ACT CONSORTIUM GUIDANCE ON ECONOMIC EVALUATION

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PURPOSE OF THE GUIDANCE

This guidance has prepared for ACT Consortium members. It is intended to provide an introduction to economic evaluation and outline the principles and methods for undertaking cost-effectiveness analysis.

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UNDERTAKING ECONOMIC EVALUATION

1. INTRODUCTION TO ECONOMIC EVALUATION

1.1 Why undertake an economic evaluation?

Economic evaluation has increasingly become part of decisions on health policy and care. Resources (people, time, facilities, equipment and knowledge) are scarce and choices must be made concerning their deployment. In particular, rising costs, often associated with new technologies, and spending limits have prompted a search for greater technical and allocative efficiency. An intervention is technically efficient if it is not possible to decrease one or more of the inputs of the intervention without also decreasing the health benefits of the intervention. Allocative efficiency involves comparing costs and effects of interventions of different health problems to determine the optimal mix of interventions resulting in the lowest level of total costs.

1.2 What is an economic evaluation?

An economic evaluation is defined as the ***comparative analysis of two or more alternatives in terms of both their costs and consequences***.

1.3 What are the different types of economic evaluation?

Economists have developed methods to evaluate health programmes. These methods include: cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis. The identification and measurement of the various types of costs is similar across these methods, though they differ in their consequences.

- ***Cost-effectiveness analysis (CEA)*** measures health benefits in ***natural units*** such as ilife years saved or cases cured. Since costs and consequences are measured in non-comparable units, the relative (technical) efficiency is presented as a ratio: ***cost per unit of effect***. The comparison between two alternatives (e.g. intervention group and control group) is presented as the incremental cost-effectiveness ratio (ICER).

$$\text{ICER} = \frac{\text{Difference in cost}}{\text{Difference in effect}} = \frac{(\text{Mean cost}_{\text{Intervention}} - \text{Mean cost}_{\text{Control}})}{(\text{Mean effect}_{\text{Intervention}} - \text{Mean effect}_{\text{Control}})}$$

  An intervention is considered technically efficient, relative to an alternative, if it results in higher (or equal) benefits at lower cost. A limitation of CEA is the inability to compare interventions with differing natural effects. For example, interventions aimed at increasing life years gained cannot be directly compared with those that improve physical functioning, and cannot therefore directly address allocative efficiency.

- ***Cost utility analysis (CUA)*** is an adaptation of CEA, which measures an intervention's effect on both the ***quantity and quality of health*** using a utility based measure, such as a disability-adjusted life year (DALY) or quality-adjusted life year (QALY). Like CEA, relative efficiency is assessed using an incremental ratio. The use of a single measure of health

benefit enables diverse healthcare interventions to be compared so CUA can address both technical and allocative efficiency. Evaluations which use DALYs are sometimes also referred to as CEAs.

- ***Cost-benefit analysis (CBA)*** involves ***measuring costs and benefits in monetary terms***. Welfare economics shows that under certain conditions any net excess of monetary benefits over costs represents the gain in welfare by society. CBA makes it possible to determine whether an individual intervention offers an overall net welfare gain and how the welfare gain from that intervention compares with that from alternative interventions. Practical measurement difficulties and objections to valuing health benefits in monetary terms have limited the use of cost benefit analysis in health care, though recent approaches have applied the concept of "willingness to pay" to value the health improvement.

METHODS: Summary of types of economic evaluation

Type of economic evaluation	Outcome can be measured by:	Examples of outcomes relevant to ACT consortium studies
Cost effectiveness analysis (CEA)	Clinical end points Mortality Years of life Condition specific outcome measures Generic quality of life scales	Fever cases receiving biological diagnosis Biologially confirmed malaria cases receiving and ACT
Cost utility analysis (CUA)	Utility based quality of life scales eg Disability Adjusted Life Years (DALYs)	
Cost benefit analysis (CBA)	Willingness to pay Conjoint analysis	

Given the practical challenges the ACT Consortium studies are unlikely to undertake cost-benefit analysis. Thus, the remainder of this note provides guidance on conducting cost-effectiveness analysis and cost-utility analysis.

1.4 What are the relevant costs and consequences?

There is no single answer to this question, and the relevant costs and consequences depend on several factors including: the problem being tackled, the institutional framework, practical measurement challenges and the perspective of the analyst.

The possible components of an economic evaluation are presented below. The costs can include the resources consumed by the health sector, other sectors, the patient (or their family) and any associated losses in productivity. The consequences can include the change in health state (which can be measured in several ways) and any resource savings to the health sector, other sectors, the patient (or their family) and any productivity gains associated with the intervention.

METHODS: Possible components of an economic evaluation	
Costs	Resources consumed: Health sector (C_1) Other sectors (C_2) Patient / family (C_3) Productivity losses (C_4)
Consequences	Change in health state: Measure the health effect in natural units (E) Value the health state preferences using a utility measure (U) Resources saved: Health sector (S_1) Other sectors (S_2) Patient / family (S_3) Productivity gains (S_4)

Source: Adapted from Drummond, Sculpher et al (2005).

Health economics typically argue that economic evaluations should take a ***societal perspective*** and include all costs and resource savings (C_1, C_2, C_3, C_4 and S_1, S_2, S_3, S_4). This means that the evaluation should take into account the impact of the intervention on the welfare of the whole of society, not only the individuals or organizations involved. However, it is not uncommon for economic evaluations to take a ***health provider perspective*** and include only health sector costs and resource savings: C_1 and S_1.

1.5 How to present the results of an economic evaluation

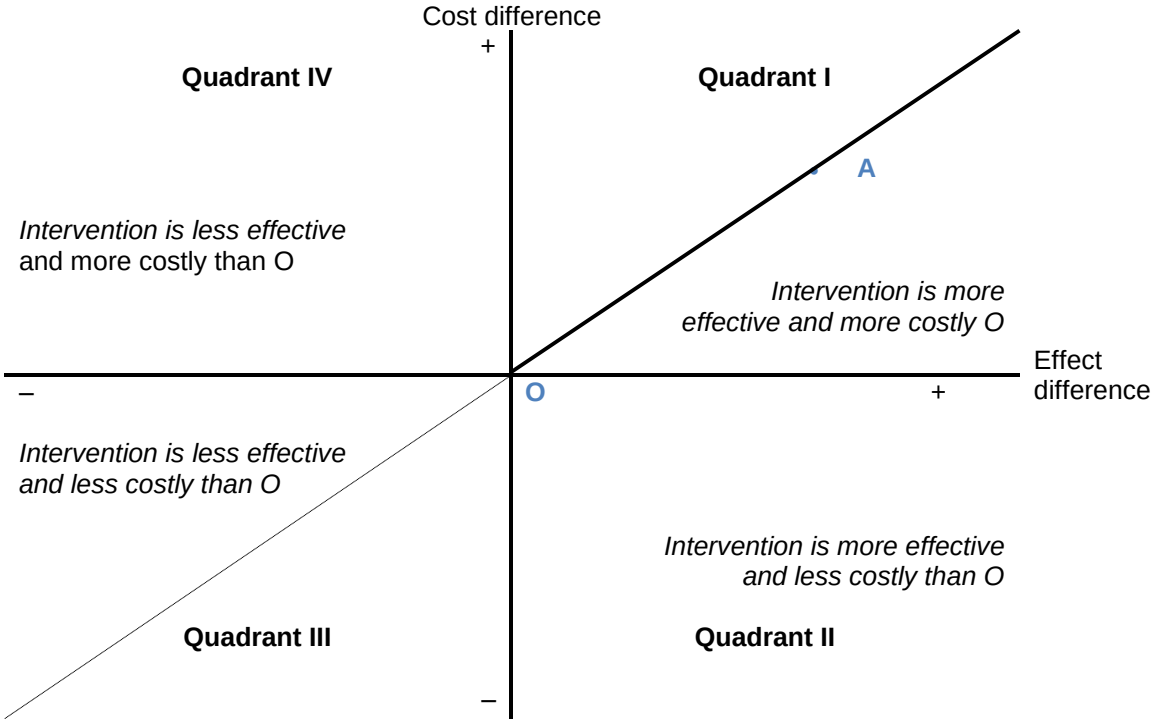
The results of CEA (and CUA) are usually presented as an incremental ratio showing the difference in cost over the difference in effect / utility between two alternatives.

$$\text{ICER} = \frac{\text{Difference in cost}}{\text{Difference in effect}} = \frac{(\text{Mean cost}_{\text{Intervention}} - \text{Mean cost}_{\text{Control}})}{(\text{Mean effect}_{\text{Intervention}} - \text{Mean effect}_{\text{Control}})}$$

It can also be useful to visualize the results using a ***cost-effectiveness plane***. In the diagram below the horizontal axis represents the difference in effect between the intervention of interest (A) and the relevant alternative (O), and the vertical axis represents the difference in cost. Intervention A could be treatment of malaria with ACT after having tested the patient using a rapid diagnostic test while intervention O might be presumptive treatment of fever episodes with ACT.

