ECONOMIC EVALUATION OF INTERVENTIONS FOR PROBLEM DRINKING AND ALCOHOL DEPENDENCE: COST PER QALY ESTIMATES

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Abstract — Aims: To compare the performance of competing and complementary interventions for prevention or treatment of problem drinking and alcohol dependence. To provide an example of how health maximising decision-makers might use performance measures such as cost per quality adjusted life year (QALY) league tables to formulate an optimal package of interventions for problem drinking and alcohol dependence. Methods: A time-dependent state-transition model was used to estimate QALYs gained per person for each intervention as compared to usual care in the relevant target population. Results: Cost per QALY estimates for each of the interventions fall below any putative funding threshold for developed economies. Interventions for problem drinkers appear to offer better value than interventions targeted at those with a history of severe physical dependence. Conclusions: Formularies such as Australia’s Medicare should include a comprehensive package of interventions for problem drinking and alcohol dependence.

INTRODUCTION

Formularies such as Australia’s Medical Benefits Scheme (MBS) and Pharmaceutical Benefits Schedule (PBS) are typically compiled by a combination of history and revision at the margin. Due to a separation of budgets and because different types of intervention are required to clear different hurdles, public subsidy may be easier to obtain for care than for prevention, for drug-therapy than for counselling, or for inpatient care than for treatment in a community setting. Given the potential for distortions when selecting interventions into (or out of) a formulary, identifying the health maximising package of interventions provides a useful point of reference when allocating limited resources.

To reduce the burden of harm arising from problem drinking and alcohol dependence, the optimal package of interventions should maximise the objective function contingent upon any constraints with respect to funding and distribution. Consider the simple case of health maximisation over independent clusters of mutually exclusive interventions. Whereas the mutually exclusive interventions within each cluster treat the same problem in the same target population, different clusters treat different problems or different target populations (or both). Within each cluster, interventions with a lower effectiveness per unit cost than a less expensive alternative should be excluded (by extended dominance) before selecting the most effective affordable intervention. Independent clusters then compete for a limited budget and health benefits are maximised by selecting clusters where the cost per quality adjusted life year (QALY) gained of the most effective affordable intervention is no greater than the estimated shadow price of a QALY (Johannesson and Weinstein, 1993).

For the prevention and treatment of problem drinking and alcohol dependence, inter-dependency between different target populations complicates the task of prioritising over competing interventions. Early-intervention for problem drinkers, for example, may reduce the number of patients progressing to alcohol dependence such that the line between target populations becomes blurred. The extent of any substitution in favour of early-intervention would turn firstly, on the extent of any inter-dependency and secondly, on distributional and budgetary constraints. So, while the task of prioritising over a diverse set of competing interventions putatively requires no more than an appropriate set of performance indices and the application of simple decision-rules, difficulties in the interpretation of data and the application of decision-rules may arise due to the existence of distributional constraints and errors in defining independent clusters.

The aim of the current study is to compare the performance of competing and complementary interventions for the prevention or treatment of problem drinking and alcohol dependence. Issues surrounding interpretation of performance indices and application of decision-rules are then discussed by considering how health maximising decision-makers would prioritise over competing and complementary interventions.

INTERVENTIONS

Interventions were selected to provide an example of the choices facing policy-makers when allocating funding for the treatment and prevention of problem drinking and alcohol dependence. The evaluated interventions can be divided into three clusters of mutually exclusive programs: (i) brief interventions for problem drinking (Saunders et al., 1991; Babor and Grant, 1992; Wilk et al., 1997; Moyer et al., 2002), (ii) psychotherapy for mild to moderate dependence (Heather et al., 2000; Sellman et al., 2001) and (iii) drug-therapy adjuvant to counselling for detoxified patients with a history of severe physical dependence (Streten and Whelan, 2001). This section describes some of the key features of the evaluated interventions. Further details with respect to the intervention, comparator, and target populations are given in Table 1.

