1. INTRODUCTION

To aid priority setting in prevention, the Assessing Cost-Effectiveness in Prevention Project (ACE-Prevention) applies standardised evaluation methods to assess the cost-effectiveness of 100 to 150 preventive interventions, taking a health sector perspective. This information is intended to help decision-makers move resources from less efficient current practices to more efficient preventive action resulting in greater health gain for the same outlay.

Cost-effectiveness analysis is about comparisons, about differences in costs and outcomes between a situation where an intervention is present, and one where it is not. The focus is usually on options for change to current practice. In the health sector, measurement of outcomes concentrates on health gains such as the Disability Adjusted Life Year (DALY). The DALY is a summary measure of population health which captures the impact of both premature mortality and morbidity as years of healthy life lost adjusted for illness severity.

The gross costs of an intervention and its comparator concentrate on the costs to the health care system and to patients/families involved in the delivery of the intervention. From this is deducted any cost offsets (i.e. the difference in future health care costs that will arise as a result of the intervention or its comparator), to derive the net cost of the intervention and comparator scenarios. The differences in costs and outcomes are usually combined into a summary performance measure; the incremental cost-effectiveness ratio (ICER).

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\text{ICER} = \frac{\text{(Net cost of intervention} - \text{Net cost of comparator)}}{\text{(Health gain of intervention} - \text{Health gain of comparator)}}
\]

When both differences in costs and outcomes are positive the ICER can be interpreted as the price of an additional DALY bought with the intervention under evaluation. When the price of the additional DALY is less than a specified threshold – say $50,000 – the option for change is considered to be ‘cost-effective’. The level at which the cost-effectiveness threshold is set is a matter for decision-makers and reflects, among other things, the size of the available budget, the number of potential options for change and precedent.

The ACE-Prevention ICER results are presented in several ways:

1. ICERs with uncertainty ranges;
2. ICERs on the cost-effectiveness plane; and
3. intervention pathways.

The first two are attempts to capture the uncertainty that surrounds the point estimate of the ICER; the intervention pathway is a way to show the optimal sequence of multiple potential interventions for the same health problem. We will first discuss uncertainty and next the intervention pathway.
2. **UNCERTAINTY**

Uncertainty in health economic evaluation originates from several sources. The first of these is the uncertainty in the model parameters that is due to sampling. Usually the most important here is the 'effect size'. The effect size, based on a clinical trial or a meta-analysis, has a confidence interval that expresses the uncertainty caused by the trial population being a sample of the total population. Other important parameters involving uncertainty include the relative risk of disease given exposure to a risk factor; expected participation in programs; expected adherence to treatment; side-effects; anticipated cost offsets; etc.

In ACE-Prevention we use parametric bootstrapping to quantify this uncertainty. In this procedure we replace uncertain model parameters with suitable distributions, and recalculate the model many (say 2000) times, each time drawing a random value from each of the distributions. This results in a large number of ICER results. The distribution of ICER results reflects the uncertainty in the input parameters.

**Uncertainty range**

ACE-Prevention reports 95% uncertainty ranges around the ICER, which means that of the large number of ICERs calculated in the parametric bootstrap, 95% is within this range. The interpretation is that, given the uncertainty in the input parameters, there is a 95% chance that the ICER will be inside the reported range.

**Cost-effectiveness plane**

Figure 1 the cost-effectiveness plane. Incremental costs are on the vertical axis, incremental benefits on the horizontal axis.

The cost-effectiveness plane is a graphical way of presenting cost-effectiveness results, with the difference in costs on the vertical axis and the difference in health benefits on the horizontal axis (Figure 1). Since incremental costs and health benefits can both be either positive or negative, there are 4 possible combinations, which are reflected in the 4 quadrants of the cost-effectiveness plane.

Decision-making is easy when the ICER falls in quadrant 2 (called “dominant” - more benefits, lower costs: accept) or quadrant 4 (called “dominated” - less benefits, higher costs: reject). Decision-making is harder in quadrant 3 (less benefits, lower costs). In economic terms, it is 'efficient' to accept an option for change with this result when the costs saved can be used elsewhere to generate more benefits than are lost by discontinuing current practice. However, replacing current practice with a less effective (but cheaper) intervention often has important ethical implications and is not an easy decision to make.
Most of the action is in quadrant 1, where interventions yield more benefits, but involve higher costs (often this is the only quadrant that is shown). The economic merit of an intervention depends, among other things, on whether the ICER (i.e. the cost per DALY) is lower than the threshold cost the policy-maker is prepared to pay for an increase in health outcomes.

Figure 2 shows the results of an evaluation with all ICERs in quadrant 1 of the cost-effectiveness plane. Each ICER is represented by a dot, all 2000 producing a cloud of pair-wise combinations of incremental net costs and benefits. The figure also shows a $50,000 per DALY threshold line (representing an estimate of how much the community is prepared to pay for an extra DALY). When an ICER dot is below (to the right) of this threshold line, the ICER is less than the threshold, and vice versa. In Figure 2 all ICERs are below the threshold and we conclude that this is a 'cost-effective' intervention.

Figure 2: Quadrant 1 of the cost-effectiveness plane with 2000 ICERs and a $50,000 per DALY threshold line

While Figure 2 is unequivocal in that all ICERs are below (or to the right of) the threshold, this is not always the case. The threshold line may cross through the cloud of ICERs, or you may have a different threshold than the one in Figure 2. How many dots are below the threshold is reported in a table of results as the probability of the intervention being under $50,000 per DALY.

Other uncertainty

For some parameters, such as patient travel costs, as a rule no formally estimated uncertainty is available. In such cases we include point estimates with reasonable, but arbitrary upper and lower bounds in the uncertainty analysis (e.g. +/- 10%).

Uncertainty due to other causes is not dealt with in the probabilistic uncertainty analysis described above. Uncertainties such as "what happens if we broaden the study perspective beyond the health sector"; "what is the appropriate discount rate"; or "should time and travel costs be included"? We try to capture the effect of these uncertainties by presenting two or more scenarios in a sensitivity analysis; for example, by presenting results for various discount rates or presenting results with non health sector impacts included/excluded.

3. INTERVENTION PATHWAYS

For most health problems there are multiple interventions each with a different effectiveness and cost. In this decision context, there is a strong case for arguing that maximal efficiency is obtained by implementing the intervention with the lowest ICER first, then the intervention with the next lowest ICER, etc. Plotting the successive ICERs on the cost-effectiveness plane can be used to generate an intervention pathway graph.
Figure 3 Intervention pathway of the cost effectiveness of reducing blood pressure and cholesterol in Australia.

Figure 3 shows an intervention pathway for interventions to lower blood pressure and cholesterol, with the dots representing specific interventions and the slope of the connecting lines representing the ICER. Since we start with the intervention with the lowest ICER, the slope becomes increasingly steep.

The interpretation of this graph is that of an efficiency frontier – that is, we can do no better than this (given current technology and prices). However, we certainly can do worse. In Figure 3 current practice is also plotted. From the graph we can see that we would get about 125% more health gain at net current expenditure if we had implemented the optimal combination of interventions.

For more information, please visit website www.sph.uq.edu.au/bodce-ace-prevention

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C. Key assumptions underlying the economic analysis
D. Interpretation of ACE-Prevention cost-effectiveness results
E. Indigenous Health Service Delivery

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2. Combined effects

Indigenous population results
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2. Diabetes prevention
3. Screening and early treatment of chronic kidney disease

General population results
1. Adult depression
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13. Psychosis
14. Renal replacement therapy, Screening and early treatment of chronic kidney disease
15. Salt
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