If point A is in quadrants II or IV the choice between the programmes is clear. In quadrant II the intervention of interest is both more effective and less costly than the alternative and is said to dominate the alternative. In quadrant IV the opposite is true. In quadrants I and III the choice depends on the maximum cost-effectiveness ratio one is willing to accept. The slope of the line OA is gives the cost-effectiveness ratio.

METHODS: The cost-effectiveness plane



The remainder of this guidance note provides more detail on the aspects of an economic evaluation provided in this introduction. The following sections are intended to outline the key steps in undertaking a cost-effectiveness analysis.

The references to this guidance note provide additional sources of information. The standard text on health economic evaluation is: Drummond MF, Sculpher MJ, Torrance GW, O'Brien B, Stoddart GL. *Methods of Economic Evaluation of Health Care Programmes. Third Edition.* 2005 Oxford, Oxford University Press. A series of papers in Health Policy and Planning also discuss in more detail many of the issues covered in this guidance note.

2. SCOPE OF THE COST-EFFECTIVENESS ANALYSIS

In undertaking a cost-effectiveness analysis it is important to clearly set out the purpose and scope of the evaluation. This involves defining the health intervention, its comparator(s) and the target population, and determining the implementation period and the time horizon for the analysis.

2.1 Framing the study question

In framing the study question the analyst should define the patient population, intervention and the appropriate comparators. The perspective of the study may also be stated in the question. Patients or populations can be defined in terms of the health condition, demographic characteristics, or setting. The intervention and comparator(s) can take a variety of forms and may, for example, be treatment strategies or different medicines. The perspective of the study typically reflects the interests of the target audience, such as the government and health ministry. Although the primary analysis may take the perspective of the publicly funded health system, secondary analysis which also takes into consideration the costs of patients and their families is desirable (see Section 4 on Identifying Costs).

2.2 Defining the health intervention(s) and its comparator(s)

The health intervention should be carefully described using all information essential to interpret the estimated costs and benefits. The definition of an intervention should include: information on the setting where the intervention is delivered or undertaken (e.g. facility or community based care); the target population covered by the intervention; the time frame; the regimen of therapy; the frequency of obtaining the intervention, and any other important information.

The description of the intervention should also define the treatment pathway for clinical interventions, and where are there are alternative treatment pathways it is usually recommended that they are evaluated separately. For example, the health intervention to treat malaria with an ACT may include the option of conducting a diagnostic test. In this case it would appropriate to evaluate both i) treatment with ACT (and no diagnosis) and ii) the combination of diagnosis and treatment with ACT.

Cost-effectiveness analysis is comparative, and in addition to defining the health intervention(s) it is necessary to define the counterfactual. It is crucial to set the appropriate comparators as they will determine the cost-effectiveness of the intervention and the relevance of the study to policy makers. The usual approach is to compare the intervention with the current practice, or what would happen if none of the interventions were implemented (“do nothing”). Possible comparators to the earlier example include “treatment with a less effective antimalarial”, and “no treatment”.

2.3 Specifying the target population

The cost-effectiveness of an intervention depends on the population being evaluated. The evaluation should analyze the entire population defined in the study question. Target populations may be defined using baseline demographic features that describe the type of patient (e.g. age, sex, socioeconomic status) with a specific condition (e.g. fever), of a certain severity or stage, with or without co-morbidities or risk factors. In addition populations can be defined by their setting (e.g. community or hospital), geographical location, usual adherence rates, or typical patterns of treatment.

It may be appropriate to conduct a stratified analysis of small, more homogeneous subgroups where there is variability in the target population. Variability may relate to differences in access to care, health outcomes, patient preferences, and costs of the intervention among subgroups of patients.

2.4 Determine the time horizon for analysis

The implementation period and length of time over which the intervention is evaluated will vary and should be based on the natural course of the condition and the likely impact that the intervention will have on it. The time horizon applied to costs and outcomes should be the same. It is important to ensure that the time horizon is long enough to capture all relevant differences in future costs and outcomes of the alternatives being analyzed. Thus, the choice of follow-up period should not bias the analysis in favour of one intervention over another. In ACT consortium studies, where outcomes are measured in terms of treatment effectiveness, the follow-up period would normally be at least one month. For those studies focusing only on the more immediate outcome of changing provider behaviour, there may be no follow-up beyond the consultation.

As the costs of implementing the health intervention may be higher in the first year, many interventions are evaluated for a typical year, with start up and capital costs annualized. This means that the costs are adjusted over the useful life of the asset to obtain an annual economic cost, and the method is explained later in this note (see 4.5 and 4.6).

To extend the time horizon of the cost-effectiveness analysis beyond the timeframe of the study, modelling techniques can be used which extrapolate from the data in the initial period (see section 6.3).

3. IDENTIFYING COSTS

In undertaking an economic evaluation it is necessary to determine which costs should be considered in the evaluation. This involves specifying the costing ***perspective*** for the analysis.

3.1 What are the different types of cost?

A variety of resources are used in the implementation of the health intervention, all of which incur a cost. There are costs incurred by the provider of the health intervention, and for some interventions the costs may be incurred by other agents, such as other government departments. There may be costs to the patient or their family in accessing the health intervention, such as in user charges, transport costs or the out-of-pocket expenditure on medicines. Economists also consider the cost relating to the impact on productivity that arises from the patient or their families taking time off work to access the health intervention. A summary of the main categories of costs, with examples, are provided in the table below.

METHODS: Types of Costs

Perspective				Types of Cost	Examples
Societal perspective	Public sector / Government			***Direct costs to publicly funded services*** *(other than health care)*	• Social services • Education
		Health sector	Public health provider: Health Ministry	***Direct costs to publicly funded health care provider*** *(may include contributions from international donors and similar agencies)*	*Capital costs:* • Buildings • Medical Equipment • Vehicles *Consumables:* • Medical supplies • Laboratory supplies and rapid diagnostic tests • Medicines • Training materials • Insecticide Treated Nets *Overheads:* • Utilities (water, electricity, telephone) • Administration, • Buildings and vehicle maintenance • Other central services (e.g. catering or laundry) *Labour costs:* • Health professionals (e.g. doctors, nurses, lab technicians) • Administrative staff • Support staff (e.g. cleaners)
			Patients	***Direct costs to patients and their families***	• Out-of-pocket expenditure (including co-payments) for consultation, drugs, treatment etc • Cost of travel for treatment • Paid caregivers
				Lost productivity: time costs to patients and their families	• Patient's time spent for travel and receiving treatment • Lost time at paid and unpaid work (e.g. housework) by patient and family caring for the patient

Source: adapted from Canadian Agency for Drugs and Technologies in Health (2006). Guidelines for the Economic Evaluation of Health Technologies: Canada, 3rd Edition.

Notes: The classification system in the table excludes some (indirect) time costs to patients and families caring for them. Lost leisure time is usually not considered to be a cost. The costs to private insurers (i.e. insurance premiums received from, and benefits paid to, patients) have been included as a direct cost to the patient. These amounts can usually be assumed to cancel out, unless there is a good reason to do otherwise

Research costs are typically excluded from the analysis. However, any resources that are donated to provide the health interventions (such as from a donor agency) should be included. Community (including in-kind) contributions may also be relevant, though this will depend on the perspective of the analysis.

Double counting of costs should be avoided. For example, if the user fees paid by the patient are included in the costing then it is also necessary to exclude the revenue from user fees received by the health care provider.

The health intervention may generate some ***resource savings,*** which could be included in the analysis. For example, a health intervention providing insecticide treated bed-nets to prevent malaria should reduce the number of cases of malaria that would need to be treated and generate resource savings for the health sector providers and for the households and communities. Another example is the potential saving resulting from the reduction in inappropriate prescription of ACTs as a results of increased use of rapid diagnostic tests. The resource savings associated with a health intervention depend on the potential reduction in health service use, such as measured by the difference in the absolute number of clinic visits to the local health centres. It can be challenging to estimate resource savings and for this reason the analyst may opt not to include them, or only take them into consideration in a secondary analysis.

The ***cost classifications*** outlined in the previous table are predominately by input category, though it is also possible to classify costs by the intervention activity (e.g. administration, planning, and supervision) or organizational level (e.g. national, district, hospital). The choice of classification system will vary by context. The decision is largely a practical one, though it is important to ensure that all relevant costs are included and that the classification categories do not overlap. In selecting an approach it may be useful to consider the data sources and any existing systems employed to account for resource utilization and their associated costs. For example, in those situations where the health intervention is managed and implemented by activity it may be appropriate to use an activity-based costing approach. In other scenarios, such as when using facility records and accounting data, it may be easier to categorize costs by the department utilizing the resources (e.g. maternity ward, pharmacy, administration etc). Further guidance from the WHO on the types of activities that may be incurred by the provider of the health intervention at the central level is in Annex A.