Despite differences in programme logic, intensity, and target population, all but one of the interventions emphasised moderation of alcohol consumption rather than abstinence. Babor and Grant (1992), for example, in the WHO project in which Australian centres took part, evaluated brief interventions of varying intensities in a sample of heavy drinkers

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Psychotherapy for mild to moderate dependence

Brief interventions for problem drinking
- Various brief interventions (BIs) characterised as ‘motivational with a self-help orientation’
- Intensity varied from 1–4 sessions
- ≤1 h total counselling time but some BIs included just 10 min
- Three BIs with different intensity: simple (5 min), brief (20 min), or extended (120–150 min over four sessions)

Psychotherapy for mild to moderate dependence
- Pre-trial assessment including severity of alcohol dependence and alcohol problem questionnaires
- Moderation-oriented cue exposure (MOCE): a form of extinction procedure where patients asked to resist cravings after priming doses
- Emphasis on controlled drinking
- Average length of MOCE: 88 min over 7.67 sessions
- Motivational enhancement therapy (MET). MET is a brief, psychotherapeutic intervention with the aim of first building motivation to change and then strengthening commitment to change
- Four sessions over 6 weeks
- Non-directive reflective listening (NDRL). NDRL subjects talked about anything they wanted, with no attempt to steer towards alcohol problem
- Four sessions over 6 weeks

Drug-therapy for detoxified patients with a history of severe physical dependence
- Naltrexone plus counselling
- Counselling ranged from weekly group therapy to weekly one-to-one CBT to intensive inpatient treatment
- Naltrexone is an opioid receptor antagonist that reduces pleasurable effects of alcohol thereby masking the cue for further consumption
- Dose of 50 mg/day over 12 weeks

Table 1. Details of interventions, comparators, and target populations

<table>
<thead>
<tr>
<th>Intervention (Rx)</th>
<th>Comparator (C)</th>
<th>Target population</th>
<th>Study</th>
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<tbody>
<tr>
<td>Brief interventions for problem drinking</td>
<td>No alcohol-related Rx</td>
<td>Heavy drinkers</td>
<td>Wilk et al., 1997</td>
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<td></td>
<td>Initial 20 min interview re general health, nutrition, stress, sleep and smoking</td>
<td>Hazardous alcohol consumption</td>
<td>Saunders et al., 1991</td>
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<td></td>
<td>No alcohol-related Rx.</td>
<td>Not physically dependent</td>
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<td></td>
<td></td>
<td>Aged 17–70 years</td>
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<tr>
<td>Psychotherapy for mild to moderate dependence</td>
<td>Pre-trial assess as per Rx</td>
<td>Patients seeking help for alcohol problems with a preference for moderation rather than abstinence</td>
<td>Heather et al., 2000</td>
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<td></td>
<td>Behavioural self-control training (BSCT)</td>
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<tr>
<td></td>
<td>Emphasis on controlled drinking</td>
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<td></td>
<td>Average length of BSCT: 63.49 min over 6.56 sessions</td>
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<tr>
<td></td>
<td>No further counselling after initial assessment and feedback/education</td>
<td>Mild to moderately dependent drinkers</td>
<td>Sellman et al., 2001</td>
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<tr>
<td></td>
<td></td>
<td>Aged 15–59 years</td>
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<tr>
<td>Drug-therapy for detoxified patients with a history of severe physical dependence</td>
<td>Placebo plus counselling</td>
<td>Recently detoxed</td>
<td>Streton and Whelan, 2001</td>
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<td></td>
<td>Counselling as per Rx</td>
<td>No significant psychological disorder</td>
<td></td>
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<td></td>
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<td>No coexisting drug-use</td>
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</table>

aged 17–70 years who were not physically dependent. At the lowest level of intensity, intervention amounted to simple advice lasting 5 min. Higher intensity interventions entailed advice plus brief counselling and problem solving strategies totalling 20 min or advice plus extended counselling followed by two ‘booster’ sessions including feedback of lab results totalling 120–150 min.

Sellman et al. (2001) evaluated motivational enhancement therapy (MET) and non-directive reflective listening (NDRL) in a sample of physically dependent drinkers aged 15–59 years. MET is a brief, psychotherapeutic intervention based on five key principles of motivational interviewing: (i) expressing empathy, (ii) deploying discrepancy, (iii) avoiding argument, (iv) rolling with resistance to change, (v) supporting self-efficacy. The aim is to first build motivation to change and then strengthen commitment to change. The NDRL intervention allowed subjects to talk about anything they wanted, with no attempt to steer discussion towards drinking behaviour. Both interventions were delivered in an outpatient setting by trained therapists. Despite targeting patients at the more severe end of the spectrum and (perhaps necessarily) employing a more intensive intervention, the NDRL intervention retained an emphasis on moderation (in this case, drinking within New Zealand’s National Guidelines).

