# The Economic Analysis of Prevention in Mental Health Programs

Cathrine Mihalopoulos,[1] Theo Vos,[2] Jane Pirkis,[3] and Rob Carter[1]

[1]Deakin Health Economics, Deakin University, Burwood, 3125, Melbourne, Victoria, Australia; email: cathy.mihalopoulos@deakin.edu.au

[2]Centre for Burden of Disease and Cost-Effectiveness, School of Population Health, University of Queensland, Herston, QLD 4006, Australia

[3]Centre for Health Policy, Programs and Economics, University of Melbourne, Victoria, 3010, Australia

## Keywords

economic evaluation, priority setting, mental disorders, cost-effectiveness

## Abstract

This article introduces the role economics can play in deciding whether programs designed to prevent mental disorders, which carry large disease and economic burdens, are a worthwhile use of limited healthcare resources. Fortunately, preventive interventions for mental disorders exist; however, which interventions should be financed is a common issue facing decision makers, and economic evaluation can provide answers. Unfortunately, existing economic evaluations of preventive interventions have limited applicability to local healthcare contexts. An approach to priority setting largely based on economic techniques—Assessing Cost-Effectiveness (ACE)—has been developed and used in Australia to answer questions regarding the economic credentials of competing interventions. Eleven preventive interventions for mental disorders and suicide, mostly psychological in nature, have been evaluated using this approach, with many meeting the criteria of good value for money. Interventions targeting the prevention of suicide, adult and childhood depression, childhood anxiety, and early psychosis have particular merit.

## Contents

## INTRODUCTION

This paper is divided into five distinct but related sections, each following the main argument described below.

The prevention of mental disorders is an important health priority given the large disease and economic burden associated with such disorders (first section). Fortunately there are a number of interventions that are able to prevent the emergence of such disorders (first section). However, the question of which interventions should be adopted within any healthcare system is difficult, particularly given limited healthcare resources. Economics, via the tool of economic evaluation, can help answer such questions from the perspective of determining the comparative value for money credentials of such interventions (second section). Many existing economic evaluations have limited local context applicability, since the design, delivery, and cost of healthcare systems around the world greatly vary (second section). An approach to priority setting of competing healthcare interventions based on economic methods has been developed in Australia—the ACE (Assessing Cost-Effectiveness) approach (third section). This approach has been applied to preventive interventions for mental disorders and has provided important information regarding the comparative value for money of different interventions (fourth section). This information is valuable to decision makers faced with the difficult task of allocating scarce healthcare resources across a number of competing diseases/ disorders, though important caveats need to be considered rather than simplistic acceptance of such information (fifth section).

Unless noted otherwise, all costs in this review are expressed as Australian dollars.

## SETTING THE CONTEXT

Mental disorders are highly prevalent and account for a large proportion of disease burden within most countries. Burden of disease studies provide a description of the health burden associated with various diseases and disorders incorporating premature mortality and disability into a single metric, the disability-adjusted life year (DALY). The disease burden associated with mental disorders in Australia is substantial, ranking third behind cancer and

cardiovascular disease (Begg et al. 2007, Mathers et al. 1999). Internationally, major depression is the third leading cause of disease burden worldwide (World Health Org. 2008) and the first leading cause in middle- and high-income countries. The majority of the disease burden associated with mental disorders is attributable to disability rather than mortality. This is in contrast to diseases such as cancer, where most of the burden is associated with premature mortality.

Direct health expenditure on mental disorders is substantial in developed countries. In Australia, $5 billion was spent on mental disorders in 2003, and this amount is projected to increase to $12 billion by 2033 (135% increase) (Goss 2008). However, broader costs associated with mental disorders are not well captured by these estimates. Mental disorders have large economic impacts in other areas, including lost productivity, carer/family costs, and costs in government sectors (such as welfare, housing, and the judiciary). Australian and international cost-of-illness studies in both depression and psychosis have found, for example, that half the total costs are due to nonhealth-sector costs (Carr et al. 2003, Luppa et al. 2007).

Australian estimates for the treatment of depression suggest that current treatment averts 13% to 16% of the disease burden, and even if all depression were treated using evidence-based treatments, only 24% to 52% of the disease burden would be averted (Andrews et al. 2004, Vos et al. 2004). It is unsurprising that the prevention of mental disorders is being viewed as an important way to avert a proportion of the burden associated with such disorders.