EXAMPLE: Cost categories used in a cost-effectiveness study of malaria drug combinations

Cost perspective	Cost Category	Item
Provider / Hospital	*Recurrent costs*	Drugs
		Staff salaries
		Rental of building
		Utilities
		Consumables
	Capital costs	Microscope
Patient and family	*Direct costs*	Medication
		Hospital fees
		Transportation
		Miscellaneous
	Indirect costs	Time spent at hospital
		Time spent travelling to hospital
		Time spent caring for sick child at home

Source: Taken from Wiseman, Kim et al (2006).

3.2 What is the perspective for the cost analysis?

The perspective of the analysis determines which costs should be included in the evaluation. Specifying the perspective is important because an item may be a cost from one viewpoint, but not from another. For example, a patient's travel costs may be a cost from the patient's perspective and from a societal perspective, but not from a health sector perspective. Possible perspectives include: ministry of health, other government ministries, public sector, the health sector, patient or the whole of society. The table of different types of cost in Section 3.1 is organized by costing perspective.

Many economic evaluations are undertaken from the perspective of the health service provider, though given its foundations in welfare economics, health economists argue that where possible an evaluation should consider the impact of an intervention on society, not only on the individuals and organizations directly involved. The choice of perspective often depends on the target audience for the study, data available and practical constraints (such as in estimating the productivity losses associated with a health intervention).

EXAMPLE: Costing from a societal perspective in an evaluation of ITNs in Tanzania

"The cost-effectiveness analysis included project implementation costs (donor and provider perspective), user contributions (payments for nets and insecticide), travel and time costs incurred by users in connection with the purchasing of nets, and in-kind community contributions to the running of the distribution system. All research costs were excluded. The project implementation costs included the cost of initial set-up activities and the costs associated with the supply of nets, including the establishment of distribution channels, product promotion and publicity, training and distribution."

Taken from Hanson, Kikumbih et al (2003).

3.3 Is it reasonable to exclude any costs?

Sometimes, largely for pragmatic reasons, it is possible to exclude some costs from the analysis. However, any exclusion needs to be carefully justified to ensure that they would not affect validity of the study results. It may be possible to justify excluding costs for the following reasons:

- If the programme is restricted to the interventions immediately under study, any costs that are identical to both need not be considered as they will not affect the choice between

programmes. The elimination of these costs can save a considerable amount of work, though it may limit the broader comparability of the results.

- If the consideration of some costs are expected to merely confirm a result that might be obtained from considering a narrower range of results.
- If the costs are small and unlikely to make any difference to the study result, while would take considerable time and effort to collect them.

4. MEASURING AND VALUING COSTS

Household costs

Collection of data on costs incurred by patients and their families, is usually done through interview with patients or their carer's, asking about direct costs and time spent, as in the example above. If this is done only at the time of a consultation, the estimate of costs will be limited to those up until the point of consultation. To measure the full impact of correct targeting or increased access to ACTs, some ACT consortium studies, should ideally collect both effectiveness and household costs 4 (or 2) weeks after an initial consultation. The collection of household costs is described in the Guidance Note to Household Costs with an example questionnaire. The core ACT consortium core staff will be happy to help in the design and analysis in individual studies.

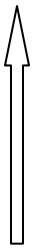
Provider costs

Once the relevant range of costs has been identified, the individual items must be measured and valued. This involves two elements: ***measurement of the quantities of resource use*** and the ***assignment of unit costs or price weights***. Typically the resources will be amounts of labour input, use of bed days or medicines obtained, but may also include patients' or carers' time. Market prices are usually used to assign a value to many of the resource items; though where they are not available other techniques need to be employed. This section provides more detail on these issues.

4.1 How accurate does the costing have to be?

Analysts need to make a judgement about how accurate or precise cost estimates need to be within a given study. For example, there are different levels of precision in health facility costing, with the least precise estimates based on average per diems (or daily costs) and the most precise based on micro-costing.

Figure X: Levels of precision in health facility costing

Most precise 	Micro-costing:	Each component of resource use (for example, laboratory tests, days of stay by ward, drugs) is estimated and a unit cost derived for each.
	Case-mix group:	Give the cost for each category of case or hospital patient. Takes account of length of stay. Precision depends on the level of detail in specifying the types of cases.
	Disease-specific per diem (or daily cost)	Gives the average daily cost for treatment in each disease category. These costs may still be quite broad (for example, orthopaedic surgery).
Least precise	Average per diem (or daily cost).	Averages the per diem over all categories of patient. Available in most health care systems.

Source: Drummond, Sculpher et al (2005)

In some countries national tariffs are available and an accepted source of unit cost data for costing health service use. For example, the UK National Health Service publishes reference cost data that can be used to assign values. For studies in developing countries the WHO lists regional and some country specific prices that can be used for cost analysis and additional guidance such as on the assumptions on resource use for programme costs of health interventions (see http://www.who.int/choice/costs/en/).

Measuring and valuing costs at the patient level provides the most accurate estimates, and enables the analyst to complete more sophisticated cost analysis, though this level of data is more time consuming and expensive to collect. The choice of whether to assign national costs, centre-specific or intervention-specific costs for each cost category is a judgement for the analyst. There may be some concerns about the accuracy of national unit costs, and centre-specific or intervention-specific costs may be a more precise estimate of the costs incurred in the study. It may also be important to take into account some interaction between cost and service use.

The decision of whether to undertake detailed costing is likely to depend on the ease with which unit costs can be collected and quantitative importance of each cost category in the evaluation, taking into account the estimation of resource quantities and the unit cost of those resources. In other words, some costs will be straightforward to collect (e.g. direct costs of the intervention) while others are more challenging (e.g. cost of a hospital stay or the expected resource savings associated with the intervention). Moreover, efforts should be focused on collecting unit cost data for those costs that are likely to have a substantial impact on the results.

EXAMPLE: WHO-CHOICE Costs and Prices

The WHO publishes information on the cost per hospital stay by hospital level, outpatient visits, and cost of outpatient visits at different population coverage levels. Country specific costs are provided for unit cost per hospital stay by hospital type, hospital outpatient visits by hospital type, and health centres at different population coverage levels.

Example of Hospital Costs (2005 prices)

Country	*Facility type*	*Unit cost per bed day*		*Unit cost per outpatient visit*	
		US $	*Local currency*	*US $*	*Local currency*
Ghana	Primary hospital	15.00	4.32	4.05	1.17
	Secondary hospital	19.57	5.63	5.74	1.65
	Tertiary hospital	26.72	7.70	8.50	2.45

Example of Health Centre Costs (2005 prices)

Country	*Population coverage*	*Unit cost per visit at health centre by population coverage for 20 minute visit*	
		US $	*Local currency*
Ghana	50%	6.95	1.89
	80%	7.08	2.04
	95%	10.65	3.07

Notes: public facility, at different population coverage, excludes drugs and diagnostics
The WHO-CHOICE website also provides data on prices for programme cost inputs under the following headings: personnel costs, media and information, education and communication (IEC) operating costs, transportation operating costs, utilities, other costs, building capital costs, and transportation capital costs. Additional unit costs are provided for a variety of tradable goods, such as vehicles, furniture and stationery, along with suggested useful lives for capital goods. Further information can be obtained from http://www.who.int/choice/costs/en/.

4.2 How to measure quantities of resources used?

The measurement of resource quantities often depends on the context for the economic evaluation and the nature of the resource. For example, if an economic study is being conducted alongside a clinical trial, data on resource quantities may be collected on the case report forms. On the other hand, if the economic study is free standing, resource quantities may be estimated by a review of patients charts, case notes, or from routine data systems such as hospital records. The quantities of some resources may be estimated by asking patients to report their use or costs incurred.

The unit of measurement depends on the nature of the resource being measured, and usually applies a large degree of common sense. For example, it would be appropriate to measure the number of outpatient visits, the length of inpatient stay in days, the amount of time of a health workers involved in implementing the health intervention, and so on. For some items the resource use may be collected in monetary terms. For example, it is usually simpler and more accurate to obtain for the annual costs of electricity or water directly from bills.

A number of methods can be used to assess the time that health professionals spend providing care. These include time and motion, work or activity sampling, logging and historical average. These methods may involve observation, beeper-prompted recording or self reporting. Each method has its strengths and weaknesses, in terms of accuracy, cost, convenience, and ease of observation.

METHODS: Measuring time spent providing care: time and motion studies

Time and motion studies are the most commonly used method for measuring the time spent by health professional providing care. The steps involved are: i) identify and define each activity (e.g. clinic visit made by patient); ii) define a time standard for each service by observer measurement, self measurement, self estimation via recall (e.g. minutes per visit, reported by provider) and; iii) define a measurement of frequency for each service (e.g. number of visits per day). Additional steps include identifying the supplies and equipment used by each service, and the corresponding fixed and variable costs.

Sample size estimation of time and motion estimates are often based on the desired precision of the mean for the time estimates. For example, the analyst may be primarily interested in the mean time for an activity or determining whether the mean time for one activity differs from that of another. Other methodological issues include accounting for patient variability, identifying boundaries between activities, establishing rules for how to count time when an activity starts and stops and also for when providers perform multiple activities at the same time.

