

A GUIDE to the development



implementation

**How to compare the costs and
benefits: evaluation of the
economic evidence**

and evaluation

of clinical practice

guidelines



NHMRC

*National Health &
Medical Research Council*

How to compare the costs and benefits: evaluation of the economic evidence

**Handbook series on preparing clinical practice
guidelines**

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NHMRC

National Health and Medical Research Council

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PREFACE

Clinical practice guidelines are systematically developed statements that assist clinicians, consumers and policy makers to make appropriate health care decisions. Such guidelines present statements of 'best practice' based on a thorough evaluation of the evidence from published research studies on the outcomes of treatment or other health care procedures. The methods used for collecting and evaluating evidence and developing guidelines can be applied to a wide range of health care options, including the use of technology and pharmaceuticals, surgical procedures, screening procedures, lifestyle advice and so on.

In 1995, recognising the need for a clear and widely accessible guide for groups wishing to develop clinical practice guidelines, the National Health and Medical Research Council (NHMRC) published a booklet to assist groups to develop and implement clinical practice guidelines. In 1999, a revised version of this booklet was published, called *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines* (NHMRC 1999), which includes an outline of the latest methods for evaluating evidence and developing and disseminating guidelines.

The emerging guideline processes are complex, however, and depend on the integration of a number of activities, including collection and processing of scientific literature, evaluation of the evidence, development of evidence-based recommendations or guidelines (including evaluation of cost-effectiveness), and implementation and dissemination of the guidelines to relevant professionals and consumers. The NHMRC therefore decided to supplement the information in the guideline development booklet (NHMRC 1999) with a series of handbooks with further information on each of the main stages involved. Experts in each area were contracted to draft the handbooks. An assessment panel was convened in June 1999 to oversee production of the series. Membership of the assessment panel and the writing group for this handbook are shown at Appendix A.

Each of the handbooks in the series focuses on a different aspect of the guideline development process (review of the literature, evaluation of evidence, economic assessment, dissemination and implementation, consumer publications and so on). This handbook provides essential information to help a committee developing guidelines to weigh up the cost-effectiveness of clinical management options for which review and assessment of the scientific literature has shown evidence of clinical benefit. In doing so, it builds on the information presented in two companion handbooks in this series — *How to Review the Evidence: Systematic Identification and Review of the Scientific Literature* (NHMRC 2000a) and *How to Use the Evidence: Assessment and Application of Scientific Evidence*

(NHMRC 2000b) — drawing on the most recent methods that have emerged in this rapidly developing area.

The way in which the guidance provided in this handbook fits into the overall guideline development process recommended by the NHMRC is shown in the flow chart on page ix. Other handbooks that have been produced in this series so far are:

How to Review the Evidence: Systematic Identification and Review of the Scientific Literature (NHMRC 2000a)

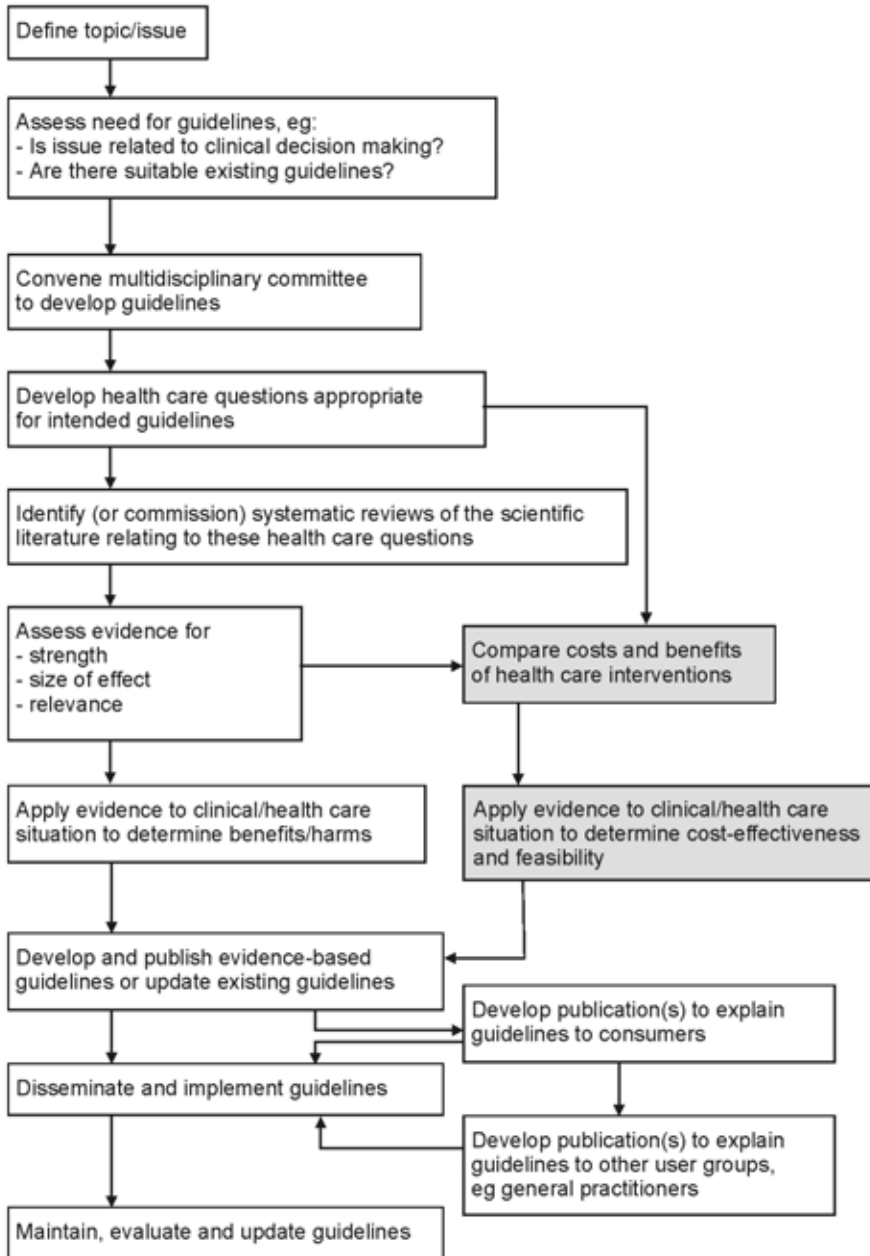
How to Use the Evidence: Assessment and Application of Scientific Evidence (NHMRC 2000b)

How to Put the Evidence into Practice: Implementation and Dissemination Strategies (NHMRC 2000c)

How to Present the Evidence for Consumers: Preparation of Consumer Publications (NHMRC 2000d)

The series may be expanded in the future to include handbooks about other aspects of the guideline development process, as well as related issues such as reviewing and evaluating evidence for public health issues.

Flow chart 1 Clinical practice guidelines development process
(Shaded boxes show the stages described in this handbook)



INTRODUCTION

Development of evidence-based guidelines

The process for developing clinical practice guidelines is described in the National Health and Medical Research Council (NHMRC) publication *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines* (NHMRC 1999). This recommends that guidelines should be developed by a multidisciplinary committee, the initial tasks of which are to determine the need for, and scope of, the guidelines, define the purpose and target audience and identify the health outcomes that will improve as a result of their implementation.

The membership of a guideline development committee depends on the nature of the particular guidelines being developed but should include clinicians, health professionals, consumers, health policy analysts, economists and regulatory agency representatives, industry representatives and bioethicists (see NHMRC 1999 for a full list and further discussion of the multidisciplinary committee). The inclusion of consumers is particularly important, to ensure that patient-relevant outcomes and evidence are considered.

The development and implementation of clinical practice guidelines endorsed by NHMRC need to be underpinned by economics. This handbook explains what the multidisciplinary committee must do to ensure that this requirement is met. It assumes that the committee will incorporate economic considerations in the development of the guidelines, rather than first developing guidelines and then undertaking an economic evaluation.

Clinical practice guidelines range in their complexity: some cover the whole health care protocol for a complex disease whereas others may focus on one specific component of a protocol. Similarly, the economic evaluation that is appropriate may focus on one specific component of health care for a condition or it may encompass care for a complex disease or set of conditions. The principles of economic evaluation remain the same whatever the complexity of the guideline or the phase of disease control it addresses.

This guideline brings together a range of methods used in the economic evaluation of clinical practice and provides an overall approach with wide applicability for different health care issues. There are a variety of guides for economic analysis currently used in Australia and overseas, with areas of both agreement and disagreement. Though desirable in the future, this guide has not attempted a harmonisation of the various Australian standards.

Definitions

In the handbook *How to Review the Evidence: Systematic Identification and Review of the Scientific Literature* (NHMRC 2000a) five different types of clinical questions are considered, involving different study types.

- *Interventions* — ‘What are the effects of an intervention (eg prevention, screening, rehabilitation)?’
- *Frequency or rate* — ‘How common is a particular condition or disease in a specified group in the population?’
- *Diagnostic test performance* — ‘How accurate is a sign, symptom, or diagnostic test in predicting the true diagnostic category of a patient?’
- *Aetiology and risk factors* — ‘Are there known factors that increase the risk of the disease?’
- *Prediction and prognosis* — ‘Can the risk for a patient be predicted?’

For an economic evaluation, questions involving interventions and diagnostic test performance are relevant, and the study types are the same as those for a clinical evaluation.

In this handbook, the terms ‘*health care*’ and ‘*health care option*’ are used to denote the whole process of patient care from the initial consultation, through diagnosis (work-up) to any resulting intervention. Information about aetiology, risk factors, prediction and prognosis and frequency might be required for the evaluation. Other terms used in this handbook are:

- *guideline practice* — refers to the practice recommended by the guideline;
- *current practice* — refers to the patterns of practice that are in place before a new guideline is disseminated;
- *new practice* — refers to the patterns of practice that become established once a new guideline has been disseminated;
- *consequences* — refers to the health outcomes, both positive and negative, that result from different health care options; and
- *costs* — refers to the cost of the resource use involved in health care.

Of course, some current practice may be consistent with the guideline recommendations. However, it is assumed that there is some difference

between current practice and the new guideline practice — otherwise the guideline would not be needed.

Why is economic evaluation needed?

When it comes to the allocation of health care resources, it is well accepted that there is a pressing problem to solve. Continual pressure is placed on limited health care budgets by increasing wants and demands. Allocating these scarce resources in ways that are most effective in improving health outcomes continues to be a challenge.

An important first step in undertaking an economic evaluation is to understand why such a process is relevant for developing clinical practice guidelines. As long as society limits what it is prepared to spend on health services, it is important to consider both the effectiveness and the costs of health care options. Economic evaluation can help to maximise health gain within a given health budget.

The focus of clinical practice guidelines is to distinguish effective from ineffective care on the basis of the scientific evidence. The systematic identification, review, assessment and clinical application of such evidence is described in two accompanying handbooks in this series (NHMRC 2000ab). Eliminating ineffective clinical practice is good for individuals undergoing health care, but it is also good for society, as health care spending is not wasted on ineffective care. Clearly, the health of the population may be improved if spending on health care can be directed to effective options.

Where there is a range of effective health care options, the most effective outcome can be identified, so that health benefits can be maximised. However, health care options vary in their costs as well as their effectiveness. The most cost-effective option is not necessarily the cheapest; but neither is the most effective option always the most cost-effective. It depends on the balance of costs and consequences.

What is economic evaluation?

Economic evaluation is the systematic, explicit analysis of alternative courses of action, assessed in terms of both costs and consequences. It is concerned with choice. Indeed, economic issues pervade almost every aspect of our daily lives and economic evaluation is needed to find efficient solutions to resource allocation problems. In health care, an economic evaluation provides a framework and a set of techniques that enable decision makers to incorporate

economic criteria into decisions about whether, and how, to allocate scarce resources to particular health care options.

Efficiency is evaluated by assessing alternative courses of action in order to identify those that, if implemented, maximise the expected benefit, such as number of life-years gained or quality-adjusted life-years (QALYs) gained. Equally, efficiency can be couched in terms of minimising the cost of achieving a given level of benefit. Inefficiency is said to exist when it is possible to reallocate resources to increase the benefits obtainable. Economic evaluation used in this way is concerned with benefit maximisation rather than cost cutting.

Economic evaluation offers another advantage. As judgments are an inevitable part of most aspects of health care decision making, an important component of economic evaluation is sensitivity analysis. This is the systematic exploration of the influence that key variables and assumptions have on the economic evaluation. The analysis allows the user of economic results to gain insight into their robustness.

Economic evaluation of health care options builds on clinical effectiveness; therefore it is typical to find health economists working closely with clinicians, epidemiologists and other health service professionals.

Essential to an evaluation are:

- identification of all main clinical event pathways and their associated resource implications, and the consequences (health outcomes) for each relevant option;
- estimation of the probabilities of the main event pathways occurring;
- identification and measurement of resource use associated with each pathway; and
- identification and measurement of the consequences to be valued.

Scope of an economic evaluation

The overall development process for clinical practice guidelines consists of:

- formulation and consultation;
- implementation and dissemination; and
- evaluation and revision (NHMRC 1999).

The overall question, from an economic perspective, is whether proposed clinical practice guidelines lead to a more efficient allocation of scarce health care resources. Thus, economics could be included in any of these aspects of the process.

Formulation

In developing guidelines, the committee should consider the cost (ie resource use) as well as the effectiveness of the health care options available, in order to ensure:

- greater health gains for less cost;
- the same health gain for less cost; or
- greater health gain for an additional cost deemed worth paying.

Implementation

A change in clinical practice will almost certainly affect resource use. A new practice may cost more than the current practice (eg if there is an effective health care option for patients who are currently untreated) or less (eg if a treatment is replaced by a less expensive treatment). In either case it should be more efficient. Estimating the net cost of the new practice also requires some prediction of the success of the guideline in changing practice. Unless there is 100% adoption of the proposed practice, the costs of new practice patterns will not be the same as the anticipated cost of the guideline practice.

There may also be a budget constraint that affects the implementation of clinical practice guidelines — identifying cost-effective practice per se does not necessarily mean that a proposed guideline is affordable within a current budget. It may be that a procedure or treatment that is cost-effective when considered against other options on a per person basis has to be so widely applied (eg as in a population screening program) that the costs would exceed the available health care budget.

Dissemination

The guideline dissemination process also has associated costs and an economic evaluation can be used to analyse alternative strategies of dissemination to determine the most cost-effective approach. The total cost of the process is the cost of the guideline formulation plus the cost of dissemination and this cost can be compared with the costs of changing from current to new practice patterns. The greater the cost savings in changing practice, the greater the amount that is worth spending on dissemination. The cost-effectiveness of a particular guideline can be assessed by the estimated change in health outcomes

for the net costs, that is, the cost of development and dissemination plus any additional costs of new practice patterns.

Evaluation and revision

Economic evaluation can be used in the evaluation process for clinical practice guidelines to determine whether the actual costs and consequences achieved were those estimated.

Focus of this handbook

In this handbook, attention is concentrated on the formulation and implementation aspects of the guideline development process, including the impact of a new guideline on the total budget. These are the parts of the process where economic issues are crucial and are most likely to influence decision making.

An economic evaluation could be conducted on different strategies for disseminating clinical practice guidelines but this is outside the scope of this handbook. The use of economic evaluation in developing the guidelines will provide a basis for including an economic analysis in the subsequent evaluation process, but this issue is not addressed explicitly here.

Financial and other incentives may affect the adoption of clinical practice guidelines, either encouraging or discouraging recommended practice. Financial incentives may be used deliberately to reinforce recommended practice. However, the analysis of incentives also lies outside the scope of this handbook.

The role of a health economist

Although the NHMRC recommends that the multidisciplinary guideline development committee should include a health economist as one of its members, such professionals are in short supply and one may not be available. It is therefore crucial to recognise *when* it is important to have a health economist as part of the team. If a group is formed without a health economist, it may be necessary to at least consult with one at some stages of the process. How much of the work proposed can be undertaken by a group without a health economist will depend on the complexity of the guidelines under investigation and on the experience and skill of the group members with respect to economic issues. However, if a new economic study is needed (see stage 5, below), consultation with a health economist will be essential, either as a member of the team or as externally commissioned specialist help.

Although in some cases it may be possible for a multidisciplinary committee to undertake an economic evaluation with little input from a health economist, the economist could not undertake the work without significant input from the other members of the committee. This is because economic analysis requires not just an appreciation of resource allocation problems (which are the generalist skills held by health economists) but specialist knowledge of the clinical evidence, the patient groups involved and clinical practice in Australia. The committee must therefore work as a team throughout the stages outlined in this handbook, which is written for the guideline development committee as a whole, and lays out step by step the processes that must be followed in an economic evaluation of proposed clinical practice guidelines.

About this handbook

The handbook is divided into two main parts.

Part 1 addresses the question: ‘Which of the health care options is the most cost-effective?’ That is, it describes the economic evaluation of the alternatives considered in formulating clinical practice guidelines.

Part 2 addresses the question: ‘Is the proposed clinical practice guideline economically feasible?’ That is, it describes the economic evaluation of the change from current practice to new practice as a result of dissemination of the proposed guideline practice. It also includes information on how to assess the impact of the proposed guideline on the total budget and how to incorporate the economic guideline into clinical practice guidelines.

Within these two parts, nine stages are described which the guideline development committee must work through. Part 1 includes stages 1–6 and Part 2 includes stages 7–9, as follows.

PART 1: Is the proposed clinical practice cost-effective?

1 — Setting up an economic framework

An economic framework is established and the extent of analysis needed is assessed. This requires the committee to outline the costs and consequences of the options being considered. Sometimes the evidence will be sufficiently clear and strong at this stage that no further formal economic evaluation is needed. If this is not the case, the committee must proceed through the next stages. The objective of these is to estimate a cost per additional unit of effect gained (such as life-year or QALY gained for each option), using a consistent and standard method.

2 — Defining the economic question

The key issues for economic evaluation relevant to the particular clinical

guidelines being developed are defined. Where guidelines cover a range of health care options for a complex disease, there will be many clinical decisions, each of which could have a separate economic evaluation. This would be unwieldy and not a good use of scarce resources, so this stage provides guidance for defining the key components of clinical practice where economic questions are relevant.

3 — Collecting and appraising the economic literature

Relevant economic studies are collected, reviewed and critically appraised.

4 — Appraising external validity and transferability

The study findings are assessed to determine whether they can be transferred from their original setting (which may be a different country or a different time) to the current situation in Australia. At the end of stage 4, the committee will have assessed the available evidence. However, sometimes the available evidence may not be adequate to answer the important questions identified in stage 2. In this case, the committee proceeds to stage 5 and undertakes further analysis.

5 — Undertaking a new economic evaluation

If necessary, new studies are set up to obtain the data required for economic evaluation. Setting up a study in this context does not mean setting up a new clinical trial and collecting new primary data. It does mean commissioning a new economic analysis. This stage also provides information relating to commissioning the services of a health economist to assist the committee in this task.

6 — Determining the cost-effectiveness of options

The cost-effectiveness of the proposed guideline practice is determined relative to its alternatives. The committee must decide whether the proposed guideline practice is a cost-effective option based on a consensus view of the size and certainty of the cost and effectiveness data drawn together from stages 3–5.

PART 2: Is the proposed clinical practice guideline economically feasible?

7 — Determining the costs under current practice

The baseline resources and costs associated with current clinical practice are assessed.

8 — Predicting the resource and cost implications of guideline practice

The cost implications of implementing the new guideline practice are estimated. Stages 7 and 8 identify the impact on total costs and implications for individual funding organisations. Stage 8 also shows how the committee can synthesise the economic information and reach a

recommendation on whether to proceed with the clinical practice guideline on the basis of cost-effectiveness.

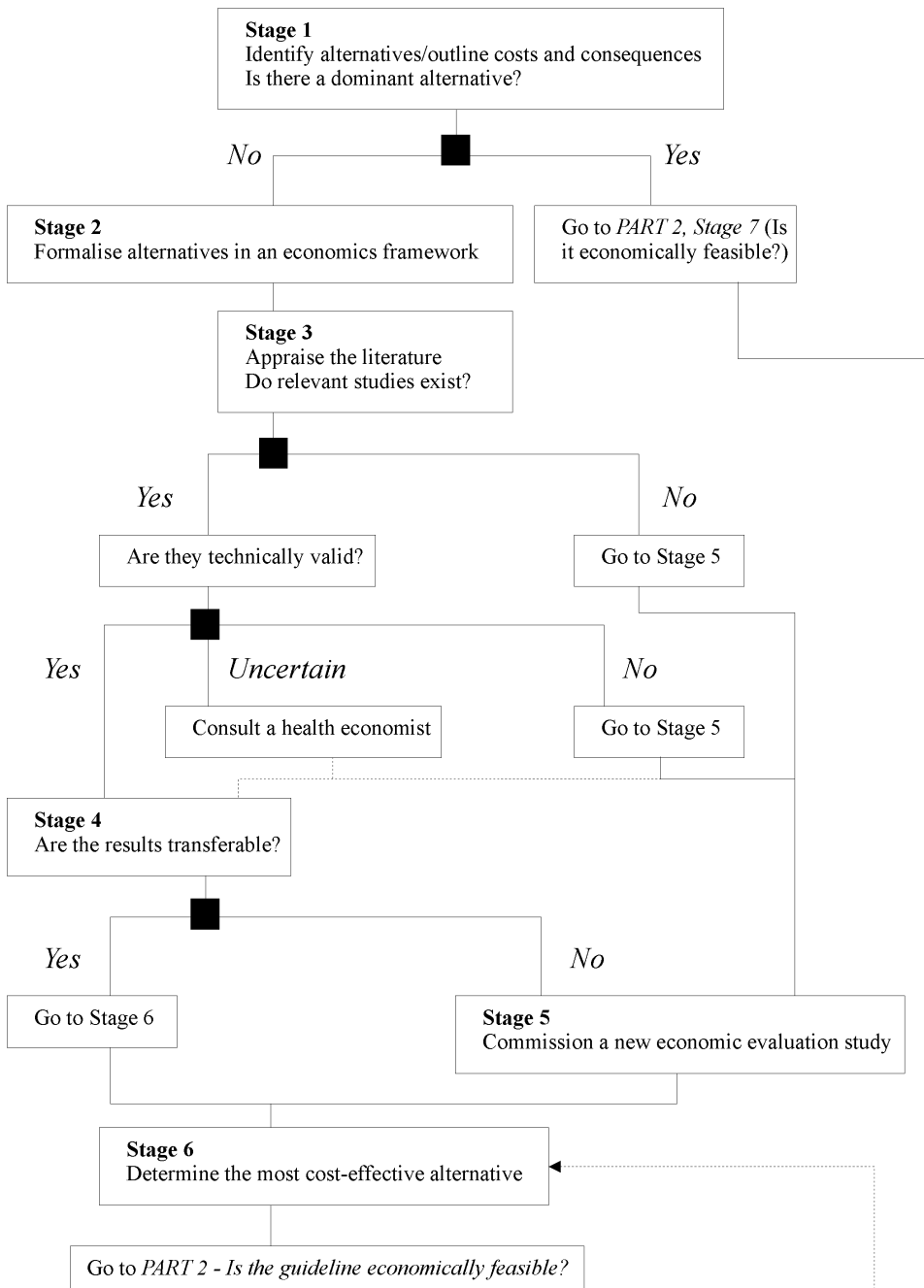
9 — Presenting the economic evidence

The evaluation of economic evidence is incorporated into appropriate clinical practice guidelines.

