สำนักงานวิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

CHAPTER 2

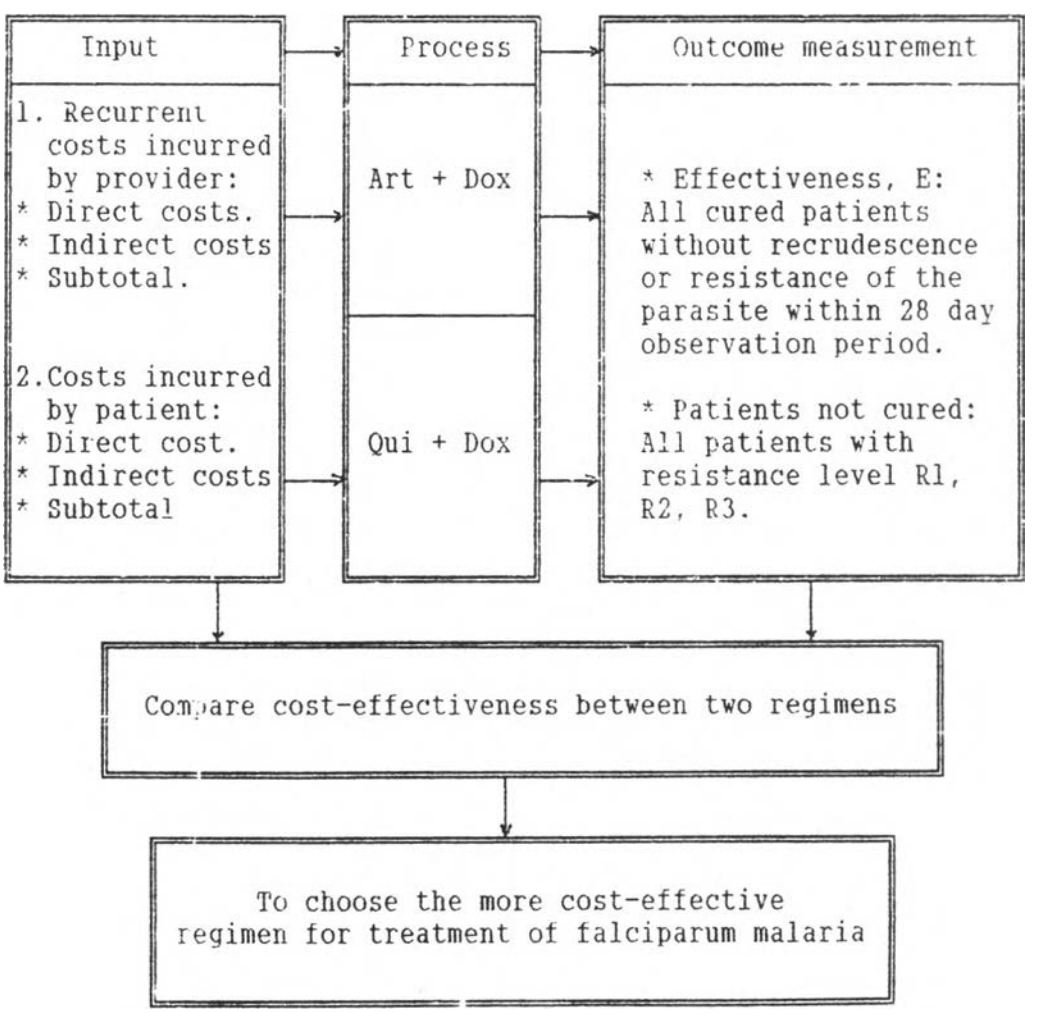
CONCEPTUAL FRAMEWORK

In order to analyze costs and effectiveness of the two regimens Art + Dox and Qui + Dox in falciparum malaria treatment, the study should:

1 Identify the cost input and components of cost in each regimen.
2 Identify the effectiveness and level of effectiveness in each regimen.
3 Compare the cost-effective between two regimens and choose the more costs-effectiveness for falciparum malaria treatment.
4 Test statistical significance and clinical significance of outcome between the two treatment regimens.

The conceptual framework is summarized in the Figure 2.1.