4.3 How are values assigned for the unit costs?

4.3.1 Financial costs and economic costs

Economists define a cost as the value of resources used to produce a good or service, though the way these resources are valued can differ. There are two main approaches to costing: financial costs and economic costs. Financial costs represent the actual monetary flows on goods and services purchased. Costs are described in terms of how much money has been paid for the resources used by the project or service. Economic costs recognize that the cost of using resources also means that these resources are then unavailable for productive use elsewhere.

There are three main ways in which economic costs differ from financial costs: economic costs include the estimated value of donated goods or services; capture the cost of a good when the price does not reflect the cost of using it productively elsewhere; and allow for people's preferences for receiving goods and services now rather than later.

4.3.2 Valuing market items

For many items it will be possible to assign a unit cost using market prices. For example, market prices should be available for the cost of obtaining equipment, or the cost of medicines. Gross salaries (including all benefits and employer costs) are typically used to determine the cost of health worker inputs, with the cost calculated based on the proportion of time associated with the intervention.

4.3.3 Valuing non-market items and productivity losses

A key non-market resource input to health interventions is the time (including travel time) of patients (and their families) to access the health intervention. For salaried individuals one approach to the valuation is to use market wage rates, and adjust for the period of time utilized. For non-salaried workers or volunteers it is possible to use unskilled market wage rates.

The market value of leisure time is harder to assess. However, in the base case, the most common practice is to value leisure time at zero.

Although these approaches are frequently used, some concerns have been highlighted. For example, productivity losses are usually estimated using gross earnings of those in employment, and some studies impute an equivalent value for non-salaried workers (such as subsistence farmers or homemakers). However, it can be argued that these valuations over-estimate the

costs because losses in production could be compensated by colleagues or household members. Given the challenges in valuing the lost productivity, especially in a developing country context where many of the individuals will be non-salaried workers, productivity losses may not be included in the primarily analysis.

Further guidance on the valuation of market and non-market items in a developing country context can be found in: Hutton G, Baltussen R Cost valuation in resource-poor settings. *Health Policy and Planning* 2005;20(4):252-259.

4.4 How should shared (or overhead) costs be handled?

The term overhead costs refer to those resources that serve many different departments and programmes, and include, for example, the costs of general hospital administration. If individual interventions are to be costed then these shared costs need to be attributed to the interventions. There is no single method for doing this, though often the approach is to allocate overheads on a basis that is judged to be related to the usage of the overhead item.

One method for allocating the costs incurred in the delivery of health services is step-down cost accounting. This approach involves identifying the range of line item costs, allocating them to a variety of cost centres. The cost centres include indirect costs such as administration, intermediate costs such a pharmaceutical or laboratory services as well as final costs centres, such as the maternity ward or outpatients department. Each of the costs of indirect and intermediate cost centres are then reallocated to the final cost centres to generate a total cost and a unit cost.

Further details are provided in the box below and in the paper: Conteh L, Walker D. Cost and unit cost calculations using step-down accounting. *Health Policy and Planning* 2004;19(2):127-135.

METHODS: Six stages of step-down cost accounting

The method of step-down cost accounting should be approached in these six stages.

1. Define the purpose of the cost analysis and determine which services or departments are to be assigned unit costs

2. Define cost centres (those that correspond to the existing organizational structure of the health facility's accounting methods often facilitate data collection, analysis and presentation). Three levels of cost centres are usually identified:

- *Final (or direct) cost centres*: end-points of the production line that deliver services to clients and beneficiaries (e.g. maternity ward; outpatients department; paediatrics ward)
- *Intermediate cost centres*: diagnostic and departmental support to the final level: e.g. pharmacy; laboratory
- *Indirect cost centres*: general services, mostly related to overheads: e.g. admin; transport;

3. **Identify and then group all individual line items.**

Grouped Line Items	*Line Items*
Personnel costs	*Salaries; Overtime and pensions; Travel and subsistence; Accommodation*
Administrative costs	*Insurance; Telephone/fax charges; Electricity/water charges; Office supplies*
Transport costs	*Vehicles; Maintenance and servicing; Fuels*
Pharmacy costs	*Drugs; Storage and handling costs*
Laboratory costs	*Laboratory equipment; Laboratory supplies*

4. Assign inputs to cost centres

Sources of information on resource utilization and cost in a health facility include management and administration records, such as on staff allocation, pay scales and other benefits, drug and supplies management, vehicle log books, and other hospital records. Personnel costs should be assigned to the different cost centres depending on the activities of the different staff. Where some staff may be assigned to a single cost centre (e.g. a driver to transport costs) others may have responsibilities that should be assigned to more than one (e.g. nursing staff may work on more than ward).

5. Allocate all costs to final cost centres

The costs allocated to indirect and intermediate cost centres, now need to be allocated to the final cost centres. The basis upon which the costs are reallocated will depend on the nature of the cost. For example days of care may be used to allocate catering costs, while the floor area may be used to allocate cleaning costs. The totals for each of the indirect and intermediate cost centres are in turn reallocated to the other cost centres, until the only the final cost centres remain. Annex B presents an example of step-down cost accounting taken from a paper by Conteh and Walker (2004).

6. Compute total and unit costs for each final cost centre

Total costs for each final cost centre are determined by the step-down cost accounting. To calculate the unit cost, activity data is required that provides a measure of units of service. For example, the cost per hospital inpatient can be measured by the length of stay in bed-days and the cost per outpatient can be measured by the number of visits. The unit cost calculations are then:

Final cost centre	*Total costs ($)*	*Unit of service*	*Units of activity data*	*Unit cost ($)*
Maternity ward	3685	Day	350	$10.53 per bed day
Outpatients	4281	Visit	1500	$2.85 per visit
Paediatric ward	2700	Day	400	$6.75 per bed day

Source: Conteh and Walker (2004).

4.5 How should capital outlays be handled?

Capital costs are the financial costs to purchase the major capital assets required by the programme: generally equipment, buildings, and land. Capital costs differ from operating costs in that they represent investments at a single point in time, often at the beginning of an intervention. Capital costs represent an investment in an asset that is used over time. Most assets, such as equipment and buildings, depreciate with time. On the other hand, land tends to maintain its value.

In an economic evaluation there are several methods of measuring and valuing capital costs, and the preferred method is to annuitize the initial capital outlay over the useful life of the asset and calculate the equivalent annual cost (E).

METHODS: How to annuitize capital costs to derive the equivalent annual cost

If the capital outlay is K, we need to find the annual sum E which over a period of n years (the estimated life of the asset), at an interest rate of r, will be equivalent to K. The approach can be generalized to include the situation where the equipment of buildings have a resale value at the end of the intervention, such that

$$E = \frac{K - \left(S/(1+r)^n\right)}{A(n, r)}$$

where:
E = equivalent annual cost
K = purchase price / initial outlay
S = resale value
n = the useful life of the asset
r = discount (interest) rate

and *A(n, r)* is the annuity factor and given by: $\frac{1-(1+r)^{-n}}{r}$

For new equipment this method can be applied unambiguously, while for old equipment the recommended approach it to use the replacement cost of the equipment.

In determining the useful life and resale value of an asset (n and S) it may important to make a distinction between the physical life of a piece of equipment and its useful clinical life (which is depends on technological change).

In choosing a discount rate, r, analysts have typically chosen one of two conventions. In some countries, including the UK, the government announces a common discount rate for all public sector projects. Alternatively, where there is no announced rate, the convention has been to use a rate consistent with the existing literature, and a 3% discount rate has been the de facto convention for health economic evaluation.

Source: Glick, Doshi et al (2007).

EXAMPLE: Annutizing the cost of vehicle in a cost-effectiveness study of ITNs in Kenya

A cost-effectiveness study of ITNs in Kenya involved the purchase of four vehicles, each costing US $20,000 (in 1996 prices). The cost of vehicles (a total of US$ 80,000) was annuitized over an expected life of 10 years and at a discount rate of 3%. The resale value was assumed to be zero.

Using the formula above the annual economic cost was calculated to be $9,378 (in 1996 prices)

$$A = \frac{1-(1+0.03)^{-10}}{0.03} = 8.5302$$

$$E = \frac{80000}{8.5302} = 9378$$

where K = 80,000; n =10; r = 0.03; S = 0

Source: Adapted from Wiseman, Hawley et al (2003)

Further details on annualization of costs can be found in Walker, Damian and Lilani Kumaranayake (2002). "Allowing for differential timing in cost analyses: discounting and annualization". *Health Policy and Planning*; 17(1): 112-118.