An overview of this process is shown in Flow chart 2 (How to use this handbook).

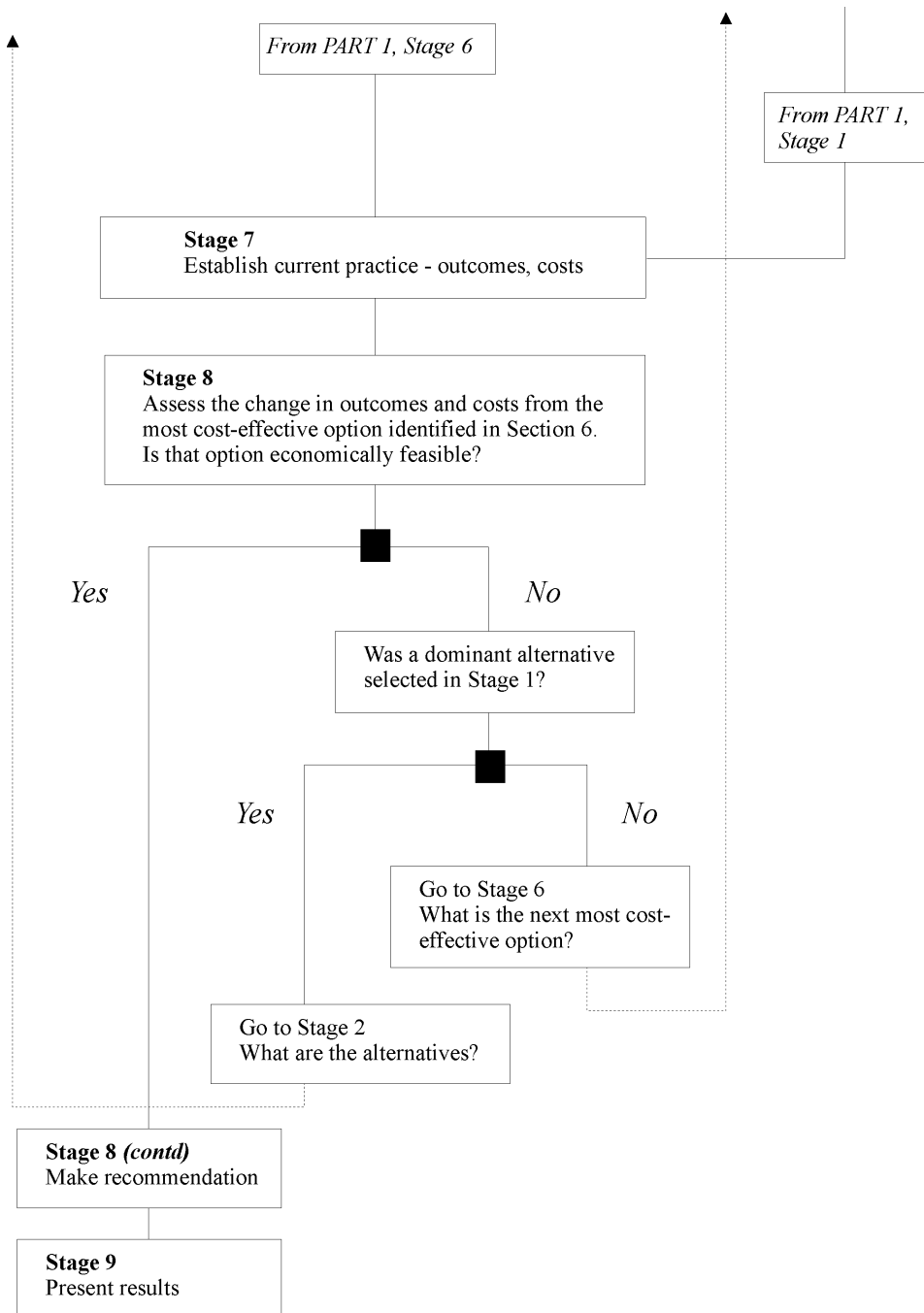
Finally, there is much agreement among economists about what constitutes a good economic evaluation. These criteria are summarised in a number of checklists for critical appraisal. One such checklist is given in Table 3.2. However, some aspects of economic evaluation remain open to debate and there is variation in methods between studies. This is partly because of methodological issues that are not entirely resolved, but also because of differences in the contexts in which the studies are undertaken. Valid comparison across economic evaluations relies on the use of a standard or reference case to ensure consistency in methods. This handbook provides such a reference case in Section 4, which is used both to assess published economic studies and to structure any new analysis.

Flow chart 2 How to use this handbook



continued

Flow chart (contd)



Part 1

Is the proposed clinical practice cost-effective?

1 SETTING UP AN ECONOMIC FRAMEWORK

Objectives

- To outline the costs (resource use) and consequences (health outcomes) of options for the clinical topic under consideration.
- To determine whether it is appropriate to proceed with a formal economic evaluation and, if so, to set up an economic framework for the evaluation.

Steps

- Start thinking in an economic framework.
- Identify relevant health care options.
- Identify relevant health consequences and flow-on effects.
- Decide on a timeframe for analysis.
- Determine whether there is a clearly dominant outcome.

1.1 Start thinking in an economic framework

The economic perspective on developing clinical guidelines will, not surprisingly, differ from a clinical view. There are two aspects to thinking like an economist in this context. First, every possible clinical action will use resources and produce health outcomes. Second, developing a guideline requires choosing the best from the possible options, that is, the option that maximises production of health outcomes from available resources. The options can be compared in terms of their costs (resource use) and consequences (health outcomes).

Economic evaluation always involves a comparison of one option with at least one other (a comparator). One option may be to 'do nothing' but often in health care even this has costs and consequences (for example, comparing a screening program with a no-screening option will still involve opportunistic case detection and costs of treatment).

Economic evaluation compares alternative courses of action in terms of their costs and consequences. There are four different types of economic evaluation, which are summarised in Table 1.1. In each case, resource use is valued in monetary terms because quite disparate resources (doctor time, transport, sterile supplies and drugs) can be measured in terms of dollars.

However, the different types of economic evaluation differ in the way they measure the consequences and in the type of question they can address. To

make the comparison meaningful, the different clinical endpoints under consideration have to be measured in the same units. For example, it is not meaningful to compare effectiveness in terms of reduction of blood pressure for one intervention with control of blood sugars for another.

Hence, the comparison of costs and consequences is generally expressed as a monetary cost per unit of effectiveness. The most general unit approach is to estimate a cost per life-year saved, with or without some adjustment for differences in quality of life. This allows the widest range of health programs to be compared.

Table 1.1 Types of economic evaluation

| Type of economic evaluation | Consequence measurement | Questions that can be answered |
|------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cost-minimisation analysis ^a | Not measured (health care options assumed to be equally effective) | Given that we want to achieve this health care goal, which options would cost the least? What is the most efficient way to spend a given health care budget? |
| Cost-benefit analysis ^a | Monetary units | Is it worth achieving this health care goal? What level of resources should we allocate to this health care goal? |
| Cost-effectiveness analysis ^a | Natural units (eg strokes avoided) | What is the cost per natural unit (eg stroke avoided)? |
| Cost-utility analysis ^a | Health state preference values (eg quality-adjusted life-years) | What is the cost of gaining the improvement in health state? |

^a See the Glossary for more detailed definitions.

In cost-minimisation analysis, the effectiveness of the two health care options is assumed to be the same. Therefore, the difference between the options is only in the cost. In the cost-benefit analysis the consequences (health outcomes) of the options are given an explicit monetary value; therefore both the costs and the consequences are measured in monetary units. This can allow comparison outside the field of health care.

Cost-effectiveness analysis uses as its measurement of consequence an outcome that can be counted and is of interest, for example, life-years saved, strokes

averted, blood pressure lowered. The output from a cost-effectiveness analysis is the cost per unit. Cost-utility analysis measures the consequence of different options in health preference values such as QALYs. The output from a cost-utility analysis is cost per QALY. There is considerable overlap between cost-effectiveness analysis and cost-utility analysis.

The cost-effectiveness of a particular health care option is determined from the ratio of the net change in health care costs to the net change in consequences relative to the comparator (ie the comparison of outcomes and costs for each option). The simplest example is to consider two health care options, A and B. If B is compared with A, then the result can be fitted into a cell within the matrix given in Table 1.2.

Table 1.2 **Classifying incremental cost-effectiveness results**

| Cost of B compared to A | Effect (consequences) of B compared to A | | |
|--------------------------------|-------------------------------------------------|--------------------|--------------------|
| | <i>Less</i> | <i>Same</i> | <i>More</i> |
| <i>Less</i> | ? | Y | YY |
| <i>Same</i> | X | – | Y |
| <i>More</i> | XX | X | ? |

Y= B more cost-effective than A; X = B less cost-effective than A; ? = uncertain;
 – = same costs and consequences (centre box)

B is clearly more cost-effective than A when B delivers more health gain for the same or lower costs. This is represented by the three cells with a Y or YY. This occurs when B costs less than A but provides the same effectiveness; B costs less and is more effective; and B costs the same as A but is more effective. It is not difficult to see why spending on B will deliver more effectiveness for the dollars spent. In this situation B is said to ‘dominate’ A clearly.

Similarly an X or XX represents the situation where B is clearly less cost-effective than A. This occurs when B costs the same as A but is less effective; B costs more than A and is less effective; and B costs more but provides only the same effectiveness as A.

This situation becomes more complicated in the cells marked with ‘?’. This is because trade-offs between the estimated consequences and costs have to be made; B is more (less) effective than A, but also more (less) costly. The question is whether the additional gain in (loss of) effectiveness justifies the additional (lower) cost.

In the unusual situation that the costs and the consequences are exactly the same (as in the centre cell), A and B cannot be distinguished on economic grounds; they are identical.

1.2 Identify relevant health care options

The choice of options is important in economic evaluation. Once the committee has decided on the clinical content of the proposed guidelines (eg which drugs should be recommended in the treatment of atrial fibrillation in the elderly), the economic inquiry will need to focus on the range of health care options available. All the realistic options may be considered, including current practice. For each option, a clear description is required, including what is done (prevention, screening, etc), to whom (the patient population of the proposed guideline), and how (the process and resources used to treat, screen, etc).

Although it is critical to ascertain the 'right' options in economic evaluation, there is no single correct way of doing this. Instead, this process will rely on the expertise of the clinical area specialists on the committee. Four approaches may help identify the range of options:

- introspection — drawing on the clinical expertise and experience of committee members;
- identification of the current practice of those who work in the area — bearing in mind that current practice may be different in metropolitan, rural and remote areas;
- examination of the literature; and
- examination of previous guidelines issued for the same clinical area.

Example 1.1 Health care options

Condition to be treated: atrial fibrillation — an irregular rhythm of the heart that predisposes those who have it to stroke (Barnett et al 1995).

Alternative treatments: both warfarin and aspirin have been used as alternative methods to reduce the chance of stroke. While these drugs reduce the risk of a blood clot causing a stroke (ischaemic stroke), they raise the risk of bleeding and therefore of haemorrhagic stroke.

Minimum set of options for economic evaluation:

- aspirin
- warfarin
- do nothing

It is very important to get the health care options right. This is because the cost-effectiveness of a health care option is influenced by the alternatives chosen as comparators. This is what we do intuitively in other walks of life — for example, when deciding how to travel between cities, it is reasonable to compare air travel to bus or car travel but it might be considered ridiculous to

compare it to walking. Thus, if a health care option is compared with a highly costly and inefficient practice (that is not current practice), it may seem artificially cost-effective by comparison. Or if a comparison is made between a new effective health care option and an out-of-date, ineffective alternative, the former will appear comparatively effective, but may not do so if appropriately compared to current health care.

Overall, the committee must describe each option clearly, including the population of interest (ie the population that is the subject of the guideline). It is important to state this explicitly to ensure that a consistent approach is taken.

1.3 Identify relevant health consequences and flow-on effects

Health consequences

For the purposes of guideline development it is important that all major health consequences of different care options are identified. All patient-relevant consequences (NHMRC 2000b), including both positive and negative outcomes, must be considered. Clinical or surrogate outcomes such as reduced cholesterol or reduced blood pressure can be used, as long as they are linked to, or predictive of, the patient-relevant consequences. It may be appropriate not to incorporate some more trivial consequences.

Table 1.3 Types of health consequences (outcomes)

| Consequence | Definition |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Patient-relevant | Outcomes that matter to the patient and their carers. They need to be outcomes that patients can experience and that they care about (eg quality of life, return to normal function). |
| Clinical | Outcomes defined on the basis of the disease being studied (eg survival in cancer). |
| Surrogate | A laboratory measurement or physical sign used as a substitute for a clinically meaningful endpoint that measures directly how a patient feels, functions or survives. |

Source: Definitions from NHMRC (2000b)

Flow-on effects

For the economic analysis, all resources used (or saved) associated with a health care option and with its flow-on and side effects are relevant, irrespective of who actually pays for them. In this context, the flow-on effects are the predictable occurrences that happen as a result of the health care option. It is

important to recognise that the costs of the use of a particular health care option can span more than one time period and that all these costs must be captured in the analysis. The option chosen will impact on current and future resource use and may use extra resources in one time period while freeing them up later on (eg preventive medicine). However, if a care option increases the life expectancy of a patient and the patient contracts another, unrelated disease, those costs should not be considered. Although some commentators disagree with this approach, it is the standard for most guidelines on economic evaluations (Drummond et al 1997, Gold et al 1996)

Example 1.2 Flow-on effects of health care options

Example 1

Health care option: mammography screening as a method of detecting early breast cancer in appropriately aged women.

Restricted evaluation: detection of cases.

Flow-on effects: (i) increased need for treatment of early breast cancer (such as surgery, hormonal therapy, radiotherapy and chemotherapy); and (ii) potential benefits of early detection and potential cost savings due to earlier less invasive surgery compared to later more radical surgery and other therapy.

Example 2

Health care options: streptokinase and t-PA (tissue plasminogen activator) are two intravenous medications used for the treatment of acute myocardial infarct.

Restricted evaluation: reduction in 30-day mortality rate of myocardial infarct, with t-PA being slightly more efficacious (GUSTO Investigators 1993).

Flow-on effects: because more people survive with t-PA there may be more resource requirements for cardiac survivors (eg cardiac rehabilitation, post myocardial infarct angiograms and stress tests and perhaps even a higher demand for cardiac surgery).

1.4 Decide on the timeframe for analysis

The next step for the committee is to outline the relevant timeframe for the inclusion of all the important health consequences and costs.

An economic analysis might have to consider a longer timeframe than is traditional for some clinical evaluations, to capture all the costs and consequences that arise from the health care option. This is especially important when one considers the move from clinical outcomes to patient-relevant outcomes, which mostly occur at a point removed in time from the diagnosis and treatment. The resource use that is relevant can therefore span timeframes from as short as a month for a simple procedure (eg antibiotics for a throat

infection) to a lifetime for a preventive intervention or a chronic disease treatment.

It is important that the timespan used to assess costs is the same as that used to measure health consequences. For example, if the outcome measure is the number of heart attacks prevented over a 10-year period, then the costs should similarly be measured over the 10-year period.

Example 1.3 Timeframe for analysis

Health care option. Screening for bowel cancer with annual faecal occult blood detection.

Timeframe for benefits. Improvement in 10-year survival.

Timeframe for costs. Should also be 10 years, including the costs of screening for 10 years, the cost of confirming the cancer and the costs of treating the cancer, including any relapse.

1.5 Determine whether there is a clearly dominant option

Once a framework for economic analysis is in place (options specified, range of relevant consequences and costs identified and an appropriate timeframe determined), the next step is to consider the costs and consequences of each option and determine whether one is clearly dominant.

A full economic evaluation is not necessary at this stage: estimates are all that is required. However it is important that these estimates incorporate all relevant costs and consequences. For each option, the relative health consequences are either *better, about the same, less* or *not clear*. Similarly, with relative costs, each option can be considered as costing *more, about the same* or *less* than the others. If the lowest cost option provides the same or better health consequences than any of the others, then it is clearly the most cost-effective and this is said to be a *dominant option* (XX or YY in Table 1.2).

Example 1.4 Identification of a dominant option

Problem. Diabetic nephropathy in type I diabetes.

Options. Captopril or blood pressure control without Captopril.

Results. The use of Captopril reduced the progression of nephropathy, the use of dialysis and the costs of treating the condition.

Conclusion. The use of Captopril dominates other blood pressure control in type I diabetes with overt nephropathy.

Source. Rodby et al (1996)

1.6 Overview and next steps

At this stage, the committee should have identified the relevant options, determined the costs and consequences and established whether or not there is a clearly dominant option.

If a clearly dominant option has been identified, there is no need to proceed with the assessment of whether the proposed guideline is cost-effective. The committee can proceed directly to Part 2 of this handbook to assess whether the guideline is economically feasible. (In such cases, Part 2 will involve more data collection, as some of the input for Part 2 would otherwise be amassed during the stages outlined in the remainder of Part 1.)

If there is no dominant option, then a more sophisticated analysis is required to identify the most cost-effective option. The stages involved in this analysis are outlined in the remainder of Part 1.

Those comparisons that fall in the centre cell should continue through the stages outlined in Part 1 because it would be inappropriate to consider two options to be identical from the relatively superficial analysis that has been undertaken at this stage.

2 DEFINING THE ECONOMIC QUESTION

Objective

- To provide a statement clearly identifying the important economic question(s) relating to the proposed guideline, including:
 - a clear description of the perspective to be taken;
 - who (medical personnel) does what (tests, treatments, etc) to whom (clinical group of interest); and
 - the consequences (health outcomes) of interest.

Steps

- Select the key issues based on the health care options identified.
- Define and describe the health consequences.
- State the perspective for the economic evaluation.
- Interpret the results.
- Define the question.

2.1 Select the key issues

This stage moves on to the practical issues of how to obtain the economic information needed to answer the question: 'Is a specified health care option cost-effective?'

The descriptions of the options from Section 1 can be used in the development of a decision tree to identify alternative clinical pathways.

Using decision trees

A decision tree is a diagram that depicts all the clinical events for each option, branching at decision or chance points where choices exist or events happen. Following a particular pathway of the tree leads to a particular endpoint (for a more detailed explanation, see Weinstein and Fineberg 1980). Whilst the decision tree as a tool may be familiar to many members of the committee, the purpose here is to emphasise the specific use it can have in economic evaluation. Clinical event pathways do not only represent clinical outcomes. For each event, the associated cost and flow-on effects of management can also be attached. Thus, the decision tree can show the costs and consequences of different clinical pathways. As mentioned earlier, to identify all relevant economic consequences may require the decision tree to follow a longer timeframe than the related clinical decision tree. One reason for this is that economic evaluation is often interested in final outcomes — occurring later in time than reported clinical outcomes. For example, economists tend to think of

final outcomes, such as life-years saved or QALYs, rather than intermediate outcomes, such as blood pressure reduced or cases found. The advantage of representing this in the model of a decision tree is that the assumptions made about important information are made explicit.

One of the great advantages of this approach is that a large number of potential decisions and options can be recognised. However, using economic evaluation appropriately to develop a clinical guideline may be complex since the topic addressed by any clinical guideline may be quite broad and may encompass a range of health care options covering diagnosis and interventions at different stages of disease and rehabilitation. Conceivably, every decision down to the micro-level could be analysed, for example, whether to discharge from hospital one day earlier, or to give antibiotics for six days instead of seven. If each one of these possible decisions were subject to economic evaluation, then the potential workload of the committee would be prohibitive. An example of a decision tree is given in Appendix C, outlining prevention and treatment options for stroke. The challenge is to focus on the decision points that are of key importance in an economic sense and pinpoint the nature of economic information needed to address these questions.

The key decisions concern health care that contributes significantly to the total cost of an option, options with very different costs or care that contributes significantly to health outcomes. On the other hand, decisions are unimportant if they concern health care that is uncontroversial, options that are not economically viable or options for which there are no large resource implications. An example of an unimportant point in a guideline for the treatment of myocardial infarct would be the use of aspirin, which is uncontroversial, known to be effective, has few alternatives (except for doing nothing) and has no large resource implications.

