PHARMAC

Pharmaceutical Management Agency Ltd

A PRESCRIPTION FOR PHARMACOECONOMIC ANALYSIS

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Table of contents

SUMMARY

Within the health system, we don't have the resources to do everything we want to do. Consequently, we need a means of deciding how to allocate resources to those activities that we most desire. Cost benefit analysis provides guidance for resource allocation decisions.

PHARMAC chooses to use **cost-utility analysis** (CUA) because it is achievable and practical, yet still enables comparisons across different health interventions. This helps prioritise competing programs and opportunities, without the problems of valuing benefits in money terms.

In performing cost utility analysis, PHARMAC considers the relevant health benefits and the direct costs of the intervention to the health sector. Where indirect costs and non-health related benefits are important, it is likely that they will be recognised within PHARMAC's Decision Criteria.

Cost utility analysis is subject to PHARMAC's larger Operating Policies and Procedures, which outline our framework and Decision Criteria for incorporating the range of need, efficiency, equity and commercial considerations.

All future costs and health consequences are stated in terms of their "present value". This involves adjusting costs and benefits for differences in their timing. "Discounting" is the computational process used to obtain present values of future costs and benefits. A key element to discounting is selecting a discount rate that reflects the populations' preference for present over future outcomes.

All major assumptions used in analysis should be subject to sensitivity analysis. Sensitivity analysis allows us to assess to what extent the results depend on the assumptions used in the analysis.

PERSPECTIVES

The following pages describe the main ideas behind and methods used by PHARMAC's cost utility analyses. They draw heavily on health economics guidelines and consensus statements published internationally,[1] [2] [3] [4] but vary where PHARMAC and District Health Boards (DHBs) have particular operating constraints, or take account of the funded universal coverage of the New Zealand public health service.

General Perspectives

A General Introduction to Economic Evaluation

Cost Utility Analysis facilitates economic evaluation of a range of spending opportunities.

Economic evaluation is a tool for assisting decision-making given assumptions about how society wishes to maximise the benefits from limited health care spending.

Economic evaluation involves identification of the benefits and costs of such spending, where:

- the benefits include improvements in the maintenance of, or prevention of deterioration in, health status (including improvements in length of life, reductions in illness and improvements in quality of life); and

- the costs are the resources that are used to generate the benefits.

Economic evaluation can only ever be a tool to aid decisions. Economic evaluation aims to identify the extent to which a particular decision or set of decisions meets the goal of promoting efficiency. Yet efficiency may not be the only goal that society has, and other criteria may be equally or more important (for example, equity). The advantage of undertaking economic evaluation however is to measure the costs and benefits of various decisions and the trade-offs which might be made between efficiency and other criteria.

What is Cost Benefit Analysis?

Cost benefit analysis is the explicit consideration of the perceived costs and benefits of a proposed course of action.

We implicitly weigh the costs and benefits of courses of action on a daily basis. The analysis discussed in this paper merely extends this weighing up process by clarifying the values used and assumptions made in valuing the attractiveness of a proposed action.

Why use it?

Within the health system, we don't have the resources to do everything we want to do. Consequently, we need a means of deciding how to allocate resources to those activities that we most desire. Cost benefit analysis provides guidance for resource allocation decisions.

The explicit nature of this analysis allows for clear definition of issues. This clarity is an essential prerequisite for a robust decision making process. Assumptions are open to scrutiny and debate, allowing all relevant issues to be considered and weighed when coming to a decision.

Also, the explicit listing of costs and benefits creates a record against which future (and past) decisions can be reviewed, thereby, aiding consistency.

Types of cost benefit analysis

Difference types of analyses reflect the different levels of analysis that can be performed in pharmacoeconomic cost benefit analysis. They are listed in order from the least complex to the most.

Cost Minimisation Analysis (CMA): where no benefit changes are involved (i.e. assuming the same levels of the outcome). Hence, the decision can be made on the basis of costs alone. The benefits from listing a generic pharmaceutical at a lower price than the original brand product, delivering the same health benefits for less cost, is an example of a "cost minimisation" decision.

Cost effectiveness Analysis (CEA): where we assess the costs of achieving directly comparable outcomes. For example a drug trial may show that treating 100 patients for 5 years may avoid 10 heart attacks. Cost effectiveness analysis divides the cost of treating the 100 patients for 5 years by the number of heart attacks avoided to give us a figure of $Y per heart attack avoided. The resulting cost effectiveness measure can be compared with those for other interventions that also enable people to avoid heart attacks.

This analysis has a major drawback in that we cannot directly compare interventions that treat different disorders. For example, how do we compare a cost effectiveness analysis of $X per heart attack avoided with a $Y per hip fracture avoided?

Cost Utility Analysis (CUA): where we compare the possible health outcomes using a common currency. Rather than having a certain end-point relevant to the treatment in question, such as heart attacks avoided, the analysis has a common value end-point, such as a quality adjusted life year (QALY). We can, therefore, derive figures of $Y per QALY across all interventions treating disorders as diverse as infections, heart attacks or osteoporosis. The smaller the $Y per QALY, the more cost effective the intervention.

CUA has the advantage that investment opportunities in different areas of health care can be compared. For example, the cost effectiveness of interventions to prevent heart attacks can be compared with the cost effectiveness of drugs to cure gastric ulcers. In contrast, CEA can compare investment opportunities for only one area of health care, in the example above, that of avoiding heart attacks.

We note that there are still some issues to be addressed in using cost-utility analysis. For example, there is currently no commonly agreed technique for measuring quality of life. Secondly, there are issues involved in interpreting QALYs. For example, should a QALY be worth the same to every person who gains one regardless of age or current quality of life?

Full Cost Benefit Analysis (CBA): Where we set out all costs and benefits in dollar terms. Investment opportunities can be compared across all areas of government spending, extending beyond health. However, it has two major drawbacks.

Firstly, there are significant difficulties in placing a dollar value on health benefits. We know of no robust technique for doing this that is systematically used by funding authorities in any country. We note that there is interest in developing techniques for valuing benefits, but that further research is required before such approaches can be considered more seriously. For this reason, it is not a practical option for PHARMAC to use in its analysis.

Secondly, it implicitly assigns different values (weights) to different types of health benefits. For example, people may be willing to pay more for life saving interventions over those that raise quality of life. We aim to do this explicitly, which is more easily done using cost-utility analysis.

Of the above alternatives, we choose to use **cost-utility analysis** because it is achievable and practical, yet still enables comparisons across different health interventions.

This helps us prioritise competing programs and opportunities, without the problems of valuing benefits in money terms.

What do we do with cost utility analysis?

Decision making with many investment opportunities but limited funds involves rationing.

Rationing inevitably includes explicitly comparing one intervention against others when deciding which programs to fund. To do this, each possible health intervention needs to be prioritized (ranked) in terms of value for money, and benchmarked against other decisions. This applies to all new investment decisions (through the application of incremental analysis) and to reviews of decisions made in the past (through the application of decremental analysis).

An example could be that PHARMAC receives an application to fund a new drug "A", that offers significant health benefits. However, expenditure forecasts indicate that PHARMAC cannot afford to buy the new drug without reducing funding of other drugs. Therefore, as PHARMAC must work within a fixed budget, it has three options:
1. to not fund drug A, or
2. to fund drug A and reduce the funding for less-effective pharmaceuticals.

Under option 2, the total health gains from the resources available are maximised.

A hypothetical example is set out below.