Figure 2.1 Conceptual Framework



2.1 Identify the Cost Input and Components of Cost

The costs of each regimen for falciparum malaria treatment include costs incurred by provider and costs incurred by patient. Provider costs and costs incurred by patient will be broken down into direct and indirect costs.

2.1.1 Costs Incurred by Provider

To estimate costs incurred by provider, it is necessary to classify its components. Cost elements can be broken down in several ways. The costs incurred by provider in this study were classified by input, which composed capital costs and recurrent costs.

In this study, some costs are covered by provider (protocol driven cost). So that the costs incurred by provider will be higher than normal treatment practice for both of the treatment regimens. In normal treatment practice, patients should pay for service and diagnostic tests and non antimalarial drugs.

Provider costs include capital costs and recurrent costs. however since the building was ereted over 20 years and equipment is old (over 5 years). Only the capital costs have been written off.

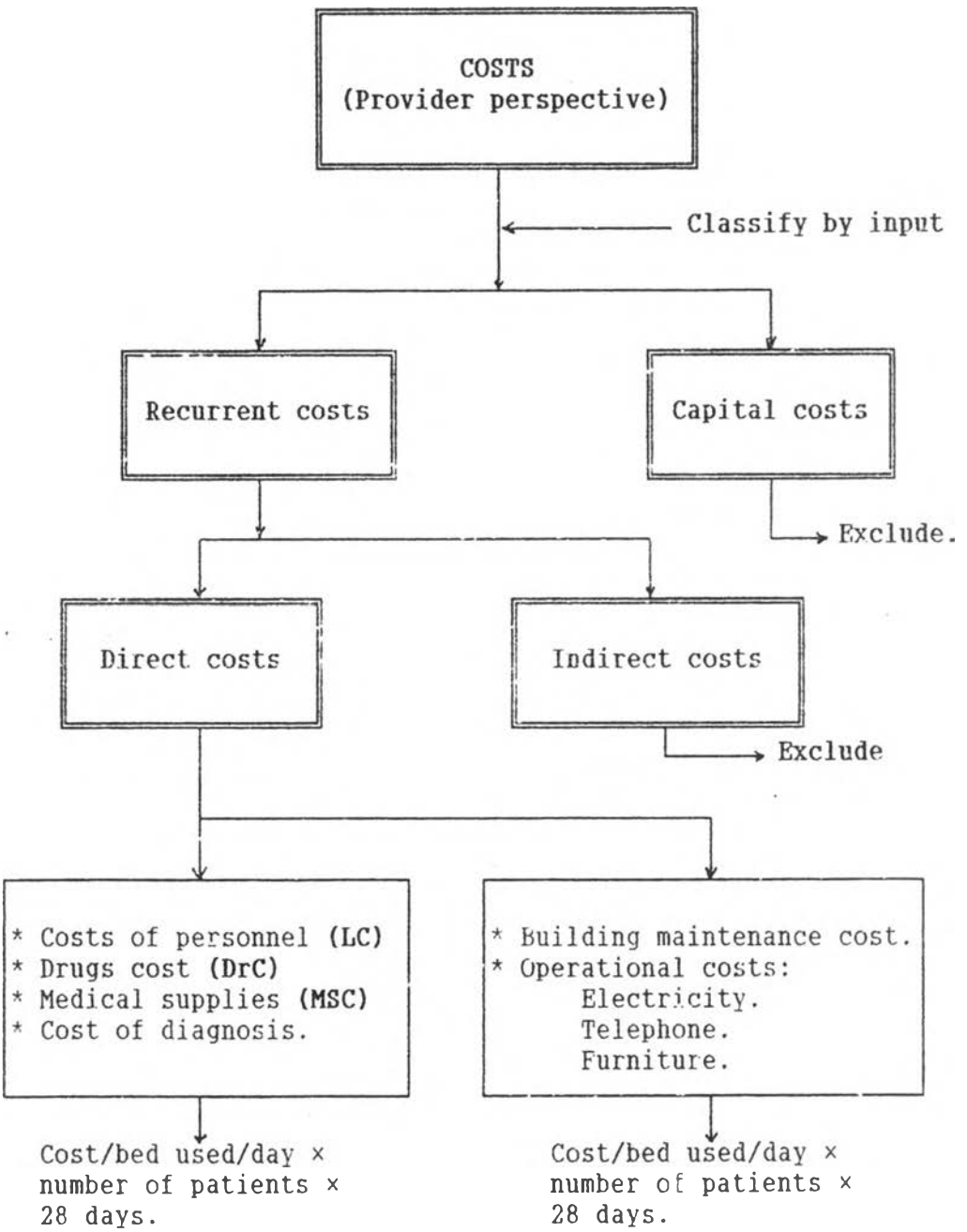
Recurrent costs therefore considered included direct and indirect costs. In this study, indirect costs wewe not mention because it was not possible evaluate and measure the training costs of medical staff in the hospital. Therefore only direct costs were measured.