## Prevention of Mental Disorders

Preventive interventions can be classified according to target population—comprising universal interventions (whole populations), selective interventions (targeting at-risk population groups, such as children of divorced parents) or indicated interventions (targeting people showing minimal signs of disorders) (Mrazek & Haggerty 1994).

A number of published meta-analyses and reviews (including Cochrane reviews) have investigated the prevention of mental disorders (Cuijpers et al. 2005, Durlak & Wells 1997, Mrazek & Haggerty 1994, Nicholas & Broadstock 1999). These reviews examine different interventions, though the majority are selective or indicated rather than universal strategies—probably because universal interventions are harder to evaluate and are not amenable to the types of studies included in meta-analyses.

The majority of studies use surrogate outcomes (such as reductions in problematic behaviors) rather than final outcomes (defined as reduction in the incidence of mental disorders). The study by Cuijpers et al. 2005 has particular merit since the purpose was to conduct a meta-analysis of the effects of preventive interventions on the incidence of formally diagnosed mental disorders using quality randomized studies. Thirteen studies were included in this analysis across a number of different disorders, with half targeting children/adolescents. The overall results were encouraging [relative risk (RR) = 0.73, 0.56–0.95] and showed that it is possible to reduce the incidence of mental disorders.

One of the most influential and best-cited references in this area is the 1994 U.S. Institute of Medicine review (Mrazek & Haggerty 1994). Even though this review is quite dated now, the recommendation regarding a focus on interventions aimed at early life is still current. This is not surprising because evidence suggests that most adults with mental disorders have a juvenile history (Kim-Cohen et al. 2003).

There have also been two Cochrane reviews investigating preventive interventions for mental disorders. One review reported evidence for the prevention of depression in children and adolescents using targeted or indicated interventions (Merry et al. 2004); the other found evidence for the prevention of postnatal depression using indicated interventions (Dennis & Creedy 2004).

In addition, a number of reviews have focused on the improvement of psychosocial

**Economic evaluation/appraisal:** the comparative analysis of the costs and consequences of two or more competing programs/interventions

**Priority setting:** the process of making decisions about what gets funded and the relative priority of different interventions/diseases in this process

**ACE:** Assessing Cost-Effectiveness

**Burden of disease:** a measure of the total cost, usually in terms of mortality or morbidity, of various diseases/disorders

**Disability-adjusted life year (DALY):** measure of illness that includes mortality (years of life lost) and morbidity (years lived with disability)

**Cost-effectiveness analysis (CEA):** economic evaluation technique where costs are valued in monetary terms but consequences are valued in clinically meaningful physical units (e.g., life years)

**Cost-utility analysis (CUA):** economic evaluation technique where costs are valued in monetary units but consequences are valued using generic preference-based metrics (e.g., quality-adjusted life years)

**Cost-benefit analysis (CBA):** economic evaluation technique where both costs and consequences are valued in monetary terms. Different techniques can be used to monetarize consequences

outcomes (such as prevention of child abuse), often thought to be risk factors for mental disorders (Barlow & Parsons 2003, Coren & Barlow 2001). The limitation of these reviews is that although effects on surrogate risk factor outcomes are demonstrated, reduction in disorder incidence is not.

Finally, there are recent studies suggesting that anxiety disorders in children can be prevented, and psychotic disorders can at least be delayed (Bayer et al. 2009, McGorry et al. 2009).

Importantly, primary prevention of mental disorders (classically defined as the reduction of incidence of first-ever cases) is difficult to evaluate purely in the mental health context for a number of reasons. For example, most studies that use diagnostic outcomes at follow-up cannot definitely exclude people with a prior history of mental illness because exclusion criteria are usually limited to the presence of a mental illness within the past 12 months. The reason for this limitation is that there is no psychometrically validated diagnostic tool that reliably assesses lifetime incidence. Therefore, people offered these interventions are possibly a mix of people with no history of mental illness and people with some prior history (particularly in adult studies, where it is known that most adult mental illnesses are preceded by childhood conditions, though not necessarily the same ones) (Kim-Cohen et al. 2003). Studies that are classified as "treatment" of mental illnesses would of course make no such distinction and usually require the person to be currently ill at baseline assessment. One recent study evaluating the prevention of depression in 14-year-old adolescents attempted to distinguish between adolescents with no prior history of depression and those with some possible prior history (Arnarson & Craighead 2009). Importantly the effectiveness of the intervention was not impacted by the possible presence or absence of a prior depressive episode. From a public health perspective, treatment would not be withheld either way.

