CHAPTER 1

INTRODUCTION

1. Problem Statement

Many countries of high malaria endemicity and high rate of drug resistance such as Thailand is intending to apply new rapid on the spot diagnostic test. The question is whether outcomes are worth test costs or not.

On WHO statistics, 1985, the most intensive foci of Plasmodium falciparum resistant malaria in the world are confined to the countries of South East Asian and Western Pacific Regions. Resistance of P.falciparum to 4-aminoquinolines is highly prevalent in almost all countries of the region. Resistance of P.falciparum to sulfadoxine-pyrimethamine combination has developed in vast areas of Thailand (Ketrangsee 1992), some parts of Myanmar, Bangladesh, Bhutan, Indonesia (Kondrashin and Rooney, 1992), the Philippines (Asinas, 1992), Malaysia (Lim, 1992), Cambodia (Denis and Meek, 1992), Vietnam (Annual Report of the Malaria Control Program, 1993). An increasing trend of P. falciparum resistance to mefloquine (Karbwang, 1992) has been reported from the Thai Cambodian border, particularly from Borai district; somewhat sensitivity to quinine has also been seen in the same areas (Kondrashin and Rooney, 1992).

The resistance of P. falciparum to antimalarial is reported to be among the major reasons explaining why malaria control programs in many countries has not been completely successful (Björkman and Philippshoward, 1990; Peters, 1985; Looreesuwan, 1992).

In the case of Thailand, despite the large budget from external international assistance and the regular health budget of the

Government allocated to the malaria eradication program over many years, malaria incidence is still high enough to be a major public health problem. Up to 1991, in Thailand: malaria incidence and mortality rate were 3.74 per 1,000 and 2.1 per 100,000 population respectively (Malaria Division, 1993; Tanpradist and others, 1993; Saowanit, 1993).

The inappropriate drug consumption (presumptive treatment and self treatment) is considered as one of the factors leading to the spread of malaria drug resistance (Kamolratanakul and others,1992; Verdrager, 1986; McDonnel, 1993 b). Extension of service points providing "on the spot diagnosis" seems to be the most attractive among measures (change of treatment strategy, restriction of drug access, improvement of drug packaging and labelling) to combat inappropriate drug consumption. It will reduce presumptive treatment and may reduce self treatment which depends upon user behavior (Fungladda and others, 1986; Hongvivatana and others, 1985).

At the moment, on the spot diagnosis and treatment for malaria can only be provided at malaria clinics and hospitals where they have microscopes and trained personnel. Extending the number of service points able to provide on the spot diagnosis and treatment could be achieved by 2 means: 1) provide existing technology (microscopes and trained personnel) to other types of established health clinics and 2) provide alternative technology to health clinics and perhaps to village malaria volunteers.

A major concern of introducing either alternative is costs to the supplier. But weighed against costs should be the potential benefits in a reduced cost to patient, a reduced waiting time for diagnosis and treatment, a reduced rate of presumptive treatment and self treatment, and an expected reduced rate at which drug resistance develops. A number of economic studies on analysis of the existing technology have been done (Kaewsonthi and others, 1988; Keawsonthi and Harding, 1989a; Pornchaiwiseskul, 1993).

This study is concerned with the introduction of a new test, in particular deciding how the costs to suppliers and outcomes could/should be determined on the assumptions that the new test is introduced to one or more of the existing types of service points both singly and in combination: malaria clinics, health clinics, village health volunteers, taking into consideration previous experiences (Mills and Drummond, 1987; Creese and Parker, 1991; Drummond and others, 1991; Guyatt and others,1993; Kaewsonthi and Harding, 1986 a,b; 1989 b).

2. ParaSight Test

Waiting time is believed to be the cause of inappropriate drug consumption which is thought to be among the factors leading to drug resistance. Recently, Becton Dickinson Advanced Diagnostics introduced a new test by the name of ParaSight. This is an on the spot test.

The new technology, the ParaSight test currently under development is likely to be based upon the detection of the histidine rich protein II (HRPII)) antigen of Plasmodium falciparum. HRPII is a water soluble protein released from parasitized erythrocytes. It was found in all natural isolates of P. falciparum tested and has been detected in plasma as well as in whole blood.

On statistical data (1992) of the Malaria Division, 168,370 positive cases were found in 5,575,282 examined slides. That means about 30/1,000 are found to be positive. On the basic of the same statistical data, 96,696 were P.falciparum positive. That means about half of positive cases. The actual ParaSight test can presently detect only P.falcifarum. Consequently the use of ParaSight test can detect only 15/1,000. The remaining number (985) of cases may receive presumptive treatment. Therefore, any useful rapid test must be able to detect both major species of malaria, otherwise the drug wastage will be very high. This ParaSight could be the best choice for the following

reasons as compared to standard thick and thin blood smear examination:

* Instrumentation: No requirement of expensive instruments
* Performance: Easy to perform
* Training Time: Very short (less than 1 hour)
* Performance Time: Rapid on the spot (4-5 minutes).