The brief interventions included in the Wilk et al. (1997) meta-analysis were delivered in a variety of settings including outpatient clinics, hospitals and community centres. Once again, the intensity of the interventions varied widely (between 10 and 60 min counselling time and between one and five follow-up sessions) but all were defined as being ‘motivational with a self-help orientation’ and as having the objective of moderation rather than abstinence. Likewise, the behavioural interventions evaluated by Heather et al. (2000) emphasised controlled drinking and excluded patients with a preference for abstinence.
Only one of the evaluated interventions targeted abstinence in preference to moderation. Streton and Whelan (2001) reported a meta-analysis of seven trials comparing naltrexone plus counselling against placebo plus counselling in detoxified patients with a history of severe alcohol dependence. Abstinence was the key outcome in five of the seven trials that were included in the Streton and Whelan (2001) meta-analysis suggesting that moderation is either less than ideal or less than realistic in patients with a history of severe physical dependence.

For a number of studies, the control group received an active intervention or follow-up that may have increased the likelihood of moderation or cessation of alcohol consumption. For example, intervention and control arms in the Streton and Whelan (2001) trials received detoxification and counselling as the agreed minimum standard of care for severely dependent patients. Similarly, controls in the Sellman et al. (2001) and Heather et al. (2000) trials received alcohol-related treatment that could be considered the minimum acceptable care for mild to moderately dependent drinkers. Specifically, controls in the Sellman et al. (2001) trial attended a feedback/education session that reviewed personal drinking history over the 6 months to baseline. The significant other of each control-participant was also encouraged to attend the feedback/education session. In addition, all participants in the Sellman et al. (2001) trial were given pamphlets and information booklets on responsible drinking and encouraged to drink within national guidelines. Likewise, Heather et al. (2000) compared moderation-oriented cue exposure (MOCE) against behavioural self-control training (BSCT)—a commonly used active intervention for dependence. In each case, the control group received elements of active intervention that approximate to usual care for the relevant target population.

Interventions evaluated in the Wilk et al. (1997) meta-analysis and the Saunders et al. (1991) trial targeted heavy drinkers at a lower level of severity than the mildly to severely dependent drinkers selected into the Sellman et al. (2001), Streton and Whelan (2001) and Heather et al. (2000) studies. In line with this lower level of severity, controls in the Wilk et al. (1997) and Saunders et al. (1991) trials received no alcohol-related treatment consistent with usual care in the target population. Table 1 describes the interventions, comparators, and target populations for which we derive cost per QALY estimates.

METHODS

Incremental costs and incremental benefits are estimated from a societal perspective, but the range of costs and consequences included in the analysis is limited due to various practical considerations in estimation. Specifically, the base-case analysis excludes possible downstream cost-savings arising, for example, from a future reduction or delay in treatment costs for liver cirrhosis; largely due to the high-level of uncertainty associated with these estimates. Productivity gains and private costs to access services, such as waiting time and transport costs were also excluded from the base-case analysis. A detailed description of the cost-analysis—including identification, measurement, and valuation of individual cost components for each intervention—is available from the authors upon request. Incremental programme costs have been estimated in 2003 Australian dollars (AUD) based on a description of resource-use in intervention and control groups obtained from the study reports.

Evidence as to the magnitude and direction of behaviour change in the presence of the intervention is drawn directly from the study reports. Key health outcomes were typically the proportion of patients drinking either side of a specified threshold (e.g. ‘safe limits’, NZ guidelines, ‘in moderation’) at 6- or 12-month follow-up. Likewise, evidence as to the persistence (or otherwise) of any behaviour change after the intervention has been discontinued is drawn from the study reports where possible. [Results from a 10-year follow-up were reported for the Saunders et al. (1991) trial but the 10-year data is difficult to interpret due to attrition and the established age-gradient in alcohol consumption. Evidence from Streton and Whelan (2001) suggests that a degree of pessimism would be advisable with regards to the persistence of any treatment effect. ‘At the end of one 12-week trial, the study medication was discontinued, but outcomes were reevaluated after 6 months. Results indicated that the benefit of naltrexone appears to be lost within 6 months of discontinuing pharmacotherapy’ (p. 544). In another meta-analysis of brief interventions, Moyer et al. (2002) noted that effect sizes are largest at the earliest follow-up points suggesting decay in intervention effects over time. In the base-case, relapse rates are derived from comparison between treatment effect at early and late follow-up.