There appears to be reasonably good evidence that mental disorders can be prevented. It is unsurprising that Australian as well as international health policy documents (Commonw. Aust. 2009, World Health Org. 2004) highlight the importance of preventive interventions for mental disorders. Although the importance of mental disorder prevention is acknowledged, these documents are less prescriptive about which interventions should be provided. A number of interventions can be provided across the different disorders; however, which ones should be provided is far from clear, particularly within the context of a limited health budget used to finance a range of both preventive and treatment health services across different diseases.

## ECONOMIC EVALUATION

Economic evaluation is a method for considering the benefits and costs of alternate uses of healthcare resources to aid decision makers in allocating and prioritizing health resources (Drummond et al. 2005). It is a useful technique whereby interventions can be compared and their respective value for money or worth determined. Economic evaluation has two defining features: The first is that both the costs and consequences (or benefits) of alternative interventions/programs are considered; the second is that choices between different interventions/programs must be made (Drummond et al. 2005). The first criterion, although challenging in pragmatic terms (e.g., ensuring all appropriate costs and consequences are identified and valued), is simple to understand. However, the second criterion of choice, and setting priorities, is more complex in that choices are often made on the basis of different motives, which may or may not be explicit. Therefore, economic evaluation of preventive interventions can provide decision makers with information regarding the economic value of interventions and assist with the difficult decision of healthcare resource allocations.

There are three main economic evaluation techniques: cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). The main difference between

them is the method used to measure and value the consequences or benefits of health interventions. CBA values benefits in monetary terms. CEA and CUA value benefits in physical units. The defining difference between CEA and CUA is that CUA combines both morbidity and mortality into a single unit of measurement [such as a quality-adjusted life year (QALY) or a DALY prevented], whereas CEA utilizes symptomatic or diagnostic indicators meaningful to clinicians (e.g., cancers detected, number of arthritic joints, or pain-free days).

Apart from three key evaluation techniques, there are three main theoretical schools of thought that can influence the preferred technique used in economic evaluation. The first is orthodox neo-classical economic theory, sometimes termed welfare economics. Welfare economics has its foundation in utilitarianism, whereby individual choices and consumer sovereignty are the drivers of resource allocation decisions. CBA is founded in this school of thought and is sometimes thought of as being "theoretically superior" because of this. However, most societies believe healthcare to be different from other goods and services (i.e., a merit good) because social justice and the concept of "need," not individual preferences, are considered fundamental to healthcare (Rice 2002). Therefore, most international healthcare systems do not rely on the premises of orthodox welfare economics to decide which healthcare services are provided.

The second school of thought is termed extra-welfarism and was developed in response to the perceived weaknesses of utilitarianism, as applied to health. Extra-welfarists believe that there are social objectives over and above personal utility that motivate people; in its most common manifestation, it is thought that health should be the key objective of healthcare (Culyer 1989), though other objectives such as equity may also be considered (Brouwer et al. 2008). Cost-utility analysis has foundations in this school of thought whereby "health" is the key outcome to be maximized in resource allocation, though other objectives, such as equity,

can be accommodated (e.g., via equity weights in CUA).

The third school of thought is the decision-making school. It has the premise that whatever is useful to decision makers should be considered in economic evaluation—it could be health or equity or other objectives (Carter et al. 2008, Sugden & Williams 1978). Importantly, any of the existing techniques can be used under the decision-making school depending on what is consistent with the objectives of the decision makers. In a recent article, Richardson & McKie (2005) introduced "empirical ethics" as a way of determining what the objectives of a health system should be and therefore what should be considered in economic evaluation. This school of thought is similar to the decision-making school because both are based on the idea that the objectives of healthcare should not be dictated by economic theories, but rather by what societies (or decision makers) consider important.

In summary, different evaluation techniques are based on different normative theoretical foundations, and each presents results differently, which makes the ranking of interventions in terms of their economic merit impossible. Therefore, to evaluate the economic credentials of preventive interventions for mental disorders, a starting point is a review of any existing economic evaluation studies.