Any new diagnostic test in testing should be considered with its own characteristics such as sensitivity, specificity, predictive values, etc...by comparing with a standardized test being called the gold standard or by comparing with typical clinical symptoms. In this case, blood slide examination is considered as the gold standard. Preliminary observations are as follows:

	BECTON DICKINSON	FRENCH HOSPITAL	THAILAND
Sensitivity	95.6%	99.0%	100% (18/18)
Specificity	86.8%	94.0%	80.0% (4/5)
(+) Predictive value	83.7%	88.6%	
(-) Predictive value	96.5%	99.4%	

In this study, we put emphasis on specificity for cost-benefit analysis as the most interesting issue being whether an on the spot malaria diagnostic test can reduce inappropriate drug consumption or not, for those who get a false positive diagnosis have to take radical treatment, involving drug wastage. Of cause sensitivity of the test is equally important as specificity. However, it is not so straightforward

to calculate accurately. There, both the ParaSight test and blood smear will have false negative rates neither can be considered to be gold standards, and ideally both need to be judged against the best available standard, polymerase chain reaction (PCR). When this is done (as is planned in future field trials in Thailand), it will be possible to calculate costs attributable to sensitivity. Hence, such calculations are omitted in this study.

The ParaSight test utilizes a paper like strip imbedded with antibody and dye containing microcapsules which mark a positive reaction. It can be summarized in the figure 1.

3. Previous Work

Some economic analyses of malaria surveillance were conducted in Thailand (Kaewsonthi and others, 1986 a; 1988; 1989 a, b). In these analyses 3 models were developed:

* Pool of infection model.
* Cases prevented model.
* Short run cost and aggregate cost model.

Internal costs were analyzed on survey data with emphasis on apportioned versus measured costs; costs and performance of zones and sectors; costs and performance of field services.

External costs or costs incurred by patients include direct and indirect costs incurred by patients, direct and indirect costs incurred by positive cases and labor substitution.

Surveillance costs vary between 30-90 Baht per blood slide and 3,300-3,400 Baht per positive case. Costs per blood slide and cost per positive case at zone level depend on where they are managed (figure 2)

Figure 1. ParaSight Test

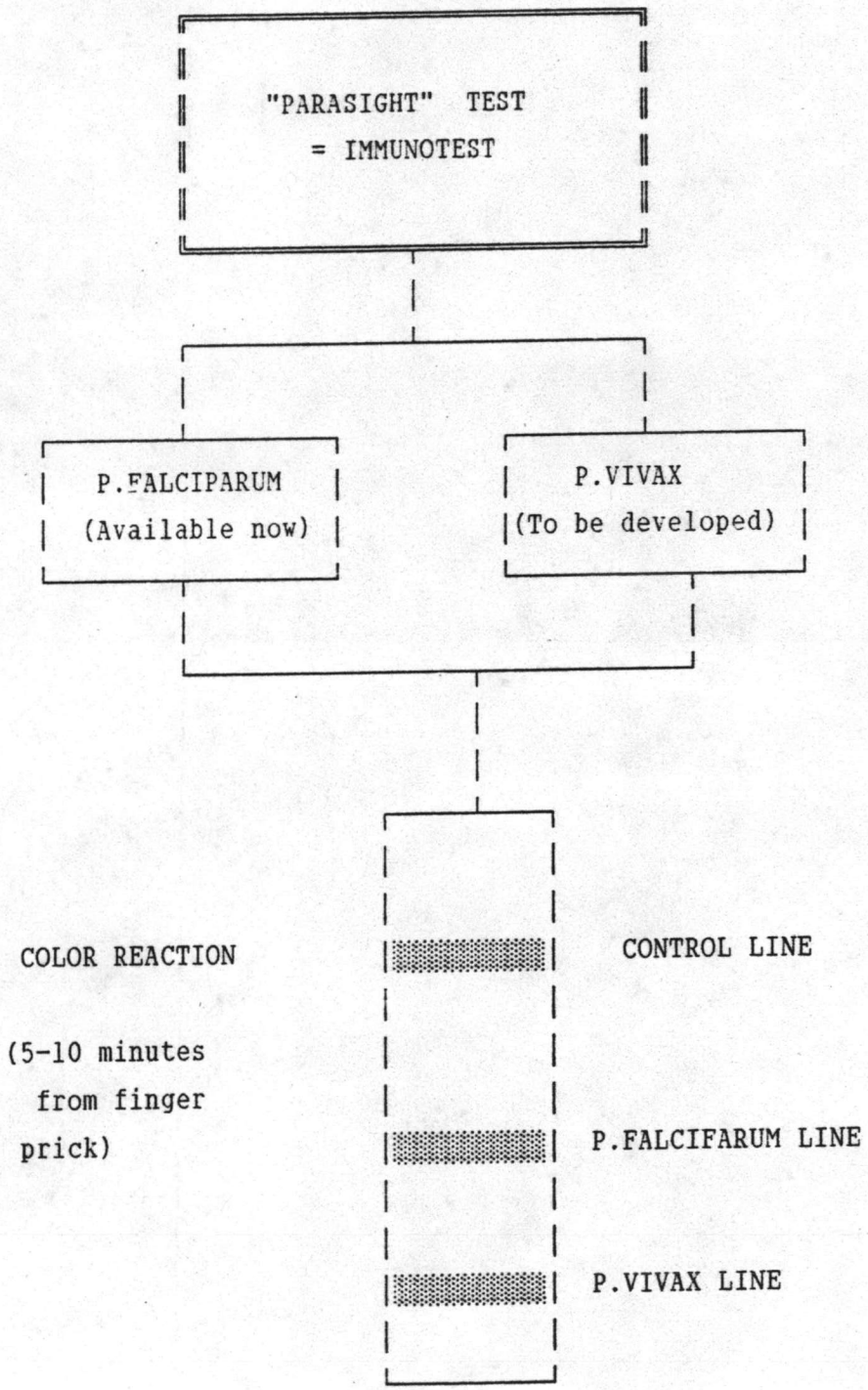


Figure 2. Cost per Blood Slide and Cost per Positive Case.