Direct costs (DC) included:

Personnel: Doctors, nurses, health workers, technicians,
Drug: Antimalarial drug & other drug used.
Medical supplies: Small equipment and material in laboratory.
Building maintenance costs.
Operational costs: Electricity.
Telephone.
Furniture.

The provider costs were summaried in Figure 2.2

Figure 2.2 The Elements of Provider Costs



2.1.2 Costs Incurred by Patient

Costs incurred by patients also include direct costs and indirect costs. Each component was classified into medical and non medical costs to identify costs of medical side and othe side.

* Direct medical costs incurred by patient (**DMCp**) included:
  Drug costs (non antimalarial drug).
  Costs of laboratory tests.
  Cost for services.

* Direct non medical costs incurred by patient (**DNMCp**) included:
  Travel costs of patient to the hospital.
  Cost of food.

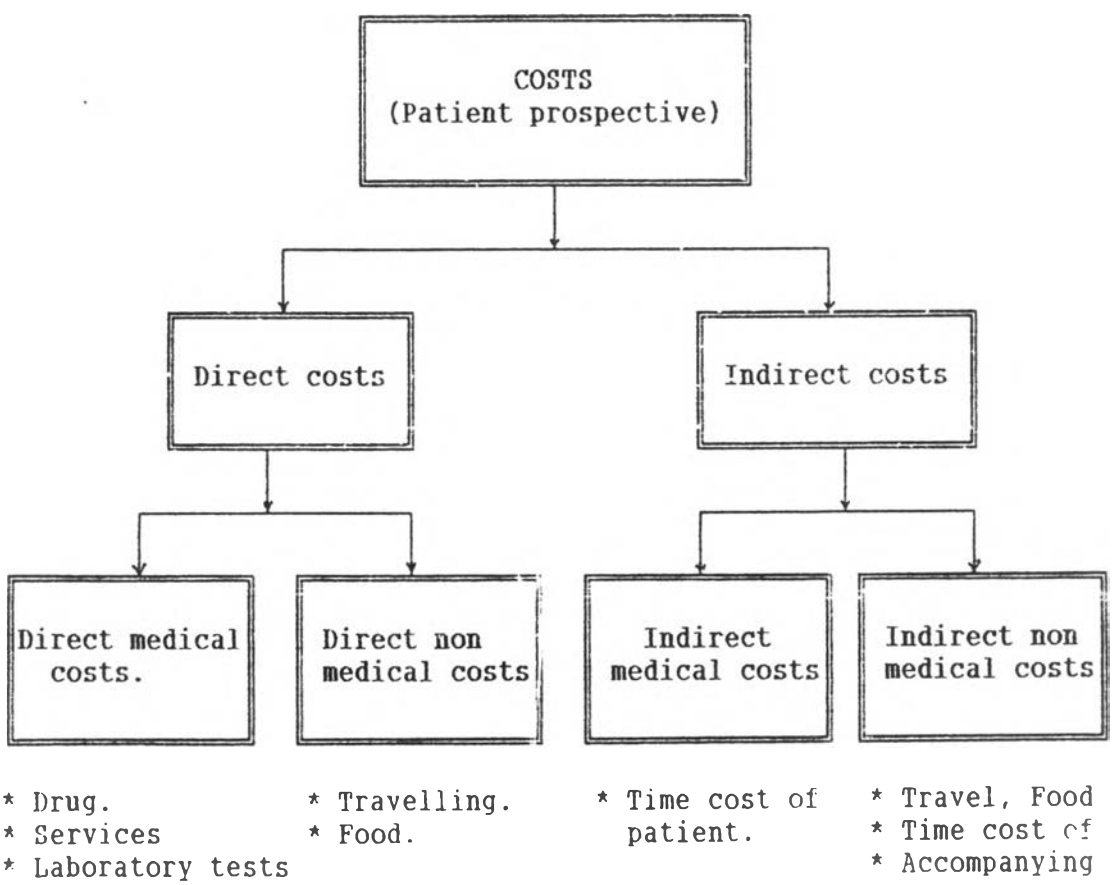
* Indirect medical costs incurred by patient (**IDMCp**) include:
  Time costs of patient, time costs is income loss because of the illness or by treatment period, eg.time absent from the work.