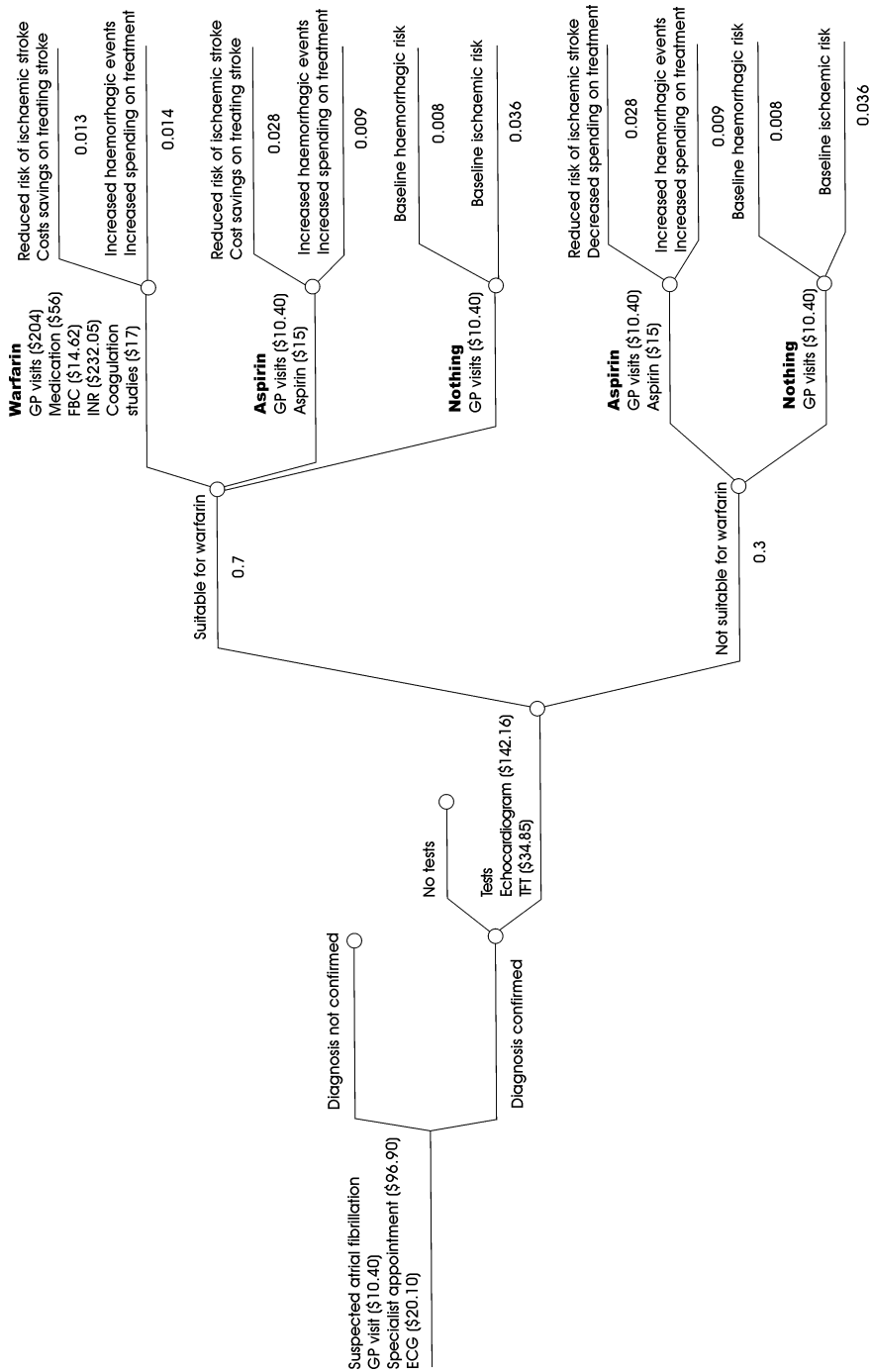
Setting out the decision tree shows what information is required — the probabilities of different clinical events and decisions, and their associated costs. Required information includes identification of resources used in the health care option, follow-on implications of the condition (eg hospitalisation for a complication) and a measurement of the resources used (eg cost of the hospital admission for that case type).

An accompanying handbook in this series, *How to Use the Evidence: Assessment and Application of Scientific Evidence* (NHMRC 2000b), provides useful information in this setting, especially for the generation of effectiveness information and risks.

It may be necessary to create a different version of the decision tree for different groups of patients, if they differ in terms of clinical risks or likely resource use.

Figure 2.1 shows a decision tree built using the example of atrial fibrillation and its treatment in the elderly. This has been assumed to be an important factor for the complicated stroke management guideline shown in Appendix C. Atrial fibrillation is an irregular heart rhythm, which predisposes patients to a higher risk of stroke. This risk may be reduced by the use of drugs that reduce the chance of blood clotting; two such agents that are proposed for this are aspirin and warfarin. While these drugs reduce the risk of a blood clot causing a stroke (reducing the risk of ischaemic stroke), they may raise the risk of bleeding and therefore increase the risk of haemorrhagic stroke. A decision tree for this disorder might be drawn as below (this decision tree is simplified at the top with options around the diagnosis of the atrial fibrillation not being discussed; also, the consequences are not explored in detail).

As is conventional for decision trees, the points where decisions are made are depicted with squares and are known as choice nodes; the points where the outcomes are determined by chance are depicted with circles and are known as chance nodes. A patient with suspected atrial fibrillation is seen by their general practitioner and an investigation is done to either confirm or reject the diagnosis. If the diagnosis is rejected, the patient 'leaves' the guideline; if the suspected diagnosis is confirmed then the patient sees a specialist and an echocardiogram and thyroid function tests are done. The patient is then treated by one of three mutually exclusive options: warfarin, aspirin or no medication. The outcomes, resource implications and potential savings are listed beside each health care option. For example, if the patient is treated with warfarin, the effect of the drug must be monitored with international normalised ratio (INR) tests, which require additional visits by health care workers.



Note: This example is for illustrative purposes only
 FBC = full blood count; INR = international normalised ratio; TFT = thyroid function tests;
 ECG = electrocardiogram

Figure 2.1 A decision tree for treatment of atrial fibrillation

Example 2.1 — Key area of interest

Condition: atrial fibrillation.

Decision points of interest: there are a number of potential points of interest on the decision tree shown in Figure 2.1, for example:

- the alternative forms of diagnosis;
- the search for the cause; and
- the choice of which therapy to use for prevention of stroke: aspirin, warfarin or nothing.

However, the choice of which therapy to use is probably the point of most interest as it has the largest implications for cost-effectiveness and flow-on costs.

Key points to consider in considering health care options are listed below.

- The options considered determine what will ultimately be recommended.
- The options selected for consideration should include all the relevant choices for the guideline subject.
- Poor selection of options can bias the results.
- It is important that each option is described clearly.
- Decision trees can be used to identify alternative clinical pathways.

2.2 Define and describe the health consequences

Relevant health consequences for an economic evaluation are any which have a value for those involved. In health care, this generally means survival and quality of life. Thus, while a focus on a surrogate or clinical outcome (see Table 1.3) may be appropriate for some health care options, it may miss other relevant outcomes that may also be important.

Example 2.2 — Relevant health consequences

Condition: non-insulin dependent (or type II) diabetes.

Clinical outcome: achieving normal glucose levels (because it is known that controlling the blood sugar reduces the chance of undesirable consequences of diabetes (UK Prospective Diabetes Study Group 1998).

Economic focus: improvement in the patient's welfare.

Other relevant outcomes: (i) changes in the undesirable consequences of diabetes; (ii) the occurrence of clinically relevant hypoglycaemia; and (iii) drug reactions between the alternatives.

2.3 State the perspective for the economic evaluations

For an economist conducting an economic evaluation, one of the most important considerations is from whose viewpoint or perspective this should be done, as this will change which costs and consequences are included. For health-care economic analysis in Australia, there are a number of potential viewpoints that could be considered, for example:

- individual patient — all consequences that accrue to the patient and all costs that are borne by the patient;
- health funder — for example, the costs that fall on a State health authority;
- health care sector — all costs that fall to the health sector, including, but not limited to, hospitals, specialists, general practitioners, ancillary services and community services (includes all health improvements or health-related quality-of-life improvements but does not include such things as informal carer costs, patient transport costs or time off work); and
- society — all costs and consequences that arise from the options no matter who pays or who receives benefits from them.

The use of different viewpoints will identify different costs and consequences, and thus may result in different cost-effectiveness ratios. Consequently, a consistent approach across all guideline development is important.

For the development of clinical practice guidelines, the appropriate perspective is most often that of the health sector. The goal is to maximise the health gains from available health spending, so the health sector budget is the relevant constraint. This is the perspective adopted in the reference case (explained in Section 4).

However, in some cases, a health care option will shift costs. This could be from the health sector to another sector (eg from the medical sector to the community sector), from one health funding organisation to another (eg from a hospital to general practitioners or from one hospital to another) or from the health sector to patients and carers. Therefore, the extent to which cost shifting occurs should be considered for all options. If the extent of cost shifting is large or important, the evaluation may include an additional analysis from a societal perspective and/or an analysis of the distribution of costs and consequences. Where substantial costs are shifted to the patient or another sector (eg the community sector) it may be appropriate to adopt a broader perspective for the analysis. Where substantial costs are shifted between funding organisations, the appropriate perspective is still that of the health system, but it may be

appropriate to include an analysis of how costs are shifted as a result of a particular health care option.

Example 2.3 — Perspective in economic evaluations

Setting: hospital.

Subject of guideline practice: mastectomy.

Options considered: early discharge versus standard discharge.

Perspective: costs to hospital.

Costs omitted: the cost of community medical costs (general practitioner costs, private consultations with surgeons and the costs of scripts of the Pharmaceutical Benefits Scheme).

Conclusion: not including the community medical costs inappropriately reduces the cost of early discharge.

2.4 Interpret the results

The results of an economic evaluation are expressed as a cost per unit of effect (unit of consequence). The costs should include the cost of the health care option itself, plus the costs from any adverse effects (such as complications) and minus the cost savings from any reduction in morbidity or mortality directly resulting from the health care option. For each option, the cost of the health care divided by the outcome is the average cost-effectiveness ratio. Comparing a number of options, the one with the lowest cost-effectiveness ratio is the most efficient. If the least costly option is also the most effective (analogous to YY in Table 1.2) then this is the most cost-effective option. This is known as a dominant solution.

However, the most effective option may cost more (corresponding to the upper left-hand box in Table 1.2). The question then is whether the additional gain in effectiveness (over the option) is worth the additional cost. To answer this question, incremental cost-effectiveness ratios must be calculated. Each option should be ranked in order of (increasing) cost and then the relative change in effectiveness compared.

For example, if there are three health care options available — the base case, option A and option B, each of these have associated costs (C) and effectiveness (E) as follows (Table 2.1).

Table 2.1 Calculating incremental cost-effectiveness ratios

| Option | Cost | Effect | Incremental cost-effectiveness ratio^a |
|------------------------|-------------|---------------|---------------------------------------------------------|
| Base case (least cost) | C1 | E1 | – |
| A | C2 | E2 | $\frac{C2-C1}{E2-E1}$ |
| B (highest cost) | C3 | E3 | $\frac{C3-C2}{E3-E2}$ |

^a The incremental cost-effectiveness ratio is the additional cost per unit of effect.

As stressed in Section 1.2, it is important to choose the right options to assess. Example 2.4 shows how the interpretation of the results of economic evaluation for the three options already described for treatment of atrial fibrillation for the prevention of stroke varies according to which combination of options is considered. Only when all three options (aspirin, warfarin or do nothing) are considered is the true picture apparent.

The incremental cost-effectiveness ratio gives the cost per effect for moving to a more expensive option. However, this does not answer the question: ‘Does the gain justify the cost?’ In practice, this question can only be answered if there is a benchmark for what society is prepared to pay for health outcomes. This is known as a shadow price. For example, if \$70,000 per life-year gained is set as the accepted shadow price level, then this is saying that only those health care options offering increased life-years for an extra \$70,000 or less would be regarded as cost-effective.

Example 2.4 illustrates how incremental cost-effectiveness can be calculated for the comparison of three health care options for avoiding the complications of atrial fibrillation in the form of stroke.

Example 2.4 Interpreting the results

The choice for avoiding the complications of atrial fibrillation in stroke is treatment with warfarin, aspirin or nothing, as described in Example 1.1.

The table below shows the annual rate of ischaemic and haemorrhagic stroke in a population of 65–74-year-old people with atrial fibrillation potentially suitable for warfarin, treated with nothing, aspirin or warfarin. Treatment with aspirin or warfarin lowers the rate of stroke caused by blockage (ischaemic stroke) but may increase the risk of stroke due to bleeding (haemorrhagic stroke). The overall rate of stroke decreases with treatment due to a large reduction in the ischaemic stroke rate. Further details of the figures given below are contained in the tables in Appendix D.

Annual rates of stroke in a population with atrial fibrillation (%)

| Option | Haemorrhagic | Ischaemic | Overall |
|---------------|---------------------|------------------|----------------|
| Nothing | 0.8 | 3.6 | 4.4 |
| Warfarin | 1.4 | 1.3 | 2.7 |
| Aspirin | 0.9 | 2.8 | 3.7 |

Source: See Appendix D, Table D2

If the choice is aspirin or nothing, then the guideline might recommend aspirin as the best treatment, but this may be incorrect because the option of warfarin has not been considered. Alternatively, if warfarin is considered without the option of aspirin, then its relative cost-effectiveness will be exaggerated because a low cost option that is potentially effective has not been considered. The appropriate manner in which to assess this is to consider all three options — aspirin, warfarin and nothing — and then decide between them. The costs and consequences of aspirin and warfarin, compared to the ‘do nothing’ option, are shown in the table below.

Assuming 27,104 people are eligible for warfarin treatment, the cost of the warfarin option is \$22.2 million per year (including \$8.5 million for diagnosis) and this prevents 462 strokes. This is an average cost per stroke avoided of \$48,000. If the use of warfarin is compared to the ‘do nothing’ option (which still contains the cost of diagnosis) the incremental cost is \$30,000 per stroke avoided, (calculated from the \$13.6 million extra spent on warfarin divided by the 462 avoided strokes). If aspirin is used, then the cost is \$8.9 million, preventing 178 strokes at a cost per stroke avoided of \$50,000. If this is compared to the ‘do nothing’ option, the incremental cost is \$2,250 per stroke avoided (calculated from the \$400,000 extra spent on aspirin divided by 178 avoided strokes).

...contd

Example 2.4 (contd)

Comparison of costs and consequences of health care options to reduce risk of stroke in 27,104 people

| Health care option | Effect (strokes averted) | Cost | Incremental cost per stroke avoided |
|---------------------------|---------------------------------|----------------|--------------------------------------------|
| Nothing | 0 | \$8.5 million | – |
| Aspirin | 178 | \$8.9 million | \$2,250 |
| Warfarin | 462 | \$22.2 million | \$30,000 |

Source: See Appendix D

Comparing warfarin and aspirin, warfarin prevents 284 (the difference between 462 and 178) more strokes for the cost of \$13.3 million (the difference between \$22.2 million and \$8.9 million) so the incremental cost per stroke avoided is \$46,800 per stroke avoided (\$13.3 million divided by 284).

Only the comparison of warfarin, aspirin and nothing shows the true costs and consequences of these options relative to one another.

Note: This example is an illustration only. The treatment of atrial fibrillation should be discussed with an appropriate medical practitioner and not be based on these examples of guidelines.

2.5 Define the question

The final step at this stage is to translate the findings into a clear question that can be answered by the economic evaluation. In defining the question, several important components must be included. For the proposed guideline practice, and its alternatives, a clear description of the health care option or program must be given. A statement should include who (medical personnel) does what (treatment, tests, etc) to whom (clinical group of interest), the perspective being used (the health sector) and the outcomes of interest (see Example 2.5).

Example 2.5 — Statement and question

Condition: atrial fibrillation and its treatment to prevent stroke in the elderly.

Population: 65–74-year-olds who have no contraindications to warfarin.

Economic area of interest: prevention of stroke by treatment of atrial fibrillation with aspirin, warfarin or nothing.

Perspective: the health sector.

Consequences of interest: (i) progression onto stroke, or (ii) major haemorrhage.

The economic question

What is the relative cost-effectiveness in preventing stroke of treating patients with atrial fibrillation with the three identified options: nothing, aspirin or warfarin?

Statement

The three identified health care options are described in terms of resources required to treat the population of interest.

Option 1 — do nothing

No active treatment of the atrial fibrillation, initial diagnosis with electrocardiogram and echocardiogram, yearly GP visits, specialist review and blood tests.

Option 2 — aspirin

150 mg of aspirin once a day, initial diagnosis with electrocardiogram and echocardiogram, yearly GP visits, specialist review and blood tests.

Option 3 — warfarin

Warfarin as required to keep the international normalised ratio between 2.0 and 3.0, full blood count, coagulation profile before treatment, fortnightly international normalised ratio tests, initial diagnosis with electrocardiogram and echocardiogram, GP visits, specialist review and blood tests.

Note: This example is for illustrative purposes only.

Key points to be considered in interpreting results of economic evaluation of different options include the following:

- all important consequences should be included in a complete economic evaluation but in order for them to be compared there needs to be a common measure;
- deciding on the perspective is important and can alter the results; and
- incremental cost-effectiveness gives the cost per unit gained of moving from one option to another.

2.6 Overview and next steps

Having finished this stage, the committee should have an appreciation of the economic evaluation perspective and the health care options available for the clinical practice under consideration. The committee should have formulated their findings into a clear question, suitable for economic evaluation and should have a clear description of the economic question(s) they want to answer in association with their clinical practice guideline. The next two stages, Sections 3 and 4, look at how to critically assess whether any available literature exists to inform these questions.

3 COLLECTING AND APPRAISING THE ECONOMIC LITERATURE

Objectives

- To locate and review the existing literature addressing the economic questions compiled in the previous stage.
- To assess the internal validity of studies obtained.

Steps

- Collect and appraise economic literature relevant to evaluation.
- Conduct a systematic literature review.
- Critically appraise economic evidence for internal validity.
- Assess overall internal validity.

3.1 Collect and appraise economic literature relevant to evaluation

The first step is to search the existing literature to assess whether a study relating to the relevant economic questions has already been done. Economic evidence used in the development of earlier guidelines has generally been of limited use, either because such evidence was difficult to identify and retrieve, or because the committee was unclear on how to assess the quality of the evidence. Assessing the quality of a study involves identifying whether valid methods have been used (*internal validity*) and the extent to which the results are transferable to other settings (*external validity* or *generalisability*; see Section 4). The committee needs explicit appraisal criteria in order to undertake an informed assessment of how the published evidence may or may not apply to their own area of clinical practice.

3.2 Conduct a systematic literature review

The purpose of a literature review is to identify and appraise all the available research evidence that may provide information relating to resource or economic implications of the key choices to be made in developing the guidelines. The complementary handbook *How to Review The Evidence: Systematic Identification and Review of the Scientific Literature* (NHMRC 2000a) gives useful information on how to conduct a systematic review. It is important to remember that the aim of a systematic review is to answer a question based on all the evidence — both published and unpublished. In the previous section, the

committee was led through the steps of how to consider the options in order to specify the important economic question(s). The findings from that exercise should be used to inform the relevant search topic(s) and strategy(s) for this literature review.

Useful databases

Two specialist economic evaluation databases are recommended as an initial point of contact with the literature. These cover a large portion of published (as well as some grey area) economic literature.

- *National Health Service (NHS) Economic Evaluation Database* — this is one of the databases of the Centre for Reviews and Dissemination at the University of York, United Kingdom, and is accessible online free of charge.¹ The database contains structured abstracts of economic evaluations of health care options that have been assessed by health economists according to a set of quality criteria: economic study design; assessment of effectiveness; estimation and valuation of consequences used in the economic analysis; costing methodology; method for synthesis of results; and handling of uncertainty. Material for the database is identified from published sources by regular, comprehensive searching of key databases, including Current Contents Clinical Medicine (weekly), MEDLINE and the Citation Index for Nursing and Allied Health Professionals (CINAHL), by hand-searching relevant journals and by scanning the grey literature.
- *Health Economic Evaluations Database (HEED)* — this database has been developed as a joint initiative between the Office of Health Economics and the International Federation of Pharmaceutical Manufacturers' Association and is available online (a charge is levied for access).² The database includes 25 of the leading medical, health economics and health policy journals and some other journals not available through online databases. Academic and government publication lists are regularly searched for new literature.

As these databases may not cover all the relevant material in the timeframe of interest, the committee should also conduct their own literature search. This should include the health-related databases such as MEDLINE, HealthStar, Embase and CINAHL; the psychology databases PsycINFO and PsycLIT; the business database ABI/Inform; and the economic-specific database EconLit. (As a minimum the committee should search both MEDLINE and EconLit.)

¹ <http://nhscrd.york.ac.uk>

² www.ohe-heed.co

In searching these databases, a number of key words and phrases should be used, such as:

Medical subject headings (MeSH):

cost benefit analysis, costs, cost analysis, economics

Key words:

economic evaluation, cost-effectiveness analysis, cost-utility analysis

These terms need to be supplemented with specific key words relevant to the health care option/strategy of interest. For example, in searching for economic evaluations of atrial fibrillation, the following search would be appropriate:

atrial fibrillation AND (economic evaluation OR cost-effectiveness OR cost utility analysis)

Other sources of information that may be useful, especially for finding current research not yet published in refereed journals, are specialised organisations. Useful organisations and their Internet addresses are given in Table 3.1. Many of these provide links to other organisations.

Table 3.1 Useful organisations and websites

| Organisation | Internet address |
|-----------------------------------------------------|--------------------------------------------------------------------------------------------|
| Centre for Health Economics Research and Evaluation | www.chere.usyd.edu.au |
| Centre for Health Program Evaluation | ariel.unimelb.edu.au/chpe/ |
| Health Economics Research Group | www.brunel.ac.uk/depts/herg/ |
| Centre for Health Economics | www.york.ac.uk/inst/che/ |
| Health Economics Research Unit | www.abdn.ac.uk/public_health/heru/ |
| Centre for Health Economics and Policy Analysis | hiru.mcmaster.ca/chepa/ |

Duplicate publications are likely to be easily identifiable in this field, as usually there are only a small number of studies on any one topic. Following standard literature review practice, the abstracts of identified studies can be used to narrow down the relevant set of studies. Key words are commonly misused in economic evaluation literature (eg a study may be entered into a database as a cost-effectiveness study but on closer inspection it may provide no systematic data on costs and consequences). Identifying and culling such studies is an important part of the review process.

3.3 Critically appraise economic evidence for internal validity

A number of reputable organisations have issued guidelines on how to assess the quality of economic evaluations. Such guidelines aim to maintain methodological standards, facilitate the comparison of results of economic evaluations of different health care options and improve interpretation of study results from one setting to another. The criteria referred to in the remainder of this section are consistent with two such guidelines (Drummond and Jefferson 1996, Drummond et al 1997).

The quality of economic evaluations should be assessed using a set of standard questions and a system for grading responses to each question. A recommended set of 12 core questions is summarised in Table 3.2 and given in more detail below. Once the guideline development committee has checked the relevant economic evaluations against this list of questions, and graded the responses, an overall assessment of each study's internal validity can be made (addressed in Section 3.4).

In the remainder of this section, the 12 questions shown in Table 3.2 are discussed as a guide to help grade each item and thus appraise each study.