Management points	Cost / blood slide	Cost/positive case
Village Health Center	14- 47 Baht	1,200 - 5,800 Baht
Village malaria volunteers	80 Baht	5,000 -18,000 Baht
Malaria clinic	66- 109 Baht	620 - 1,500 Baht

The document shows that 35.25% (in zone 3) and 17.69% (in zone 7) of the patients got self treatment before attending malaria clinics. Another study found a higher rate of previous self treatment (78%) in patients attending malaria clinics of westerns Thailand (Fungladda et al, 1986a). According to Fungladda and others,(1986b), the cost of self treatment varies with the number of visits to malaria clinics:

* Cost of 1st treatment before visiting malaria clinics is 25.11 Baht in average (on interview of 126 patients).

* Cost of 2nd treatment before visiting the clinics is 116.25 Baht in average (on interview of 12 patients).

In a study of cost incurred by patients, Kaewsonthi (1988) found that a large proportion is for time cost. The average income was 12,200 Baht/year. Based on the average income and 6 working days a week, the real income was 39 Baht/day. There were no data on waiting time cost in relation to drug consumption cost which will be investigated in detail in this study.

4. Objectives

The general objective of the study is to make a simulation modelling analysis of costs and potential outcomes from introducing a new rapid malaria diagnostic test.

Specific objectives are:

1) To develop a simulation model for evaluating costs and outcomes from introducing a new rapid malaria diagnostic test, with emphasis on intermediate outcomes, especially drug consumption.

2) To test the model, developed under objective (1) for its feasibility by using hypothetical data from estimations made on the development of the ParaSight test.

5. Conceptual Framework

In order to design a simulation model for evaluating costs and outcomes from introducing a new rapid malaria diagnostic test, the study should:

- identify indicators of simulation model for evaluating costs and outcomes;
- develop input cost system for costing;
- predict and cost outcomes;
- determine elements of the simulation model establishing mathematical relationships between costs and outcomes for judgment.

In order to test the developed simulation model, the study should describe cost components of the ParaSight test and cost inputs and value outcomes on simulation model for judgment from data estimated by the Malaria Division of the Thailand Ministry of Public Health.

5.1 Identification of Quantifiable Elements

Identification of quantifiable elements include

* Input quantifiable elements : Input costs (C).
* Outcome quantifiable elements:
- Reduction of waiting time (No of cases shifting from waiting time more than 1 day to less than 1 day) and cost saving incurred to consumers (patients) (B1);
- Reduction of presumptive treatment and (No. of cases prevented from presumptive treatment) and cost saving incurred to providers (Malaria Control Program) (B2);
- Reduction of self treatment (No. of cases prevented from self treatment)and cost saving incurred to consumers (B3).

Note: Reduction of drug resistance is thought to be the consequence of above elements but data for this evaluation has not been available.

* Modelling equation: The modelling equation is based on cost-benefit analysis within a defined time frame (short run or long run) taking into consideration the annual interest rate. The higher the ratio the better the test.

$$\frac{B1 + B2 + B3}{C}$$

Relationships between input costs and outcomes are illustrated in figure 3.

5.2 Cost System and Costing Inputs

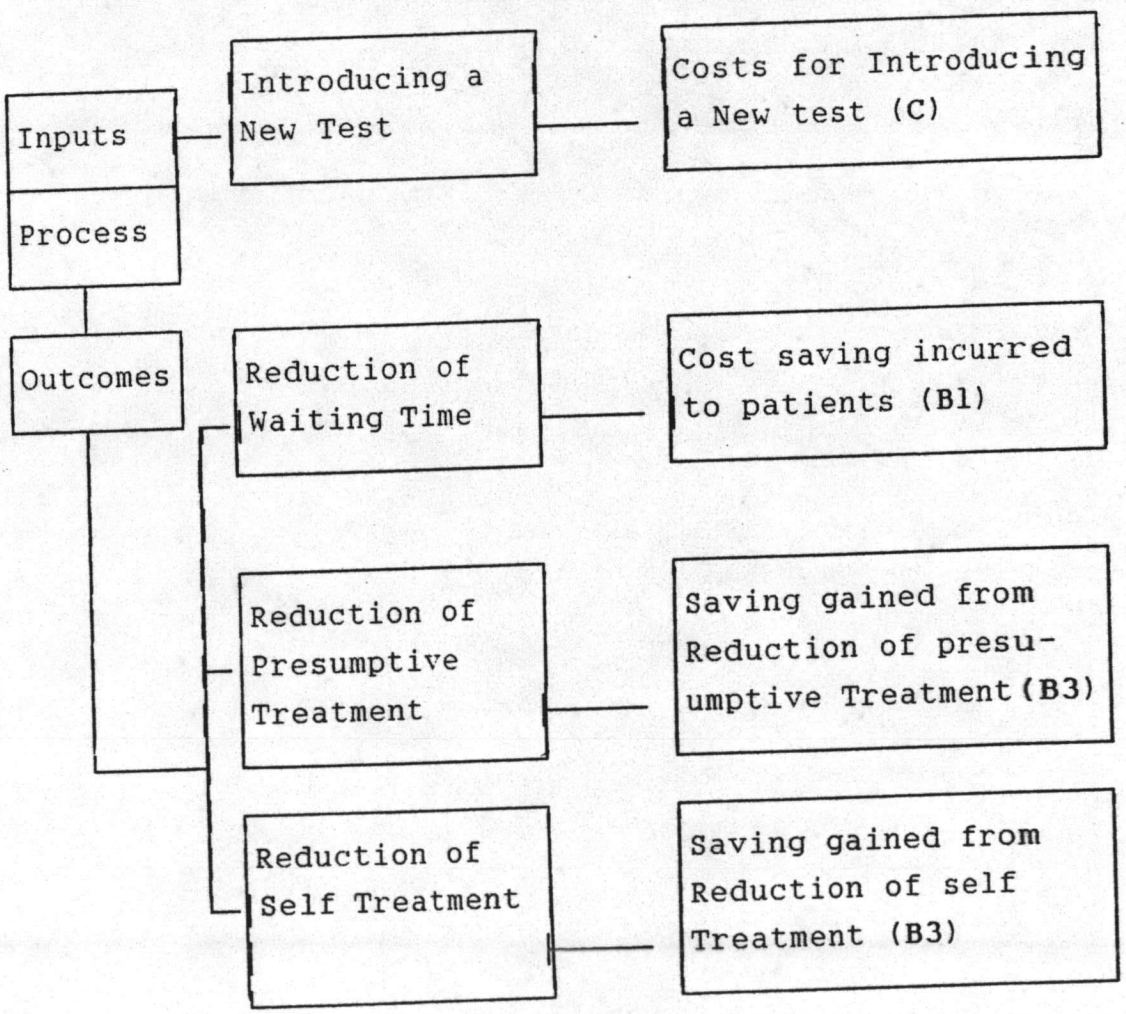
Costing inputs consist of developing input cost system and setting relationships between costs and influencing factors.