* Indirect non medical costs incurred by patient (**IDNMCp**) included:
  Travel costs of accompanying person to the hospital take care patient.
  Time costs (working days loss of accompanying person).
  Cost of food of accompanying person.

* Total costs incurred by patient = direct costs + indirect costs.
  = DMCp + DNMCp + IDMCp + IDNMCp

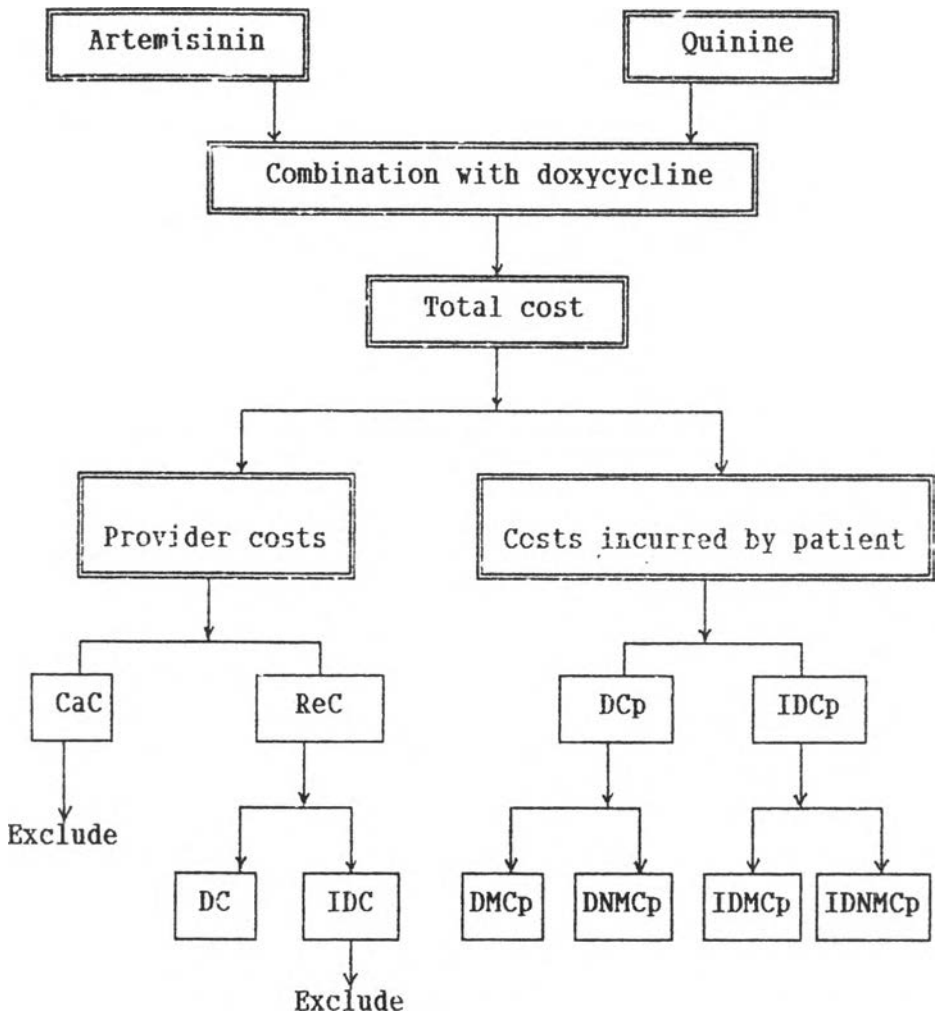
The elements of costs incurred by patient are presented in Figure 2.3.