Table 3.2 Checklist for appraising economic evaluation studies

| Appraisal item for internal validity | Comments/ grading ^a |
|-----------------------------------------------------------------------------------------|-------------------------------------------|
| 1. Was the study question well defined? | |
| 2. Were appropriate health care options chosen and clearly described? | |
| 3. Was an appropriate study type used? | |
| 4. Was the effectiveness of the health care options established? | |
| 5. Were the cost estimates related to baseline population risk? | |
| 6. Were all the relevant costs and consequences identified for each health care option? | |
| 7. Were costs and consequences measured accurately? | |
| 8. Were costs and consequences valued credibly? | |
| 9. Was differential timing considered? | |
| 10. Was incremental analysis performed? | |
| 11. Was a sensitivity analysis performed? | |
| 12. Were modelling techniques used in a clear and reasonable way? | |

^a See Table 3.3 for an example of a grading system

3.3.1 Was the study question well defined?

The question, or hypothesis, being addressed should be clearly stated and should include a comparison of costs and outcomes of relevant options. The viewpoint for the evaluation should be clearly stated and justified.

3.3.2 Were appropriate health care options chosen and clearly described?

All appropriate, realistic options should have been identified. Maintaining the status quo is a frequently omitted strategy. Another mistake is to view options as being 'all or nothing' rather than being able to operate at different levels or in combination. Using the atrial fibrillation example, a relevant option could be a strategy that includes the use of aspirin and warfarin in different people or a different INR range.

The comparisons that can be made are often limited by the data. Shortcomings of individual trials may mean that economic evaluations have to be based on a synthesis of evidence from multiple sources. By necessity, a number of assumptions must come into play. The committee may have to assess the

methodology of the primary studies used in the economic evaluations and decide whether such studies are really comparable. For example, if primary studies included groups with different baseline risks or measured clinical outcomes in a different way, this would be cause for concern.

Each option compared should be described in sufficient detail to enable the committee to assess who did what, to whom, where and how often.

3.3.3 Was an appropriate study type used?

The type(s) of evaluation used should be clear. There should be reasonable justification to show how the form of evaluation chosen helps to answer the questions posed.

For example, if using a cost-minimisation evaluation, there should be justification that the consequences of the options are equivalent in type and magnitude (cost-minimisation analysis is used when consequences of the options are the same). If the study used a cost-effectiveness framework, the consequences of the health care options should be measured in the same units.

3.3.4 Was the effectiveness of the health care options established?

The claimed effectiveness of health care options in an economic evaluation study should be assessed using criteria laid out in the complementary handbook *How to Use the Evidence: Assessment and Application of Scientific Evidence* (NHMRC 2000b). It is important to establish that there is sound evidence for the effectiveness of any health care option.

The most rigorous evidence of effectiveness is drawn from clinical trials but these may impose restrictive conditions that do not reflect normal clinical practice (eg the trial may impose restrictions on those patients who are included). Therefore, effectiveness data may need adjustment (to reflect the population the health care will be applied to). This is discussed in detail in the accompanying handbook in this series *How to Use the Evidence: Assessment and Application of Scientific Evidence* (NHMRC 2000b) and is also discussed in Section 4.

Effectiveness data are generally measured in natural clinical units and may have been converted to more general measures of benefit, such as life-years saved and QALYs (see Section 1.1). The methods used to extend measures of effectiveness beyond the endpoint of the trials, or to convert to other measures of benefit, should be clearly described.

3.3.5 Were cost estimates related to baseline population risk?

Dividing patients into risk categories is common in clinical practice. Costs and consequences of health care options, and therefore cost-effectiveness, are likely to differ over risk categories. Therefore, the committee may need to think about the relevance of a cost-effectiveness analysis in terms of relevant subgroups. In this context, risk refers to the absolute risk within subgroups and cost-effectiveness is dependent on the reduction of absolute risk. For example, the risk of stroke complicating atrial fibrillation increases as age increases; therefore it might be expected that the cost-effectiveness of treatment might improve with age, all other things being equal.

3.3.6 Were all the relevant costs and consequences identified for each health care option?

Direct costs can be divided into the three subcategories listed below, one within and two outside the health services sector.

- Health care resources consumed in running the health care option, including dealing with adverse events or other flow-on costs. These are the relevant costs from the health service sector perspective described in this handbook.
- Patient and family resources such as time and any out-of-pocket expenses (eg for adjustments to the house to enable the patient to recuperate at home). If a health sector perspective is taken these may not be measured and valued, but it is good practice to acknowledge these costs.
- Resources consumed from other sectors. Certain health care options may change the pattern of resource use in other sectors of society, such as community services or education. This may be especially important for options directed at groups such as the elderly or mentally ill.

It is important to use a timeframe that is long enough to encompass all the important costs and consequences. Similarly, consequences of a health care option may impact on the physical, social or emotional functioning of the patients. All relevant aspects of health consequences should be included.

All relevant and significant costs and consequences within the specified viewpoint should be identified. In cases where some costs and consequences have been omitted, the committee should be satisfied by the reasoning given by authors that such omission does not greatly affect the results and conclusions.

3.3.7 Were costs and consequences measured accurately?

Resources should be measured in physical units such as number of physician visits, hours of nurse time or quantity of drugs taken. Reasonable criteria must

be used to allocate a measure of shared resources (eg hospital overheads such as power might be distributed according to floor space and porters according to the number of patients) to a health care option.

When measuring resources used in a clinical trial, adjustments should be made for those that are not typical of usual practice but are part of the research costs themselves (eg tests undertaken for the purposes of randomisation).

Outside the trial setting, estimates of resource use should be based on real patients, either followed prospectively or identified retrospectively from medical records. Use of expert panels may be necessary when there are no alternatives but this is not ideal as estimates from expert panels have been found to be inaccurate.

For consequences, the units used to measure outcome should be logically specified. For example, if a treatment saves lives then the number of lives saved or the number of life-years gained may be chosen, whereas if a treatment improves morbidity then some index of health status may be used. The committee should be satisfied that those consequences included in the final economic evaluation were measured with sufficient accuracy.

3.3.8 Were costs and consequences valued credibly?

Price is the unit most commonly used to cost resources. Prices may need to be adjusted if they are clearly an inaccurate proxy for the opportunity cost, that is, the value of what must be given up in order to obtain something (opportunity cost is the value of the other benefits forgone). For example, the price of heavily subsidised goods does not reflect their true cost. Additionally the cost of volunteer labour does not reflect its true cost.

The importance of accurate estimates of opportunity costs of a particular resource depends on how much the resource contributes to the estimate of the overall cost. For example, patients in Australia are often classified into an Australian diagnosis-related group (AN-DRG) according to their presenting diagnosis and the procedures they have received. Standard cost-weights are derived that apply to all patients within a DRG³. The importance of using a general per diem or DRG cost-weight for a hospital stay depends on how this relates to total costs of the health care option, and on whether the valuation used is sufficiently sensitive to capture any differences between the options being considered.

³ For example see Commonwealth Department of Health (1993) or the appropriate State Australian Diagnosis Related Group cost-weights guide.

If consequences have been valued, details should be provided of the valuation methods used and of the individuals who provided the valuations (eg patients, general public, health professionals). Examples of valuation methods include a standard health status index, such as Australian quality of life (AqoL), and direct estimates of value from standard gamble and time trade-off.⁴

Prices should be dated so that they can be adjusted for inflation or currency conversion where necessary. The conversion of one currency to another with the use of purchasing power parity (PPP) rather than exchange rates probably represents the true value more appropriately.

3.3.9 Was differential timing considered?

The time horizon in the study should be given. This should be long enough to capture all the effects of the options under consideration. If the time horizon is shortened for practical reasons this decision should be justified and an estimate of any possible bias introduced should be given.

It is conventional to discount future costs and consequences to their present value using a discount rate.⁴ Most analysts agree that consequences should be discounted at the same rate as costs in the baseline analysis. The choice of discount rate should be stated and an explanation given if costs or consequences are not discounted. Most studies will include a sensitivity analysis around the issue of the discount rate.

A discount rate of 5% is recommended in this document as the reference case method (see Section 4.2). The guideline development committee may wish to adjust a study's results to reflect this. If discounting is included, a note should be made to indicate whether or not it was at the 5% level.

3.3.10 Was incremental analysis performed?

An incremental analysis comparing the options should be reported, unless one therapy is dominated by another (ie the dominant therapy produces more health gain with lower costs), in which case an incremental comparison is not needed. The incremental cost-effectiveness ratio will be critically dependent on the comparison being made.

3.3.11 Was a sensitivity analysis performed?

Uncertainty in economic evaluation arises from lack of precision in estimation, from extrapolation or from analytical methods. The impact of this uncertainty on the results should be tested. The convention is to undertake a sensitivity

⁴ See Glossary.

analysis where key variables are systematically altered to assess their impact on the cost-effectiveness ratio. There are a number of ways in which this can be done (Drummond et al 1997).

The committee should be satisfied that all key areas of uncertainty were tested. The range of values tested should be justified and should be based on evidence or logic. Firm conclusions may be shown to hold despite considerable uncertainty (ie the conclusion is not changed by the sensitivity analysis) and is considered to be robust. However, if it is found that relatively small changes of parameters in the sensitivity analysis create substantial uncertainties regarding the implications of the study findings, then either more effort is needed to reduce the uncertainty or less confidence can be placed in the results.⁵

3.3.12 Were modelling techniques used in a clear and reasonable way?

Modelling techniques allow an evaluation to be extended beyond a single set of direct observations. Models are necessarily simplified, and the extent to which the simplification is appropriate will be a matter of judgment. Modelling may involve explicit statistical and mathematical techniques or it may simply bring together data from a variety of sources into a single conceptual framework. Modelling can be used to:

- extrapolate clinical outcomes beyond the trial horizon (eg a trial might continue for 10 years but the economic evaluation might consider a lifetime of costs and consequences [Whynes et al 1998]);
- move from intermediate measures to final outcomes (eg using the number of those giving up smoking in a smoking cessation trial to calculate life-years saved [Stapleton et al 1999]);
- look at data from multiple sources to undertake decision analysis (eg the decision tree modelling in an economic evaluation of school-based screening options for tuberculosis in children [Slater et al 1998] was constructed with information from several different sources, including surveys, journals and professional opinion); or
- look at evidence from trials to estimate what might happen in a different clinical setting or population (eg the trial data might be adjusted for the age mix in the general population [Whynes et al 1998]).

⁵ See Appendix E for more information on sensitivity analysis

Any modelling should be explicit and clear, and assumptions used in the construction of models and inputs to them should be tested in a sensitivity analysis.

3.4 Assess overall internal validity

Economic evaluations will always involve a number of judgments. Methods of economic evaluation cannot be applied in a cookbook fashion; rather, a general set of evaluation tools is applied to a particular problem using economic theory to guide decisions. One approach to grading the answers to the 12 questions described above is shown in Table 3.3. Although this is intended as a guide to appraising the economic evidence located in the literature review, the advice applies equally to new economic evidence produced specifically for clinical practice guidelines (see Section 5).

The grading suggested in Table 3.3 clearly calls for value judgments to be made. These should be made collectively by the guideline development committee. It is important to remember that the answers relate to the validity of the study in its own setting (internal validity). For example, if the comparator given is relevant to the United States (where the study is set) but is not relevant to the Australian setting, this is an external validity issue, addressed in Section 4.

Researchers often have limited space in journals or other outlets in which they can report their results, so it may sometimes be difficult to tell whether or not a study is valid. In such cases the committee should contact the authors to ask for a more comprehensive report or to clarify issues. Where it is not possible to clarify a point, it is recommended that the group err on the side of caution and grade the study conservatively.

Table 3.3 Key to grading evidence on the 12 core questions

| Description | Grade |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| The item is clearly demonstrated and appropriately carried out. | Y |
| <p>There is some concern that this item of the study may not have been appropriately carried out.</p> <p>This category is applied if the study methodology is not as clear or as detailed as it could be but does not by itself make the study invalid. For example, if discounting (item 9) was not conducted or incremental analysis (item 10) not performed, these could be performed later, given sufficiently detailed data. Another example might be that a study does not discuss whether individuals in a health care group might have been likely to attend a GP clinic more often than those in the comparator group (item 6). If the cost of an item is likely to be small in relation to total costs, the committee might decide that, although there are concerns, they are not sufficient to invalidate the results.</p> | ? |
| <p>There are clear concerns about the item.</p> <p>This category is applied if there is a flaw in the study that may be significant enough to seriously affect the results, or if insufficient information is given to judge whether such a flaw might be there — for example, if the effectiveness results in the study are based on the view of one clinician and no good reasoning is given for the selection of that clinician (item 4). Another cause for serious concern might be if the comparators used are not ideal — for example, if a new diagnostic test was compared with no test when there is another test in routine use that the new test would replace (item 2).</p> | ?? |
| <p>The item is not applicable in the context.</p> <p>This may apply, for example, where the study was dealing with a highly defined group of patients. In this case, estimates related to population risk (item 5) may not be applicable. Similarly, if all costs and consequences relevant to the study (eg considering a medicine for the common cold) occurred in the first six months then differential timing (item 9) would not be applicable.</p> | NA |

Different analysts may make different decisions at points throughout an analysis; however, it is hoped that they would agree on the crucial points and that even if the end results differ slightly there are no substantial differences.

With the above points in mind, the committee needs to assess whether, overall, a study is internally valid. Minor contentions about the methodology or data may arise at several points but what is important is whether or not these points cause enough concern to seriously doubt whether the results are valid. In making a judgment on this point, the committee should use the completed

Table 3.2 as a reference. If contention or uncertainty remains, a health economist should be consulted.

On finishing this stage, the committee developing clinical practice guidelines should provide a summary of the relevant economic evidence in terms of:

- a systematic review of the literature;
- the search strategy used for identifying the literature; and
- an assessment of the internal validity of relevant studies.

3.5 Overview and next steps

This section covered the process of searching for relevant existing literature relating to the question(s) formulated in the last stage. The internal validity of each relevant study should have been assessed against the provided checklist and a consensus arrived at regarding the overall internal validity of each study.

If one or more internally valid study has been located, the committee can proceed to the next stage, which looks at how the findings of a study can be applied to the clinical practice guideline being developed. If no internally valid studies have been located, the committee should proceed directly to Section 5, which provides guidance on how to conduct a new economic evaluation.

4 APPRAISING EXTERNAL VALIDITY AND COMPARABILITY

Objective

- To assess whether the results of existing studies assessed as being internally valid are generalisable to the proposed guideline setting (externally valid).
- To use a reference case to ensure that the available studies are consistent so that comparison of results is valid.

Steps

- Assess the external validity of a study.
- Assess the study against a reference case.
- Assess the study overall.

4.1 Assess the external validity of a study

In Section 3, the internal validity of an economic evaluation was assessed. However, even if a study is sound in its own setting, this does not necessarily mean the results can be applied to another place and/or time. Assessing generalisability requires an assessment of differences in the health care system, practice patterns, types of patients (eg the severity of their illness, risk status), patterns of resource use and costs.

The question of whether a result is generalisable is especially important when the cost-effectiveness of an expensive health care option largely relies on its ability to offset other health care expenditures.

The following issues are some of the key aspects affecting the generalisability of a study to the guideline setting. Each of these needs to be carefully considered before the results of a study can be justifiably recommended and used in the development of a guideline. Each issue should be discussed with respect to both the proposed health care and the alternative(s). In addition, each study type and clinical practice area is likely to have specific issues relating to generalisability, which should be carefully considered and addressed. A worksheet, such as that shown in Table 4.1, can be used to record the assessment. The grading, which requires value judgments to be made, and comments recorded in this table can be used by the committee to make an overall assessment of a study's external validity with respect to the proposed guideline setting.

Table 4.1 Criteria for assessing the generalisability of economic evaluation studies

| Appraisal issue | Comments/ grading^a |
|-------------------------------------------------|------------------------------------------|
| Patient group | |
| Health system setting | |
| Health care option | |
| Resource costs | |
| Marginal versus average cost | |
| Other specific issues relating to the guideline | |

^a Suggested grading for generalisability issues

A = The study is generalisable to the proposed guideline setting with regard to this issue.

B = There are some concerns relating to generalisability for this issue.

C = The study is not transferable to the proposed guideline setting with regard to this issue. There is sufficient concern about this issue to believe the study results are not generalisable.

4.1.1 Patient group

Different costs and outcomes may be associated with different patient groups. Therefore, it is important to determine whether the patients in the study differ from the patients who would be covered by the proposed guideline in terms of demographics, clinical indicators and comorbidity profiles. If the patient characteristics considered for the proposed guideline meet the inclusion and exclusion effectiveness criteria of the original study(ies), then there is little difficulty in judging that the patients are similar.

In many circumstances, the study patients and the proposed guideline patients may not be an exact match (eg they may differ in the severity of their illness and/or their risk status). In these cases, patients treated under the proposed guideline may respond differently to the treatment and/or consume a different level of resources from those included in the study. In some cases, subgroup or sensitivity analyses in the original study may aid this comparison.

4.1.2 Health system setting

It is also important to assess whether the availability of treatments, the levels of health sector personnel and equipment, and the local supporting care patterns differ between the study setting and the anticipated setting for implementation of the guideline in Australia. Factors that may affect the applicability of studies to the proposed guidelines include:

-
- equipment and care used in the original study no longer being in use;
 - differences in the institution size or type of experience of the personnel across disciplines;
 - differences in the urban and rural mix in health care delivery between the study setting and the Australian setting;
 - possible supply constraints in Australia that could impact on how a health care package would be offered in practice; and
 - differences in incentive structures (to professionals, institutions or patients) between the setting used in the original study and the proposed guideline setting (findings may also differ even when a study removed the usual incentives surrounding medical care).

4.1.3 Health care option

The health care used in the reported study needs to be compared with the health care and/or clinical management considered for the guideline. For the study results to be generalisable, the components of the health care (eg the proportions of inpatient treatment and ambulatory care for the same condition) should be the same.

4.1.4 Resource costs

In considering the transferability of cost estimates, it is useful to remember that the cost of a health care option is the product of physical resources consumed (eg drugs, tests and professionals' time) and respective unit prices. Cost data may not be transferable for two reasons. First, clinical practice patterns and settings may vary in such a way that resource consumption associated with the treatment, supporting care and diagnostics differs from that reported in the study (see Sections 4.1.1 and 4.1.2). Second, local prices for resources may differ from those used in the study. If the relative prices of two or more health care options differ between (or even within) countries, then the relative cost-effectiveness of the options will differ also. To assess these aspects of generalisability, study data on resource use and prices need to be disaggregated. Disaggregated data may or may not be available from published studies.

The unit costs from a study may not be in Australian dollars (if the study was conducted overseas) or may not be in current prices (if the study was conducted in a previous year). These issues alone are not of serious concern — if the study data are provided in a sufficiently disaggregated form, a health economist will be able to adjust the prices to current Australian resource costs.

4.1.5 Marginal versus average cost

The correct cost approach needs to be identified. Some authors claim the superiority of marginal costing over average costing, where marginal costing is costing a good or service at the extra cost of producing the next unit of the good or service.⁶ However, the most appropriate approach needs to relate to context and timeframe and must be decided by the committee. In the short term, few costs may be variable if a change in health care is introduced. Over a longer timeframe, all costs may be variable. If the published study results are aimed at the manager of a hospital, then short-run marginal costs of various options may be appropriate within the current budget. However, if the study results are being used to assess a national policy (which may be the case for many clinical practice guidelines) then average costs are likely to be more appropriate because they reflect the costs when many services are provided in a large number of facilities across the country.

Example 4.1 Transferability of economic study findings

O'Brien et al (1997) have outlined an approach for interpreting economic analyses and the application of study findings to a specific clinical practice situation. They proposed a spectrum for the certainty with which information can be transferred from one setting to another, with **efficacy data (does it work?)** more transferable than **effectiveness data (how well does it work?)**, which are in turn more transferable than **economic information**.

The implication is that, along the spectrum from efficacy data to economic data, increasingly stringent proof of equivalence is needed before study results can be transferred to the local setting.

Some would argue that clinical applicability should be the first criterion addressed in determining study portability. If it is not possible to verify that comparable clinical efficacy/effectiveness exists, there may be little benefit (and a lot of work) involved in proceeding with the verification of other clinical and cost data to complete the transfer. Whatever the approach, each of the major components of the evaluation (ie clinical, economic, epidemiological, health care patterns, treatment comparators) must be verified versus local conditions before a study's results can be considered transferable.

Source: Canadian Coordinating Office for Health Technology Assessment (1997).

4.2 Assess the study against a reference case

Comparability of studies is improved by the use of a standard set of methods, or a 'reference case'. This does not prescribe or proscribe what the analyst can

⁶ World Bank glossary (www.worldbank.org/healthreform/class/module1/glossary.htm)

do but ensures that there is a consistent basis for comparison across different studies and gives some basis for judging the quality of an economic evaluation.

A reference case should be used to assess and (where necessary) adjust the results of published studies to ensure comparability. The recommended reference case methods for economic evaluation studies are shown in Table 4.2. These methods are based on the reference case developed by Weinstein et al (1996), adapted to relate specifically to clinical practice guidelines in Australia. This approach is also consistent with most of the economic recommendations of the Pharmaceutical Benefits Advisory Committee (PBAC; Commonwealth Department of Human Services and Health 1995)

Where valid studies do not conform to the reference case standards, adjustments will need to be made.

4.3 Assess the study overall

The results of the above assessment of generalisability (the completed Table 4.1) and comparability (compliance with the reference case) can be used to determine whether a study is, overall, externally valid. Minor contentions about various aspects of the study may arise but the important decision is whether, and to what extent, these points would change costs and outcomes, and hence the cost-effectiveness ratio between the study findings and the proposed guideline setting. Consultation with a health economist may help determine responses to any specific issues relating to the particular proposed guideline, and responses to the appraisal issues. Furthermore, a health economist can advise on conversion of different units of currency to current values through techniques such as the use of purchasing power parity.