Input Cost System: Cost input system for costing of introducing a new rapid test includes:

- Costs for establishing the test (capital costs)
- Costs for running the test (running costs).

Cost components for establishing the test are those to be used for a long time such as training, major equipment, space and vehicles. Costs for establishing the test should take into consideration the use time frame in years within the time frame of cost benefit analysis.

Figure 3. Relationship between Costs, Inputs and Outcomes of Introducing a New Rapid Malaria Diagnostic Test:



Cost components for running the test are:

* Retraining : every year, a certain proportion of staff have to under go retraining. The proportion depends on the technique used and the real situation: this has been estimated by experts of Malaria Division.

* Materials, supplies, chemicals: these are consumable costs, depending on the quantity of services performed.

* Maintenance of equipment :this item includes depreciation and small repairs of equipment.

* Maintenance space: As mentioned above, this consists of both depreciation cost and repair cost. The space used for performance test or quality control test is shared with other activities if some activities are done in the same place. The calculation of sharing is based on the time and the space which is used by a certain activity.

* Administration and logistics: water, electricity, etc.

* Gasoline, maintenance of cars, transportation: Cars or gasoline are cost sharing together with other activities.

Costs for running the test should be calculated for 1 year. Cost per year for introducing a new test is the sum of cost per year for establishing a new test and annual cost for running a new test. This cost (C) should be judged against total savings gained (B1 + B2 + B3) from annual outcomes for evaluation, accepting or rejecting the test on economic analysis.

The calculation of costs should also consider cost levels (field level, intermediate levels or country level). A cost system should be developed for costing of inputs on identification of what activity of each cost component has to be implemented in what level (figure 4).

Cost elements of each activity should be identified, for exemple,

* A.I-1: Per diem for teachers of the courses on ParaSight test for performers.
* A.I.2: Travelling fare for teachers of the courses on ParaSight test for performers.

The cost system should be in detail so that any expected cost element for introducing a new diagnostic test can be included.

Figure 4. Cost System

	Field level I	Intermediate level II	Country level III
Establishing components A. Training	A.I Course on test for performers A.I-1,...	A.II Course on test for supervisors A.II-1,...	A.II Course on test for trainers A.III-1,..
B. Equipment	B.I-1,...	B.II-1,...	B.III-1,..
C. Space	C.I-1,...	C.II-1,...	C.III-1...
D. Vehicles	D.I-1,...	D.II-1,...	D.III-1...
Running components E. Retraining	E.I-1,...	E.II-1,...	E.III-1...
F. Materials	F.I-1,...	F.II-1,...	F.III-1...
G. Maintenance	G.I-1,...	G.II-1,...	G.III-1...
H. Administration	H.I-1,...	H.II-1,...	H.III-1...
I. Transport	I.I-1,...	I.II-1,...	I.III-1...

Factors influencing costs

The model should estimate quantitative relationships between above cost system and various elements of endemicity, malaria service network and the number of diagnostic cases for costing of inputs as follows:

* Incidence and number of diagnostic cases

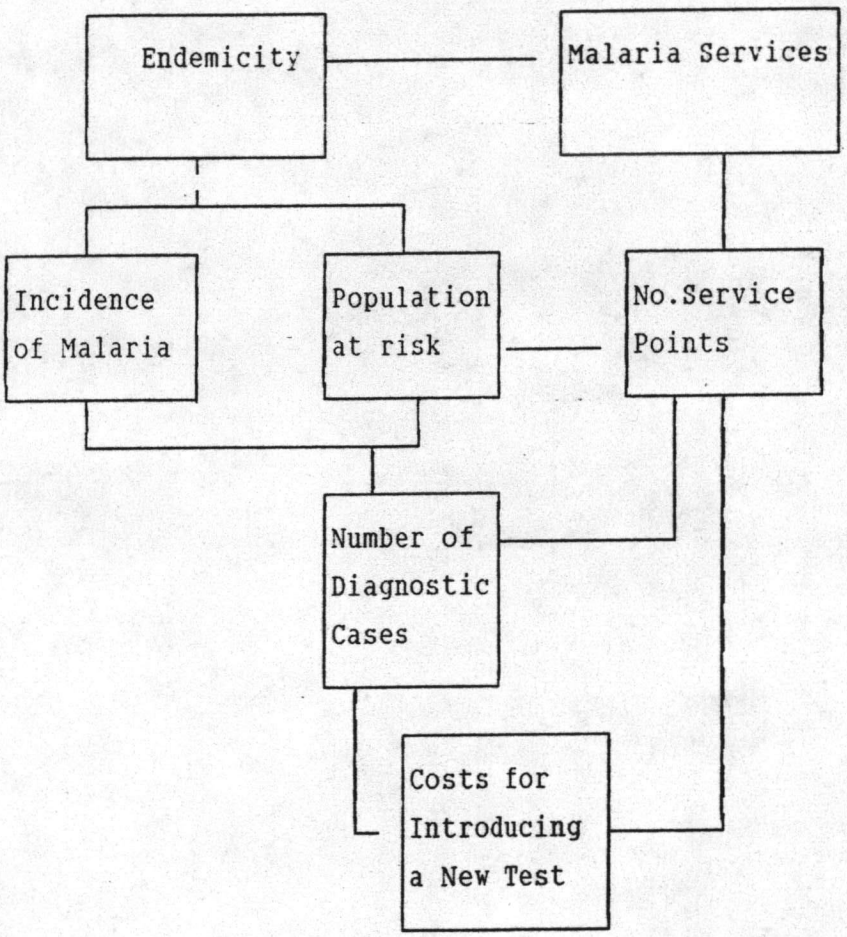
* Population at risk and number of diagnostic cases.

* Population at risk and number of service points

* Number of service points and the quantity of material and equipment.

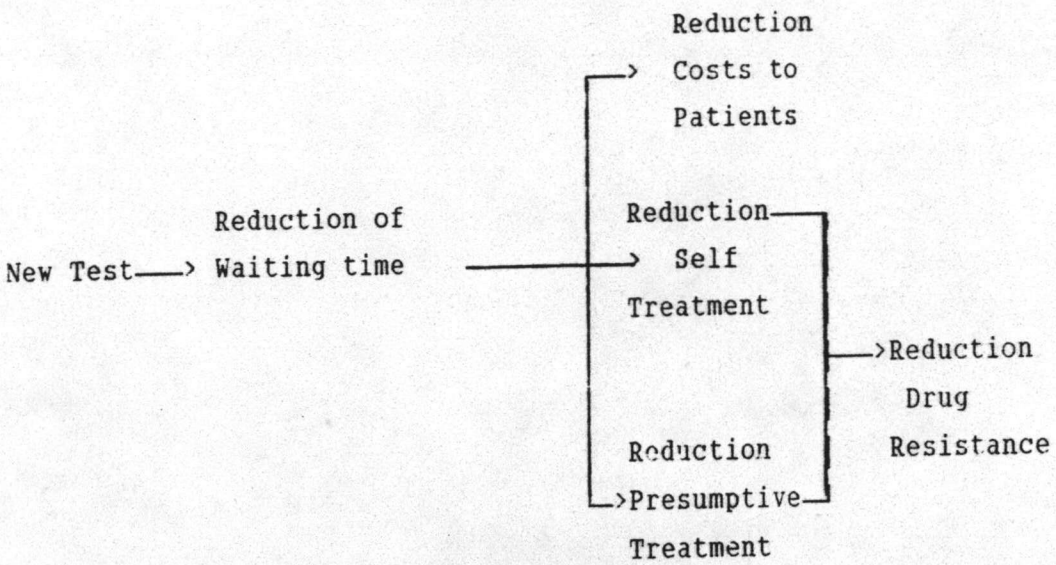
Such interrelationships are illustrated in figure 5. Figure 5 shows that malaria endemicity and malaria services affect costs for introducing a new test via the number of service points and the number of diagnostic cases; malaria endemicity determines partly malaria service points and number of diagnostic cases determines partly number of service points.

Figure 5. Factor Affecting Costs for Introducing New Rapid Malaria Diagnostic Test.



5.3 Predict and Value Outcomes:

Introducing a new diagnostic test reduces waiting time and consequently reduces costs incurred to patients, presumptive treatment, self treatment then finally drug resistance.



Waiting time is the time from diagnosis to radical treatment. Waiting time less than one day (Wt=0) is considered as on the spot diagnosis and treatment. The existing technology (microscopes and trained personnel) provides on the spot diagnosis and treatment only in malaria clinics and hospitals where required facilities are available.

Waiting time more than one day (Wt>1) often requires presumptive treatment and may affect behaviour of patients in using self treatment. The value of outcomes includes:

* Reduced costs incurred to patients;
* Value of prevented cases from presumptive treatment;
* Value of prevented cases from self treatment;
* Costs of prevented cases from drug resistance (actual data not available).