Decision type	Drug	Benefit (QALYs)	Cost ($)	$/QALY
Applications for	A	200	1,000,000	5,000
funding new	B	100	2,200,000	22,000
drugs	C	50	1,600,000	32,000
	D	50	4,800,000	96,000
Review of	E	200	2,000,000	10,000
already funded	F	80	1,200,000	15,000
Drugs	G	250	4,500,000	18,000
	H	50	1,050,000	21,000

In this case, if PHARMAC concentrated only on the cost utility framework in its decision making, PHARMAC would maximise the QALYs gained by funding drug A and delisting drug H.

Breaking down the data for QALY rankings

The above framework relies on reliable data about the patient groups to be treated. A group can be defined as a set of patients having roughly equal ability to benefit from a treatment. If a drug gives varying benefits across different groups of patients, then each group of patients will need to be treated separately.

Patient groups can differ by combinations of age, sex, symptoms, disease severity, and other factors. Hence, we ultimately need cost-utility ratios for each potential target population.

This means that for each funding decision, we may need to estimate costs and QALYs for each combination of:

■ treatment regime x

- disease group x

- symptom complex x

- severity of disease x

- patient characteristic (e.g. age x sex x other factors)

Disaggregating the analysis by patient groups will require that we can define a manageable set of groups that are mutually exclusive, comprehensively exhaustive and relevant to any treatment or targeting regime that might be implemented.

The necessary detail will depend on the intervention involved. Due to their nature, some interventions may not need analysis of individual patient sub-groups. In other cases, the clinical data may be so lacking that no reasonable distinctions can be made. As such, the amount we disaggregate the analysis will vary according to the specific issue.

The treatment groups used for analysis may determine PHARMAC's targeting criteria for patient access to a drug or other. It may be a good investment to fund a drug for one patient group, but not another. For example, better value (i.e. greater health benefit per dollar spent) is obtained if we fund statins for high risk patients (such as patients aged 60 years with pre-existing coronary heart disease and total cholesterol >7.5mmol/l)[5] rather than lower risk patients (e.g. 10-15% 5-year CHD risk with moderate total cholesterol levels). Such conclusions, made by analysing the net costs and expected QALY gains of treating a diverse range of patients, may help targeting decisions.

The CUA approach can be used to consider past funding decisions as well as future funding decisions. For example, it can provide the analytical basis for decisions to restrict access to medicines where the evidence suggests these drugs are only cost effective for patients with certain conditions or severity. Such divestment can free up funds for more worthwhile interventions currently waiting funding.

Clarity is essential

The major advantage of using cost utility analysis is that, when done properly, it clarifies the assumptions and methods used in coming to a decision. For example, when calculating a cost per QALY, one has to decide, amongst other things:

- what costs are included and why?

- what benefits are included and why?

- is a QALY for one person equal to one for another?

- what time frame is relevant?

Each of these issues influences the final result. A change in any one will usually significantly change the result.

Consequently, when using CUA to inform a decision, the perspectives taken should be clearly stated.

This paper undertakes to clearly outline the assumptions and perspectives taken by PHARMAC when commissioning or performing CUA.

PHARMAC Objectives and Perspective Used in CUA

PHARMAC is a Crown entity established by the New Zealand Public Health and Disability (NZPHD) Act 2000. The Agency is directly accountable to the Minister of Health.

Prior to PHARMAC's establishment as a stand-alone entity under the 2000 NZPHD Act, PHARMAC was owned by the Health Funding Authority (HFA) and, prior to that, the Regional Health Authorities (RHAs). Under this relationship, PHARMAC advised the HFA on which pharmaceuticals to subsidise compared to other pharmaceuticals or other health interventions which the HFA had the option of purchasing. Hence, PHARMAC would undertake cost utility analysis from the HFA's perspective for the specific purpose of improving New Zealanders' health and independence.

Since the introduction of the 2000 NZPHD Act, PHARMAC's primary objective has been "to secure for eligible people in need of pharmaceuticals, the best health outcomes that are reasonably achievable from pharmaceutical treatment and from within the funding provided". This objective is accomplished through the management of a list of subsidised pharmaceuticals, the Pharmaceutical Schedule, on behalf of the Crown.

The perspective taken by PHARMAC in conducting CUAs is that of the health sector, in accordance with PHARMAC's primary objective (achieving the best health outcomes possible from pharmaceutical treatment). This implies that any patient benefits and/or costs that accrue beyond being either healthy or unhealthy are outside the scope of PHARMAC analysis (where "health" is defined by default in the Health and Disability Services Act 2000 as amenable to health services interventions). The role of health services is to put an individual in the position where he/she has the greatest capacity possible to choose their lifestyle, be it economically or socially productive or otherwise.

This means that extra economic production stemming from an individual being healthier is outside the scope of our analysis. Otherwise we might discriminate against those less economically productive, such as children and the elderly.

Following this argument implies that PHARMAC should concentrate on those costs that are:

- *Pertinent to DHBs.* Obviously direct health funding costs will be included in all analyses. This extends beyond just drug costs, to include costs and savings in hospitalisations and other health and disability support services.

  Also, direct costs to patients of a treatment are incorporated. We include items such as prescription co-payments and surcharges for general practice consultations that are a sharing of resource costs between DHBs and patients. We note though that we would not want to include costs that the patient chooses to bear when they have the option not to. For example, patients paying manufacturer's surcharges for drugs where there is a fully subsidised alternative drug available.

  Other patient costs such as travel time etc. could be incorporated under these definitions, but they run afoul of the next criteria, ease of measurement.

- *Pragmatic to measure.* Indirect costs such as patient travelling times and productivity losses are not easily measured. There is usually no available data on these issues or how to cost them across patient sub-groups. Consequently, we feel that incorporating these into the analysis will entail using significant and untestable assumptions. Given the large uncertainties involved we feel it best to avoid incorporating these estimates into base case analysis.

- *Neutral across all New Zealanders.* If we incorporated productivity losses we could easily bias a decision toward those sectors of society that are most economically productive and

away from other groups, e.g. children, elderly, caregivers etc. This conflicts with the public priorities as stated by the Government.

In summary, the PHARMAC perspective in CUA is to consider only health benefits and direct health sector and patient costs.

Where indirect costs and non-health related benefits are important, it is likely that they will be recognised within PHARMAC's Decision Criteria.

Best health vs best care for those with need.

The goal of maximising health can conflict with the goal of creating the best care for the needy. For example, a patient group with a severe condition may not receive a new service (A) because another service (B) for another patient group may deliver significantly greater quality of life gains per dollar spent.

Cost utility analysis is a tool used for maximising health. CUA cannot explicitly assist in any debate about the ethics of maximising health compared to treating the "needy". CUA does clarify the size of the efficiency trade-off if a decision to treat the needy is made (where the needy will gain less benefit per dollar spent than patients who would benefit from an alternative proposal). However, this is the only exception where CUA informs ethical debate.

For this reason, we have adopted cost utility analysis as one part of our decision-making framework. Decisions can, and have, been made to treat the needy on grounds other than maximising health. In short, CUA results are considered a guide to decision making, not a substitute.

Defining the comparator

Where relevant, PHARMAC will conduct CUA on an intervention comparing it to no treatment as well as to close comparators, where they exist.

Most of the analyses PHARMAC has performed concentrated on comparing an intervention to existing treatments. However, we cannot assume that all existing treatments are in fact worthwhile. Hence, it is helpful to perform CUA on an intervention on both an untreated and an existing treatment basis. For example, when considering the funding of tacrolimus for use as a last resort to rescue transplanted kidneys, the analysis investigated the cost utility of tacrolimus and the incremental cost effectiveness of tacrolimus as summarised in the table below.