## Results of a Systematic Review of Economic Evaluations of Preventive Interventions for Mental Disorders

To source any existing economic evaluation, a search using the keywords prevention AND (mental disorder* OR depression OR psychosis OR anxiety OR suicide OR conduct disorder) AND (cost OR economic) was undertaken in Medline, Psychinfo, and Econlit. References relevant to dementia or substance abuse were not included in the current review. To qualify for inclusion to the review, the studies had to be comparative economic evaluations of interventions designed to prevent mental disorders. Simple cost comparisons or descriptions were ineligible. There has been one

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**Quality-adjusted life year (QALY):** measure of health status that includes mortality (years lived) and morbidity (quality of years lived)

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**ICER:** incremental cost-effectiveness ratio

systematic review of the literature up until 2008 (Zechmeister et al. 2008). Two of the studies quoted in this review were not relevant because their subject matter was the detection of depression rather than prevention of depression. Another four studies also were not relevant because they were concerned with reductions in risk factors and did not directly address the prevention of mental disorders (or even mental health problems) (Aos et al. 2004, Lynch 2004, McAuley et al. 2004, Schweinhart et al. 2004). A further four studies, published subsequent to 2006, were retrieved. However, upon closer inspection, it was found that one of these was not a full economic evaluation (Fleischmann et al. 2008). This left 11 economic evaluations that were eligible for the current review.

The quality of the studies was assessed using a ten-item checklist (Drummond et al. 2005). Briefly, these criteria include assessments of the quality of the research question; the description of the competing alternatives; establishment of program effectiveness; identification of costs and consequences; the measurement of costs and consequences; the valuation of costs and consequences; adjustment for differential timing (discounting); incremental analysis of competing alternatives [i.e., costs of program 2 are subtracted from the costs of program 1, which are divided by the benefits of program 2 subtracted from the benefits of program 1—commonly referred to as an incremental cost-effectiveness ratio (ICER)]; allowance made for uncertainty in both the costs and consequences; and the presentation of results and discussion that are of concern to study users. Although other criteria also exist (Gold et al. 1996), all are generally similar, and the criteria developed by Drummond et al. (2005) are well known, are commonly used, and are the basis of criteria for judging the quality of economic evaluation in the *British Medical Journal* (Drummond & Jefferson 1996). Unfortunately, the criteria are somewhat less prescriptive about how such quality should be rated. In the current context, a score of 1 was awarded for fully meeting the criteria, half a point was awarded for partially meeting the criteria, and no point was awarded

when criteria were not met. The ratings were undertaken by the primary author of this review (C.M.) to determine the quality of the published economic evidence base for use in healthcare rationing decisions. The studies along with their quality ratings are summarized in **Table 1**.

The majority of studies are of good quality, although there are a number of important methodological differences between them (such as economic framework, perspective, outcome measurement, and time horizon; for a description of these terms, refer to the General Methodology for ACE-Prevention section), making direct comparisons almost impossible. Most of the studies appraise interventions for the prevention of depression and suicide. Five studies evaluated various interventions for the prevention of depression (two focused on postnatal depression, and the others on childhood, late life, and adult depression, respectively). Neither of the studies evaluating interventions for postnatal depression reported that the interventions were effective. The other two depression studies, which included diagnostic measures at follow-up, found that the interventions reduced depression, although the effectiveness measures in one study in particular (Smit et al. 2006) were limited (small sample size with significant effect in a one-tail test of significance). Only Lynch et al. (2005) used a cost-utility framework, reporting an ICER of U.S. $9,000/QALY (Lynch et al. 2005). However, this study used symptomatic, not diagnostic, measures of outcome and modeled the QALY benefit. The majority of studies included a short horizon of time, and their generalizability outside their own study context is limited. Only one study has been undertaken in an Australian setting (Mihalopoulos et al. 2007), although some of the cost estimates used in this study were sourced from overseas.

