuming that the period in which detected and treated VL cases live with disability is considerably small (less than a year).
5. The formula gives equal weights to all population.

3.11 Translation of effectiveness into monetary terms

A simple formula was developed in order to translate effectiveness estimated using above discussed methods (cases detected and deaths averted). Translation of effectiveness into monetary terms considered only the value of potential life years saved by averting deaths among detected cases

Other benefits of detection program such as future medical costs averted and third-party benefit of the value of assurance in correctly ruling out of cases, etc were not considered, for the want of estimates of some key variables.

In order to estimate the value of potential life years saved, **Human Capital Approach** was used, in which it is assumed that human years of life is like a capital which if remains healthy generates income (Drummond, 1997). The formula used in this study is:

$$\textbf{Value of potential life years saved} = \sum_{x=1}^{L_e} \{N_{dx} (L_e - x) (1-p_0) Y_x\}$$

(Modified from Murray, 1996)

Where, L_e = Potential limit to life = 58 years (Average Life Expectancy)

(Source: Appendix B)

x = Age of an individual diagnosed as having VL at the time of case detection

p_0 = Probability that a case dies due to VL even after treatment

Y_x= Estimated yearly income at age x

N_{dx} = Number of cases detected and treated at age x

Underlying assumptions of this formula:

1. Not all cases detected as having VL and consequently given treatment will survive.
2. Potential limit to life for all cases detected now is assumed to be the same, i.e L_e, irrespective of how old the case is now. The presence of ailment other than VL in these cases, which might cause his/her death in future, is also assumed to have no effect on potential limit to life.
3. Younger population's life is assumed to be more important than older ones.
4. For a case detected now, his/her income is assumed to remain the same until s/he dies at age L_e.

The value of income attached with this formula came from the real data collected for this study. The daily income thus collected was multiplied by 365 to get the yearly income. A value of zero was assigned to younger population's income (that is, income of the population less than 7 years). Those of above 7 years of age in the sample had actual income data.

3.12 Cost-Effectiveness Analysis

Cost-effectiveness ratio (C/E) was calculated using the costs and effectiveness estimations. Two levels of cost-effectiveness ratio were calculated:

Level I: Cost Effectiveness ratio = Costs incurred per case detected

Level II: Cost Effectiveness ratio = Costs incurred per death averted

The reasons why two levels of effectiveness were considered is already discussed in sections 3.2 and 3.4.

A **cost-effectiveness analysis** was then performed and the alternative, which minimized the cost per effectiveness, was designated most cost-effective. However, care was taken to discuss the differences in results between the two cost-effectiveness ratios and their implications. Chapter V discusses about this in details.

Sensitivity Analysis

A sensitivity analysis was carried out on those parameters of costs and effectiveness, which was subject to appreciable uncertainty. The effectiveness formula (deaths averted) and the process of translating effectiveness into monetary term include several underlying assumptions, which might be subject to appreciable uncertainty. Probability of survival of a detected case was considered to be one and a sensitivity analysis was carried out with two different values of this probability. Another variable chosen for sensitivity analysis was the discount rate.