Reduction of costs incurred to patients

Costs incurred by patients include:

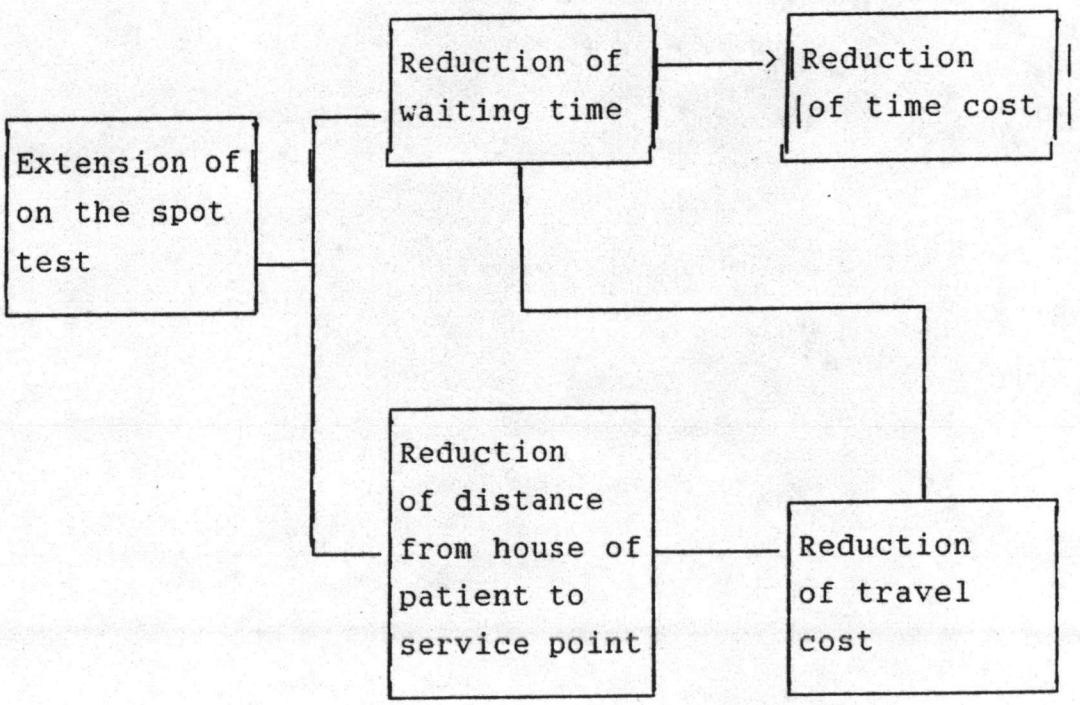
* Direct costs or costs for patients themselves:

- Time cost of patients: We assume that those who get no on the spot malaria diagnostic test have to wait for some days (without working) for treatment. - Travel costs for patients: for those who do not take on the spot malaria diagnostic have to go to the health service two times (one time for taking examination and other for getting the result). So if they take on the spot malaria diagnostic test they will save one time of round travel cost. They can also save some cost due to the reduction of distance from house to the service point if the service points for the new test are more than those for existing test.

* Indirect costs or costs for accompanying persons: Travel costs for accompanying persons as the same above mention.

Reasons why costs incurred to users are considered as outcomes are illustrated in figure 6.

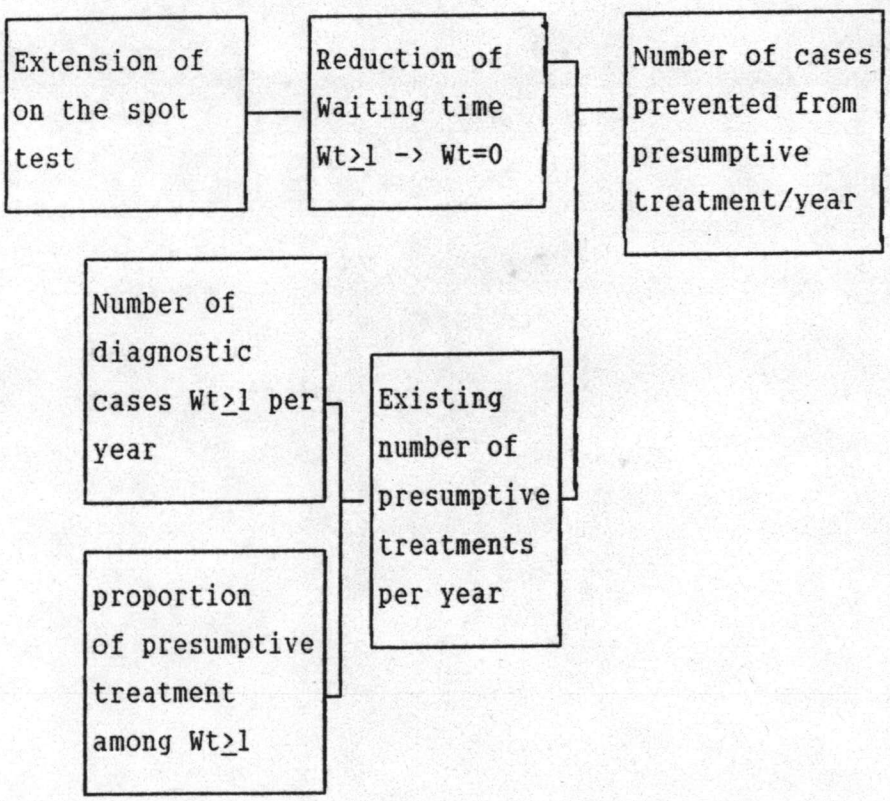
Figure 6. Relationship between Extension of on the Spot Test and Cost Incurred by Patients:



Predicting and costing reduction of presumptive treatment

Predicting reduction of presumptive treatment means predicting the number of prevented cases from presumptive treatment in one year. This number depend on the number of diagnostic cases in one year; the proportion of presumptive treatment among diagnostic cases with waiting time more than one day (Wt>1) and the reduction rate of waiting time from more than one day to less than one day (Wt>1 -> Wt=0) by the extension of an on the spot test (figure 7).