Table 4.2 Reference case methods recommended for economic evaluation studies for Australian clinical practice guidelines

| Factor | Reference case methods |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Perspective | The analysis should be from the perspective of the health sector (to maximise the health gain from the health budget). Costs from outside the health sector should not be considered. |
| Time horizon | The timeframe of the study should be long enough to capture all relevant future effects (costs and consequences) of a health care option. There is often little evidence on long-term effects but a recommendation about the use of a practice cannot wait for such evidence. The same time horizon must be used for both costs and consequences; and the lack of evidence on long-term effects noted. |
| Options | All the relevant health care options (see Section 1.2) should be compared. |
| Costs | |
| – numerator | All health sector costs should be identified. In practice, the decision about which costs to include in the study should strike a balance between expense, difficulty and potential importance. All cost items that have a significant impact on the results should be included. Costs that fall outside the health sector (eg to community care services or to patients) should be identified. If there are likely to be important differences between options, then these should be measured and valued but presented separately from the cost-effectiveness ratios. For example, if in one option care occurs in the home and in another it occurs in the hospital, this should be noted, if it is considered important. Other distributional aspects should be identified if there is a major change in the burden of costs. |
| – indirect costs | Indirect costs, such as productivity gains and losses, and time costs of patients in health care, should not be included. A monetary cost for years of life gained should not be imputed. |
| – measurement | All costs should be measured using unit costs relevant to the proposed guideline setting (usually Australia-wide). If cost estimates have been based on one hospital, they should be adjusted to reflect Australia-wide hospital costs. For example, if costs have been estimated at different times, these should be adjusted to constant dollars. Costs from other countries may have to be adjusted for differences in resource use (eg substitution of nurses for medical practitioners, shorter hospital stays) and unit costs (eg higher earnings). A 5% per year discount rate should be used for future costs and consequences. |

...contd

Table 4.2 (contd)

| Factor | Reference case methods |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| – opportunity cost | Wherever possible, the opportunity cost should be identified and measured (generally in prices). If prices do not represent a sufficiently accurate approximation to opportunity costs, they should be adjusted and justified. Costs associated with new, unrelated diseases that are likely to affect patients in added years of life due to effective health care should not be included in the analysis. |
| Health consequences | |
| – identification | All relevant health consequences should be included. |
| – denominator | Ideally, the consequences of a health care option should be assessed in terms of final consequences, such as life-years saved or QALYs. Modelling may be required to link surrogate outcomes to final outcomes. Quality adjustment weights should be based on community preferences, and scaled appropriately. |
| – probabilities | Probabilities of outcomes should be determined from the best designed studies (NHMRC 2000b). Expert judgment should only be used where no adequate data exist or if the parameter is of secondary importance to the analysis. Modelling can be used to estimate or extrapolate effectiveness values. |
| Uncertainty | The impact of uncertainty on the results should be assessed. At a minimum, one-way sensitivity analysis should be conducted. It is desirable that two-way sensitivity analysis be undertaken for important parameters (see Appendix E). |

4.4 Overview and next steps

This section covered the process of assessing the generalisability (or external validity) of the results to the proposed guideline setting, and the comparability based on reference case methods.

If the study or studies have been assessed as being generalisable to the particular guideline setting and they meet the reference case standards (ie are comparable), the committee should move directly to Section 6. This looks at how the assessments of internal and external validity are used to come to a decision about the usefulness and interpretation of published cost-effectiveness evidence.

If no externally valid study findings have been located, or if the results need re-analysis (ie are not comparable), the committee should proceed to Section 5, which provides guidance on how to conduct a new economic evaluation.

5 UNDERTAKING A NEW ECONOMIC EVALUATION

Objective

To provide guidance on how to conduct a new economic evaluation for a proposed guideline.

Steps

- Assess whether a new economic evaluation is needed.
- Identify the methods required for economic evaluation.
- Consult a health economist.

5.1 Assess whether a new economic evaluation is needed

There are several reasons why a new economic study may be needed. These include:

- there is no available economic evidence;
- available studies are of poor quality or out of date (not internally valid; see Section 3);
- evidence is not generalisable to the setting and patients being considered (not externally valid; see Section 4); or
- the results need conversion into the reference case.

Economic analysis is increasingly conducted prospectively as part of a clinical trial, but this does not mean that if there is no economic evidence available a new trial has to be conducted. Often a new economic analysis can be based on existing data. Data on outcomes and effectiveness are available from the literature. Appropriate cost data can be obtained by building up a picture of resource use and by using benchmark costs, such as AN-DRG cost weights (Commonwealth Department of Health and Aged Care 1999) or the standardised unit costs produced by the PBAC.

Sometimes, published data can be augmented by readily acquired new primary data. In this stage, the emphasis is on developing an economic analysis from readily available data. Most commonly, an appropriate model can be constructed from a range of published studies and data with the skill of a health economist.

5.2 Identify the methods required for economic evaluation

For any economic evaluation, the steps to be followed mirror the questions that were asked in the critical appraisal steps of Sections 2–4. The steps are:

- defining the scope of the study;
- collecting data on costs and consequences; and
- analysing the data.

The methods adopted should conform to the reference case (see Table 4.2). If it is necessary to depart from one of the reference case rules, especially the costs, the rationale for this should be made explicit and study results for both the reference case and the alternate should be reported.

5.3 Consult a health economist

Whilst the principles of economic evaluation are readily grasped, their application can be more complex, often requiring a comprehensive understanding of microeconomics. Thus, it is important to consult a health economist at this stage to obtain relevant input and specialist knowledge. Depending on the make-up of the committee and size of the task at hand it may be necessary for the group to commission additional specialist help.

Table 5.1 describes the steps in an economic evaluation and the respective roles of the guideline development committee and the health economist.

Table 5.1 Checklist for conducting a new economic evaluation

| Steps | Who does what? |
|------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Define the question for the evaluation ^a | GDC defines the clinical question HE defines the approach for economic evaluation and outlines resources required GDC refines economic study question |
| 2. Describe the options in sufficient detail to identify resource inputs | GDC |
| 3. Identify the full range of important consequences | GDC and HE collaborate to ensure the consequences are appropriate clinically and economically |
| 4. Estimate/obtain appropriate evidence of effectiveness | GDC |
| 5. Transform measures of effectiveness into appropriate measures of benefit ^b | HE |
| 6. Identify full range of costs | HE and GDC collaborate |
| 7. Measure and value resource inputs | HE |
| 8. Adjust for differential timing | HE |
| 9. Incremental analysis | HE |
| 10. Sensitivity analysis | HE |
| 11. Recommendations | GDC and HE collaboratively |

GDC = guideline development committee; HE = health economist

^a The other handbooks in this series will be valuable at this step.

^b Other professionals such as clinical epidemiologists may be of help at this stage.

Health economics is a relatively new subdiscipline of economics. There is an international shortage of experienced health economists and economic evaluation is only one of many areas of research within the subdiscipline. It is therefore unlikely that every guideline development committee will include a health economist and one may need to be identified for this stage.

The earlier the health economist meets with the committee, the more familiar they will be with the issues the economic evaluation has to address. However, if the committee has not defined the specific issue for the economic evaluation, the health economist will have little to contribute. The best approach is to involve the health economist once the scope of the project is clear but to allow the economist to help refine the study question. Health economist resources can be found at the following websites and postal address:

-
- www.chere.usyd.edu.au – this has link pages to other health economics organisations;
 - www.healtheconomics.org/databases.htm – this is a searchable worldwide database requiring either the name of a health economist (if one is known) or a country/organisation name (to produce a listing of health economists); or
 - the Australian Health Economics Society Inc., which covers health economists in Australia and New Zealand. Information can be obtained from The Secretary, AHES Inc., Health Economics Unit, Monash University, PO Box 477, Tel: (03) 9496 4406; Fax: (03) 9496 4424.⁷

5.4 Stage summary and next steps

This section gave a broad overview of the situations in which a new economic evaluation may be required. The new economic evaluation(s) should have been based on the reference case (see Table 4.2), and a health economist should have been consulted, as appropriate.

By following this guidance, the committee should be able to conduct a valid economic analysis to answer any questions from Section 2 that have not already been adequately addressed by the existing literature. The new data generated will add to a series of studies that are consistent in quality and have comparable results.

In the next stage, all the evidence gathered in Sections 3–5 must be assessed to determine whether the proposed guideline is, in principle, cost-effective.

⁷ Also online at www.uq.edu.au/economics/ahes

6 DETERMINING THE COST-EFFECTIVENESS OF OPTIONS

Objective

To decide on the preferred clinical practice, using both clinical effectiveness and economic evidence.

Steps

- Assess whether any options are dominant or dominated.
- Calculate incremental cost-effectiveness.
- Assess the quality of the evidence.
- Consider other factors.
- Make the decision.

6.1 Assess whether any options are dominant or dominated

The results of the economic analysis will show (at least) the costs of each option being considered, and the consequences expressed in some clinically meaningful way. This may be the number of cases occurring, the number of adverse events or complications, or the number of deaths — it does not matter how consequences are measured, as long as they are measured in the same way for all options. The first step is to identify any options that dominate others or are dominated themselves.

Where there is an option that costs more and delivers less care than another, it is said to *be dominated*. It should no longer be considered a relevant option, as the other option is clearly better. This is the XX cell in Table 1.2.

If one option is preferred, over all others, on both the clinical and cost evidence, it is said to *dominate* the others (YY in Table 1.2). In this situation, there is no need to calculate incremental cost-effectiveness ratios.

Example 6.1 shows a hypothetical example of a dominated option. Three possible health care options, A, B and C, have been identified for a health problem and the total costs and consequences are shown. Option B is dominated by option A because A costs less (\$10,000 versus \$40,000) and gives a larger health gain than B (5 life-years versus 4 life-years). For this particular health problem, B is dominated by A and should not be considered further. Option C costs considerably more than A but gives a larger health gain; thus, options A and C will have to be considered further.

Example 6.1 — A dominated option

| Option | Cost (\$) | Life-years resulting from the health care |
|---------------|------------------|--------------------------------------------------|
| A | 10,000 | 5 |
| B | 40,000 | 4 |
| C | 140,000 | 8 |

6.2 Calculate incremental cost-effectiveness

A common outcome to the assessment is that a more effective health care option will cost more ('?' in Table 1.2). The second step is therefore to consider the incremental cost-effectiveness ratios (as described in Section 2.4). In the same way that effectiveness can be measured in any meaningful clinical unit, so the cost-effectiveness ratio can be measured as additional cost per case detected, additional cost per event avoided, additional cost per death prevented, additional cost per life-year gained and so on. The question that has to be answered is: 'What is the additional benefit worth?' This can only be answered if there is a known shadow price (or cost) that the community is prepared to pay.

The shadow price is the predetermined maximum willingness to pay for health gains. As suggested previously, there is a pressing allocation problem that must be solved in health care. The comparison of the costs and consequences of a health care option needs to include indications of when the comparison is favourable and when it is not. The shadow price is one such indication; it can be used as a guide when comparing different options as to whether the consequence is worth the cost. In this context, the shadow price is the mechanism ensuring that the least costly option will not always be chosen. It should be remembered that the use of the shadow price is a guide.

The magnitude of the shadow price is contentious. It may be revealed directly or indirectly through the endorsement of particular guidelines. However, it is helpful to draw on PBAC and others for information and experience to guide this decision (see Box 6.1).

**Box 6.1 Shadow prices used by the Pharmaceutical Benefits
Advisory Committee****Purpose**

It has been mandatory for some time that new drugs are subject to economic evaluation before being recommended for listing by the PBAC.

Shadow prices

Data are available on the range of shadow prices implied from actual decisions taken to list drugs on the Pharmaceutical Benefits Schedule during 1993–96 (costed at 1995–96 prices).

If a drug fell within the range of \$36,000 to \$69,000 per life-year gained, then it was mostly listed at the price recommended but sometimes a lower price was recommended.

If it fell below the \$36,000 per life-year gained threshold, it was unanimously accepted.

If it fell over the \$69,000 per life-year gained limit, there was unanimous agreement by the committee to reject requests for listing, or occasionally to recommend listing only at a lower price.

Source: George et al (1998).

Consistent with the analysis of the PBAC decisions and others, but also taking into account clinical practice guidelines representing a much wider range of health service care options, the following is recommended. If the incremental cost-effectiveness ratio is expressed as cost per life-year gained, it is suggested that:

- health care options that fall below the threshold of \$30,000 per life-year gained are considered good value and are recommended;
- health care options that exceed a threshold of \$100,000 per life-year are not recommended without strong justification; and
- health care options that fall between \$30,000 and \$100,000 per life-year are given further consideration.⁸

The committee may be considering a range of options, each one involving more resources than the last and achieving more benefit. The question then becomes whether any of the health care options are cost-effective within the shadow price range given above. If more than one health care option is deemed cost-effective the question then becomes, 'which option is the preferred clinical practice?' The answer is that the health care option offering the highest benefit

⁸ It should be noted that these are the recommendations of the authors and there is some debate around this issue.

should be deemed the preferred practice. Some hypothetical figures are given in Example 6.2.

Example 6.2 — Incremental cost-effectiveness ratios

| Health care option | Cost (\$) | Life-years resulting from the health care | Incremental cost (\$) | Incremental life-years gained | Incremental cost-effectiveness (\$/life-year saved) |
|--------------------|---------------------|-------------------------------------------|--------------------------------|-------------------------------|-----------------------------------------------------|
| Do nothing | 10,000 ⁹ | 5 (baseline) | – | – | – |
| A | 40,000 | 6 | 30,000 (40,000 – 10,000) | 1 (6 – 5) | 30,000 (30,000 ÷ 1) |
| B | 140,000 | 8 | 100,000 (140,000 – 40,000) | 2 (8 – 6) | 50,000 (100,000 ÷ 2) |
| C | 380,000 | 10 | 240,000 (380,000 – 140,000) | 2 (10 – 8) | 120,000 (240,000 ÷ 2) |

In Example 6.2, option A is clearly cost-effective (it falls under the shadow price level). Saving additional lives for \$50,000 each by replacing A with B may be cost-effective, as it falls between \$30,000 and \$100,000 thresholds, but this will depend on the level of evidence and other factors, as explained below. However, saving additional lives for \$120,000 by replacing B with C is not cost-effective. Here, if the committee ascertains that B is cost-effective then it is the preferred practice; if they determine that B is not cost-effective, then A is the preferred option.

It is important to recognise that there may be different conclusions for a health care option under different conditions. For example, the incremental effectiveness and/or cost may differ depending on the group of individuals it is being applied to, or according to varying institutional factors or settings. The groups of individuals may be split according to varying clinical indicators (such as age, sex, ethnicity, comorbidities). For example the use of warfarin might be more cost-effective in the over 65 age group than in the under 65 age group. The institutional factors or settings may be split according to urban/rural settings, size of the hospital or facility, or availability of technology or skilled workers. For each of these different groups it may be necessary to produce a separate statement about what the evidence points to in terms of whether the health care option is cost-effective.

⁹ There is a cost to the 'do nothing' alternative because the natural history of the disease causes contact with medical services.

If the economic results are not given in terms of cost per additional life-year gained, there are potentially an enormous number of intermediate outcome measures and it is not possible to find benchmarks for all of them. However, the issue of what an additional unit of outcome is worth has to be addressed. Judgment will be needed to assess whether the results it has (in whatever units) are consistent with the benchmark of \$30,000 to \$100,000 per life-year gained. For example, suppose a treatment for asthma provides an additional night of uninterrupted sleep at a cost of \$30 per night. If three years of uninterrupted nights is considered the equivalent of one life-year saved, then this treatment represents around \$30,000 per life-year saved.

6.3 Assess the quality of the evidence

The next step is to consider the confidence that can be placed in the economic results. Just as the evidence on effectiveness can be judged (based on the strength of the evidence, the size of the effect and the relevance of the outcomes), the evidence on costs can be judged according to relevant criteria. The higher the evidence is judged to be, the more confidence can be attached to recommending the health care option and therefore the higher the cost per life-year that can be accepted as a threshold. There are two components to the economic evidence, the evidence of the effectiveness of the options and the evidence of their costs.

A scheme for judging the strength of evidence of effectiveness has been produced in another handbook in this series (NHMRC 2000b). This contains dimensions of level (study design), quality and statistical precision. When considered with the relevance of the evidence this gives an indication of the degree of confidence that can be placed in the results. Although a single dimension loses a lot of the information, for the purposes of the calculation of the shadow price it is recommended that the committee rate the strength of evidence as high or low. A judgment of a high level of evidence is aided by a number of large, good-quality studies giving the same result.

Sensitivity analysis can play an important role in the judgment of the evidence on costs (see Appendix E for details of sensitivity analysis). When sensitivity analysis is conducted on the study model or structure, the results can be labelled as either robust (insensitive to plausible changes in the assumptions/model) or not robust (sensitive to plausible changes in the assumptions/model). If multiple studies are available, the sensitivity analysis should include the important differences between them, where appropriate. If the results are robust to changing the model and the identification and measurement of cost data, the cost evidence may be considered strong; if the results are not robust, the cost evidence should be considered weak.

The quality of evidence on costs is based on the level of confidence that can be placed in the studies (ie to what extent the evidence is based on criteria for internal validity, generalisability and sensitivity analysis). If multiple studies show consistency in the results for costs and consequences, this will lead to increased confidence in the data. The committee or the health economist working with the committee should rate the evidence on costs as strong or weak. Strong evidence on costs comes from internally valid studies that are generalisable (or have been adjusted) and are robust as determined by sensitivity analysis. The more the studies deviate from this, the weaker the evidence. A small concern over one aspect of a study does not make the evidence weak, but a number of concerns or one large concern weakens the evidence.

The evidence on both costs and effectiveness can be compared, giving the range of possibilities shown in Table 6.1. This also shows how the threshold cost per life-year should vary with the quality of evidence. The lower the ranking of the evidence, the more likely the committee is to not recommend an option where the cost has been assessed to fall in the range \$30,000 to \$100,000.

- If highly ranked evidence is available on effects and there is strong evidence on costs, then options that cost less than \$70,000 per life-year saved are recommended and those that cost \$100,000 are rejected. Those that cost between \$70,000 and \$100,000 should be considered.
- If effectiveness evidence is ranked as low and the cost evidence as weak, options that cost more than \$30,000 per life-year saved are rejected.
- If neither of the above cases applies, then options of less than \$30,000 are recommended and those greater than \$70,000 are rejected. Those that are between \$30,000 and \$70,000 should be considered.

Table 6.1 Assessing evidence using shadow prices

| Ranking of evidence on costs | Ranking of evidence on effects | |
|------------------------------|--------------------------------------------------|-------------------------------------------------|
| | High | Low |
| Strong | Recommend if: < \$70,000 per life-year | Recommend if < \$30,000 per life-year |
| | Do not recommend if > \$100,000 per life-year | Do not recommend if > \$70,000 per life-year |
| | Weak | |
| Weak | Recommend if < \$30,000 per life-year | Recommend if < \$30,000 per life-year |
| | Do not recommend if > \$70,000 per life-year | Do not recommend if > \$30,000 per life-year |

6.4 Consider other factors

Health care options might require further consideration if they fall in the range \$70,000–\$100,000 per life-year saved and rank highly for evidence on costs and effects, or if they are in the range \$30,000–\$70,000 per life-year saved and rank highly on one but not the other. Factors that may make a health care option more attractive and move the threshold towards a higher price are:

- quality of life as well as survival is improved;
- quality of life or functional status is a major factor;
- the condition is severe and preventable;
- the condition leads to permanent effects in children and young people;
- the disease is rare and there are no other health care options;
- quality of life for family members is seriously affected;
- the option prevents adverse flow-on effects into other sectors; and
- there are equity implications.

6.5 Make the decision

The committee can now decide on the preferred, cost-effective option for the guideline, taking into account:

-
- the cost per unit of outcome (which should be consistent with the threshold cost per life-year saved of \$30,000–\$100,000);
 - the quality of the evidence of effectiveness of the health care option (if placed at the higher end of the range, evidence on costs and effectiveness needs to be ranked highly); and
 - other factors that increase the option’s attractiveness (important if the option is placed at the higher end of the range).

In cases where there is more than one economic question relating to the proposed guideline, the same principles apply. In more complex cases, where there is interaction between the economic questions relating to a proposed guideline, or where the evidence is conflicting, it will be necessary to consult a health economist.

6.6 Overview and next steps

This section described how to calculate cost-effectiveness ratios based on the ranking of both the clinical effectiveness evidence and economic evidence. Based on this and the other considerations highlighted, the group should have come to a consensus decision on which (if any) of the options considered should be the preferred practice, in principle, on the basis of clinical effectiveness and cost-effectiveness.

The next step is to assess whether the preferred practice is economically feasible. Only if the practice is economically feasible as well as cost-effective should it be recommended as a clinical practice guideline. This stage is described in Part 2.

Part 2

Is the proposed clinical practice economically feasible?

This part of the handbook describes a framework to assess the economic feasibility of cost-effective guidelines. To do this, three key pieces of information are required:

- an estimate of the resources and costs incurred under current practice, identified by the relevant health agencies;
- a projected estimate of the resources and costs under the new guideline practice; and
- assumptions made about supply-side factors, including a projection of guideline uptake rates.

This information can be used to form a view on whether the health sector can afford the magnitude of the cost of the resource change arising from the implementation of the cost-effective guideline. It will also indicate which funding organisations incur the costs and/or cost savings from implementing the guideline and whether there are barriers to implementing the guideline that can be modified.

The final section of Part 2 suggests how the evaluation of economic evidence can be incorporated into clinical practice guidelines.

7 DETERMINING THE COSTS UNDER CURRENT PRACTICE

Objective

To set up the framework for estimating the resources and costs associated with current practice.

Most of the component pieces of data to be included in this framework have been collected previously (see Sections 2–5), making the committee’s task largely a matter of reorganising existing information.

Steps

- Identify and quantify the target population.
- Identify and quantify the range and frequency of use of current health care options.
- Quantify total resources and costs associated with each current health care option.
- Tabulate the profile of current practice.

7.1 Background

Several situations can arise that may cause a health care option that has been found to be cost-effective *in principle* to be not economically feasible.

- The implementation cost of moving from current to guideline practice may be too high. For example, encouraging all general practitioners (GPs) in Australia to use a specific antihypertensive drug therapy as the best practice clinical guideline for the treatment of hypertension may require a high investment in educating this large group of practitioners about the guideline and how to change from their current practice.
- The guideline, though cost-effective, may become so frequently used under guideline practice that the total cost of implementing it would be prohibitive, exceeding budgets. For example, prescribing tamoxifen for the prevention of breast cancer in postmenopausal women may appear to be cost-effective on an individual basis but to prescribe this medication to all postmenopausal women in Australia would exceed the pharmaceutical budget.
- Practical barriers may exist. For example, the use of anti-D immunoglobulin to reduce Rhesus incompatibility in future pregnancies has been shown to

be cost-effective. However, because the agent is in short supply, additional costs are needed to find ways to increase supply. This adds an additional tier of costs and thus reduces the overall cost-effectiveness.