The modelled cost-utility analysis for the evaluated interventions is based on a common structure, adapted to reflect the characteristics of the target population for each intervention. The following assumptions are common across all evaluated interventions:

- Time-dependent state-transition model.
- Tunnel sequences used to delay the health effects of moving from one state to another.
- Cycle length = 6 months (except naltrexone model where cycle length = 3 months).
- Modelled out to full life-expectancy.
- Health-related quality of life (HRQoL) gain directly attributable to behaviour change varies depending on severity of alcohol problems as per disability-weights from Stouthard et al. (1997) such that returning problem- and dependent-drinkers to a ‘safe’ consumption pattern is assumed to imply annual QALY-gains of 0.110 and 0.330, respectively.
- Mortality differential based on Rehm et al. (2001).
- Exclude downstream cost-offsets in the base-case analysis.
- Annual discount rate of 5% applied to both costs and health gains.

Building on this common structure, a number of intervention-specific assumptions were made to reflect differences in the magnitude and persistence of treatment effect for each intervention and to specify important characteristics of the relevant target population (e.g. with respect to age and severity of alcohol misuse). For example, a time-dependent state-transition model with seven non-absorbing states and one absorbing state (dead) was used to estimate QALYs gained per person for the brief interventions evaluated by Wilk et al.
The seven non-absorbing states comprised a tunnel sequence of three problem drinking states (problem1, problem2, and problem3), a tunnel sequence of three moderate drinking states (moderate1, moderate2, and moderate3) and a single ‘dependence’ state to capture the differential rate at which problem drinkers might progress to dependence in the absence of intervention or where brief intervention is ineffective. There is no ‘abstinent’ state because all subjects in the pooled sample from the Wilk et al. (1997) meta-analysis were problem drinkers on entry to the trials and because the only outcome measure is a moderation of consumption rather than abstinence. Because brief interventions are ineffective in treating physical dependence on alcohol, the model structure does not permit recovery from ‘dependence’ to either ‘problem’ or ‘moderate’. Due to gender differences in pooled estimates of treatment effect and the availability of supporting data by age/sex band, the model was run for men and women separately.

In contrast, the model used to estimate QALYs gained per person for the naltrexone plus counselling intervention included just six non-absorbing and one absorbing state (dead). The six non-absorbing states comprised a tunnel sequence of three dependence states (dependence1, dependence2, and dependence3) and a tunnel sequence of three recovered states (recovered1, recovered2, and recovered3). There is no ‘abstinent’ state because relapse was defined as a return to consumption of five or more drinks in a day for males and four or more drinks in a day for females rather than a lapse in abstinence. Neither ‘moderate’ nor ‘problem’ states appear in the model because all subjects in the pooled sample from the Streeton and Whelan (2001) meta-analysis were dependent but recently detoxified on entry to the trials. All persons in the model population therefore commence in the ‘recovered1’ state. The risk of death is elevated for persons characterised as ‘recovered’ (but lower than for ‘dependence’) and a return to either an ‘abstinent’, ‘moderate’, or ‘problem’ state is not permitted because it is difficult to completely undo the damage done during dependence (Rehm et al., 2001).

Note that the two models described above can be viewed as sub-trees of a larger state-transition model describing disease-pathways and treatment options for problem drinking and alcohol dependence. Applying the relevant sub-tree to each target population is equivalent to applying the larger model across all target populations because transitions beyond each sub-tree would only be permitted when consistent with the characteristics of the target population and the intervention. Table 2 describes the model structure and key assumptions used to derive cost per QALY estimates for the evaluated interventions.