Figure 2.3 The Elements of Costs Incurred by Patients



The cost components of two the treatment regimens were summarized in Figure 2.4.

Figure 2.4 The Cost Components of Two Treatment Regimens



Where:

- CaC = Capital cost.
- ReC = Recurrent cost.
- DC = Direct costs incurred by provider.
- IDC = Indirect costs incurred by provider.
- DCp = Direct costs incurred by patient.
- IDCp = Indirect costs incurred by patient.
- DMCp = Direct medical costs incurred by patient.
- DNMCp = Direct non medical costs incurred by patient.
- IDMCp = Indirect medical costs incurred by patient.
- IDNMCp = Indirect non medical cost incurred by patient.

2.2 Identify Effectiveness Oucome

2.2.1 Definitions

Unit of Outcome

Unit of outcome is the number of cured patients or effectiveness. Unit of cost is cost per cured patient or cost-effectiveness.

Definition of Cutcome.

In this study, outcome was measured in term of effectiveness (or cured patients).

Effectiveness (E): All cured patients without recrudescence or resistance of parasite within 28 days follow up period.

Effectiveness Measurement

Effectiveness can be expressed by the following formula:

$$E\ (\%) = \frac{(T - R) \times 100}{T}$$

Where:

T = Total treated cases.
R = Total recrudescent cases.

Resistance

Drug resistance in malaria has been defined as the "ability of a parasite strain to survive and/or to multiply despite the administration and absorption of a drug given in doses equal to or higher than usually recommended but within the limits of tolerance of the subject" (WHO, 1965, 1973). This definition can be applied to all species of malaria parasite but commonly refers to resistance of P.falciparum to the available blood schizonticide.

The response of the parasite to antimalarial drugs ranges from a low level of resistance with a loss effect demonstrable only by occasional recrudescence (R1), to a high level of resistance at which the drug apparently has no suppressive affect on the parasite (R3) and results in severe malaria infection.

In 1967, the WHO Scientific Group on Chemotherapy of Malaria proposed an arbitrary grading system based on the response to normally recommended dose of chloroquine, a slightly amended version of which is presented in Table 1.2. This grading is also used for other blood schizontocides and other species of human plasmodia but modification may be required for each drug on the basis of speed of action, half-life and the biological characteristic of the Plasmodium species, e.g. the follow up period for chloroquine, quinine or artemisinin derivatives should be 28 days but for mefloquine should be 42 days. The grading system is still generally used for the purpose of comparison of drug efficacy, (Looareesuwan and Chongsuphajaisiddhi, 1992).

In Vivo Test (WHO Extended Test 28 Days Observation)

In vivo test is the standard test for determining the response of malaria parasite to antimalarial drug within 28 days observation. It has been recommended by World Health Organization (WHO, 1973). This test will distinguish between sensitivity (S) and the kind of resistance (R) that is demonstrable only by recrudescence following a normal initial response. It is interpreted as follows :

(a) **Sensitivity**

If no asexual parasites are found by day 6 and if asexual parasites do not reappear by day 28, the parasites are sensitive (S) .

(b) **Resistance level 1 (R1)**

If asexual parasites disappear as in (a) but return within 28 days reinfection having been excluded, the parasites are recrudescent or resistant at the R1 level.

(c) **Resistance level 2 (R2)**

If the asexual parasitemia does not clear but is reduced to 25% or less of the original pre-test level during the first 48 hours of treatment, the parasites are resistant at the R2 level.

(d) **Resistance level 3 (R3)**

If asexual parasitemia is reduced by less than 75% during the first 48 hours or if it continues to rise, the parasites are resistant at the R3 level.

The response of falciparum parasites to antimalarial drugs by the in vivo test is summarized in the Table 2.1.