Costs and benefits of rescuing transplanted kidneys

	Cost	QALYs	Cost/QALY
Tacrolimus rescue (a)	$10,452,261	372	$28,094
Dialysis (b)	$9,880,066	145	$67,941
Increment	$572,195	227	$2,525

- NPV is calculated over 23 years using an annual discount rate of 11.4% - the capital charge applying to government departments at the time of this analysis (Note: data shown are for purposes of illustration only. Incremental cost per QALY equals [cost of (a) less cost of (b)] divided by [QALYs gained under (a) less QALYs gained under (b)]).

The incremental cost utility of tacrolimus for use in renal rescue indicates that funding it for this use would be money relatively well spent (cost per QALY ratios of around $2,500). However, part of the reason for this is that the alternative, dialysis, is relatively costly per QALY gained. If this alternative was not currently available, the cost utility estimate for tacrolimus rescue shown above of between $26,000 and $30,000 indicates that allocating funds to tacrolimus for kidney rescue may be an option that compares poorly with other interventions looking for funding.

Time horizon and discounting

Cost and benefits are measured over a given time horizon, long enough to capture all the differential effects of an intervention. All costs and benefits should be discounted to reflect:

- An investment's opportunity. Investing money in health takes resources away from other investments that may earn a return. The opportunity cost of the resource use is the return that would be made elsewhere.

- People's time preferences. It is human nature to prefer to gain benefits sooner rather than later, in particular, because of uncertainty about what the future holds.

This is, however, an issue of considerable debate. Some argue against discounting, others for a rate equal to Government's long term cost of capital, while others argue for even higher rates to reflect perceived risks that the DHBs and PHARMAC face in managing public health expenditure. PHARMAC currently uses an annual discount rate of 10% but presents analyses using a range of rates.

Other HFA/PHARMAC perspectives on CUA

There are three fundamental concepts that have been kept in mind while developing PHARMAC's CUA framework. These have a significant impact on the type of analysis chosen and the tools used.

Grass-roots involvement

To have any appreciable impact in improving decision making systems, those involved in contracting and negotiating the investment decisions must also be involved in the economic analysis. This requires that the Therapeutic Group Managers (TGMs) are involved in the CUA, along with members of the analysis team, during consideration of an investment.

Analysis prior to decision making

Analysis should be done before an investment decision is made, as well as after. There is no point in working out whether an investment is worthwhile after you've spent your money on it. And once in place, it can be difficult to retract those services if they are found to be poor value. However, we also note that on-going programmes should be reviewed to check that the funding assumptions still hold.

Manageable implementation

The changes in decision making processes must be manageable if people are to adopt CUA. For this reason we are keen to make minimal changes to existing PHARMAC processes.

Putting it all together

$$
\text{Incremental cost / QALYs} = \text{discounted incremental costs / discounted QALYs}
$$

$$
= \frac{(\text{net costs of intervention}) - (\text{net costs of alternative}), \text{ discounted by year}}{(\text{net QALYs of intervention}) - (\text{net QALYs of alternative}), \text{ discounted by year}}
$$

Limitations of CUA, and hence its more limited role in PHARMAC's decision-making

Ideally, CUA could give us a clear ordering of which interventions will give the best value-for-money when compared with other interventions (by comparing any intervention against its current or next-best alternative). But in reality this can be difficult. CUA is often hampered by poor data. In particular, there may be difficulties with:

- a lack of data about <u>marginal</u> non-drug health sector costs (rather than average costs),

- a lack of data about the effectiveness of an intervention and patients' compliance in real life,

- incomplete agreement on defining generic health states and measuring utilities,

- potential bias in how disease states and health status improvements are mapped to generic health states and utilities.

CUA's role in PHARMAC's decision-making

Given these potentially serious limitations, CUA is but one part of PHARMAC's decision making process.

As set out under its Decision Criteria in its Operating Policies and Procedures, PHARMAC takes into account the following factors (where applicable) when deciding whether to fund new treatments:

> The health needs of all eligible people within New Zealand;
>
> The particular needs of Maori and Pacific peoples;
>
> The availability and suitability of existing medicines, therapeutic medical devices and related products and related things;
>
> The clinical benefits and risks of a pharmaceutical;
>
> The cost-effectiveness of meeting health needs by funding pharmaceuticals, rather than by purchasing other health care and disability services;
>
> The budgetary impact (in terms of the pharmaceutical budget and Governement's overall health budget) of any changes to the Pharmaceutical Schedule;
>
> The direct cost to health service users;
>
> The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere, and
>
> Any other criteria that PHARMAC thinks are relevant. PHARMAC will carry out the necessary consultation whenever it intends to take any 'other criteria' into account.

Using these factors can sometimes mean arriving at a different decision than that which would be advised by CUA alone.

For example, when considering *"The overall budgetary impact of any changes to the Pharmaceutical Schedule"*, two interventions A and B may appear equally cost-effective in

terms of cost per QALY, but B costs five times as much as A. The decision may be made to fund only intervention A at this stage.

	Cost	QALYs	Cost/QALY
Intervention A	$2,000,000	167	$12,000
Intervention B	$10,000,000	833	$12,000
Intervention C	$10,000,000	139	$72,000

Other examples of alternative outcomes are when:

- Government has created a special priority area

  Two programmes may have similar costs and total QALYs gained, but the population group of one falls into a Governmental priority group, such as Maori, and, therefore, is given higher priority for funding.

- Commercial considerations

  The recommendations of CUA may be less relevant in light of a wider set of supplier negotiations or where PHARMAC perceives significant commercial gain to be made in negotiations.

- Equity considerations

  The purpose of CUA is to guide decisions aimed at maximising the number of QALYs for a given amount of money. There are times when this may result in recommendations that conflict with current views of equity.

  For example, by stratifying analysis by age, one may obtain results indicating that fewer QALYs per $ can be gained by treating the elderly compared with younger generations. This may reflect that the elderly have lower life expectancies, and perhaps in some cases, a lower quality of life than younger people.

  PHARMAC ran across this circumstance in its consideration of de-restricting "statin" pharmaceuticals for New Zealanders with cholesterol problems. In this case, on an equity basis, the PHARMAC Board decided age would not be a criterion for access to the drugs, despite the elderly gaining significantly fewer benefits.

  Another situation where ethical considerations may override economic ones is when the "rule of rescue" is invoked. In this case, economic evaluation may favour an intervention that saves no lives but improves the quality of life of a large number of people, whereas decision-makers may prefer to fund another intervention that saves lives. However, it should be noted that the problem is seldom this simplistic and that in reality the question is how much of both interventions should be funded - with more of one meaning less of the other.

Summary

Despite its limitations, CUA can give important guidance. This is particularly when weighing up interventions that cover a range of different diseases, patient groups and outcomes.

CUA explicitly formalises the weighing up which implicitly - and inevitably - occurs when one decides to fund one intervention over another.

MEASUREMENT OF COSTS

The incorporation of different types of costs will depend on the interventions being studied and the type of analysis undertaken, i.e. comparing an intervention to no treatment, or comparing one intervention to another.

Costs are measured in dollar terms and include:

Net costs = direct costs of intervention

+ costs of treatment side effects (if any)

+ other health sector costs

- savings from decreased use of other drugs or treatment regimes

- savings from decreased hospitalisations and other health sector costs (e.g. disability support services)

What costs do we measure?

Direct costs of intervention

For PHARMAC's cost-utility analyses, direct costs of interventions are (usually) the price of the pharmaceutical ex-manufacturer, exclusive of Goods and Services Tax (GST). Dispensing fees associated with the pharmaceutical only need to be taken into account if it is to be dispensed on a monthly basis whereas the comparator is dispensed stat.

Costs of treatment side effects

Costs of treating adverse effects include hospitalisations, primary health care costs, and drugs to treat side effects (for example, use of H2 antagonists to offset stomach ulceration caused by non-steroidal anti-inflammatory drugs). These, too, should be measured ex manufacturer, excluding GST.