Figure 7. Factors Determining the Number of Prevented Cases from Presumptive Treatment in One Year.



Saving gained from reduction of presumptive treatment depend on costs per presumptive case and proportion of presumptive treatment among waiting cases.

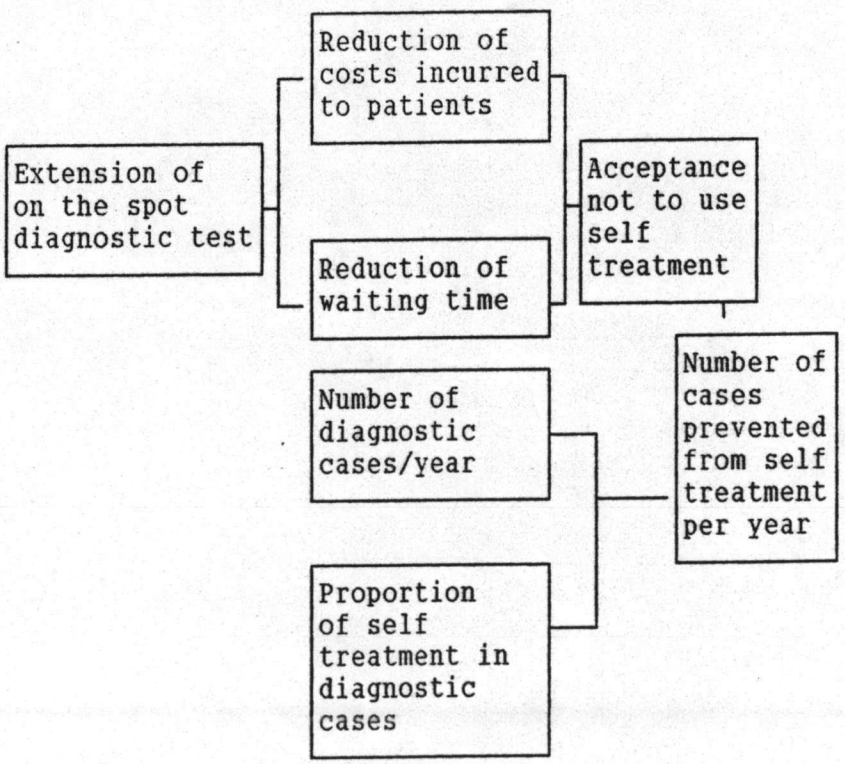
Predicting and costing reduction of self treatment

Predicting reduction of self treatment is predicting the number of cases prevented from self treatment per year. This number depends on:

- behavior of patients
- the number of diagnostic cases in one year
- the proportion of self treatment among diagnostic cases;
- cost per self treatment case.

Behavior or acceptance of patients is one of main factors determining the proportion of self treatment among diagnostic case awes. Factors determining the number of prevented cases from self treatment are illustrated in Figure 8.

Figure 8: Factors determining the number of prevented cases from self treatment in one year.



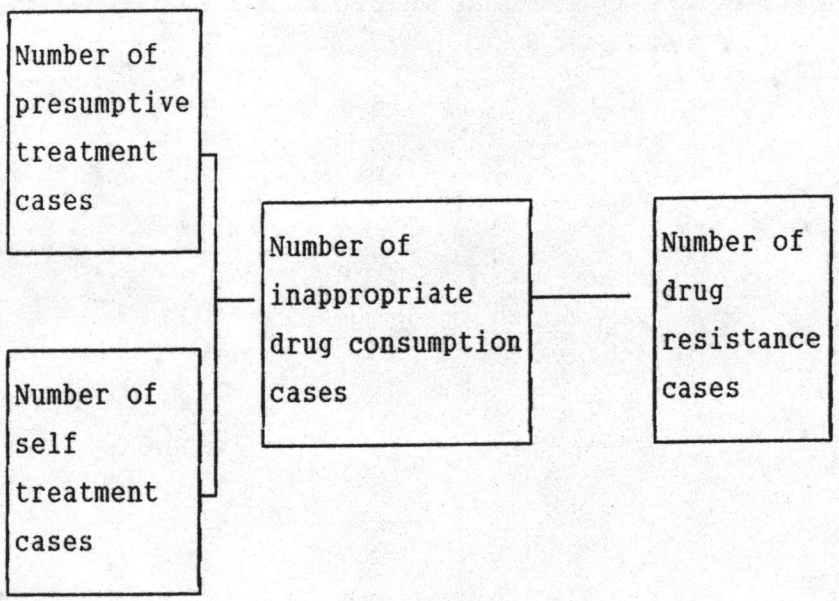
Value of saving from reduction of self treatment depend on:

- cost per self treatment case,
- number of cases getting diagnosis;
- proportion of self treatment among those who get diagnosis.

Predicting and costing reduction of drug resistance

Reduction of inappropriate drug consumption (presumptive and self treatment) contributes to reduction of drug resistance (figure 9).

Figure 9. Relationship between Inappropriate Drug Consumption and Drug Resistance.