4.6 When and how to adjust costs to account for timing differences?

When costs and effects are incurred at substantially different times it is necessary to account for differences in timing. The two main adjustments relate to inflation for cost and time preference for cost and effect. ***Inflation*** refers to the general upward price movement of goods and services over time. Inflation becomes important when comparing costs measured in monetary units through time. Without adjusting for inflation it would not be possible to determine whether an increase in costs represents an increase in the real resources used or a decline in the value of the money those costs are measured in. ***Time preference (or discounting)*** refers to a differential valuation of a good or service depending on when the good or service is consumed). Individuals are assumed to have a positive rate of time preference, which means a preference to benefits today rather than in the future. This is based on the assumption that individuals have a short-term view, the future is uncertain and they consider given amount has a higher value today than it would at some time in the future

The presence of inflation and time preference indicate that costs and effects in different time periods are not directly comparable. Comparison requires converting to a common time period. It is necessary to adjust for inflation of the unit costs are from different points in time, but not if they are from a constant time period. It is necessary to discount costs and effects to take into account time preference if patient follow-up extends beyond one year. The table below summarizes when it is necessary to adjust for inflation and discount costs.

METHODS: When to adjust for inflation and discount costs

Unit cost	**Per patient follow-up**	
	Less than 1 year	**More than 1 year**
Constant	Do not adjust for inflation; Do not discount	Do not adjust for inflation; Discount
Time varying	Adjust for inflation; Do not discount	Adjust for inflation; Discount

Source: Glick, Doshi et al (2007)

Having determined the year at which costs and prices will be reported, prices from earlier or later years need to be adjusted using an inflation adjustment factor. An example is provided and the following paper provides further guidance: Kumaranayake, Liliani (2000). "How to do (and not to do)… The real and the nominal? Making inflationary adjustments to cost and other economic data". *Health Policy and Planning*; 15(2): 230-234.

EXAMPLE: How to adjust for inflation

Suppose the selected base year is 2007. The unit cost per bed day is $15.00 (at 2005 prices) and inflation was 4% in 2005 and 6% in 2006. The unit cost per bed day in 2007 prices is obtained by multiplying the unit cost by an inflation adjustment factor for each year (1.04 for 2005 and 1.06 for 2006). The resulting unit cost is: $16.536 (= 15 * 1.04 * 1.06).

Similarly, unit cost data from later years needs to be deflated to 2007 prices. Suppose the unit cost per visit in 2008 prices of $8.00 and inflation in 2008 was 5%. The unit cost per visit in 2007 is $7.60 (=8.00 * 0.95).

The method for discounting is similar to the adjustments made for inflation. Discounting at the rate of 3% involves dividing the values for future years by successive powers of 1.03. With the start at year 1, that means dividing values in year 2 by 1.03, in year 3 by 1.03^2 (or 1.0609), in year 4 by 1.03^3 (or 1.092727), and so on.

Further details on discounting are given in the box below and in the paper: Walker D, Kumaranayake L. Allowing for differential timing in cost analyses: discounting and annualization. *Health Policy and Planning* 2002;17(1):112-118.

METHODS: How to discount costs

The present value of future costs is achieved by discounting future costs, using an annual interest (or discount) rate:

$$P = \sum_t \frac{F_t}{(1+r)^{(t-1)}}$$

where:

P = present value

Ft = future cost at year t

r = discount rate (or inflation rate)

This assumes that all costs are incurred at the beginning of each year, such that the costs of year 1 do not need to be discounted.

Example: Programme A is a 3-year intervention that incurs $5000 in costs in year 1, $10,000 in year 2 and $15,000 in year 3. A discount rate of 5% is used to adjust future costs. The present value of the future costs is equal to $28,129:

$$P = 5000 + \frac{10000}{(1+0.05)^1} + \frac{15000}{(1+0.05)^2} = 28129$$

where F_1 = 5,000, F_2 = 10,000, F_3 = 15,000, r = 0.05, t = 3

4.7 What is the difference between average cost and marginal cost?

The importance of the distinction between average cost and marginal cost is apparent when examining the effects on costs of small changes in output as it is likely that these will differ from average cost. For example, the extra cost of keeping patients in hospital for another day at the end of their treatment might be less than the average daily cost for the whole stay (and accordingly the resource savings from a reduction in one day's stay are usually lower than the average daily cost).

While it is important to acknowledge the difference between marginal and average costs (or savings), in practice this issue can only really be explored in the context of specific locations or

situations. For example, it is likely the marginal cost will depend on the extent to which there is spare capacity (infrastructure, equipment or staff) that can be readily utilized.

METHODS: Various definitions of cost

Total cost (TC)	= cost of producing a particular quantity of output
Fixed cost (FC)	= costs which do not vary with the quantity of output in the short run (about a year). That is, costs which vary with time rather than quantity. For example, rent, equipment lease payments, some wages and salaries.
Variable cost (VC)	= costs which vary with the level of output, for example, supplies food, fees for service
Cost function (TC)	= f(Q), total cost as a function of quantity
Average cost (AC)	= TC/Q the average cost per unit of output
Marginal cost (MC)	= the extra cost of producing one extra unit of output = (TC of x+1 units) – (TC of x units) = d(TC)/dQ evaluated at x

Source: Drummond, Sculpher et al (2005)

5. MEASURING AND VALUING HEALTH EFFECTS

The use of cost-effectiveness analysis for prioritizing resource allocation across health interventions requires the health effects to be represented in common units in order to facilitate comparisons across interventions, diseases or conditions. This section provides a brief overview of some of the issues in measuring and valuing health effects.

5.1 Health effects: outcomes and utilization

Analyses typically start with a health effect measured in a natural unit, such as cases treated or deaths averted. All interventions that avert death for a population of a given age are comparable, though where lives are saved at different ages then the measure should account for the difference in years of life saved. In selecting an outcome measure a key issues to consider is whether the measure is relevant given the objectives of the study and the policy context.

To identify health effects it can be useful to describe the clinical path following the intervention. For example, the final outcome for an intervention that seeks to improve the performance of those providing of ACTs may be cases of severe malaria averted or deaths averted. However, it may not be possible to measure these accurately and therefore more appropriate to consider some of the intermediate outcomes including: cases of fever treated with ACT, cases of malaria (with confirmed clinical diagnosis) treated with ACT, cases that receive correct dosage of ACT, and cases that report adherence to ACT treatment course.

5.2 DALYs: a measure for mortality and morbidity

Another measure for health effects that enables comparison across interventions is the disability-adjusted life year (DALY). This measure was introduced by the WHO and World Bank and incorporates assumptions about the severity of nonfatal conditions, age at incidence or intervention, duration with and within intervention, and remaining life expectancy at that age.

Health interventions are intended to reduce disability adjusted life years (DALYs) and are the sum of years of life lost and years lived with disability. Or in a more formal definition: the present value of future lifetime lost through premature mortality and the present value of future lifetime adjusted for average severity (frequency and intensity) of any mental or physical disability caused by a disease or injury.

Some ACT Consortium studies may estimate the impact of the intervention in terms of DALYs by using modelling techniques (see section 6.3).

5.3 Discounting health effects

As with costs, health effects followed for more than one year need to be discounted to take into account time preferences (see section 4.6 for an explanation of time preference).

6. ANALYZING AND REPORTING COST-EFFECTIVENESS

6.1 Analyzing and reporting costs

6.1.1 Presenting financial and economic costs

The summary financial and economic costs of the intervention(s) and its comparator(s) often highlight the main cost drivers. As discussed in section 4.3.1, financial costs cover actual expenditure while economic costs represent the value or opportunity cost of all resources used. The following example shows the presentation of the financial and economic costs in a paper reporting on the cost-effectiveness of ITNs in Kenya.

EXAMPLE: Financial and Economic Costs (1996 prices)

The financial costs present the actual expenditure at the time it was incurred and adjusted to 1996 prices. Economic costs were calculated by annualizing capital costs on the basis of a 3% discount rate. It was assumed that vehicles had a useful life of 10 years and ITNs had a useful life of 5 years.

	Total financial cost				Average annual economic cost
	1996	**1997**	**1998**	**1999**	
Programme Capital Costs					
Vehicles (4)	80,000	0	0	0	9,378
Equipment	10,000	0	0	0	1,172
ITNs	92,000	138,000	0	0	60,193
Programme Recurrent Costs					
Insecticide	0	22,080	33,120	0	13,707
Staff	25,000	60,000	80,000	60,000	31,311
Fuel/maintenance	10,000	15,000	24,000	20,000	16,805
Office rental	1,000	1,000	1,500	1,000	1,100
Training	5,000	5,000	0	0	2,479
Supplies	10,000	10,000	12,000	10,000	10,266
User/community Recurrent Costs					
Water					845
Transport					500
Time/Labour					1,100
TOTAL	**233,000**	**251,080**	**150,620**	**91,000**	**148,856**

Source: Adapted from Wiseman, Hawley et al. (2003).

6.1.2 Estimating resource savings

Some interventions may generate resource savings which ought to be taken into account in the cost analysis. For example, interventions may reduce the number of children falling sick and reduce the number or length of visits to the health facilities. The assumption underlying an estimation of resource savings should be clearly stated and based on the evidence from the study or the wider literature. The resource savings may be achieved by both the provider and the user.