In order to identify key drivers and to evaluate the robustness of estimates of cost per QALY gained, univariate sensitivity analyses were conducted by varying parameters such as age on entry to the model (from 20 to 70 years), HRQoL gain (from base-case to zero such that the lower bound estimate captures mortality effects only), annual discount rate (3, 5, and 7%), initial rate of relapse (from base-case to 0.40), relative risk of death (95% CLs from Rehm et al., 2001), treatment effect (95% CLs from the study reports), and incremental cost (from 50 to 150% base-case). Upper and lower bound estimates of treatment effect were therefore intervention-specific. Similarly, adjustments to the HRQoL gain accrued in moderate or recovered states differed in line with the characteristics of the target population for each intervention. A detailed description of the sensitivity analysis is available on request from the authors.

Threshold analysis was used to estimate the minimum downstream cost-offset (health care costs avoided in future periods due to a second-order reduction in disease-incidence) in the moderate or recovered state that would be required for each intervention to dominate (cheaper and more effective) its usual care comparator. When interpreting the threshold analysis, it should be remembered that downstream cost-offsets are likely to be age/sex dependent and accrue in an episodic (rather than constant) manner. In an attempt to incorporate some of this complexity, no downstream cost-offsets accrue during the initial two cycles in the moderate or recovered state but otherwise the dollar-value of downstream cost-offsets remains invariant with respect to duration and age.

**RESULTS**

Based on the modelled cost-utility analysis, the brief interventions evaluated by Wilk et al. (1997) are estimated to deliver 0.091 QALYs gained per treated male and 0.125 QALYs gained per treated female. The average incremental cost of the brief interventions as compared to no alcohol-related treatment was estimated at 60.98 AUD per treated person. The cost per QALY gained is therefore estimated at 671 AUD in men and 490 AUD in women.

At the lowest level of intensity, brief intervention of simple advice alone is estimated to deliver up to 0.225 QALYs gained per treated person at an incremental cost of 14.91 AUD per treated person as compared to no alcohol-related treatment. More intensive intervention produced additional QALY gains, with the potential to deliver up to 0.406 QALYs gained per treated person at an incremental cost of 90.03 AUD per treated person. The cost per QALY gained is therefore estimated at well under 1000 AUD for initiation or escalation of brief interventions.

Heather et al. (2000) reported that treatment response for MOCE was no better than for BSCT when responders were defined as either ‘non-problem drinkers’ or ‘abstinent’ at 6-month follow-up. MOCE is also considerably more expensive than BSCT such that the BSCT would dominate the MOCE (cheaper but no less effective). That said, a differential effect with respect to partial responders is evident when partial responders are defined as ‘much improved’, ‘non-problem drinkers’ or ‘abstinent’ at 6-month follow-up. MOCE is then estimated to deliver 0.116 QALYs gained per completer at an incremental cost of 249 AUD per completer as compared to BSCT. Based on these figures, the cost per QALY gained is estimated at 2145 AUD in a predominantly male population with moderate dependence.

In a predominantly male population with mild to moderate dependence, NDRL was inferior to the usual care comparator based on the proportion remaining within national guidelines at 6-month follow-up (Sellman et al., 2001). NDRL is also more costly than usual care such that usual care dominates the NDRL intervention (cheaper and more effective). MET is estimated to deliver 0.116 QALYs gained per completer at an incremental cost of 389 AUD per completer as compared
to usual care. The cost per QALY gained for MET is therefore estimated at 3366 AUD as compared to usual care of no further counselling after initial assessment and feedback/education.

Finally, naltrexone plus counselling is estimated to deliver 0.0528 QALYs gained per completer at an incremental cost per completer of 685 AUD as compared to placebo plus counselling. The cost per QALY gained for the naltrexone plus counselling vs placebo plus counselling comparison is estimated at 12 966 AUD as compared to usual care. The cost per QALY gained for MET is there-

Table 2 summarises results from base-case, sensitivity, and threshold analyses.

Decision-rules for the constrained maximisation of health benefits can be applied to base-case estimates of cost per QALY gained. Recall that the evaluated interventions can be divided into three clusters of mutually exclusive programs: (i) brief interventions for problem drinking (Babor and Grant, 1992; Saunders et al., 1991; Wilk et al., 1997; Moyer et al., 2002), (ii) psychotherapy for mild to moderate dependence (Heather et al., 2000; Sellman et al., 2001) and (iii) drug-therapy adjuvant to counselling for detoxified patients with a history of severe physical dependence (Streeton and Whelan, 2001). For problem drinking, none of the brief interventions can be excluded by extended dominance so the most intensive of the brief interventions (i.e. the most effective affordable intervention) would be selected to treat problem drinkers.