Table 2.1 The Response of Malaria Parasite to Antimalarial Drugs

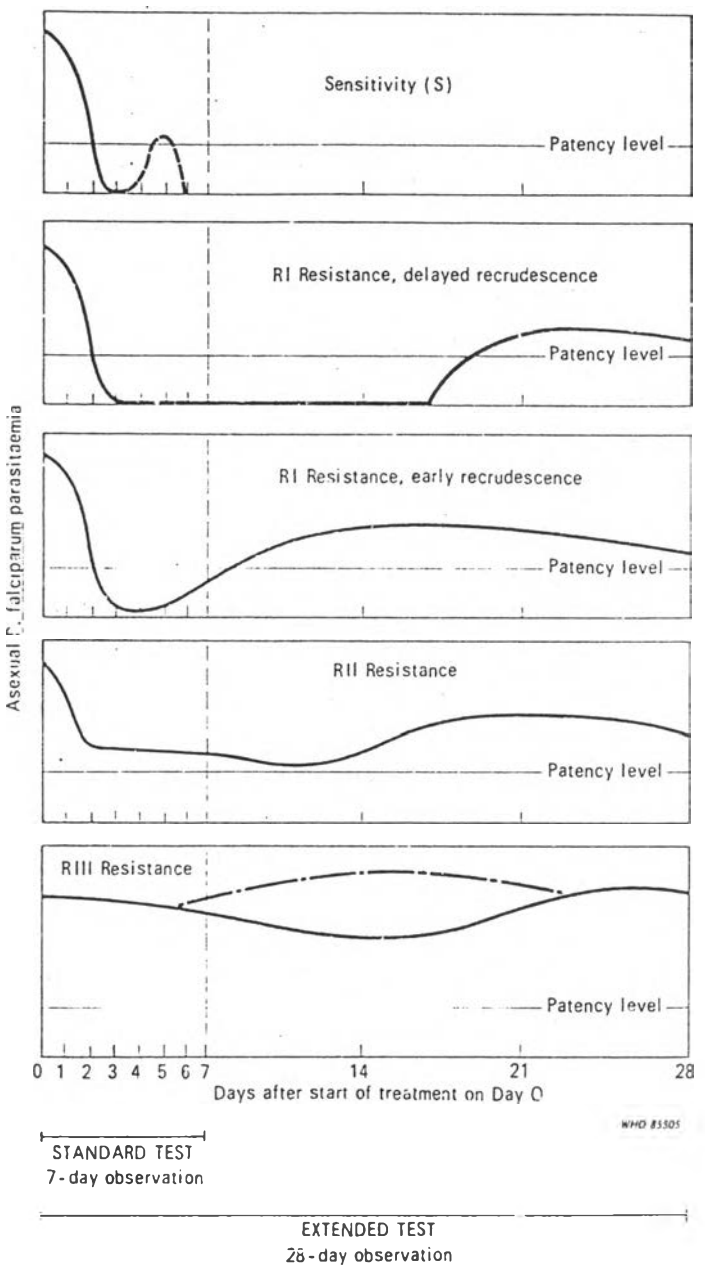
Response	Recommend symbol	Evidence
Sensitivity	S	Clearance of parasitemia within 7 days of initiation of treatment,without subsequent recrudescence.
Resistance	R1	Cleanse of asexual parasitemia as in sensitivity,followed by recrudescence.
	R2	Marked reduction of asexual parasitemia,but no clearance
	R3	No marked reduction of asexual parasitemia.

Definition of side effects

Side effects are therapeutically undesirable but unavoidable consequences of taking a drug, e.g nausea and vomiting after chloroquine taken on an empty stomach, or fall of blood pressure after an intravenous injection of quinine, etc. (Rosenheinm, 1958 and Bruce - Chwatt, 1986).