- There may be unacceptable cost shifting between funding organisations. For example, a health care option that shifts costs between State/Territory-funded services and Commonwealth-funded services may contravene current funding arrangements.
- Flow-on effects from the implementation of a guideline may have substantial ramifications for other services or staffing. For example, greater detection rates for cancer through implementation of screening programs can lead to greater demand for best practice health care option services such as specialist surgical services and multidisciplinary teams. These may themselves be in short supply, meaning that new practice will not be realised.

Factors such as these need careful consideration to determine whether a cost-effective guideline will be economically feasible and should therefore proceed. Some of the information that is required for this assessment may have already been gathered in Part 1; for example, the information used for the specification of options may be information that can be used for the determination of current practice techniques.

Assessing the economic feasibility of a proposed cost-effective option is not a dismissal of best practice but rather a cohesive and comprehensive evaluation of the proposed best practice, in order to ensure that its introduction is sensible in a wider framework.

7.2 Identify and quantify the target population

The target population fits predetermined criteria about who will be directly affected by implementation of the guideline. For example, this may be people aged 65 years and over, living in New South Wales. Clearly, the size of the target population will have substantial implications for resource use and costs when measuring the absolute value of resources. Identification and definition of the target population is addressed in the accompanying handbook *How to Use the Evidence: Assessment and Application of Scientific Evidence* (NHMRC 2000b).

Quantification of a target population requires the following steps:

- define the scope of the guideline;
- identify the size of the general population;

- estimate the prevalence of the health condition in the population to be covered by the guideline;
- identify and quantify demographic features within the target population; and
- calculate the number of people covered by the guideline.

See Appendix F for further details on how to calculate a target population.

The estimated number of people to be covered by the guideline should be tabulated so that a decision can be made about whether there are important subgroups within the target population (eg age groups, gender, ethnicity or geographical location) that need to be considered. It is also advisable to tabulate all the data sources and assumptions used in estimating the target population. Example 7.1 gives an example of this process. It is important to tabulate the data sources and assumptions to allow the validity of this step to be judged by others and to allow the information to be updated in the future.

| Example 7.1 Calculating target population estimates | | | |
|------------------------------------------------------------|----------------|-------------------------------------------------|---------------------------------------------------------------|
| Variable | Target | Source | Comments/assumptions |
| Coverage area | All Australia | Committee decision | |
| Population 55 years and over | 3,730,899 | Australian Bureau of Statistics (series 3201.0) | Total potentially relevant population |
| Prevalence rate of atrial fibrillation | 3.4% | Review of literature (five studies cited) | Assumed study results applicable to the Australian population |
| Total target population | 127,904 | | |

Note: This example is for illustrative purposes only.

If demographic features within the target population are important then a similar disaggregated table should be constructed. For example, in the clinical practice guidelines for prevention of stroke (NHMRC 1996), because the prevalence of atrial fibrillation increases with age, the population was disaggregated to give atrial fibrillation rates by age groups to gain more accurate estimates of the target population (Example 7.2).

Example 7.2 Disaggregated target population estimates

| Age group (years) | Total population | Prevalence of atrial fibrillation | Target population |
|--------------------------|-------------------------|------------------------------------------|--------------------------|
| 55–64 | 1,529,414 | 1% | 15,294 |
| 65–74 | 1,290,650 | 3% | 38,720 |
| 75–84 | 708,194 | 7% | 49,574 |
| 85+ | 202,641 | 12% | 24,317 |
| Total | 3,730,899 | | 127,905 |

Note: This example is for illustrative purposes only.
Source: NHMRC (1996).

7.3 Identify and quantify the range and frequency of use of current health care options

The full range of health care options used in the clinical practice situation were identified in Section 1. Current practice must be identified for the target group in question. It may be that all health care options identified in Section 1 remain relevant, or that only a subset are relevant. The task is to establish and tabulate the overall use pattern of current practice. This may require a new survey or an assessment of existing data.

Estimates of the frequency of use of each health care option depend on the context of use of that health care option. For example, health care for hospital inpatients may be estimated from descriptive epidemiological studies, or possibly from International Classification of Diseases (ICD-9-CM) codes recorded on hospital data files. Information on health care by general practitioners may be obtained from Health Insurance Commission (HIC) data. Outpatient and community health care may, in some circumstances, be more difficult to quantify. However, a sample of patients may be surveyed or a sample of hospitals may allow access to detailed records on home visits and outpatient attendances. Some of the numerous secondary data sources are listed in Box 7.1.

Frequency of use of each health care option identified with current practice may be calculated as the rate of use in the target population or the absolute numbers of a particular option by type of health care. For example, earlier it was noted that there are three alternative courses of action for prophylactic treatment of stroke in a population with atrial fibrillation: do nothing, aspirin or warfarin. Warfarin treatment is not appropriate for all of the people in the target subgroup of 65–74-year-olds with atrial fibrillation. Table 7.1 shows the treatment frequency for the three options (as assessed by survey), assuming that warfarin treatment is appropriate for 70% (27,104) and not for the remaining

30%. The population of interest is, therefore, those aged between 65 and 74 years, in Australia, with atrial fibrillation who are suitable for treatment with warfarin. Any assumptions used in this step should be documented.

Box 7.1 Possible data sources and identifying data needs

Data sources

- The Australian Bureau of Statistics (ABS):
 - demographic data — population, trends in population, by age group, by State
 - mortality data — deaths, by cause of death, age, gender, ethnicity.
- Australian Institute of Health and Welfare (AIHW):
 - mortality data
 - hospital inpatient data for all Australian public hospitals, from 1996 (unit records potentially available)
 - hospital outpatient data for some States and recent years
 - health expenditure data
- Commonwealth Department of Health and Aged Care:
 - Medicare statistics (analysis and breakdown)
 - health insurance status
 - Pharmaceutical Benefits Scheme
- State health departments:
 - hospitalisation inpatient collections — unit records potentially available
 - costs for procedures and individuals potentially available and/or costs by diagnostic related group
 - outpatient attendances by type of specialist
 - use of auxiliary health care services
- Health Insurance Commission (HIC):
 - records insurance claims by Medicare number for health care in the public sector
 - large range of procedure codes available (but not diagnosis)
 - includes nonhospital health care procedures
 - Pharmaceutical Benefits Scheme
- Surveys of populations or health care providers:
 - may be necessary to obtain accurate incidence, prevalence or cost data or to verify data obtained from secondary sources

Identifying future data needs

During the identification of current practice, any gaps in the availability of data should be addressed. Systems need to be established at this point to collect the necessary data. A separate survey may be necessary.

Table 7.1 Identifying the range of current practice options for a target subgroup of those aged 65–74 years old with atrial fibrillation and suitable for treatment with warfarin

| | Do nothing (option A) | Aspirin (option B) | Warfarin (option C) | Target subgroup^a |
|-----------|----------------------------------|-------------------------------|--------------------------------|----------------------------------------|
| Rate | 20% | 30% | 50% | 100% |
| Frequency | 5421 | 8131 | 13,552 | 27,104 |

^a Example assumes that 70% of those aged between 65 and 74 years with atrial fibrillation are suitable for warfarin treatment and 30% are not.

Note: This example is for illustrative purposes only.

7.4 Quantify total resources and costs associated with each current health care option

The next two steps — to quantify key resources associated with each health care option and to attach unit costs to resources to estimate total costs (allowing for categorisation of these costs by separate health sector funding organisations) — can be carried out simultaneously. It is important to present resources and costs separately to give a picture of total demand for specific resources within health care options and across the range of clinical practice (which can be useful for identifying supply-side issues in the implementation process) and a separate analysis of the budgetary impact. Resource use and unit cost data collected previously (Sections 3–5) are used for these estimates.

Depending on how data on resources were made available in the earlier stages, the resources associated with each health care option can be tabulated as an average amount of resource per case (ie unit) or as total resources. These can then be summarised according to the frequency of use across the range of current practice to yield total demand for particular resource types (see Table 7.2).

Unit cost data relating to particular units of resources can be directly inserted into the table in the relevant cells so that the total costs and cost savings of each health care option can be estimated by multiplying total quantity of resources by respective unit costs.

A summary of total net cost for the range of current practice may be calculated by adding up the total costs and cost savings of each health care option, weighted by the frequency of use for each practice.

7.5 Tabulate the profile of current practice

Table 7.2 shows a summary of how all the component pieces of information required for assessing resource use and costs can be presented in the treatment of atrial fibrillation for the prevention of stroke to generate a profile of current practice over a predefined period. It is important that all costs are presented in a common price base. In this example, only the total costs are presented for each resource item; details of the unit costs and number of units are given in Appendix D.

If important subgroups have been identified within the target population, separate tables may need to be constructed for each subgroup identified.

The demand for resources from different health care options may fall on different funding organisations — such as area health services, the federal government, and so on. An example of this is shown in the last column of Table 7.2. Therefore, depending on the perspective of the study, these resources may need to be separated into the different funding organisations. In addition, if the health care option varies according to other important factors, such as demographic factors, then resource use and costs should be accordingly disaggregated. In effect, this may require reconstructing Table 7.2 to represent the relevant subgroups.

If sufficient detail is obtained to identify the costs and consequences for each health care provider, then the aggregation of the data used in Table 7.2 will more accurately reflect the 'true' costs and consequences of current practice. However, if data are limited (eg from only one Australian State) and extrapolations are required to estimate the total costs for the target population, then a sensitivity analysis should be undertaken on the current practice costs. Extrapolation introduces a form of measurement error because the effect of variation over different regions and health care providers is unknown (see Box 7.2 below for issues surrounding cross-sectional variation and variations over time, including trends, cycles and epidemics).

Table 7.2 Annual health sector resources and costs for stroke prevention under current practice, Australian population 65–74 years

| Resource item | Do nothing (option A) | Aspirin (option B) | Warfarin (option C) | Total costs of current practice ^b | Funding organisation ^c |
|--------------------------------------------------|-----------------------|-------------------------------------------|--------------------------------------------|----------------------------------------------|-----------------------------------|
| | | | | | |
| GP visits | \$552,922 | \$552,922 | \$5,529,216 | \$3,041,069 | Medicare |
| Specialist visit | \$2,626,378 | \$2,626,378 | \$2,626,378 | \$2,626,378 | Medicare |
| Echocardiogram | \$3,853,172 | \$3,853,172 | \$3,853,172 | \$3,853,172 | Medicare |
| ECG | \$544,858 | \$544,858 | \$544,858 | \$544,858 | Medicare |
| TFT | \$944,574 | \$944,574 | \$944,574 | \$944,574 | Medicare |
| FBC | \$0 | \$0 | \$396,260 | \$198,130 | Medicare |
| Coagulation studies | \$0 | \$0 | \$460,768 | \$230,384 | Medicare |
| INR | \$0 | \$0 | \$6,289,483 | \$3,144,742 | Medicare |
| Medication | \$0 | \$406,560 | \$1,517,824 | \$880,880 | Medicare |
| Frequency of use ^d | 0.2 | 0.3 | 0.5 | 0.2×A+ 0.3×B+ 0.5×C | |
| Total costs | \$8,521,904 | \$8,928,464 | \$22,162,533 | \$15,464,187 | |
| Strokes averted (no.) | 0 | 178 | 462 | | |
| Resource savings of averted strokes | 0 | 1296 acute bed days 972 rehab bed days | 4120 acute bed days 3090 rehab bed days | | Medicare/ hospital Hospital |
| Cost savings (decreased stroke) | \$0 | \$3,248,091 | \$8,437,114 | | |
| Total net costs | \$8,521,904 | \$5,680,373 | \$13,725,419 | | |
| Frequency of use ^d | 0.2 | 0.3 | 0.5 | 0.2×A+ 0.3×B+ 0.5×C | |
| Total net costs of current practice ^c | \$1,704,381 | \$1,704,112 | \$6,862,710 | \$10,271,203 | |

^a A breakdown of unit costs and numbers of units used for each health care option is given in Appendix D.

^b Calculated from the frequency of use — $0.2 \times A + 0.3 \times B + 0.5 \times C$

^c For example: Medicare (Medical and PBS), public hospitals, specialists in private practice, health insurers.

^d See Table 7.1

ECG = electrocardiogram; FBC = full blood count; INR = international normalised ratio; TFT = thyroid function test.

Note: This table is for illustrative purposes only.

Box 7.2 Variations in health care option costs and consequences

Cross-section variation

Under current clinical practice, a range of different health care options in different settings may be used for care of the same condition. That is, in local settings there may be limited health care options and differences in available equipment; training, experience and skills of existing and incoming clinicians and support staff; and the availability of staff in terms of numbers and professions. Because of these variations, attempts should be made to obtain detailed information for each health care option, outcome and associated costs. This includes allowing for differences between geographical regions.

Obtaining detailed data for all practices in all regions of Australia (if the guideline is to be used as a national guideline) may require considerable time and resources. Therefore, there is a trade-off between investing in resources to acquire detailed high-quality data and using lower-quality data requiring fewer resources to obtain. It is suggested here that estimates obtained from a sample of health care providers or users can be extrapolated to the State or national levels, but with some caveats. In some instances, it may be necessary to survey a sample of the population to obtain reasonable estimates of current practices, costs and consequences.

Variation over time — cycles, trends and epidemics

The prevalence of a condition may be subject to cyclical fluctuations. If this is the case, an average of the last several years should be used. For example, infections such as meningitis may occur in cycles where the incidence in some consecutive years is greater or less than the incidence in some other set of consecutive years. This cycle should be smoothed by taking an average or median of the rate with the number of years equal to the period of the cycle.

If trends are present in the incident data, then the latest year of data available should be used to calculate the baseline costs and consequences. In estimating resource implications for the post-implementation period, trends in disease rates, treatment rates and cost data need to be considered.

Epidemics may seriously distort costs and consequences in any given year. For example, if an estimate of the costs and consequences for measles was based on the average prevalence of measles over the last five years and an epidemic of measles occurred eight years ago, then the true costs and consequences may be underestimated. Therefore, when calculating annual average costs and consequences, the year of the last known epidemic should be included. However, depending on when the last epidemic occurred, a subsequent analysis based on current prevalence rates could be undertaken. That is, if no epidemic is predicted to occur in the next 3–5 years (the time period for evaluation of the guidelines), resource estimates could be based on current prevalence rates.

7.6 Overview and next steps

This section showed how to obtain the information required to estimate the predicted resources and costs, and show who bears the costs predicted under guideline practice. The committee should have produced:

- a profile of important subgroups of the target population to be considered;
- a profile of current practice in terms of resource use, associated costs and the government sector that bears those costs; and
- a record of any assumptions made throughout this process.

This information is used in Section 8 to determine whether the proposed guideline is economically feasible.

8 PREDICTING THE RESOURCE AND COST IMPLICATIONS OF GUIDELINE PRACTICE

Objective

To evaluate the potential cost and resource requirements of the movement from current practice to guideline practice in order to determine the economic feasibility of the guideline practice (a prediction of economic feasibility is required in order to recommend the proposed guideline).

Steps

- Estimate resource use and costs under guideline practice.
- Compare current and guideline practice.
- Conduct a sensitivity analysis.
- Consider supply issues.
- Calculate net costs and resource implications.

8.1 Estimate resource use and costs under guideline practice

To predict the impact of the guideline on resources and costs, prediction of the uptake of the guideline and thus the frequency of use of the guideline practice is necessary. The impact of the guideline may be to decrease or eliminate specific health care options currently in use, in favour of guideline practices. That is, there may be a shift in the proportions of current practices used. The question to be answered is: 'what is the optimal uptake rate that can be assumed?'

The approach adopted follows the framework used in Section 7 for current practice. It will be assumed that guideline practice is applicable, generalised, and adopted throughout the target population. In essence, the costs and resources determined in this step are those of the greatest possible effect obtained from implementing the proposed guideline.

The accompanying handbook *How to Put the Evidence into Practice: Implementation and Dissemination Strategies* (NHMRC 2000c) gives detailed information on implementation and dissemination procedures. The committee may form a view by reaching a consensus through one or more of the following means:

- introspection — committee members who have particular experience in the implementation of guidelines may be able to inform discussion;
- examination of the literature; and

- consideration of previous guidelines issued for the same clinical area.

After consideration of the available information, the expected shifts in clinical practices should be tabulated, assuming the most optimistic uptake rate. For example the most optimistic use of warfarin in those with atrial fibrillation for whom it is appropriate is 100%.

In line with expected changes in patterns of clinical practice under guideline practice, the total resources and costs of guideline practice will also change. Therefore, the committee should tabulate the new resources and costs associated with new patterns of practice to arrive at resource use and cost estimates for each health care option under guideline practice, demand for total resources under guideline practice, total net costs and the distribution of costs across funding organisations. Essentially, this means replacing the frequency of use applied to the last row and second last column of Table 7.2 and recalculating the totals. This is illustrated in Table 8.1.

Table 8.1 **Estimated annual health sector resources and costs for stroke prevention under proposed guideline practice in Australian population 65–74 years with atrial fibrillation suitable for treatment with warfarin, assuming 100% compliance with the guideline**

| Resource item | Do nothing (option A) | Aspirin (option B) | Warfarin (option C) | Total costs of proposed guideline |
|----------------------------------------------------|-----------------------|--------------------|---------------------|-----------------------------------|
| Total net costs (including diagnosis) ^a | \$8,521,904 | \$5,680,373 | \$13,725,419 | |
| Frequency of use ^b | 0.2 | 0.3 | 0.5 | 0.2×A+ 0.3×B+0.5×C |
| Total net costs of current practice ^b | \$1,704,381 | \$1,704,112 | \$6,862,710 | \$10,271,203 |
| Frequency of use with 100% compliance with C | 0 | 0 | 1 | |
| Total net costs of 100% compliance with C | \$0 | \$0 | \$13,725,419 | \$13,725,419 |

^a A breakdown of unit costs and numbers of units used for each health care option are given in Appendix D.

^b See Table 7.2

A final cost component to be added is the estimated cost of implementing the guideline. Disseminating and implementing a new clinical practice guideline is not a cost-free exercise. There are several approaches that can be taken, and each one (or combination) will attract different costs. For example, if the guideline is published electronically, the costs will be different from publishing in scientific journals, popular media or as posters in the workplace. In addition,

the costs for disseminating and implementing the guideline will vary depending on the strategy used. Strategies may include educational materials, seminars and conferences, media marketing and others (see NHMRC 2000c).

For evaluation, the costs of disseminating and implementing the guideline should be added to the total costs of guideline practice. They are unlikely to be one-off costs and will probably vary for many reasons, including the dissemination strategy. These costs should not be included when calculating the change in resource use. For evaluation, however, the cost of dissemination and implementation may be obtained from a variety of sources — indirectly, from the literature, or directly, from relevant health service financial departments or a health economist.

The costs and resource use of current and guideline practices should be projected over a range of time horizons (eg one, three and five years) to differentiate between short and long-term consequences.

8.2 Compare current and guideline practice

Subtracting total net costs for current practice (ie the relevant cells in Table 7.2) from the corresponding cells in Table 8.1, enables the committee to analyse the overall cost consequences of the guideline and tabulate them in a format similar to that shown in Table 8.2.

Table 8.2 Economic feasibility predicted over one year

| | Do nothing Option A | Aspirin Option B | Warfarin Option C | Total cost | Funding organisation |
|----------------------------------------|--------------------------------|-----------------------------|------------------------------|-------------------|---------------------------------|
| Change in frequency of use of options: | -0.2 | -0.3 | +0.5 | | |
| Net costs of current practice | \$1,704,381 | \$1,704,112 | \$6,862,710 | \$10,271,203 | Medicare, hospital |
| Net costs of guideline practice | \$0 | \$0 | \$13,725,419 | \$13,725,419 | Medicare, hospital |
| Change in net costs | -\$1,704,381 | -\$1,704,112 | \$6,862,710 | \$3,454,217 | |

Source: Tables 7.2 and 8.1

Note: This table is for illustrative purposes only.

The committee may also analyse the guideline with respect to the impact on total demand for particular resource components by comparing the relevant columns in Tables 7.2 and 8.1.

These are long-term estimates of resource and cost changes, based on the most optimistic scenario. In practice, such a scenario is unlikely to occur and the committee needs to consider factors that may affect implementation of the guideline.

8.3 Conduct a sensitivity analysis

Before the committee formulates recommendations for the economic feasibility of the proposed guideline, it is important that it systematically examines the key assumptions underlying the calculations for resource use and cost estimates under current and guideline practice. For example, if there is uncertainty or variation surrounding the predicted costs of implementation, then this ought to be subject to sensitivity analysis (see Appendix E). A range of estimates should be reported in the final analysis that includes upper and lower bounds, and the most plausible estimates.

8.4 Consider supply issues

The committee also needs to address supply issues in implementing the guideline. Three issues particularly need to be considered as they may impede the move from current to guideline practice:

- ability to meet demand;
- acceptability of cost shifts between funding organisations; and
- uncertainty about the uptake rates of the guideline practice.

8.4.1 Ability to meet demand

Implementation of the guideline will be impeded if the resources are not available or supply is restricted. That is, if the preferred practice requires an increased use of a certain procedure or technology, then the committee needs to examine any labour force issues (eg the availability of adequately trained surgeons to perform a required procedure) and/or the availability of the necessary equipment required for guideline practice. In extreme situations, the guideline may not be implemented because necessary resources are not available.

Further, an increased demand for a chosen technology or skill is likely to have an effect on the price of that technology or skill; the health economist should advise on how to handle this issue.

8.4.2 Acceptability of shifts in costs between funding organisations

There may be some situations where shifts in the costs of health care options from one sector or funding organisation to another are not acceptable, which may prohibit the implementation of a guideline. The issue of whether likely cost shifts proposed under the guideline will be acceptable should be considered.

8.4.3 Uncertainty about the uptake rates of the guideline practice

Previous calculations were based on an assumed uptake rate of the guidelines (see Section 8.2). However, diffusion of guidelines may take some time and all costs and/or costs averted may not be gained instantaneously when the guidelines become available. Therefore, the task of the analyst is to determine how to estimate the costs for the most plausible uptake rate given time delays and less than optimal uptake rates of the guideline.

Estimates of guideline uptake rates may be based on, for example, acceptance and adoption of other guidelines in the institution or an opinion survey of clinicians about the guideline that includes barriers to adopting guideline practice.

The analyst should conduct additional analyses to create a profile of costs and resources based on a range of uptake rates of the guideline at various time intervals. That is, the analysis should consider the changes in proportions of current practice as it moves toward guideline practice. The introduction of a guideline such as stroke prevention may see a gradual decline in two of the three current practices and an increase in the guideline recommended practice. This has been assumed to occur over a period of three years (in this example) as illustrated in Table 8.3.