EXAMPLE: Resource savings from ITNs

ITNs were associated with a 27% reduction in the number of sick child (less than 5 years) visits to local health facilities. This translates to an annual reduction of 2,025 visits per year in a study population of 9,375 children less than 5 years old. The reduced number of clinic visits results in an annual saving to the health services of US $891 (based on US $ 0.44 per visit).

Also households in the village spent approximately US $6.50 per year less on health care for sick children under five years compared with those in control villages. There were approximately 6,700 households in the study sites with children under five years, which represents a cost saving of US $43,550.

Source: Adapted from Wiseman, Hawley et al. (2003).

6.2 Incremental cost-effectiveness ratio (ICER)

The results of cost-effectiveness analysis (and cost utility analysis) are usually presented as an incremental ratio showing the difference in cost over the difference in effect (or utility) between two alternatives.

$$\text{ICER} = \frac{\text{Difference in cost}}{\text{Difference in effect}} = \frac{(\text{Mean cost}_{\text{Intervention}} - \text{Mean cost}_{\text{Control}})}{(\text{Mean effect}_{\text{Intervention}} - \text{Mean effect}_{\text{Control}})}$$

The incremental cost effectiveness ratio shows the cost-effectiveness of an intervention in comparison to a control, which often represents either current practice or no intervention. For instance, the following example which considers the incremental cost-effectiveness of two community-based interventions designed to improve the access to artemisinin combination therapies are both compared to no intervention.

EXAMPLE: Cost of increasing access to ACTs in Cambodia

The cost-effectiveness of two community-based interventions intended to improve access to ACTs in Cambodia were evaluated: malaria outreach teams and village malaria workers. The comparator was no community based intervention (which has zero cost and has zero effect). The table shows the basic annual fixed cost of two interventions and two effectiveness measures: i) number of cases seen and tested and ii) number of cases treated.

	Malaria Outreach Team	Village Malaria Workers
Effects		
Population	19,029	100,000
Number seen and tested	3,152	57,360
Number of P. falciparum cases treated	658	13,407
Intervention costs		
Personnel	*5,422*	*20,270*
Transport	*2,224*	*37,850*
Other	*739*	*10,738*
Total basic annual cost of intervention	8,385	68,858
ICER (compared to no community based intervention)		
ICER per patient seen and tested	$2.66	$1.20
ICER per P. falciparum patient treated	$12.74	$5.14

The results of the incremental cost effectiveness analysis show that the village malaria workers scheme achieved a relatively higher coverage that the malaria outreach team and the annual fixed cost per patient treated was substantially lower at $5.14 compared to $12.74 per falciparum malaria patient treated. Further details of the results are reported in the paper by Yeung et al (2008)

Source: Adapted from Yeung S, Van Damme W, et al (2008).

6.3 Using modelling to extend the study scope or timeframe

Decision analytic modelling is an additional method used in economic evaluation and provides a framework for comparing different scenarios or interventions. Unlike the cost-effectiveness methods described in this note, which rely the collection of study-specific cost and effect data, the method is able to synthesize data from a variety of sources and consider the cost-effectiveness over a longer time horizon or scope of the study. Decision analytic modelling can therefore be used to supplement the cost-effectiveness analysis using patient level data to consider the likely cost-effectiveness of the intervention beyond the implementation period. This can be useful where the appropriate time horizon for the cost-effectiveness analysis extends beyond the project, such as when the cost and effect implications of an intervention have an impact over the patient's lifetime. In other words, an important role of decision models is to bridge the gap between what has been observed in trials and what would be expected to happen in terms of costs and effects over a long-term time horizon. Another application of decision analytic modelling is to estimate the likely impact on final health outcomes (such as life-years or DALYs) by extrapolating from intermediate natural health outcomes (such as cases treated).

A full description of the approach can be obtained from: Drummond MF, Sculpher MJ, Torrance GW, O'Brien B, Stoddart GL. *Methods of Economic Evaluation of Health Care Programmes. Third Edition.* 2005 Oxford, Oxford University Press or Briggs A, Claxton K, Schulpher M. *Decision Modelling for Health Economic Evaluation*. 2006 Oxford, Oxford University Press.

EXAMPLE: Modelling the impact on final health outcomes

In a study on the cost-effectiveness of improving malaria home management by training shopkeepers in rural Kenya measured the number of cases appropriately treated as the health effect of the intervention. However the use of this measure rather than final health outcomes prevented the comparison of the cost-effectiveness with a broader range of interventions for malaria treatment and prevention and other health needs. To overcome this shortcoming Goodman et al. developed a simple model to make estimates of the cost per DALY averted. The model is based on a simple decision tree which calculates the probability of death for a child with fever for whom treatment is first sought from a shop, with and without the intervention.

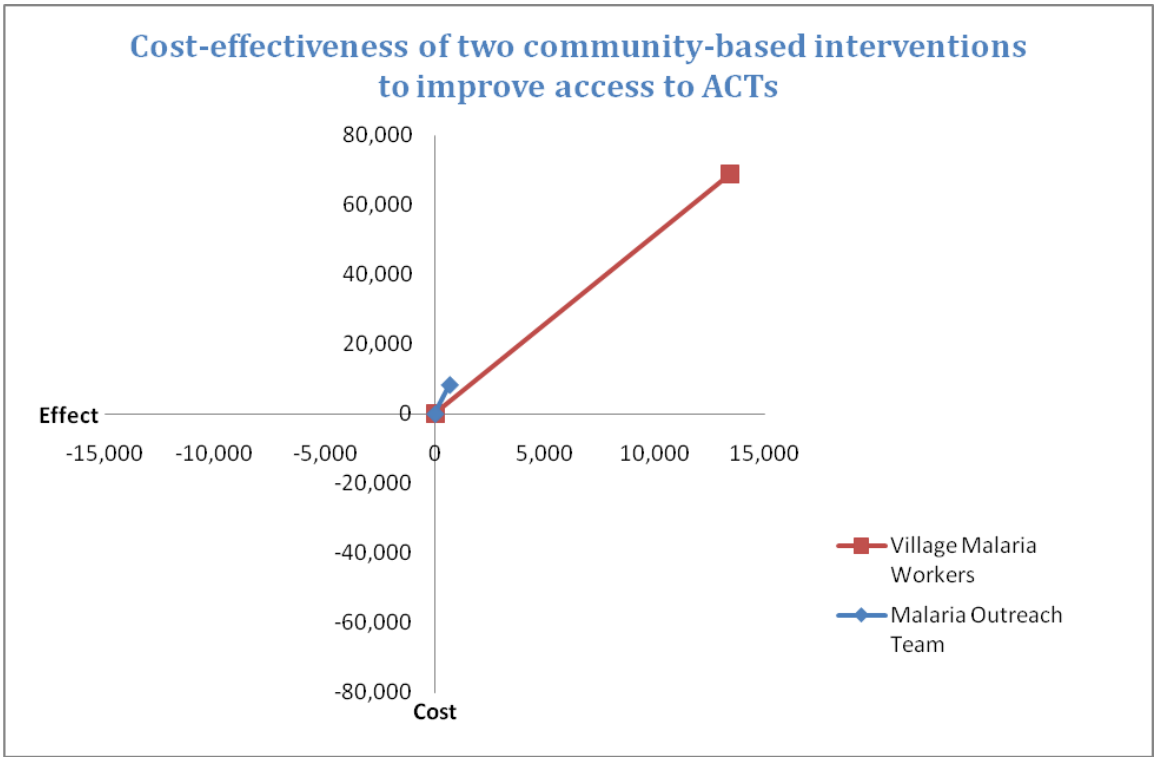
Further details of the method are provided in Goodman CA, Mutemi WM, Willetts, Marsh V. The cost-effectiveness of improving malaria home management: shopkeeper training in rural Kenya. Health Policy and Planning 2006; 21(4):275-288.

Source: Adapted from Goodman, Mutemi et al (2006)

6.4 Presenting results: using the cost-effectiveness plane

The results of a cost-effectiveness analysis can be presented on cost-effectiveness plane. As presented in the introduction (see section 1.5) the cost-effectiveness plane is two dimensional, with a horizontal axis for the difference in effect of the intervention and a vertical axis for the difference in cost of the intervention. The control or comparator is located at the origin. The interventions are plotted on the graph corresponding to the cost and effect. The top left quadrant shows interventions that are more costly and less effective that the comparator. In this case, the intervention is said to be dominated by the control. The bottom right quadrant shows interventions that are more effective and less costly that the comparator, in which case the intervention dominates. In the top right the new intervention is more effective and more costly, and in the bottom left the new intervention is less effective and less costly. In these last two scenarios the decision on whether to adopt the new intervention depends on a value judgement relating to the maximum cost-effectiveness ratio that the government is willing to accept.

The figure below graphically illustrates the results from the study by Yeung, Van Damme et al (2008). It can be seen that the two interventions evaluated were more effective and more costly that having no intervention. Of the two the village malaria workers scheme was relatively more cost-effective, and this is illustrated by the slope of the line between the origin and point, which is less steep. It can also be seen that the village malaria workers scheme was implemented on a larger scale than the malaria outreach team.