Other health sector costs

Other intervention-associated regime costs require us to estimate the number of laboratory tests and other relevant primary health service costs. This involves combining two parts:

- obtaining DHB contracted prices for the particular lab test or primary health service in question;

- estimating how many services (laboratory tests, etc.) each patient receives over the given timeframe.

General practice costs

General practice costs can be calculated, assuming X consultations at an average of, for example, $50 per consultation in the case of total analysis. In the case of incremental/marginal analysis these would only be factored in if one intervention resulted in a change in general practice utilization.

Hospitalisation offsets and savings from decreased use of other treatment

To the extent that proven offsets occur, these are incorporated into the costings.

Hospitalisation offsets can be calculated by:
1. estimating risks of hospitalisation over the given timeframe experienced by each patient, then
2. applying the average price per hospitalisation for the relevant diagnosis.

Risks of hospitalisation can be modelled from clinical trial data and uptake rates. Hospital costs are calculated using volume-weighted average WIES8C Diagnostic Related Group (DRG) costweights.

It is true that potential savings may not be realised by the DHB. For example, if hospital contracts are undefined to the extent that hospital bed-days saved through a drug's introduction are used for patients with different ailments, there may not be a financial saving to the DHB. However, we feel that even in this case, hospital cost offsets are part of the net resource use of a drug intervention and measuring net resource use is the goal of economic analysis. We note that this view is consistent with others.[6]

Patient co-payments and manufacturers' surcharges

We feel that patient co-payments should be incorporated into the analysis as they represent the sharing of an intervention's resource cost between DHBs and patients. However, manufacturers' surcharges should be incorporated only where patients have no alternative fully subsidised agent that does not carry a surcharge.

Goods and Services Tax

Goods and Services Tax (GST) is New Zealand's value added tax. It is not included in these calculations, in line with DHB policy. That is, all values presented to decision makers are presented exclusive of GST.

Caveat

Often there are few, if any, data describing some costs. This applies particularly where trial data and prevalence data are limited. Examples are data about utilisation patterns for drugs other than that being studied, and costs of treating adverse effects of the drug being studied. In addition, non-inpatient health sector cost offsets may be difficult to calculate because there are few disease-specific cost estimates for services such as outpatient clinics, community health services (domiciliary) and disability support services. In such cases, a degree of judgement will be necessary, to make a best-guess estimate.

Perspectives

Do we measure costs not borne by DHBs?

These range from:

- direct patient non health costs, for example, the costs of transportation to and from a doctor's clinic;

- patient time costs, for example, the time spent by a patient at a doctor's clinic or in receiving treatment;

- productivity costs, for example, a loss in economic productivity due to a patient's sickness, treatment or death;

- direct health costs and offsets borne by government agencies other than DHBs e.g. ACC rehabilitation costs.

For reasons explained in the introductory section of this document, we tend to concentrate on direct costs to DHBs and the patient. The one item above that was not mentioned at the beginning of the document was costs to other Government Agencies.

Generally, we are unwilling to incorporate these for the same reasons we don't incorporate patient indirect costs; we lack reasonable data to do so. Also, offsets accruing to other Government Agencies resulting from pharmaceutical investments (e.g. decreased ACC costs because of more effective osteoporosis treatments decreasing rates of hip and wrist fractures) are not necessarily matched by those agencies contributing to DHBs investment.

However, as with the other indirect patient costs, we feel that if there are individual interventions where these are likely to be significant, they can be incorporated as a sensitivity analysis to the main analysis.

Where should we count hospitalisation cost offsets?

Lower hospitalisations resulting from a health intervention should be incorporated into the model as cost offsets, using the best costing information available.

Hospitalisation offsets could be measured as QALY gains for patients who access treatments with the funds freed up from reduced hospitalisations or the hospital beds made available. This is consistent with practice where decreased hospitalisations for one condition will mean greater treatment of patients with other conditions. Thus, DHBs will not gain direct financial savings from decreased hospitalisations, instead more people will get other treatments.

Modelling this, however, is problematic. The extent of the benefit would depend on which surgical or other procedures the DHB hospital spends the funds. Effective surgery for needy patients will vastly increase the number of patient QALYs but this might not always occur and the funds may instead be spent on goods or services that offer lower QALY gains.

Without any further information on this, we propose to model hospitalisation savings as a cost offset rather than as a potential QALY gain.

Average hospital costs are only a proxy, and bias eventual cost/QALYs

We have ready information about average prices paid in New Zealand by DHBs for diagnosis-related groups or other purchasing units. These data are useful since they are condition or procedure-specific.

However, there are no ready data able to distinguish between the "fixed" costs necessary to run a service regardless of patient numbers (e.g. overheads, minimum staffing levels, etc.) compared with marginal costs, i.e. the extra costs incurred treating each new patient. This means we cannot calculate true marginal hospitalisation savings.

Thus we are forced to use average prices, since they are the only readily available data. However, we are aware that average costs are only surrogates for true marginal costs and that they may cause bias. Where we have information relating to the size of this bias, we will incorporate it into the analysis.

Adjustment of costs for patient uptake

PHARMAC considers the impact of uptake when deciding whether to invest in new pharmaceuticals or extend treatment to new indications or target populations.

Uptake rates reflect that not all patients eligible for an intervention actually receive treatment, because of:

- incomplete patient access to primary health care services (so that eligible patients are not identified as needing treatment);

- variable diagnosis by prescribers so not all at-risk patients will be diagnosed with the relevant condition;

- incomplete adherence by prescribers to guidelines and criteria (so that eligible patients do not receive recommended treatment);

- non-pharmacological improvement in health status or risk factor modification (so that previously-eligible patients no longer need treatment);

- patients not uplifting scripts from pharmacies; and

- patient non-compliance with taking medicine.

These factors accumulate, so that actual users are a fraction of those eligible. The shortfall depends on uptake, which can be defined as:

Uptake = presentation rate x screening/diagnosis rate x prescriber adherence x non-pharmaceutical improvements/risk factor modification x script uplift

Therefore:

Number of actual users = number eligible x uptake

Uptake rates affect the extent to which potential QALYs translate to actual benefits for a target population and adherence/continuation rates (which are described in the "Measurement of Benefits" section of this paper). This may affect the cost utility analysis. This will depend on the intervention in question and the data available.

Uptake effects also affect the total cost of the treatment to DHBs. As uptake effects become more prominent, total costs decrease - as do expected total benefits. This means an investment might become more affordable, because funds required will be less than needed were uptake ideal (100%). Fewer funds would need to be freed up elsewhere, and hence PHARMAC may be more willing to fund the investment.

Benefits and costs of investing in an intervention, according to uptake
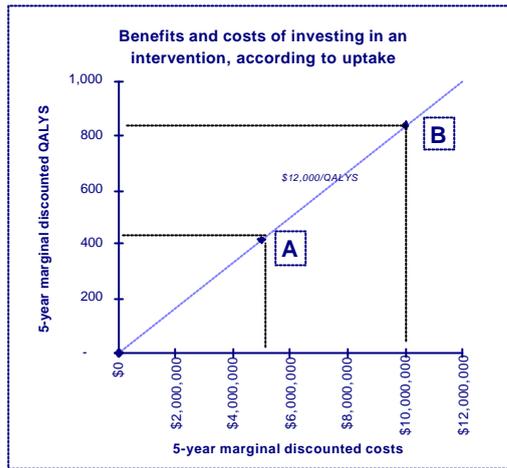
An intervention X has a cost/QALY of $12,000, costing $400/patient.