For mild to moderate dependence, the NDRL intervention is excluded and we are left with two interventions: MOCE and MET, both more effective and more costly than their comparator in the base-case analysis. However, the application of decision-rules is complicated because the performance of MOCE and MET is stated relative to two different comparators. Whereas controls in the Sellman et al. (2001) trial received feedback and education, controls in the Heather et al. (2000) trial received BSCT. Indirect comparison of MOCE and MET would require further information as to the relative performance of feedback/education and BSCT.

For detoxified patients with a history of severe physical dependence, naltrexone plus counselling is more effective and more costly than placebo plus counselling. Prioritising across the three independent clusters entails a comparison between cost per QALY estimates and the shadow price of a QALY. While the shadow price of a QALY will vary according to the characteristics of a QALY, the size of the budget constraint and societal objectives, the global budget for health care in Australia would imply a shadow price per QALY of 118 (47–1104). For MET, the budget constraint would therefore support the provision of a comprehensive package of interventions comprising intensive brief intervention for problem drinking, MOCE, or MET for mild to moderate dependence and naltrexone plus counselling for detoxified patients with a history of severe alcohol dependence.

Results from the sensitivity analysis suggest that the evidence is equivocal with respect to the relative performance of

<table>
<thead>
<tr>
<th>Intervention (Rx) vs Comparator</th>
<th>Model structure and assumptions</th>
<th>Study</th>
<th>S/QALY</th>
<th>S/QALY range from sensitivity</th>
<th>$/year for Rx to dominate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brief interventions (BIs) for problem drinking</td>
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<tr>
<td>BIs vs Nil</td>
<td>● Health states: problem1, problem2, problem3, moderate1, moderate2, moderate3, dependence, and dead</td>
<td>Wilk et al., 1997</td>
<td>&lt;671</td>
<td>(245–10 549)</td>
<td>–208</td>
</tr>
<tr>
<td>Simple vs Nil</td>
<td>● All commence in alcoprob3 at age = 40 years</td>
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<tr>
<td>Brief vs Nil</td>
<td>● Separate model for men and women</td>
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<tr>
<td></td>
<td>● Health states: problem1, problem2, problem3, moderate1, moderate2, moderate3, dependence, and dead</td>
<td>Saunders et al., 1991</td>
<td>&lt;82</td>
<td>(30–760)</td>
<td>–28</td>
</tr>
<tr>
<td>Extended vs Nil</td>
<td>● All commence in alcoprob3 at age = 40 years</td>
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<td>Psychotherapy for mild to moderate dependence</td>
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<td>MOCE vs BSCT</td>
<td>● Health states: dependence1, dependence2, dependence3, recovered1, recovered2, recovered3, and dead</td>
<td>Heather et al., 2000</td>
<td>2145</td>
<td>(599–∞)</td>
<td>–602</td>
</tr>
<tr>
<td>MET vs NFC</td>
<td>● All commence in dependence3 at age = 41 years</td>
<td>Sellman et al., 2001</td>
<td>3366</td>
<td>(679–∞)</td>
<td>–1404</td>
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<tr>
<td>NDRL vs NFC</td>
<td>● Based on ‘partial-responders’</td>
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<td>Drug-therapy for detoxified patients with a history of severe physical dependence</td>
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<tr>
<td>Naltrexone+ vs Placebo+</td>
<td>● Health states: dependence1, dependence2, dependence3, recovered1, recovered2, recovered3, and dead</td>
<td>Streeton and Whelan, 2001</td>
<td>12 966</td>
<td>(3,725–∞)</td>
<td>–3008</td>
</tr>
</tbody>
</table>