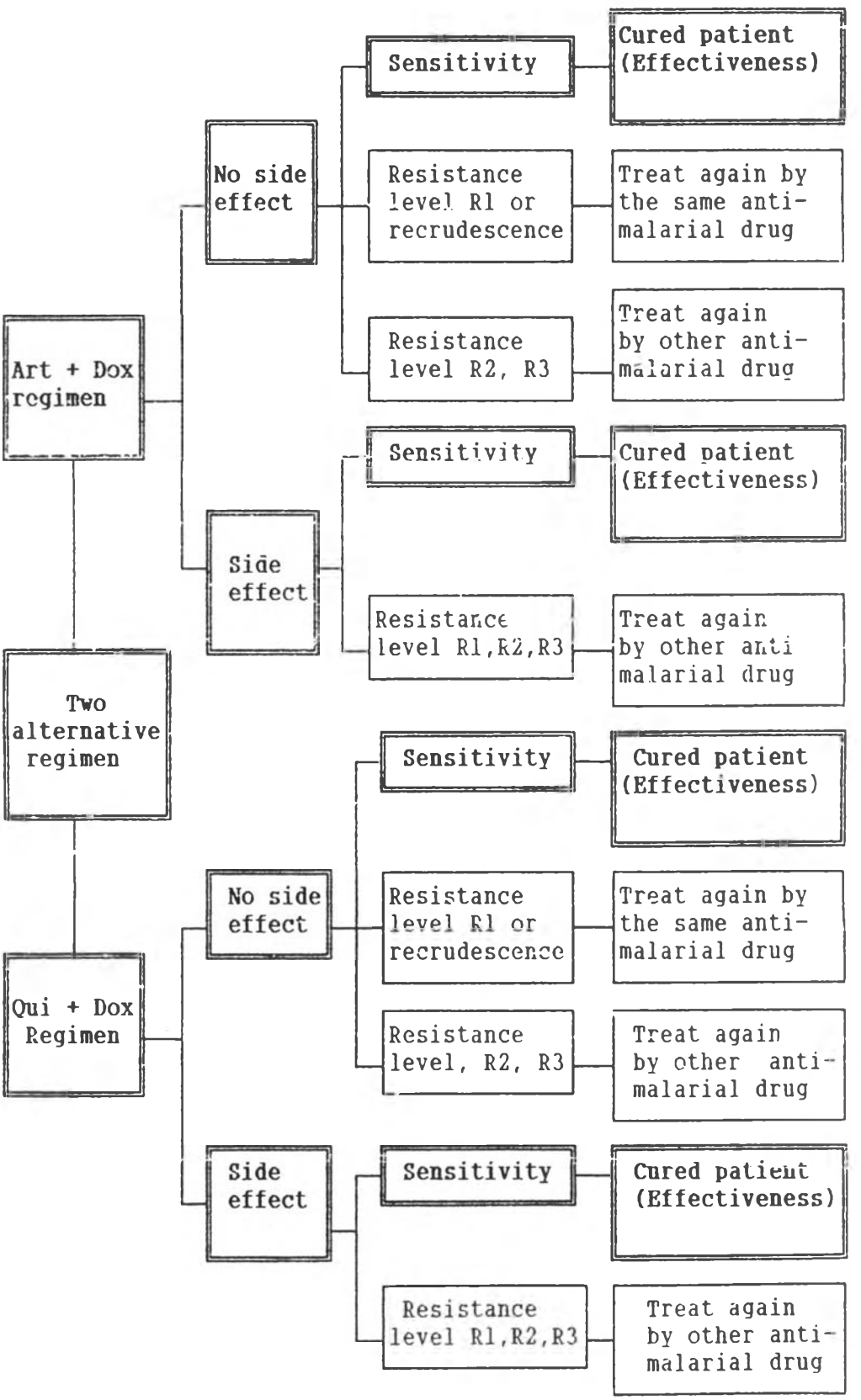
A standard procedure for determining the response of malaria parasite to antimalarial drugs in the field has been recommended by WHO (Figure 2.1). Diagram shows the degree of response ranging from sensitivity to a high resistance of P.falciparum to antimalarial drugs in a 28 day observation period.

Fig 2.1 Standard Procedure for Determining the Response of Malaria Parasite to Antimalarial Drugs.



[1] From: WHO Technical Report Series, No. 529, 1973 (amended).

Figure 2.6 Decision Tree Identified Effectiveness in Treatment



2.3 Compare Cost-Effectiveness Between Two Drug Regimens

The cost-effectiveness will be compared between two regimens to choose the more cost-effective falciparum malaria treatment. The factors required to analyze, compare and select the more cost effective treatment regimen are shown in figure 2.5.

Figure 2.6. Factors to Analysis and Select the More Cost-Effectiveness Drug Regimen