X could potentially apply to a target population of 25,000 people (see point B in adjacent graph). This would mean potentially saving 830 QALYs, but at a cost of $10m.

However, in real life uptake is expected to be only 50%. This means only 12,500 people receive treatment (at point A). So only 420 QALYs are saved, but only $5m is needed.

Expected uptake rates therefore need to be estimated for each investment decision, both now and in future.

MEASUREMENT OF BENEFITS

Benefits are measured in quality adjusted life years.

Benefits include both improvements in life expectancy and improvements in health state, and take into account treatment side effects.

Quality-adjusted life years (QALYs) saved

The aims of health interventions are to cure or ameliorate illness and disability, and to prevent the onset or worsening of illness, disability and premature death. These different outcomes can be covered by a single measure such as quality-adjusted life years (QALYs) saved. This differs from what happens in formal cost-benefit analyses, where benefits are all measured in monetary terms. We use cost-utility analysis because it is achievable and practical, and yet still allows us to compare across different health interventions.

QALYs incorporate a drug's impact on both death and illness and the effects of side effects.
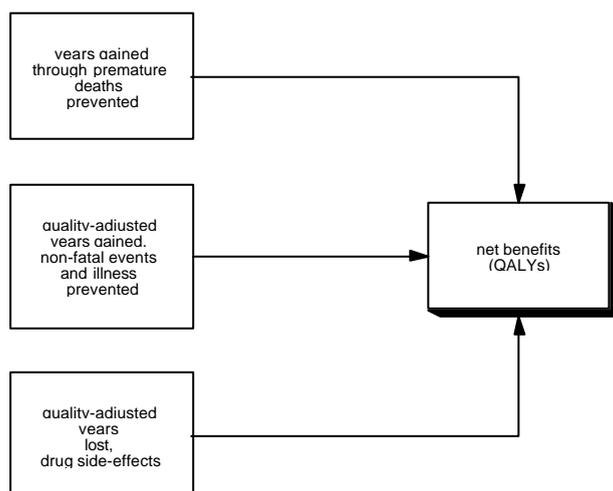
Benefits (QALYs) =

Number of quality-adjusted years saved through preventing premature death

+ quality improvement to existing life years gained through disability/suffering relieved or avoided

- quality decrease to existing life years from side effects

- loss of benefits from substitution for other drugs or treatment regimes (where relevant)

For example, when comparing a drug intervention against no treatment, the following may be taken into consideration.

Deriving quality of life adjustments

QALY scores ("utilities") are critical to calculating benefits. QALY scores are generally derived from surveys of patients, their families/carers, health professionals, and the general public.

Each survey involves asking respondents to value the quality of life where there is a change in the state of health in a particular dimension varies.

Dimensions can be defined in a number of ways, for instance in terms of distress mobility or role functioning. Health states within dimensions can also be variously defined, for instance "no problem", "mild problems", "moderate problems", and "severe problems".

Utility scores can be elicited by various methods, such as pairwise comparisons, standard gambles, time tradeoffs (TTOs), person tradeoffs (PTOs), and direct ratings using visual analogs. These methods and their features are all described in the standard health economics literature, e.g. Dolan 1998.[7]

All respondents' scores for each dimension level (Health State) are combined to form an average estimate. The estimates for each health state can be placed into a table, for instance:

Suffering	Daily activity limitations	Rating
None	None	1.00
None	Mild	0.89
None	Moderate	0.66
None	Severe	0.41
Mild	None	0.83
Mild	Mild	0.78
Mild	Moderate	0.60
Mild	Severe	0.39
Moderate	None	0.63
Moderate	Mild	0.61
Moderate	Moderate	0.51
Moderate	Severe	0.34
Severe	None	0.41
Severe	Mild	0.37
Severe	Moderate	0.32
Severe	Severe	0.18
(Death)		0.00

• Source: Hadorn and Uebersax "The Quality of Life Health Questionnaire", with linear adjustments

In this example, the collective view of the surveyed group is that someone with severe limitations to their daily activities and moderate suffering has health-related quality of life which is just 34% of that of good health.

The impact of a disease state can be "mapped" onto the resulting table of health states, by assessing how the disease affects the patient on each dimension. This enables us to measure the quality of life impact of that disease state. This quantification of quality of life impact can also extend to the quality of life gained from medical treatment.

For example, a particular asthma sufferer may be judged to experience mild physical suffering with mild activity limitation (0.78). Hence, that person's quality of life impact from asthma would be 0.22 (= 1 - 0.78).[i] If pharmaceutical use removes the activity limitations faced by this person, their quality of life is improved. Their new quality of life measure would be 0.83, and the impact of their asthma would now be 0.17 (= 1 - 0.83). We are thus able to measure the quality of life impact of drug treatment for that asthma patient as 0.05 (= 0.22 - 0.17).

So, deriving disease-state utility values when calculating QALYs involves two parts:

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[i] where 1 = rating for good health, .78 = adjusted rating for mild suffering/limitation, and .22 residual = difference between mild suffering/limitation and good health (and hence impact).

- specifying generic health states with empirically-derived utility values; and

- defining different kinds of patient groups, then mapping the severity of the Disease State and possible treatment effects to the generic health states (and hence to utility values).

Health status measures in general

There are a number of generic health status measures available for assigning values to health states. All use a scale from 0.00 (dead) to 1.00 (no distress or disability). However, each measure is different. These differences reflect that the measurement of QALYs is a relatively new and controversial area without agreement about what best to measure and how. There is no "gold standard" or any instrument to meet all needs. In a recent review of such instruments for the OECD, Erik Nord[8] concludes that measures differ greatly in terms of their conceptualisation of health and their sensitivity to changes in health.

We are aware of ten such generic health state measures identified by Nord and other sources:

- the Rosser/Kind Disability/Distress Index[9]

- the Quality of Well-Being Scale (QWB)[10]

- the 15-D[11]

- the Health Utilities Index, mark II (HUI2)[12]

- the Health Utilities Index, mark III (HUI3)[13]

- the EuroQol instrument (EQ-5D)[14]

- the Index of Health Related Quality of Life (IHRQOL)[15]

- the Quality of Life and Health Questionnaire (QLHQ)[16]

- the Australian Quality of Life instrument (AQOL)[17]

- the Years of Healthy Life Measure (YHL)[18]

Nord's review shows these instruments vary enormously in their complexity, how much they focus on different aspects of health, how they are validated, and the range of values produced.

Desirable features of a generic health state measure for use in cost-utility analysis

Selecting existing instruments or constructing new ones involves decisions about:

- which health concepts are relevant, and

- trade-offs between feasibility and sensitivity.

These decisions depend upon what we want to measure and for what purpose. The choice is important, since different measures will produce different QALY gain results, and hence ultimately different rankings of pharmaceutical interventions.

In selecting a generic health state measure, a number of *a-priori* features were considered necessary to meet PHARMAC's needs. These were that:

- health states be of **manageable number**, **mutually exclusive** and **collectively exhaustive**;

- the dimensions measured be **relevant** to aspects of life that health services can be expected to improve;

- the dimensions measured have **low interdependence/correlation** between each other – this is to prevent double counting and unnecessary complexity;

- measures within each dimension are **sensitive** to changes in severity over time;

- health states be calibrated by **empirically-derived** values;

- health state values be derived using **societal preferences**;

- **response methods** (i.e. how values/preferences are elicited) be conceptually robust;

- the measure gives consistent results regardless of who undertakes it or when they do so (ie have good **inter-rater and test-retest reliability**);

- the measure be simple to use (**feasible**), for instance, to map generic health states onto disease-specific states;

- response methods be **intuitive** (i.e. be easily understood by the average citizen);

- the measure have **face validity** (i.e. the results seem to be intuitively plausible); and

- the measure be **used and accepted elsewhere** to give greater confidence in its reliability/validity and aid any comparison with other healthcare systems.