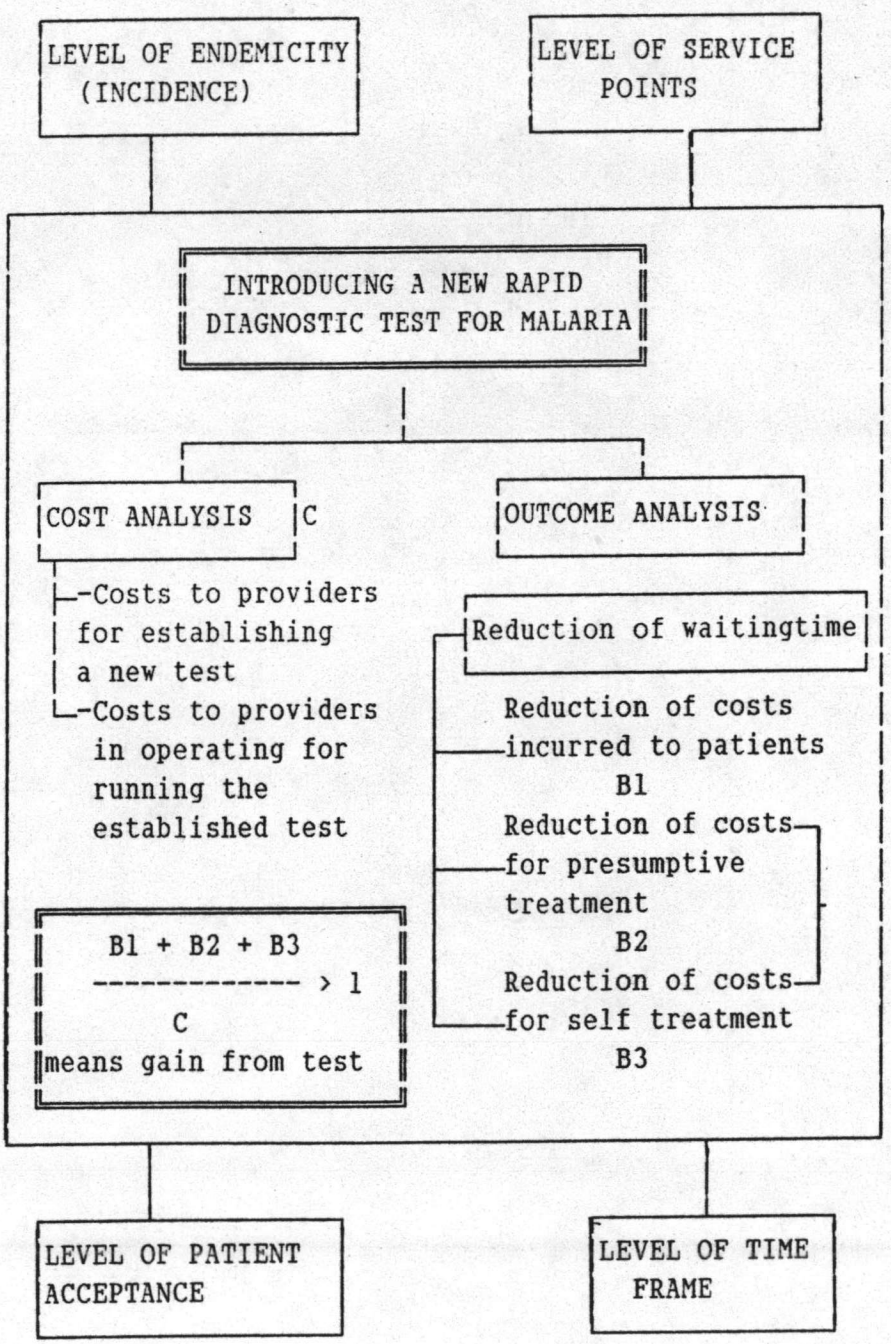


There is not actual data for the estimation of the number of drug resistant cases per year.

5.4 Simulation Modelling

Above mentioned elements can be summarized in the simulation modelling scheme as follows in Figure 10.

Figure 10. The Conceptual Framework of the Simulation Model.



The simulation modelling tries to set quantitative relationship between input costs and outcome values.

5.5 Testing the Model by Using Estimated Data from the Introduction of ParaSight Test:

Cost components, levels, activities and of the ParaSight test should be identified to be used for inputs to the model. Testing the developed modelling aims at proving the feasibility and the practicability of the modelling, that means with a given set of input data for the calculation of costs, the model can provide a set of results. Variations of input data make variations of output data. Outcome values should be judged against input costs for evaluation. Analysis of outcome variations could be made on the view of providers and users as follows:

* Costs to providers for establishing the test affect the behavior of malaria services in using or not using the test.For example, the budget is not adaptable with the high cost for establishing the new test even the quality of the new test is very good.

* Costs to providers for running the test per "unit of outcome/year time" contribute to strategic planning over time. Which the same budget, policy makers have to balance all of malaria control activities not only diagnosis.

* Costs to consumers (patients) for using the test affectpartly the behavior of communities in the restriction of inappropriate drug consumption. The more convenient the test the more motivated the patients will be to get diagnosis before taking the treatment.

* Opportunity costs to providers are mainly of social concern for political consideration in macro resource allocation. What is the benefit when policy makers spend the same money on this activity not another one?

* Financial (costs for travel, cost of drug for self treatment) and opportunity costs (time cost) to consumers are both the concern of patients. Patients are as consumers, they always concern whether the new test can reduce their travel cost, drug cost and time cost or not.