Table 8.3 Proportions of treatments used for the prevention of stroke

| | Do nothing | Aspirin | Warfarin |
|-------------------------------------|-------------------|----------------|-----------------|
| Current practice | 20% | 30% | 50% |
| End of year 1 | 10% | 20% | 70% |
| End of year 2 | 5% | 10% | 85% |
| End of year 3 (optimal practice) | 0% | 0% | 100% |

The cost estimates can now be tabulated based on the different uptake rates of the guideline. The analyst may produce a series of tables, each with different underlying assumptions or estimates about the uptake rates.

This table may help the committee to determine the strategy for disseminating and implementing the guideline. It may help to make the important decision as to whether it is worth spending more now to implement the guideline through a more effective and more costly implementation strategy.

8.5 Calculate net costs and resource implications

The next stage is to re-assess the earlier calculations of net cost and resource implications of implementing the guideline, in light of the sensitivity analysis and key supply issues. The question of how robust the guideline appears under different assumptions concerning its economic feasibility must be considered. From the range of estimates generated, the estimates that are based on the most plausible assumptions should be identified.

The estimates for costs and resources under guideline practice may need to be amended to include the implementation costs and changes in cost structures, to identify shifts in costs to different funding organisations, and to estimate costs with anticipated guideline uptake rates.

8.6 Overview and next steps

The information gathered at this stage and from the process outlined in Section 7 allows the committee to decide whether the preferred practice guideline, identified in Part I, should proceed to implementation under the proposed implementation strategy. The process for deciding this is the same as that outlined in Section 6. If it appears that the preferred practice guideline will not be economically feasible, then the committee may need to go back to the point where other cost-effective options were identified (Section 6) and consider whether one of these options might be economically feasible (ie by revisiting Section 8).

The next step is to incorporate recommendations on cost-effectiveness and economic feasibility into the clinical practice guidelines.

9 PRESENTING THE ECONOMIC EVIDENCE

Objective

To incorporate the recommendations on cost-effectiveness and economic feasibility into clinical practice guidelines.

Steps

- Decide on the appropriate format for inclusion of economic aspects in the guidelines.
- Determine the scope of the information to be included.
- Include an overall summary of the evidence (the cost-effectiveness and economic feasibility of the health care options).

9.1 Decide on an appropriate format for inclusion of economic aspects in the guidelines

The final stage of the process of evaluating the economic evidence is to incorporate the data used to make recommendations on the cost-effectiveness and economic feasibility of health care options into clinical practice guidelines. The data should be presented in such a way as to allow clinicians, patients, funding bodies or administrators to consider the evidence and weigh it up in light of their personal preferences, should they choose to do so. This can be achieved by including in the clinical practice guidelines a section on economic aspects, which outlines the recommendations and the evidence supporting them. A good example of this is the clinical practice guidelines for lower urinary tract symptoms in men (NHMRC 2000e).

An alternative approach may be to include economic evidence at several key points in the text relating to key decision points with significant economic implications.

9.2 Determine the scope of the information to be included

The section(s) on economic aspects in the clinical practice guidelines should include relevant information from each of the previous stages in this handbook. Such information should include:

- a decision tree showing the potential decisions and health care options;

-
- a summary of how the studies used meet the criteria for internal and external validity, and for comparability;
 - the rationale for basing the evaluation on existing data or undertaking a new economic evaluation, as appropriate;
 - assessment of evidence using shadow prices;
 - calculation of the relevant resources and costs for each of the options under consideration;
 - an estimation of resource use and costs under current practice;
 - assessment of resource and cost implications of moving from the current practice to the guideline practice;
 - calculation of net cost and resource implications in the light of sensitivity and key supply issues; and
 - details of the evaluation process if required (perhaps as an appendix to the guidelines).

9.3 Include an overall summary of the evidence

Based on the economic evidence presented, either in a single section or at multiple points in the guidelines, include a summary assessment of the cost-effectiveness and economic feasibility of health care options.

APPENDIX A

MEMBERSHIP OF PRODUCTION TEAM FOR HANDBOOK

NHMRC Assessment Panel

| | |
|--------------------------------|-----------------------------------------------------------------------------------------------------------|
| Professor Paul O'Brien (Chair) | Department of Surgery, Monash Medical School Member of the NHMRC Health Advisory Committee (HAC) |
| Professor Chris Silagy | Monash Institute of Public Health and Health Services Research Member of HAC |
| Professor John McCallum | Faculty of Health, University of Western Sydney Member of HAC |
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| Ms Roz Lucas, Ms Janine Keough, Ms Monica Johns | Health Advisory Unit, Office of NHMRC |
|----------------------------------------------------|------------------------------------------|

APPENDIX B

PROCESS REPORT

During the 1997–99 NHMRC triennium the Health Advisory Committee (HAC) focused its work on coordination and support rather than on collating and reviewing scientific evidence. However, the committee recognised that a key part of its coordination and support function was to provide a methodology on how to develop evidence-based guidelines.

The NHMRC publication *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines* (NHMRC 1995), which had been produced by the HAC as a resource for people wishing to develop clinical practice guidelines to a standard acceptable to the NHMRC, was revised during 1998. Early in the revision process, the committee realised that there was a need for a number of complementary handbooks to expand on the principles outlined in the document. This complementary series would cover other aspects of the identification, collation and application of scientific evidence. It was envisaged that these handbooks would be of invaluable assistance to agencies wishing to develop clinical practice guidelines of a high standard either independently or on behalf of the NHMRC.

It was agreed that there would initially be five handbooks in the series:

- how to review the evidence;
- how to use the evidence;
- how to put the evidence into practice;
- how to present the evidence for consumers; and
- how to compare the costs and benefits.

They would be published individually to allow flexibility in their production and revision, as well as to allow any later additions to the series.

Recognising the need for a transparent and competitive process for contracting the services of an expert(s), tenders were sought for the preparation of each handbook. A selection committee was then appointed by the HAC to consider the tenders.

Once the successful tenderers had been contracted to prepare the handbooks, an assessment panel, composed of HAC members, was formed to manage the progress of each project (see Appendix A).

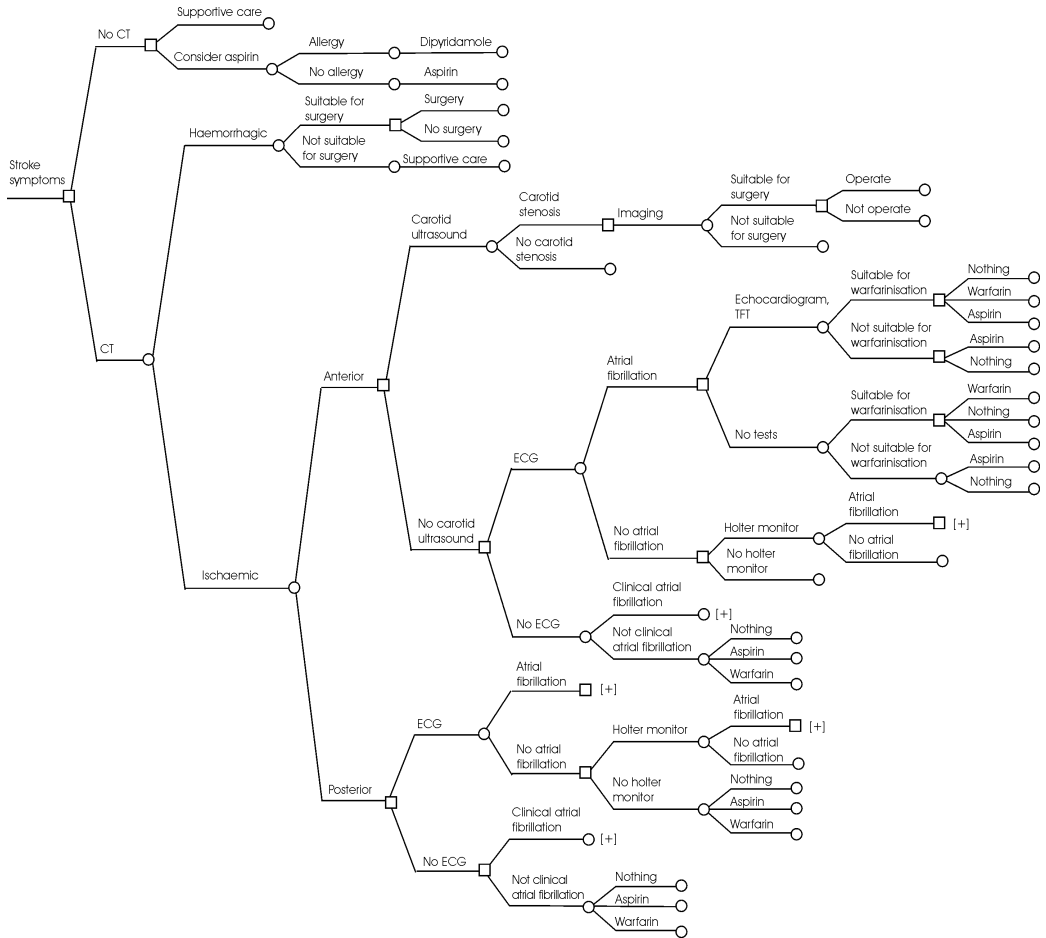
When first drafts of each handbook were received, they were distributed to a small number of experts in that particular field for peer review. The documents

were subsequently revised in the light of these comments. A technical writer was employed to ensure consistency in content and style within and between the handbooks.

The finalised documents were referred, in turn, to the HAC for approval before being forwarded to the NHMRC for endorsement.

APPENDIX C

DECISION TREE FOR STROKE MANAGEMENT



APPENDIX D

COSTS USED IN ATRIAL FIBRILLATION EXAMPLES

Table D1 shows the unit costs of the resources that it is predicted would be used in the treatment of atrial fibrillation. Most of the unit costs have been taken from the Medicare Benefits Schedule (MBS) and have been multiplied by 85%, which is the amount paid by the Health Insurance Commission to those who provide the service.

Table D1 **Costs**

| Information | Source | Quantity/cost | Annual cost |
|-----------------------------|-----------------------------|-----------------------|----------------------|
| GP visits | MBS item 3 at 85% | \$10.20 | |
| Specialist visit | MBS item 110 at 85% | \$96.90 | |
| Echocardiogram | MBS item 55102 at 85% | \$142.16 | |
| ECG | MBS item 11700 at 85% | \$20.10 | |
| TFT | MBS item 66719 at 85% | \$34.85 | |
| INR | MBS item 65120 at 85% | \$11.60 | |
| FBC | MBS item 65060 at 85% | \$14.62 | |
| Coagulation studies | MBS item 65123 at 85% | \$17.00 | |
| Medication (warfarin) | PBS item 2843P ^a | \$7.23 for 50 | \$56.00 ^b |
| | PBS item 2209G | \$7.40 for 50 | |
| | PBS item 2844Q | \$7.64 for 50 | |
| | PBS item 2211J | \$8.13 for 50 | |
| Medication (aspirin) | PBS item 1008C | \$6.70 for 100 | \$15.00 ^c |
| Cost of stroke ^d | (NHMRC 1996) | \$18,268 ^e | |
| | (Jorgensen et al. 1997) | \$17,972 ^f | |

ECG = electrocardiogram; FBC = full blood count; INR = international normalised ratio; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Schedule; TFT = thyroid function test

^a Different strengths of warfarin have different PBS item numbers; an average has been calculated.

^b Based on the average pill cost multiplied by 365 and then rounded up

^c Based on an average of 2–3 100 tablet dispenses per year

^d Represents the lifetime cost of the stroke to the health care sector

^e Patient population Australian; calculated by counting only direct costs and inflating by the consumer price index (CPI) (1.6%).

^f Patient population Swedish; calculated by converting from \$US to \$A at an exchange rate of 0.77 (1992 figures) and inflating by the CPI (13.9%).

Table D2 shows the calculation of the population at risk, the number of strokes that could potentially be averted and the data source at each stage.

Table D2 Calculation of population at risk and strokes avoided with different health care options

| | Data source | Size or rate | Calculations |
|----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|--------------------------------------------------|--------------|
| Target population | | | |
| Population aged 65–74 | ABS (1999) | 1,290,650 | |
| Population aged 65–74 with atrial fibrillation | NHMRC (1996) | 3% | 38,720 |
| Portion of 65–74-year-olds with atrial fibrillation for whom warfarin is inappropriate | Sudlow et al (1998) | 30% | 11,616 |
| Number of 65–74-year-olds with atrial fibrillation for whom warfarin is appropriate | Sudlow et al. (1998) | 70% | 27,104 |
| Rate of stroke risk | | | |
| Baseline ischaemic risk | Gage (1995) | 3.6% (2.6–4.6%) | |
| Baseline haemorrhagic risk | Gage (1995) | 0.8% (0.7–1.0%) | |
| Aspirin haemorrhagic risk | Gage (1995) | 0.9% (0.8–1.0%) | |
| Warfarin haemorrhagic risk | Gage (1995) | 1.4% (1.3–2.8%) | |
| Relative improvement in ischaemic stroke with warfarin | Ezekowitz et al (1992) Meta-analysis: Anonymous (1994) | 79% (52%–90%) 64% (51–74%) | |
| Relative improvement in ischaemic stroke with aspirin | Petersen et al (1989) Meta-analysis: Anonymous (1994) Barnett et al (1995) Anonymous (1997) | 0% 36% (4–57%) 22% (–1–39%) 21% (0–38%) | |
| Calculations | | | |
| Number of strokes in age group that could take warfarin | $0.036 \times 27,104$ | 976 | |
| Strokes avoided via warfarin | 0.64×976 | 625 | |
| Strokes avoided using aspirin | 0.21×976 | 205 | |
| Increased haemorrhagic strokes using warfarin | $0.006 \times 7,104$ | 163 | |
| Increased haemorrhagic strokes using aspirin | $0.001 \times 27,104$ | 27 | |
| Decreased total stroke with warfarin | | 462 (625 minus 163) | |
| Decreased total stroke with aspirin | | 178 (205 minus 27) | |

The rates of ischaemic stroke given in Example 2.4 are derived by applying the relative reduction in ischaemic stroke from the use of aspirin (21%) or warfarin (64%) to the base rate of ischaemic stroke (3.6%). Thus, the rate of ischaemic stroke with aspirin is 2.8% (ie $3.6 \times (1 - 0.21)$) and with warfarin it is 1.3% (ie $3.6 \times (1 - 0.64)$).

Tables D3–D5 show the costs of three health care options for atrial fibrillation.

Table D3 Annual cost of the ‘do nothing’ option for 27,104 people with atrial fibrillation

| | Price per unit | Units per person | Total units | Total price |
|------------------|----------------|------------------|-------------|-------------|
| GP visits | \$10.20 | 2 | 54,208 | \$552,922 |
| Specialist visit | \$96.90 | 1 | 27,104 | \$2,626,378 |
| Echocardiogram | \$142.16 | 1 | 27,104 | \$3,853,105 |
| ECG | \$20.10 | 1 | 27,104 | \$544,790 |
| TFT | \$34.85 | 1 | 27,104 | \$944,574 |
| Total | | | | \$8,521,769 |
| Cost per person | | | | \$314.41 |

ECG = electrocardiogram; TFT = thyroid function test

Table D4 Annual cost of the aspirin option for 27,104 people with atrial fibrillation

| | Price per unit | Units per person | Total units | Total price |
|--------------------------------|----------------|------------------|-------------|-------------|
| GP visits | \$10.20 | 2 | 54,208 | \$552,922 |
| Specialist visit | \$96.90 | 1 | 27,104 | \$2,626,378 |
| Echocardiogram | \$142.16 | 1 | 27,104 | \$3,853,105 |
| ECG | \$20.10 | 1 | 27,104 | \$544,790 |
| TFT | \$34.85 | 1 | 27,104 | \$944,574 |
| Medication | \$15 | 1 | 27,104 | \$406,560 |
| Total | | | | \$8,928,329 |
| Saving due to decreased stroke | \$18,296 | | 178 | \$3,248, |
| Net cost | | | | \$5,680,238 |
| Cost per person | | | | \$209.57 |

ECG = electrocardiogram; TFT = thyroid function test

Table D5 Annual cost of the warfarin option for 27,104 people with atrial fibrillation

| | Price per unit | Units per person | Total units | Total price |
|--------------------------------|----------------|------------------|-------------|--------------|
| GP visits | \$10.20 | 20 | 542,080 | \$5,529,216 |
| Specialist visit | \$96.90 | 1 | 27,104 | \$2,626,378 |
| Echocardiogram | \$142.16 | 1 | 27,104 | \$3,853,105 |
| ECG | \$20.10 | 1 | 27,104 | \$544,790 |
| TFT | \$34.85 | 1 | 27,104 | \$944,574 |
| FBC | \$14.62 | 1 | 27,104 | \$396,260 |
| Coagulation studies | \$17.00 | 1 | 27,104 | \$460,768 |
| INR | \$11.60 | 20 | 542,080 | \$6,288,126 |
| Medication | \$56 | 1 | 27,104 | \$1,517,824 |
| Total | | | | \$22,161,041 |
| Saving due to decreased stroke | \$18,286 | | 462 | -\$8,437,115 |
| Net cost | | | | \$13,723,926 |
| Cost per person | | | | \$506.34 |

ECG = electrocardiogram; FBC = full blood count; INR = international normalised ratio; TFT = thyroid function test

Table D6 shows the incremental cost-effectiveness of aspirin over nothing and warfarin over aspirin and nothing. The calculations do not include the potential savings due to a reduction in the amount of stroke treatment. These are the basis of the figures in Example 3: 'Incorrect choice of options'.

Table D6 Annual incremental cost-effectiveness without cost savings due to decreased strokes

| | Aspirin-nothing | Warfarin-aspirin | Warfarin-nothing |
|--------------------------------|-----------------|------------------|------------------|
| Net cost | \$406,560 | \$13,237,712 | \$13,639,272 |
| Strokes averted | 178 | 284 | 462 |
| Incremental cost-effectiveness | \$2,284 | \$46,594 | \$29,522 |

Table D7 gives the incremental cost-effectiveness of aspirin over nothing and warfarin over aspirin and nothing. This table is constructed from the previous tables; the net costs and strokes averted are the difference between the appropriate figures in tables D3, D4 and D5. The incremental cost-effectiveness

is calculated by dividing the net cost by the net number of strokes averted. The cost is actually reduced by the use of aspirin and this means that the no treatment option is a dominated solution. The choice of aspirin costs less and provides for fewer strokes and the option of no health care option should not be considered based on this analysis.

Table D7 Annual incremental cost-effectiveness with cost savings due to decreased strokes

| | Aspirin– nothing | Warfarin– aspirin | Warfarin– nothing |
|--------------------------------|--------------------------------------------------|------------------------------|------------------------------|
| Net cost | –\$2,841,666 | \$8,043,688 | \$5,202,157 |
| Strokes averted | 178 | 284 | 462 |
| Incremental cost-effectiveness | Aspirin dominates no health care option | \$28,323 | \$11,260 |

APPENDIX E

SENSITIVITY ANALYSIS

Certainty about incremental costs and consequences is often unwarranted. At best, the analyst can hope to have attained unbiased or consistent estimates but there is always uncertainty in the measurement of costs and consequences. Weinstein and Stason (1977) argue that sensitivity analyses are fundamental to cost-effectiveness analyses. Sensitivity analyses are frequently used for factors such as the discount rate, factors where analysts have had to make some assumptions about their value and factors where there is a degree of uncertainty in their measurement.

There are several approaches to undertaking sensitivity analyses. The three most straightforward approaches are described here. For more sophisticated approaches see Briggs et al (1994), Briggs and Gray (1999) or Mullahy and Manning (1996).

- *One-way sensitivity analysis:* In a one-way sensitivity analysis each critical component or parameter in the model is systematically changed by a meaningful amount within plausible bounds and the cost-effectiveness ratio recalculated while holding all other parameters constant at their baseline value. Parameters are often altered by plus or minus one standard deviation or, alternatively, are altered by plus or minus some percentage of the original parameter value. The resulting difference between the original estimate and the new estimate provides an indication of how sensitive the results are to a potential change in that parameter. This technique is useful for identifying which parameters in the model have a critical bearing on the results.
- *Two-way sensitivity analysis:* This is similar to a one-way sensitivity analysis but two critical parameters are altered simultaneously within plausible ranges while holding all other parameters constant at their baseline values. Altering more than two parameters simultaneously is known as a multiway sensitivity analysis, but it becomes difficult to detect which are the critical variables.
- *Extreme scenario analysis:* This involves simultaneously setting each variable to the most optimistic (or pessimistic) value from the point of view of the health care option in order to generate the best (worst) case scenario.

The components of an evaluation are unlikely to vary in isolation or to be perfectly correlated as in an extreme scenario analysis. Therefore, a one-way sensitivity analysis will probably underestimate the uncertainty associated with the results of an economic evaluation whereas an extreme scenario analysis will probably overestimate it.

The committee should report the approach used for any sensitivity analysis, clustering results into effectiveness and cost parameters, and report the results in terms of the effect on costs, consequences and cost-effectiveness ratios. Alternatively, results from a sensitivity analysis may be reported as the percentage change in costs, consequences and cost-effectiveness ratios compared to the base case.

An example of a sensitivity analysis is given below using warfarin for the prevention of stroke. Details of the base case scenario are reported in Appendix D (Table D5). One-way and two-way sensitivity analyses were conducted for some selected variables (Table E1). Note that the same approach can be used for a sensitivity analysis of the proportions of the population receiving the different options of aspirin, warfarin, or nothing.