Given PHARMAC's role of achieving the best health outcomes reasonable from pharmaceutical treatment for the New Zealand population, PHARMAC wishes to use societal preferences - i.e. that of New Zealand citizens, to whom the PHARMAC Board is ultimately accountable. We feel it better that generic health state scores reflect the general public's views rather than those of a specific group.

Face validity is important for acceptance by and "selling to" to those stakeholders critical to implementation, such as decision- and policy-makers, health professionals, and New Zealand society at large.

This perspective is consistent with both the consensus in health economics guidelines internationally[19] and the source of ratings obtained by QLHQ, EuroQoL, HUI-II and III, and the other major generic health state measures. Ideally, we use New Zealander's preferences for these scores.

What is available?

We are faced with two options in deriving quality of life estimates. The first is to use disease/disability-specific utility scores derived elsewhere, based on one of the above generic health states measures or similar. Currently, the only comprehensive usage of a model across a range of disease/disability states that we are aware of are those developed for the Global Burden of Disease project,[20] particularly those age-independent weights produced for the Netherlands.[21] Weights here were derived by clinical consensus of healthcare professionals/managers, using person-tradeoff and direct rating methods.

Another option is to use generic health state measures with weights obtained from the New Zealand population[22]. Devlin et al. undertook a survey using the Euroqol Group's EQ-5D questionnaire to derive generic weights specific to the New Zealand population. The survey was mailed to 3000 randomly selected New Zealanders, and was completed by 1350. Each respondent rated their health on the five EQ-5D dimensions (mobility, self care, usual activities, pain/discomfort and anxiety/depression) and assigned a global score to their profile. Valuations were sought using the visual analogue scale (VAS). Regression analysis was used to interpolate values over the 245 possible EQ-5D states.

Generic health state weights have also been derived from overseas populations for the EuroQoL, HUI-III and QLHQ instruments. These weights have been developed from surveys of large populations. However, it is likely that health state preferences of New Zealanders differ from those of people from other counties, hence it is preferable to initially use the weights derived from the New Zealand population, and compare the results with those using international health state weights (e.g. EuroQol health weights derived from the UK population).

The EuroQol

Previously, we had floated the idea of PHARMAC basing its utility analysis on the QLHQ (Quality of Life Health Questionnaire). This suggestion was strongly rejected by the parties whom we consulted with as it:

- has no international pedigree – the rest of the world doesn't use it;

- has simplicity that may come at the expense of sensitivity;

- has simplicity that may actually make it harder to use in practice;

- does not incorporate mental suffering;

- doesn't incorporate New Zealanders' utility weightings.

The majority of respondents promoted the EuroQoL as an instrument they considered an acceptable alternative. In particular, the EuroQoL's widespread use, perceived sensitivity and ability to incorporate psychological suffering were considered to be significant advantages.

In light of the extent of this advice, we recommend those supplying quality of life estimates to PHARMAC to base these on the EuroQoL- preferably using the EQ-5D weights derived from the New Zealand population.

However, in advising use of EuroQoL, we caution that EuroQoL has some important unresolved disadvantages:

- Only a small proportion of health states were empirically derived: Although EuroQoL describes utility values for all its 243 possible health states derived "from a representative survey of the UK general public", we understand the actual number of survey-derived utilities amounted to only 14 key states. The EuroQoL designers then derived synthetic values by interpolating the other 230 states from these 14 states' values.

- Less sensitivity: EuroQoL has five domains (five, viz. mobility, self-care, usual activities, pain/discomfort, anxiety/depression; six if cognition is included, as in the Netherlands Global Burden of Disease (GBD) study). However, it has only three degrees of severity. This means there is less ability to discriminate between health states and less ability to measure change over time.

- Likely interdependence between domains: Although we are not aware of any examination of the EuroQoL for auto-correlation, auto-correlation has been found in other generic health

state measures' initial domains[23]. There is, therefore, a question over whether some of the EuroQoL's domains are redundant and perhaps harmful (given the biases from any double-counting).

- Possible problems with respondent comprehension and bias (time trade-offs are complex, with potential for underestimation of non-fatal states against fatal due to respondents' risk aversion).

- Infeasiblity for any mapping, given the large number of health states (245).

The HUI-II and III measures are similarly infeasible for mapping purposes, given their enormous numbers of possible health states (as well as possible problems with respondents' miscomprehension of, and bias with, time trade offs and standard gambles).

Actual QALYs, not potential

Potential costs/QALYs are best derived from controlled clinical trials. However, such trials are thought to attract well-motivated participants who are monitored closely and, hence, may have artificially high patient continuation and compliance rates. This means it is possible that treatment may appear to be more efficacious than it would be in everyday life.

Using actual QALYs rather than those potentially gained in clinical trials is important, since continuation and adherence rates will vary according to the type of intervention and patient. For instance, preventive treatment without immediate symptom relief might be expected to have lower continuation and adherence rates than a treatment that has immediate symptom relief. Similarly lower adherence might occur with interventions with high actual or perceived adverse effects, or inconvenient therapy regimes. This compares with, say, surgical interventions, where compliance for one-off procedures is 100% (once anaesthetised). If we used cost/QALYs from clinical trials alone, interventions with better compliance would look more cost-effective than was the likely case in real life, especially when compared to say, "captive" interventions such as surgery.

There are two important factors affecting effectiveness: adherence/compliance behaviour and the existence of co-morbidities. Both dilute the potential efficacy suggested by clinical trials. This means that real-life cost/QALYs will be higher than those achieved in clinical trials because less benefit is achieved for the same spending.

Some patients in the community cannot or do not continue with their medication. Hence effectiveness and benefits are lower for each amount of drug prescribed. Although patients who discontinue their medication do not gain the benefits of treatment, pharmaceutical costs to PHARMAC may remain unchanged.

Hence, we need to calculate actual costs/QALYs, to account for incomplete patient continuation and adherence. This is proxied by adjusting potential QALY benefits derived from clinical trial data for the effects of discontinuation/non-adherence, i.e.

Actual QALYs = potential QALYs × patient continuation/adherence rate

DISCOUNTING

All future costs and health consequences will be stated in terms of their "present value". This involves adjusting costs and benefits for differences in their <u>timing</u>. "Discounting" is the computational process used to obtain present values of future costs and benefits.

A key element to discounting is selecting appropriate discount rates to reflect the HFA's time preferences for present over future outcomes.

The rationale for discounting

The arguments for discounting are twofold:

- It reflects the opportunity cost of investing in a project, where investing in project "A" prevents investing in project "B". Discounting is a way of reflecting this opportunity cost. From a Government perspective it reflects, for example, that one alternative to spending money on project A is paying off debt with a consequent lowering in servicing costs.

- People's time preferences (human psychology): we prefer to gain benefits sooner rather than later, due in a large part to uncertainty. We don't know what the future holds. For example, a life saved now is worth more than the chance of saving that life in 10 years, because in the intervening 10 years the person may have died of something else, or circumstances otherwise render analysis irrelevant.

Why is discounting important?

The timing of costs and benefits can be a significant determinant of an investment's attractiveness. For example, a DHB may face choosing between funding:

1) coronary artery bypass grafts (CABG) which have a high up-front cost with benefits accruing both immediately and over time; and

2) a new heart drug for treating patients with high cholesterol which will add varying life expectancy to large numbers of patients over the next 10-20 years (particularly after taking the drug for two years).