Source: Adapted from Yeung, Van Damme et al (2008).

6.5 Interpreting cost-effectiveness evidence

The results of cost-effectiveness analysis should be report sufficient information to enable the independent analyst to critically appraise the estimates of the costs and effectiveness studied. In addition, they should be able to interpret the findings and assess the extent to which the results can be generalizable beyond the study setting.

A cost-effectiveness report usually contains, or indicates sources for, a detailed description of the inputs and methods used to estimate costs, effectiveness and cost-effectiveness ratios for the interventions studied.

EXAMPLE: Checklist for reporting the results of economic evaluations

1. The background (importance) of the question (problem)
2. The viewpoint for the analysis
3. The reasons for selecting a particular form of analysis
4. The (patient) population to which the analysis applies
5. The comparators being assessed
6. The source of the medical evidence and its quality
7. The range of costs considered and their measurement (in physical and money terms)
8. The measure of benefit in the economic study (e.g. life years gained)
9. The methods for dealing adjusting for timing of costs and benefits
10. The methods for dealing with uncertainty
11. The incremental analysis of costs and benefits
12. The overall results of the study and its limitations

Source: Drummond, Sculpher et al (2005)

The incremental cost effectiveness ratio and the cost effectiveness plane both present the results of the evaluation. In some cases the new intervention will be unambiguously better (i.e. more effective and less costly) or worse (i.e. more costly and less effective) than the comparator. It is, however, more likely that the new intervention is more effective but also more costly than the alternative. The challenge is then for those involved in making resource allocation decisions to interpret the findings.

In an ideal world, all possible health interventions would have been evaluated. The interventions could then be ranked on the basis of their cost-effectiveness (using a common utility-based measure for effectiveness) to create a league table. The economist would then argue that the interventions should be selected in accordance with their cost-effectiveness until the finite financial health resources had been spent.

In practice not all interventions have been evaluated, different measures for cost-effectiveness have been used and the studies may not be directly comparable for other reasons, such as having applied different costing perspectives. To facilitate comparison many countries have applied a cost-effectiveness threshold to compare the results of each study against a cost-effectiveness ratio that has been deemed the maximum that they would be willing to accept. For example, in England the National Institute for Health and Clinical Excellence (NICE) which provides guidance on National Health Service provision is understood to use a cost-effectiveness threshold of between £20,000 and £30,000 per quality-adjusted life-year. The WHO provides cost-effectiveness thresholds for different developing country regions and uses the country's gross domestic product (GDP) per capita as a benchmark (http://www.who.int/choice/costs/CER_thresholds/en/index.html) . Those interventions that have ICERs of less than 3 times the GDP per capita are considered cost-effective, with ICERs less than GDP per capita very cost effective. Thus, any interventions whose ICER is greater than 3 times the GDP per capita threshold is considered not cost-effective.

7. ANALYZING VARIABILITY AND UNCERTAINTY

In addition to presenting the cost-effectiveness ratio it is useful to examine the variability and uncertainty around the cost-effectiveness results. Variability is concerned with situations where parameters may vary systematically between recipients or locations. Uncertainty refers to those situations where an input is not known precisely and can, at least in principle, be characterized as a random variable.

7.1 Analyzing Variability

The variability in the cost effectiveness analysis can be analyzed by considering the results for sub-groups of the population. This sub-group cost-effectiveness analysis can be useful as it may show that an intervention is cost-effective in some settings or patients, but not in others. Relevant sub-groups of the population will be similar to those used for equity analysis and may include: socioeconomic status, gender, age, occupation, education level, ethnic group or geographical location.

7.2 Analyzing Uncertainty

Uncertainty in the results of a cost-effectiveness analysis can occur because of methodological disagreement among analysis, the data requirements of the study, the need to extrapolate results over time or from intermediate to final health outcomes, and the desire to generalize the results of the study to another setting. The appropriate method for handling uncertainty depends on its source.

METHODS: Handling uncertainty in cost-effectiveness analysis with patient level data

Type of uncertainty	Handling uncertainty
Methodological	Reference case Sensitivity analysis
Sampling	Statistical analysis
Extrapolation	Sensitivity analysis Statistical analysis
Generalizability	Sensitivity analysis

Source: Drummond, Sculpher et al (2005).

7.2.1 Sensitivity analysis

Sensitivity analysis is an important feature of economic evaluations and study results can be sensitive to the values taken by key parameters. The traditional approach to sensitivity analysis is to examine one variable at a time: known as one-way or univariate sensitivity analysis. After calculating the base-case scenario the ICER is re-calculated holding all parameters constant apart from the one parameter chosen which is varied over the specified and justified range. This process is repeated for as many parameters as desired.

It is also possible to vary two or more of the parameters (known as multi-way or multivariate sensitivity analysis) at the same time and assess the impact on the ICER of the two mutually exclusive interventions. This approach is more realistic but unless there are only a few uncertain parameters the number of potential combinations becomes very large.

Another example of the approach is to use scenario analysis. This involves constructing a subset of potential multi-way analyses, which typically include a base case (best guess) scenario and the best case (most optimistic) and worse case (most pessimistic) scenarios. Other scenarios that are considered probably may also be examined.

An alternative is to use threshold analysis, which identifies the critical value of a parameter. For example, a decision maker might specify an increase in cost, or incremental cost-effectiveness ratio above which the programme would not be acceptable. The analyst could then determine threshold values for the combinations of key parameters that would cause the threshold to be exceeded.

EXAMPLE: Sensitivity analysis undertaken in a cost-effectiveness analysis of an ITN intervention in Kenya

Variable	Change	Effect on total costs	Effect on child death averted
Discount rate	Increasing the discount rate: from 3% to 6% and from 3% to 10%	4% and 11% increase respectively	From $1214 to $1256 and 1354, respectively
Frequency of net impregnation	Reducing the frequency of net impregnation from 6 months to once a year	29% decrease	From $1214 to $857
Cost of insecticide	A 20% reduction (or increase) in the cost of insecticide	3% decrease (or increase)	From $1214 to $1176 (or $1252)
Frequency of net impregnation and cost of insecticide	Reducing net impregnation to once a year and reducing the cost of insecticide by 20%	30% decrease	From $1214 to $839

Adapted from Wiseman, Hawley et al. (2003)

7.2.2 Statistical Analysis

When patient-level sample data are available on the costs and effects, it is possible to use formal ***hypothesis testing*** as a way of reflecting the uncertainty in the cost, effects and cost-effectiveness. In the analysis the null hypothesis is usually that there is no difference in outcome between intervention and control groups, using either a one-tailed alternative, in which the intervention is assumed to be more effective, or a two-tailed alternative, in which the intervention is may be more or less effective than the control.

There are, however, limitations to the hypothesis testing approach (see Drummond, Sculpher et al, 2005). It is generally recommended that in preference to reporting only P-values analysis should report the observed ICER with an associated ***confidence interval***. Confidence intervals provide a probabilistic range of values within which we can be confident that the true cost-effectiveness ratio lies. The confidence intervals can be calculated using parametric (e.g. Fieller's method) and non parametric (e.g. bootstrap) methods. Non-parametric ***bootstrapping*** techniques are often preferred since they do not assume that the difference in cost and effect are distributed bivariate normal.

METHODS: Bootstrap method

Rather than making assumptions about the underlying distributions in the ICER, this method re-samples from the original data to build an empirical estimate of the sampling distribution of the ICER. The steps in undertaking are:

1. Draw a sample from the observations of the intervention group by simple random sampling with replacement. Compute the bootstrap replicates of the mean cost and mean effect of the intervention group
2. Draw a sample from the observations of the control group by simple random sampling with replacement. Compute the bootstrap replicates of the mean cost and mean effect of the control group.
3. Compute the bootstrap replicate ICER using the mean costs and effects from the bootstrap sample.
4. Repeat steps 1-3 a large number of times and obtain the independent bootstrap replications. This is the empirical estimate of the sampling distribution of the ICER.
5. The confidence interval for the ICER can then be obtained by taking the 2.5 and 97.5 centiles from the empirical sampling distribution.

Source: Drummond, Sculpher et al. (2005).

Further guidance on examining uncertainty in cost-effectiveness analysis can be obtained from: Walker D, Fox-Rushby JA. Allowing for uncertainty in economic evaluations: qualitative sensitivity analysis. *Health Policy and Planning* 2001;16(4):435-443.

8. CONCLUSION

This guidance note is intended to provide an introduction to the methods for undertaking cost-effectiveness analysis. It also provides a number of examples which are intended to illustrate the key principles or issues. References are provided to guide the reader into the more detailed literature on methods of cost-effectiveness examples and applications to malaria-related interventions. Further information can also be obtained from the economists in the ACT Consortium Core Group: Dr Shunmay Yeung (shunmay.yeung@lshtm.ac.uk) and Dr Kristian Schultz Hansen (kristian.hansen@lshtm.ac.uk).