Table E1 Sensitivity analysis of warfarin treatment to prevent stroke

| | Net strokes averted (No.) | Net cost of treatment (\$) | Net cost per stroke averted (\$) |
|-----------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|-----------------------------------------|
| Base case | 462 | \$13,723,712 | \$29,705 |
| One-way analysis: | | | |
| Cost of GP visits increased to \$20.40 | 462 | \$19,254,635 | \$41,690 |
| Cost of echocardiogram increased to \$200 | 462 | \$15,293,047 | \$33,112 |
| Efficacy of warfarin reduced to 51% | 335 | \$16,042,655 | \$47,888 |
| Efficacy of warfarin increased to 74% | 559 | \$11,942,930 | \$21,349 |
| Average increased risk of intracerebral haemorrhage from warfarin decreased to 0.5% | 489 | \$13,230,283 | \$27,058 |
| Average increased risk of intracerebral haemorrhage from warfarin increased to 1.8% | 137 | \$19,667,049 | \$143,971 |
| Two-way analysis: | | | |
| Cost of GP visits increased to \$20.40 AND efficacy of warfarin increased to 74% | 559 | \$17,472,146 | \$31,232 |
| Efficacy of warfarin increased to 74% AND risk of intracerebral haemorrhage increased to 1.8% | 234 | \$17,884,560 | \$76,371 |

Increasing (or decreasing) components of cost (such as the cost of GP visits or echocardiogram) has no effect on the number of strokes averted — only the cost, and hence the cost per stroke averted. Changing the parameters for the efficacy or the risk of adverse effect (ie intracerebral haemorrhage) affects both

costs and consequences. In this example, the results are highly sensitive to both these parameters. When the risk of intracerebral haemorrhage from warfarin was increased to 1.8%, the number of strokes decreased and the cost per stroke averted increased. This scenario clearly dominates all other scenarios as the cost per stroke averted is greatest when this parameter is used. The base case is reported here for ease of comparison to the sensitivity results and should be included in sensitivity analysis results reported by the committee.

The two-way sensitivity analysis shows the effect of increasing both costs and efficacy. When both costs and efficacy are increased the dominant effect is unknown — that is, to avert a case may cost more or less, and how much more or less is unknown. Determining these effects is the purpose of sensitivity analyses. In this example, the cost per stroke averted is slightly greater compared to the base case. However, when both the efficacy and the risk of adverse effects are increased to the upper bounds, the number of strokes averted is reduced by half and the cost per stroke averted is increased 2.5 fold.

APPENDIX F

CALCULATING THE TARGET POPULATION

1. Define the scale of the guideline

The scale of the guideline, or a definition of the population it is intended to cover, will have been undertaken at the time the topic area was formulated. For example, the guideline may be targeted at a local population, such as an area health district, a State within Australia, or all of Australia. The scale may be motivated by the affiliation and purpose of the guideline development committee.

2. Identify the size of the relevant general population

The size of the general population affected by the guideline is the number of people in the region defined within the scale of the guideline. That is, it is the total population in the region that fits a predetermined criterion; for example, people aged 65 years and over normally resident in New South Wales. The Australian Bureau of Statistics (ABS) can provide estimates of these general target populations and can also supply estimates of important subgroups, when the guideline is to apply to small or highly specific groups (eg with a particular health condition).

3. Estimate the prevalence of the health condition in the population to be covered by the guideline

The prevalence of the health condition in the population group to be covered by the guideline may be estimated from a variety of potential sources. For example, local information on the incidence and prevalence of the health condition may be obtained from:

- mortality files (such as death certificates);
- hospitalisation data files;
- the Australian Institute of Health and Welfare;
- Medicare (Health Insurance Commission) data; or
- primary data generated through population and/or health care provider surveys.

Information from local data allows the direct identification of the target population as opposed to the general population. In some circumstances it may be possible to obtain unit record data. Unit records enable separation of incidents into very specific geographic areas, conditions, comorbidities and demographic groups. This local information may identify the number of people to be covered by the guideline — that is, count data.

If count data are used, then estimating the total relevant population and the prevalence (ie steps 2 and 3) may be replaced with direct estimates of the number of cases (ie counts of events). That is, the number of people in the target population is calculated directly.

In the absence of quality data, the committee may need to review epidemiological studies on the condition to estimate its prevalence. Multiplying the estimated prevalence rates by the size of the general population gives the number of people to be covered by the guideline.

4. Identify and quantify demographic features within the target population

The incidence and prevalence of health conditions may vary between different population subgroups, for example, by geographic region, age, gender, ethnicity and/or socioeconomic status. As a result, the committee needs to consider the relative importance of these factors. If some or all of these factors are important, the target population should be separated into some or all of these subgroups. Primary, and some secondary, data may enable disaggregation of data into population subgroups. The demographic features of the target population can then be more accurately described.

In addition, the stability of the population over time should be considered. For example, the absolute population may be increasing or the proportion of elderly people in the population may be increasing. The stability of the population may be examined from historical data. The ABS publishes projections of demographic trends based on low, moderate or high mortality, net emigration and natality, by State. In some circumstances it may be necessary to obtain census data from the last two or three surveys in order to make population projections for specific subgroups.

5. Calculate the number of people covered by the guideline

After defining the scale of the guideline, the population within that region, and the proportion of that population potentially affected by the guideline, the

number of people affected by the guideline is simply the result of step 2 multiplied by the result of step 3. However, if step 3 data are incomplete, it will be necessary to extrapolate local data from one region or State/Territory, area health district or hospital to a larger area to estimate the potential number of people covered by the guideline.

GLOSSARY

Allocative efficiency (*see also* technical efficiency)

When resources and production are arranged so the benefit is maximised from the available resources — in other words the health sector provides society with the amounts and types of health care that they most prefer.

Average cost

The cost per unit of an activity or output, calculated by dividing the total cost of an activity by the number of units of output it produces.

Avoided costs

Those costs that have been prevented by taking a course of action (Earl-Slater 1999).

Clinical practice guidelines

Clinical practice guidelines are systematically developed statements to assist clinicians, consumers and policy makers to make appropriate health care decisions. Such guidelines present statements of 'best practice' based on a thorough evaluation of the evidence from published research studies on the outcomes of treatment or other health care procedures.

Consequences

The health outcomes associated with a health care option.

Cost

See opportunity cost.

Cost–benefit analysis

A type of economic evaluation that measures the costs and benefits of options in monetary amounts. This allows direct comparison of programs both in and out of the health sector and is potentially the broadest form of economic evaluation.¹⁰

¹⁰ World Bank glossary (www.worldbank.org/healthreform/class/module1/glossary.htm)

Cost-effectiveness analysis

A type of economic evaluation that compares options that have a common health outcome. The output is generally displayed as cost per unit of effect. Unlike a cost–benefit analysis it does not require that health consequences be translated into dollar amounts.

Cost-minimisation analysis

A type of economic analysis that compares programs to find the least costly. Used when two or more programs are assumed to have the same outcomes.

Cost shifting

Occurs when the cost that was borne by one section of society in the health care of a medical condition is placed upon another. Examples may include early discharge after operation, which shifts costs from the hospital to the patient, patient’s relatives and community medical services. This is potentially a problem because the shifted costs may not be taken into account when decisions are made, leading to inefficient provision of care.

Cost utility analysis

A type of economic evaluation where the health outcomes are rated by preference strength, for example, quality-adjusted life years (QALYs), and the output is cost per unit of preference state. Effectively it can be a cost-effectiveness analysis, with the common endpoint being QALYs gained.

Decision tree

A graphical representation of a decision, including options, uncertain events and their outcomes (Gold et al 1996).

Direct costs

Are usually defined as those costs that are directly related to the resource use associated with a service or commodity in dealing with the prevention, treatment or rehabilitation of an illness or injury.

Discount rate

The discount rate is the rate used to convert the value of future costs and consequences into equivalent present values. The choice of rate is the subject of debate. There are two ways to derive the discount rate:

- the social opportunity cost (the interest rate forgone); and
- the social rate of time preference (a measure of society’s willingness to trade off benefits in the present for greater gains in the future).

Pragmatically, this handbook suggests that a 5% discount rate be used.

Diseconomies of scale (*see also* economies of scale)

The situation where the cost of production per unit rises (*see* average cost) as the volume of output increases.

Dominance

When one strategy or option dominates another because it is more effective and less costly.

Economic evaluation

The comparative analysis of alternative courses of action in terms of both their costs and their consequences. This can be done in a formal framework (*see* cost-effectiveness analysis, cost-benefit analysis and cost utility analysis) and is designed to help with decision-making.¹¹

Economies of scale (*see also* diseconomies of scale)

The situation where the cost of production per unit (*see* average cost) decreases as the volume of output increases (Gold et al. 1996).

Efficacy

Efficacy refers to the performance of a health care option under highly controlled circumstances.

Efficiency (*see also* allocative efficiency and technical efficiency)

Making the best use of available resources.

Effectiveness

Effectiveness is the generalisability of efficacy. This refers to the performance of a health care option in the real world with a wide variety of providers.

Equity

Fairness in the allocation of resources between individuals or groups.¹²

¹¹ Health Technology Assessment on the Net glossary (<http://hta.uvic.ca>)

¹² World Bank glossary (www.worldbank.org/healthreform/class/module1/glossary.htm)

Extrapolation

The application of results to a wider area/population than that studied. It means to infer values of a variable in an unobserved interval from values within an already observed interval (ie to extend or expand known data into an area not known so as to arrive at a usually conjectural knowledge of the unknown area).

Funding organisations

Those groups or entities that are responsible for the cost of the provision of health services. Examples include the hospital, the State and the federal government (through Medicare and the Pharmaceutical Benefits Schedule) and insurance companies. For example, in the provision of public hospital services the funding organisations include the State and the hospital.

Generalisability (external validity)

The ability to transfer the results of a primary economic evaluation study to another setting or time. This may be linked to the quality of the methodology used, study setting, and relevance of technologies. The essence of generalisability is comparing like with like.

Health care

A process that is applied to a patient or group of interest, encompassing both interventions and diagnostic procedures.

Health gain

The addition to health status that someone has or can have from health care (Earl-Slater 1999).

Incremental cost-effectiveness

The cost-effectiveness of the difference between two programs when one moves from one program to another. The difference in an outcome measure divided by the difference in price. This examines extra consequences and costs one option imposes over another.

Indirect costs

These are the costs that are not directly related to the provision of a service or commodity. Often they refer to the production losses. For example, in the prevention of stroke in those with atrial fibrillation, an indirect cost might be decreased production due to leave from work in attending appointments.

Input

Those resources that are required for the production of an output (a good or service). For example, some of the inputs required for the production of a hip replacement are a surgeon, theatre staff, anaesthetists and a prosthesis.

Internal validity

The extent to which a study measures what it is intended to measure.

Intervention

A therapeutic procedure such as treatment with a pharmaceutical agent, surgery, a dietary supplement, a dietary change or psychotherapy. Some other interventions are less obvious, such as early detection (screening), patient educational materials, or legislation. The key characteristic is that a person or their environment is manipulated in order to benefit that person.

Long run

A period of time sufficient to permit variation of all resources, for example, the time necessary to accommodate an increase in patient beds.

Margin

Refers to the extra or incremental costs or consequences of each option when compared to the other.

Marginal benefit

The extra benefit received for the consumption of one more unit of a commodity or service.

Marginal cost

The extra cost of producing the next unit of the good or service.¹³

Marginal willingness to pay

The maximum amount willing to be given for the next unit of a commodity or some specified health improvement (or to avoid a reduction in health status). This technique is sometimes used to estimate shadow prices (*see* shadow price) for a cost–benefit analysis (*see* cost–benefit analysis).

Microeconomics

The study of the economic system in terms of its individual sections.

¹³ World Bank glossary (www.worldbank.org/healthreform/class/module1/glossary.htm)

Opportunistic

Adapting actions or decisions because of expediency or favourable circumstances. For example, opportunistic cervical screening is a policy of screening women who attend medical practitioners and family planning for any reason.

Opportunity cost

This is a definition of cost used by economists. At the heart of opportunity cost is the notion of scarcity. The opportunity cost is what must be given up in order to obtain something (ie the value of time or any other input in its highest value use). Opportunity cost is the benefits forgone because the next best use was not selected (Gold et al 1996).

Options

Different courses of health service action associated with the prevention, treatment and rehabilitation of an illness or injury.

Outcome (*see also* consequences)

The result of health care on the subject. Outcomes can be divided into different categories such as patient relevant, clinical and surrogate.

Output (*see also* input)

The result of a production process. Inputs are combined to give an output.

Quality adjusted life-year (QALY)

A common measure of health improvement used in an economic analysis that combines mortality and quality of life gains (or losses) (*see* cost utility analysis).

Reference case

A series of methodological recommendations that, if included dependably in an economic evaluation, permits the user of the evaluation to identify studies of consistent quality and with comparable results (Gold et al 1996).

Resources

Those inputs that can be used in the production of goods and services. For example, buildings, surgical equipment, anaesthetic gas, and the time of doctors, nurses, physiotherapists and ancillary staff are resources that can be used to produce health care in the form of operations.

Robust

Results remain stable (ie if cost-effective they remain cost-effective, if not cost-effective they remain not cost-effective) within plausible tested bounds of variation.

Sensitivity analysis

A method used to test whether variations in the assumptions affect the conclusion of an economic evaluation. This is done by varying the items about which there is uncertainty over a specified range.¹⁴

Shadow price

The price that society is willing to pay for a particular outcome, such as lives saved. It is used in situations where it is not possible to gain a price because of the lack of a market. It can also be interpreted as the social opportunity cost of an outcome (Gold et al 1996).

Short run

The time period in which most inputs or resources cannot be varied (Earl-Slater 1999).

Standard gamble

A method of estimating health preferences using a choice between two options. One option has a certain outcome that is the health state to be rated; the other option is a gamble with a chance of full health and a chance of death. The chance of death is varied until the person choosing finds the options of equal value.

Supply-side economics

Where the emphasis is placed on the importance of supply of goods and services in a particular economic situation.

Technical efficiency

Occurs when inputs are combined to maximise a given output. May also be interpreted as minimising cost for a given output.

¹⁴ Health Technology Assessment on the Net glossary (<http://hta.uvic.ca>)

Time trade-off

A method of estimating health preferences using a choice between two options. Each option has a certain outcome. One option is the amount of time in the health state being rated and the other is perfect health for a lesser amount of time. The amount of time in the perfect health state is varied until the person choosing finds the options of equal value.

Total cost

The cost of producing a quantity of a good or service.

Uncertainty

A state in which the true value of a parameter of the structure of a process is unknown (Gold et al 1996).

Unit cost

The cost per unit of resource. For example, the unit cost of the international normalised ratio (INR) test is the cost per blood test (\$13.65). The cost for use of a resource is calculated from the unit cost multiplied by the number of units required. Some agencies produce standardised unit costs; examples are the Medicare Benefits Schedule and the Pharmaceutical Benefits Schedule.

Unit of effect

A measure of outcome of health care, for example strokes avoided, lives saved, successful treatment achieved.

Utility

A technical term used by economists to denote satisfaction or well-being. In health economics it is generally used to show the preferences that an individual, group or society has for a health state.

ACRONYMS AND ABBREVIATIONS

| | |
|----------|-----------------------------------------------------------------------------------|
| ABS | Australian Bureau of Statistics |
| AHES | Australian Health Economics Society |
| AIHW | Australian Institute of Health and Welfare |
| AMI | acute myocardial infarct |
| AN-DRG | Australian diagnostic-related group |
| Aqol | Australian quality of life |
| CHERE | Centre for Health Economics Research and Evaluation |
| CINAHL | Citation Index for Nursing and Allied Health Professionals |
| CPG | clinical practice guideline |
| CPGDG | clinical practice guideline development group |
| CPI | consumer price index |
| ECG | electrocardiogram |
| FBC | full blood count |
| GDC | guideline development committee |
| GP | general practitioner |
| HAC | Health Advisory Committee |
| HE | health economist |
| HEED | Health Economics Evaluation Database |
| HIC | Health Insurance Commission |
| ICD-9-CM | International Classification of Diseases – Ninth Revision – Clinical Modification |
| INR | international normalised ratio |
| LY | life-years |
| LYS | life-years saved |
| MBS | Medicare Benefits Schedule |
| NHMRC | National Health and Medical Research Council |
| NHS | National Health Service |
| PBAC | Pharmaceutical Benefits Advisory Committee |
| PBS | Pharmaceutical Benefits Schedule |
| PPP | purchasing power parity |
| QALY | quality adjusted life-year |
| TFT | thyroid function test |

REFERENCES

- Anonymous (1994). Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials [published erratum appears in Archives of Internal Medicine 1994 154:2254]. Archives of Internal Medicine 154:1449–1457.
- Anonymous (1997). The efficacy of aspirin in patients with atrial fibrillation. Analysis of pooled data from 3 randomized trials. Archives of Internal Medicine 157:1237–1240.
- ABS (Australian Bureau of Statistics) (1999). Population by Age and Sex, Australian States and Territories, Catalogue No. 3201.0. Canberra, ABS.
- Barnett HJ, Eliasziw M and Meldrum HE (1995). Drugs and surgery in the prevention of ischemic stroke. New England Journal of Medicine 332:238–248.
- Briggs AH and Gray AM (1999). Methods in health service research: handling uncertainty in economic evaluations of healthcare interventions. British Medical Journal 319:635–638.
- Briggs A, Sculpher M and Buxton M (1994). Uncertainty in the economic evaluation of health care technologies: the role of sensitivity analysis. Health Economics 3:95–104.
- Canadian Coordinating Office for Health Technology Assessment (1997). Guidelines for Economic Evaluation of Pharmaceuticals: Canada. Ottawa, Canadian Coordinating Office for Health Technology Assessment.
- Commonwealth Department of Health (1993). Manual of Resource Items and their Associated Costs. Canberra, Commonwealth Department of Health.
- Commonwealth Department of Health and Aged Care (1999). Australian Casemix Report on Hospital Activity, 1995-96. Canberra, Commonwealth Department of Health and Aged Care.
- Commonwealth Department of Human Services and Health (1995). Guidelines for the Pharmaceutical Industry on Preparation of Submissions to the Pharmaceutical Benefits Advisory Committee. Canberra, Australian Government Publishing Service.
- Drummond M, O'Brien B, Stoddart GL and Torrance GW (1997). Methods for the Economic Evaluation of Health Care Programmes. Oxford, Oxford University Press.
- Drummond MF and Jefferson TO (1996). Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313:275–283.
- Earl-Slater A (1999). Dictionary of Health Economics. Abingdon, Oxon, Radcliffe Medical Press.

-
- Ezekowitz MD, Bridgers SL, James KE, Carliner NH, Colling CL, Gornick CC et al. (1992). Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. *New England Journal of Medicine* 327:1406–1412.
- Field MJ and Lohr KN (1992). *Guidelines for Clinical Practice: from Development to Use*. Washington DC, National Academy Press.
- Gage BF, Cardinali AB, Albers GW and Owens DK (1995). Cost-effectiveness of warfarin and aspirin for prophylaxis of stroke in patients with nonvalvular atrial fibrillation. *Journal of the American Medical Association* 274:1839–1845.
- George B, Harris A and Mitchell A (1998). Reimbursement decisions and the implied value of life: cost effectiveness analysis and decisions to reimburse pharmaceuticals in Australia, 1993–1996. In: Harris AM (ed). *Proceedings of the 19th Australian conference of health economists*. Sydney School of Health Services Management, University of New South Wales.
- Gold M, Siegel JE, Russell LB and Weinstein MC (1996). *Cost-Effectiveness in Health and Medicine*. New York, Oxford University Press.
- GUSTO Investigators (1993). An international randomized trial comparing four thrombolytic strategies for acute myocardial infarct. *New England Journal of Medicine* 329:673–682.
- Jorgensen HS, Nakayama H, Raaschou HO and Olsen TS (1997). Acute stroke care and rehabilitation: an analysis of the direct cost and its clinical and social determinants. The Copenhagen Stroke Study. *Stroke* 28:1138–1141.
- Mullahy J and Manning W (1996). Statistical issues in cost-effectiveness analyses. In: Sloan F (ed). *Valuing Health Care*. Cambridge, Cambridge University Press.
- NHMRC (National Health and Medical Research Council) (1995). *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines*. Canberra, NHMRC.
- NHMRC (1996). *Clinical Practice Guidelines: Prevention of Stroke*. Canberra, Australian Government Publishing Service.
- NHMRC (1999). *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines*. Canberra, NHMRC.
- NHMRC (2000a). *How to Review the Evidence: Systematic Identification and Review of the Scientific Literature*. Canberra, NHMRC.
- NHMRC (2000b). *How to Use the Evidence: Assessment and Application of Scientific Evidence*. Canberra, NHMRC.
- NHMRC (2000c). *How to Put the Evidence into Practice: Implementation and Dissemination Strategies*. Canberra, NHMRC.
- NHMRC (2000d). *How to Present the Evidence for Consumers: Preparation of Consumer Publications*. Canberra, NHMRC.

-
- O'Brien BJ, Heyland D, Richardson WS, Levine M and Drummond MF (1997). Users' guides to the medical literature. XIII. How to use an article on economic analysis of clinical practice. B. What are the results and will they help me in caring for my patients? Evidence-Based Medicine Working Group [published erratum appears in *Journal of the American Medical Association* 1997 278:1064]. *Journal of the American Medical Association* 277:1802–1806.
- Petersen P, Boysen G, Godtfredsen J, Andersen ED and Andersen B (1989). Placebo-controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. The Copenhagen AFASAK study. *Lancet* 1: 175–179.
- Rodby RA, Firth LM and Lewis EJ (1996) An economic analysis of captopril in the treatment of diabetic nephropathy. *Diabetic Care* 19: 1051–1061.
- Slater J, Hall J, Lowin A and Alperstein G (1998). Cost effectiveness analysis of school based mantoux screening for TB infection in Central Sydney. Sydney, University of Sydney.
- Stapleton JA, Lowin A and Russell MA (1999). Prescription of transdermal nicotine patches for smoking cessation in general practice: evaluation of cost-effectiveness. *Lancet* 354: 210–215.
- Sudlow M, Thomson R, Thwaites B, Rodgers H and Kenny RA (1998). Prevalence of atrial fibrillation and eligibility for anticoagulants in the community. *Lancet* 352: 1167–1171.
- UK Prospective Diabetes Study Group (1998). Intensive blood glucose control of sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type II diabetes. *Lancet* 352: 837–853.
- Weinstein MC and Fineberg HV (1980). *Clinical Decision Analysis*. Philadelphia, Saunders.
- Weinstein MC, Siegel JE, Gold MR, Kamlet MS and Russell LB (1996). Recommendations of the Panel on Cost-effectiveness in Health and Medicine. *Journal of the American Medical Association* 276: 1253–1258.
- Weinstein MC and Stason WB (1977). Foundations of cost-effectiveness analysis for health and medical practices. *New England Journal of Medicine* 296: 716–721.
- Whynes DK, Neilson AR, Walker AR and Hardcastle JD (1998). Faecal occult blood screening for colorectal cancer: is it cost-effective? *Health Economics* 7:21–29.

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