When comparing the costs and benefits of the alternatives, we will need to weigh the high cost but definite morbidity and mortality reductions from a CABG against the lower up front, but continuing cost, of drug treatment for less marked morbidity and mortality reductions over the next 10-20 years. The immediate cost and benefit of the CABG surgery relative to drug treatment must somehow be taken account of in the analysis; the immediate costs as a disadvantage, the immediate benefits as an advantage. Discounting is a way of taking into account time preferences that favour immediate pay-offs and opportunity costs associated with incurring expenditure sooner (rather than later).

Where does discounting fit in the analysis?

Once all costs and benefits have been modelled over the relevant time period, the costs and benefits of future years will be discounted. Both benefits and costs are discounted at the same rate. Hence, the streams of costs and benefits are discounted so that effects accruing in future years are discounted as in the following hypothetical example:

	Year 1	Year 2	Year 3	Year 4	Totals
Costs	$1,000	$1,000	$1,000	$1,000	$4,000
discounted Costs @ 10%	$1,000	$909	$826	$751	$3,486
Benefits (QALYs)	1.00	2.00	3.00	4.00	10.00
discounted benefits @ 10%	1.00	1.82	2.48	3.01	8.31
Undiscounted CB ratio	$400				
Discounted CB ratio	$419				

Some controversy

There is no universal agreement on whether discounting should be done. It can be argued that discounting's effect of shortening a decision maker's time perspective will unduly bias decision makers against projects where the benefits accrue over the long term.

Secondly, even where there is agreement over the appropriateness of discounting, there is debate over how to discount. This debate takes three forms:

■   should benefits be discounted at all?

■   should benefits be discounted at the same level as costs? and

■   at what level do you set the discount rate, 3%, 5%, 10%?

As in any case where there is controversy one must decide which option is best depending on one's perspective. Our approach is outlined in the following sections. Please note that we are still debating some aspects of discounting, and the following approach may be modified. We welcome continual feedback.

Should we discount benefits? And both costs and benefits at the same rate?

While there is general consensus that costs should be discounted (even if actual rates need debate), this is not the case with benefits. There remains considerable controversy about how to convert future health consequences to present values, i.e.:

■   whether to discount benefits at all, and

■   if deciding to discount benefits, whether to discount benefits at the same rate as for costs.

Lipscomb et al, writing on behalf of the US Panel on Cost-Effectiveness in Health and Medicine,[24] describe the mainstream practice now as to discount future health consequences and at the same rates as for costs. They describe in detail the arguments for and against this practice.

Discounting both costs and benefits at the same rate can be justified on grounds that investments in health should be treated in the same manner as all other investment decisions. Projects that deliver health are one subset of the total set of investments decisions faced by New Zealanders. Others include employment, recreation, housing, clothing, travel etc.

Most investments have their costs and benefits measured in monetary terms and have both the costs and benefits discounted at the same rate. In contrast, health investments usually have costs measured in monetary terms but not benefits. The latter can be measured in non-monetary terms such as QALYs. Our viewpoint is that there is no valid argument for discounting time preference for QALYs at a different rate than that for dollars.

We note that some people may disagree with this, and argue that health services are somehow different and as such should be treated differently from other investment decisions.

Unfortunately, no conclusive evidence of the uniqueness of health investments vis a vis other types of investments has been produced. In the absence of such evidence we believe it best to continue on the assumption that all investments' benefits, whether monetary or not, should be discounted at the same rate as the costs of that investment.

We note that similar reasoning has been adopted in the Canadian Guidelines[25] and by the US Panel[26]. The US Panel noted that:

> Discounting the value of future expenditure requires that health effects experienced in the future all be discounted at the same rate. This conclusion is based on the observation that people have opportunities to exchange money for health and vice versa, throughout their lives.

How does discounting affect rankings?

Discounting dampens the relative importance of costs and benefits occurring in future. As discount rates rise, future benefits and costs become less and less important when compared with benefits and costs occurring at present.

Discounting's dampening of future benefits (and costs) has major effects on how programmes rank against others. Increasing discount rates tend to decrease cost-effectiveness (since with most health programmes, costs tend to occur earlier rather than later, whereas benefits and cost offsets are more likely to be delayed). However, adverse effects of discounting are more pronounced for programmes where benefits (and/or cost offsets) occur later. So, as discount rates rise, such long-term investments appear far less attractive than short-term alternatives - affecting the overall rankings of all programmes.

For example, the table below shows ten different imaginary interventions. Each costs $8 million over 10 years, but all vary as to (1) the extent of benefits and/or (2) when benefits occur and/or (3) when costs occur. When we model these scenarios, we obtain a series of cost/QALY results, along with attendant rankings:

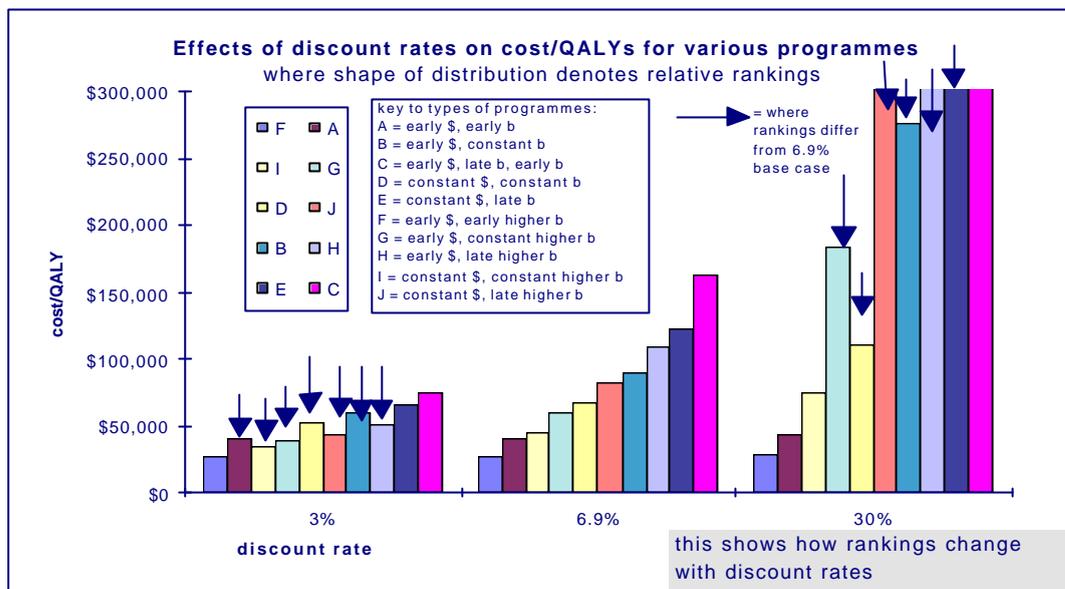Effect of discount rates on the relative ranking of programmes according to cost/QALYs

Intervention/programme (flows of costs and benefit)	Cost/QALYs at each discount rate						Ranking at each discount rate *					
	0%	3%	5%	6.9%	10%	30%	0%	3%	5%	6.9%	10%	30%
A early costs, early benefits	40,000	40,351	40,575	40,781	41,104	42,853	6	4	3	2	2	2
B early costs, constant benefits	40,000	59,440	74,344	89,555	115,723	277,029	6	8	7	7	6	6
C early costs, late benefits	40,000	75,686	113,007	162,522	283,916	4,481,041	6	10	10	10	10	10
D constant costs, constant benefits	40,000	52,225	60,277	67,552	78,217	111,338	6	7	5	5	5	4
E constant costs, late benefits	40,000	66,499	91,624	122,591	191,899	1,800,931	6	9	9	9	9	8
F early costs, early benefits (higher)	26,667	26,901	27,050	27,187	27,403	28,568	1	1	1	1	1	1
G early costs, constant benefits (higher)	26,667	39,627	49,563	59,703	77,149	184,686	1	3	4	4	4	5
H early costs, late benefits (higher)	26,667	50,457	75,338	108,348	189,277	2,987,360	1	6	8	8	8	9
I constant costs, constant benefits (higher)	26,667	34,816	40,185	45,034	52,145	74,225	1	2	2	3	3	3
J constant costs, late benefits (higher)	26,667	44,333	61,082	81,727	127,933	1,200,621	1	5	6	6	7	7

- 1 = best value for money i.e. lowest $/QALY; 10 = worst value for money i.e. highest $/QALY.