QALY, discounted at 5% per annum; $, 2003 Australian dollars; QALY, quality-adjusted life year; MOCE, moderation-oriented cue exposure; BSCT, behavioural self-control training; NFC: no further counseling; Naltrexone+, naltrexone plus counseling; Placebo+: placebo plus counseling.
MOCE and MET when compared to their respective comparators. For example, MOCE and MET are dominated when the modelled cost-utility analysis is run for lower 95% confidence limits on estimates of treatment effect. That said, it has recently been argued that the ‘rules of inference are entirely irrelevant to the decisions that clinical and economic evaluations claim to inform’ (Claxton, 1999, p. 341). For decisions that cannot be deferred and that have irreversible consequences, it is perhaps better to prioritise between competing interventions based on expected values rather than the rules of statistical inference. ‘Accepting the null hypothesis when a new treatment has positive but statistically insignificant net benefits imposes unnecessary costs’ that can be measured in wasted resources and life-years foregone (Claxton, 1999, p. 342).

Likewise, the cost per QALY estimate for naltrexone plus counselling is sensitive to increases in the initial relapse rate such that placebo dominates when the risk of relapse in the naltrexone arm is increased by a factor of three. While it is possible that relapse is higher in the naltrexone arm than in the placebo arm, the between-arm differences considered in the sensitivity analysis are unlikely to occur in practice. Finally, cost per QALY estimates for MOCE, MET, and naltrexone plus counselling exceed any putative funding threshold when the HRQoL gain arising from transition from dependence to recovered or from a moderation of problem drinking is reduced to zero. However, evidence reviewed in a companion paper suggests that the HRQoL gain has been underestimated (rather than overestimated) in the base-case due to exclusion of within-family external effects.

CONCLUSIONS

This paper reports results from a set of economic evaluations comparing interventions for problem drinking and alcohol dependence against usual care for the relevant target population. Cost per QALY estimates have been derived from a time-dependent state-transition model using the same set of core assumptions for each comparison. Under the base-case, interventions for problem drinkers appear to offer better value for money than interventions targeted at those with a history of severe physical dependence. That said, the global budget for health care in Australia (and most western democracies) would imply a funding threshold (shadow price of a QALY) well in excess of base-case cost per QALY estimates for the most effective affordable intervention in each of our three mutually exclusive clusters (George et al., 2001). While it is true that usual care dominates the active intervention under certain circumstances, priorities are increasingly set on the balance of probabilities rather than on the basis of statistical inference.

Moreover, there are good reasons to believe that (i) the cost per QALY estimates for each of the evaluated interventions are likely to be on the high side such that the evaluated interventions provide better value for money than has been reported here and (ii) that this bias might be somewhat greater for interventions targeted at those with a history of severe physical dependence. Firstly, the cost per QALY estimates reported above have not captured external effects such as the impact of alcohol-related violence on family members and we might reasonably expect these external effects to increase in line with severity. The inclusion of external effects is problematic and requires a number of potentially controversial assumptions. Methods for capturing within-family external effects and revised cost per QALY estimates are described in a companion paper.

Secondly, downstream cost-offsets have been excluded in the base-case analysis. Results from the threshold analysis suggest that the minimum downstream cost-offset per responder per year (i.e. cost-savings arising as a result of transition to the moderate or recovered state from the problem or dependent state) that would be required for each intervention to dominate its usual care comparator could be characterised as achievable and increasing in line with severity. That said, it is entirely possible that downstream cost-offsets arising from a successful transition from ‘dependence’ to ‘recovered’ would be significantly greater than those arising from a moderation of problem drinking such that the relative performance of interventions targeted at alcohol dependence is improved. For example, Palmer et al. (2000) estimated the incremental cost of relapsing from abstinence to alcohol dependence syndrome at 1452 DEM per year (including transition costs) in 1996 values, equivalent to 1465 AUD per year after currency conversion and inflation to 2003 values. More generally, there is evidence to suggest that brief physician advice (Fleming et al., 2000), psychosocial interventions for the prevention of relapse prevention (Slattery et al., 2003) (http://docs.scottishmedicines.org/docs/pdf/Acohol%20Report. pdf, accessed 13 July 2005) and acamprosate for relapse prevention (Schadlich and Brecht, 1998; Palmer et al., 2000) become cost-saving after accounting for the anticipated reduction in health service utilisation in future years. The results reported here are therefore sufficient to support the provision of a comprehensive package of interventions for problem drinking and alcohol dependence.

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