SUMMARY AND RECOMMENDATIONS

The key elements of cost-effectiveness analysis are summarized below, including any recommendations for ACT Consortium studies undertaking economic evaluation. Detailed guidance is provided in the remainder of this note on each of the points mentioned.

Study Question

Clearly define the question, which should be stated in an answerable form and relevant for policy makers. Relevant and related secondary questions should also be included (such as the impact of the intervention on sub-groups of the population).

Intervention and Comparators

Define the intervention and its comparator(s). Economic evaluation is a comparative analysis and it is necessary to evaluate the health intervention against a reference case, or counterfactual. The reference case should represent the "usual practice" that the intervention is intended to replace. In some studies "usual practice" may include more than one relevant widely used alternative, while in others the reference case may be "no practice".

Target Population

Specify the target population(s) for the intervention. Perform the analysis for the entire population, and where appropriate conduct stratified analysis of smaller, more homogeneous, subgroups.

Time Horizon

The time horizon for the analysis should be based on the natural course of the condition and the likely impact that the intervention will have on it. It is important to ensure that the time horizon is long enough to capture all relevant differences in future costs and outcomes of the alternatives being analyzed. The same time horizon should be applied to costs and outcomes. Modelling techniques can be used to extend the time horizon beyond the collection of primary data. The ACT Consortium Core Staff may assist individual studies on the option of modelling the longer-term analysis.

Type of Economic Evaluation

State the type of economic evaluation. This should be based on the nature of the research question, the intervention of interest and the availability of data on outcomes.

For ACT Consortium studies this is likely to be a cost-effectiveness analysis with outcomes such as fever cases correctly managed or malaria cases cured. The ACT Consortium Core Staff may also use modelling techniques to obtain disability adjusted life years (DALY) from the effectiveness outcome measures in order to report the results of cost-utility analysis in which outcomes are reported as cost per DALY.

Perspective

State the perspective of the study. This determines the costs to be included in the evaluation. Conceptually the societal perspective is desirable, though many studies opt to take the perspective of the publicly funded health system. The appropriate perspective should correspond to the study question and the target audience for the analysis. Interventions that involve cost-

sharing arrangements with patients should include the patients' perspective, as well as the provider perspective (at least in a secondary analysis).

All ACT Consortium studies should aim to undertake a cost-effectiveness analysis from a societal perspective. Some studies may opt to present the primary analysis from the perspective of a publicly funded health care system.

Resource Use and Costs

Systematically identify, measure, and value resources that are relevant to the study perspective (research costs should be excluded from the analysis). Resources used should be measured and reported in physical units. The costing method should be clearly explained. Measure and value with greater precision those resources that contribute most to total and incremental costs. Sensitivity analysis should be used to determine the impact of cost assumptions and analyze the impact of cost variation.

Conceptually, economic costs (that is opportunity costs) should be the basis for valuing resources. In principle, use total average costs (including capital and allocated overhead costs). Market prices should, where possible, be used to value resource use. Costs that are directly calculated or imputed should reflect the full economic cost of all relevant resources at the normal operating levels. Standard unit costs, such as available from WHO CHOICE, can also be used where they are available, though may be less accurate than directly collected costs.

Costs obtained from different time periods should be adjusted for inflation. Costs (and health outcomes) that occur beyond one year should be discounted to present values at the rate of 3% per year. Sensitivity analysis should be conducted, which uses discount rates of 0% and 6%.

Valuing Outcomes

It is expected that a variety of outcome measures may be used in the ACT Consortium studies. Some attempt to have consistent indicators, such as on prompt access to appropriate malaria treatment has been discussed, and further consideration of outcome measures would be beneficial for enabling comparisons of cost-effectiveness across the different studies. Extrapolating beyond natural health outcomes to consider utility-based outcome measures, principally the disability-adjusted life year (DALY) is encouraged (and is likely to be led by the ACT Consortium core economists).

Variability and Uncertainty

Variability can be attributed to diverse clinical practice patterns in different geographical areas or settings, or to inherent variability in the patient population. Variability should be explored by undertaking additional analysis. This involves stratifying the target population into smaller, more homogenous groups.

Some studies may want to consider the equity impact of the cost-effectiveness results. This involves identifying the equity-relevant characteristics of the subgroups that may benefit from (or be adversely affected by) the intervention. Population characteristics such as age, sex, ethnicity, geographical areas, socioeconomic group or health status may be relevant. Further guidance on equity analysis is provided in a separate Guidance Note.

Uncertainty in the cost-effectiveness analysis should be examined using sensitivity analysis. The key parameter inputs that contribute the most to the results and uncertainty should be identified.

As a minimum one-way sensitivity analysis should be performed for all key parameter inputs, though multi-way analysis may also be appropriate.

Reporting

The cost-effectiveness analysis should be reported in sufficient detail to enable the audience to critically evaluate the validity of the analysis and conclusions. This should include a summary and a conclusion that are written in non-technical language. The final results should be reported as incremental cost-effectiveness ratios (ICERs), based on the incremental differences of costs and outcomes of the alternatives. Presenting the results in graphical form, using a cost-effectiveness plane, is encouraged.

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APPENDIX

Annex A: An Illustration of the Types of Costs Included in a Selection of Intervention Activities at Central Levels

Name of Activity	Description
Administration	Includes overhead costs (e.g. space, furniture, equipment, utilities, maintenance, etc.) used by the programme and personnel in preparation for meetings or training and other administration activities.
Planning	Includes costs associated with planning. For example, per diem allowances for meetings for the endorsement and implementation of the intervention as well as other meeting costs, such as venue, supplies, transportation, etc.). It also includes payments to consultants who participated in the planning phase of the intervention.
Training	Includes special training to develop health workers' skills to deliver the intervention. It should not include under-graduate or post-graduate training as well as that occurring during the residency period. Only training that had to be provided to deliver the intervention should be included, i.e. it should be specific to the intervention studied. This will depend largely on the extent of training facilities that are available in each country. For example, in countries where most radiologists are already trained to perform this service, to add an intervention that does not require them to learn more skills but just to modify the optimum doses of radiotherapy given to cancer patients will not require prior training. In other countries where this initial experience was not available, training of providers should be included. Other examples include training of health workers to administer a new vaccine or to use a new guideline for case management. This will include costs of adaptation of the guidelines and training materials as well as the translation of the training materials to the national language if required. This should not include costs incurred at an international level, e.g. where international organizations develop guidelines for international consumption such as the development of the WHO guidelines for case management of acute lower respiratory infections.
Media and IEC	Development and production of information, education and communication (IEC) materials. This includes costs of developing the IEC materials in terms of designing the message, testing, revision and re-testing. It also includes the cost of printing those materials and/or the radio or television time to air them.
Monitoring and supervision	This includes supervision visits to health facilities in terms of per diem allowances, travel allowances and personnel salaries, if the latter is not already included in one of the activities listed above (e.g. in administration activities).
Social mobilization	This includes motivating and educating the public, and marketing health-related interventions through local markets. For example, this might involve retailers receiving some guidance on the correct use of items such as insecticide-impregnated bednets for malaria prevention. All advertising and promotion activities, seminars, technical support to retailers should be included.

Source: http://www.who.int/choice/en/

Annex B: Step-Down Cost Accounting to Estimate Health Facility Unit Costs

The first step is to reallocate the administration costs across the other cost centres on the basis of staff numbers. The sub-totals for the cost centres are then revised. Using the revised totals the second step is to reallocate the revised transport costs on the basis of the estimated vehicle usage, and determine the revised totals. This process continues until all the indirect and intermediate cost centres have been reallocated to the final cost centres.

	Cost Centres								
	Indirect Cost Centres			**Intermediate Cost Centres**		**Final Cost Centres**			
	Admin	Transport	Laundry	Pharmacy	Laboratory	Maternity ward	Outpatients	Paediatrics ward	Other services
Totals from grouped line items ($)	3000	1000	300	3200	1300	1700	1700	1500	6300
Reallocation of administration costs									
% staff numbers		10%	5%	5%	5%	20%	20%	10%	25%
Reallocate costs ($)		300	150	150	150	600	600	300	750
Revised total ($)		1300	450	3350	1450	2300	2300	1800	7050
Reallocation of transport costs									
% vehicle usage			5%	10%	15%	15%	25%	10%	20%
Reallocate costs ($)			65	130	195	195	325	130	260
Revised total ($)			515	3480	1645	2495	2625	1930	7310
Reallocation of laundry costs									
% estimated actual use				5%	5%	30%	20%	15%	25%
Reallocate costs ($)				26	26	155	103	77	129
Revised total ($)				3506	1671	2650	2728	2007	7439
Reallocation of pharmacy costs									
% based on days of care/visits					0%	20%	30%	15%	35%
Reallocate costs ($)					0	701	1052	526	1227
Revised total ($)					1671	3351	3780	2533	8666
Reallocation of laboratory costs									
% based on activity data						20%	30%	10%	40%
Reallocate costs ($)						334	501	167	668
Revised total ($)						3685	4281	2700	9334

Source: Adapted from Conteh and Walker (2004)