As can be seen in the table, increasing discount rates increases cost/QALYs regardless of the intervention considered. However, the effect is more extreme where benefits occur later (C,E,H,J), and most extreme where both benefits are late and costs are early (C,H).

In turn, this affects rankings. When compared to rankings derived from a 3% discount rate, 7/10 interventions change their rankings after discounting at 6.9% (A,B,D,E,G,H,J). When

compared to rankings derived from a 6.9% discount rate, 6/10 interventions change their rankings after discounting at 30% (B,D,E,G,H,J):

So the choice of discount rate can profoundly affect programmes' relative rankings. This is especially so when benefits and/or offsets occur much later than programme costs.

What rate of discounting to use?

In a perfect market with perfect information, the discount rate would equal the risk adjusted market rate of interest (cost of capital), which would also equal the rate of time preference for consumption. However, imperfect markets and imperfect information create a range of interest rates. This reflects varying expectations on rates of return, time preference and uncertainty across different sectors of the economy and different projects within a sector.

Which discount rate to use is controversial, and discount rates used in health economic analyses vary throughout the OECD. The US Panel recently recommended costs and benefits be equally discounted at 3% as a riskless discount rate. This is important, given the increasing credibility and use internationally of the US recommendations in establishing practice for health economic analysis. The 3% rate is consistent with what the US Panel claims is a "shadow price of capital approach to evaluating public investments" in the US, and reflects the real rates of return generated by US economic performance in the last decade. However, country of risk is important here. New Zealand's economic performance differs from the US, and discount rates (as proxied by long-term government stock yields or whatever) will be higher.

Adjustment for general inflation

Money devalues over time in terms of the amount of goods and services it can buy; this is called inflation. A dollar tomorrow will have less purchasing power than a dollar today, usually due to over-supply of money. This is a separate argument from that used in discounting where, viewed from today's perspective, a dollar in hand now is worth more than one tomorrow as we have the added option of spending it if we have it now.

We must make the same separation of arguments when considering QALYs. The life experiences of a person enjoying a full quality health year tomorrow are assumed to be the same as the health consequences of a person doing so today - in this case the value of a QALY does not devalue over time. However, in discounting QALYs we say that, from today's

point of view, a QALY gained now from a health intervention is more valuable than one gained tomorrow as the person who gains it may be sick or die from other causes.

Consequently, QALYs do not over time devalue through inflation in the same manner that money does. We need to recognise this in conducting CUA by adjusting the monetary costs to exclude the effects of inflation.

Consequently, we need to exclude general inflation from the discount rate. Thus the discount rate should equal the New Zealand Government's real cost of capital i.e. nominal rate as % less the general inflation rate.

Other possibilities?

It can be argued that one function of Government is to take a longer-term outlook for society in cases where the average of individuals' time preferences may be harmful in the short term. This "paternalistic" discount rate is, however, open to some criticism on the basis that government is not capable of choosing where and how to take such a long-term view. Adherents of this criticism point to failures of Government long term thinking (such as the 1980s Think Big projects).

Alternatively there is the bottom up approach which advocates that Government spending should finance projects with the highest rate of return first and then in the order of the rankings obtained from estimates of rate of return. Under this approach, the opportunity cost of funds is the rate of return of the last project funded by government. Using this approach, investment decisions would be made on the basis of Internal Rate of Return (IRR) calculations. A major problem with this approach is that, since government spending is, in general, relatively poorly scrutinised, this could produce an inconsistent, artificially low or even a negative rate.

Rate used by PHARMAC

PHARMAC directors' current position is that the discount rate should equate to the risk inclusive long-term cost of capital.

Treasury advised government departments that the capital charge for 2003/04 was to remain unchanged at 8.5% a year. A revision for 2004/05 has not yet been published. Given no change in the rate at this stage, PHARMAC staff anticipate making no change to the discount rate of 10% a year it uses in its new technology assessments.

Over what time horizon should we discount?

All costs and benefits over an intervention's treatment cycle should be accounted for in analysis. This allows fair comparison of interventions that either have a high up front cost or whose benefits accrue over time.

For both costs and benefits, the time horizon needed equals the maximum life expectancy expected from any of the interventions or alternatives under consideration. For instance, a 15-year time horizon is necessary when comparing statins vs alternative drugs for 65-69 year-old cardiac patients, since their life expectancy is on average 15½ years. Alternatively, a 10-year time horizon might be appropriate for certain hip joint prostheses - limited not necessarily by patients' life expectancy but by the "life expectancy" of the prosthesis itself.

However, note that discounting does reduce the effective analytical time horizon. For example discounting at 10% per annum means that costs and benefits incurred after 10 years have a relatively low weight compared with current effects.

Sensitivity analyses

Given the lack of a universally-accepted means of deriving discount rates, let alone one rate for universal use internationally, and given the volatility of rankings to discount rates, all analyses should include scenarios using discount rates of 0%, base case and high case scenarios.

DEALING WITH UNCERTAINTY: SENSITIVITY ANALYSIS

When we don't have perfect information on all aspects of a decision, we are forced to rely on assumptions. The importance of these assumptions to the final result will vary depending on the study. Sensitivity analysis allows us to assess to what extent the results depend on the assumptions made.

All assumptions should be subject to sensitivity analysis. In practice however, it is best to confine our efforts to those assumptions that we are:

■ less sure of; or

■ are likely to have a significant result on the CUA if changed.

For example, if a 10% discount rate is chosen for discounting, the results should also be tested under a discount rate of 5% and perhaps 15%. If the results are significantly different from those with the 10% discount rate, then the importance of that assumption is recognised.

A general rule of thumb is that the less sensitive a CUA result is to sensitivity analysis the more confidence can be placed in its results.

Sensitivity analysis is based on the steps below:

■ <u>Univariate</u> (one-way) sensitivity analyses for each estimate or assumption. Each assumption etc. is changed one at a time, to see how this affects the CUA's overall results. This shows which parameters substantially affect the CUA.

■ <u>Multivariate</u> sensitivity analyses for all key parameters. Key assumptions are changed at the same time, so accumulating the effects of uncertainty across all key parameters and showing how uncertainty overall affects results. Values are grouped to derive:

   ■ a "<u>best case</u>" estimate, i.e. where costs are minimised and benefits maximised (greatest absolute risk reductions, highest life expectancies, greatest disease QALY disutilities, least intervention side effect QALY disutilities)

   ■ a "<u>worst case</u>" estimate, i.e. where costs are maximised and benefits minimised (least absolute risk reductions, lowest life expectancies, least disease QALY disutilities, greatest intervention side effect QALY disutilities)

Variables for analysis will vary according to the study data and model used. However, key variables usually include:

■ net cost (intervention costs, program costs, cost offsets);

■ baseline health status and natural history of untreated disease (absolute risks of death, major events, long-term sequelae, life expectancy);

■ magnitude of effect (e.g. relative risk reduction), including 95% confidence limits;

■ quality of life scores for generic health states (e.g. adjusted QLHQs, EuroQols, Netherland GBD person trade offs, and Time Trade Offs); and

■ discount rates.

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