Overall, the conclusion of these studies is that the prevention of general depression may be cost-effective, at least in the short term, although the cost-effectiveness of the prevention of postnatal depression is questionable. The prevention of conduct disorder may be cost-effective, although the primary study design of

the Australian study was a threshold analysis (that is, the study determined how many cases of conduct disorder need to be avoided before the intervention is cost-effective), and the American study was much more cautious regarding cost-effectiveness (importantly, this study did not include cost offsets). The other four studies assessed various suicide prevention interventions. Three of these studies received only average/poor ratings. The other two average-quality studies were cost-benefit analyses and suggest that suicide prevention interventions have favorable cost-to-benefit ratios. Interestingly, the intervention that received the highest quality rating was not effective in reducing suicidal ideation. None of the studies used suicide attempts as final study endpoints. No study received a rating of excellent. This is largely because of the measures of effectiveness used. Although many studies did employ randomized designs, often the sample sizes were small, and the study designs were largely efficacy rather than effectiveness.

The existing economic appraisals of preventive interventions for mental disorders and suicide suggest that interventions, particularly for the prevention of depression, may be cost-effective; however, the better-quality studies have limited generalizability to the Australian local context, are based on single trials of efficacy, and have short time horizons. Furthermore, the value for money in comparison to other preventive interventions cannot be assessed, and hence the information from the studies for Australian (or other international) health-policy decision makers is limited. It is almost impossible for any single economic evaluation to be equally relevant to all healthcare contexts because each country has its own uniquely designed healthcare system. For example, in Australia, a large primary healthcare system acts as the gateway to the specialist system—specialist providers, including psychologists financed through the universal health insurance scheme, are only accessible after a general practitioner referral. The United States does not have such a system. Therefore, these system designs can have a major impact on the way interventions are delivered and financed, making cross-country comparisons of economic evaluation results problematic.

## THE ASSESSING COST-EFFECTIVENESS (ACE) APPROACH TO PRIORITY SETTING

Existing economic evaluations of preventive interventions for mental disorders and suicide provide limited information that is useful across multiple policy contexts. Although economic evaluation has undoubted potential as a valuable aid in healthcare decision making, the existing evidence base so far does not provide this information.

Furthermore, even when economic studies are available to guide decision making, many economists lament that their research has not been routinely used. Reasons for this include, but are not limited to, lack of generalizability, limited research questions, and lack of rigor (Hoffmann et al. 2002). Although economic evaluation is not the only decision tool used for priority setting, it can provide valuable information in terms of comparative value for money between different interventions. A number of economists have discussed the use of economic evaluation as a tool for priority setting within the healthcare sector (e.g., Carter 2001, Mitton & Donaldson 2004). Carter (2001) provides a comprehensive priority-setting framework, developed within Australia, largely based on economic principles.

Carter (2001) argues that there is no a priori theoretically correct approach to priority setting relevant to all countries and healthcare sectors. Rather, researchers and decision makers need to be explicit about what is included in the priority-setting process for each individual context. Economics offers one approach to priority setting, although alternative approaches based in epidemiology, behavioral sciences, and philosophy exist (Carter 2001). Approaches based on epidemiology focus on need (with little regard to the value for money of the interventions to address this need); behavioral science

**Table 1  Summary of economic evaluations of preventive interventions for mental disorders**

| Paper | Disorder targeted | Intervention[1] | Evaluation type[2] | Perspective and time horizon | Costs[3] | Outcomes and results[4] | Quality[5] | Comment |
|---|---|---|---|---|---|---|---|---|
| Appleby et al. (2000) | Suicide | Indicated Training of professionals | CEA using threshold analysis | Health sector, 1 year | Only intervention costs included; no cost offsets or other health sector costs | Assessed using surrogate indices based on skills gained during training; threshold analysis used hypothetical changes in suicide rate. 2.5% decline in suicide would be considered good value for money | Average-poor | Only intervention costs considered with a very simple threshold analysis framework; ungeneralizable to broader contexts |
| Byford et al. (1999) | Child/ adolescent suicide | Indicated Home-based social work intervention | CCA alongside randomized trial | Broad perspective (societal?), 6 months | Broad range of costs included but parental economic impact not included (both direct and production costs) | Assessed using suicidal ideation; no differences in costs and outcomes were observed | Good | Only surrogate outcomes considered in the analysis; parental use of services not included |
| Lynch et al. (2005) | Adolescent depression | Indicated Cognitive behavioral therapy | Randomized controlled trial with CEA and CUA | Societal, 1 year | Exact nature of non-HMO and intervention costs not specified | Reasonably assessed using depression-free days as main outcome with secondary conversion to a QALY; intervention found to be cost-effective (U.S. $9,000/QALY) | Good | Study is of high quality but not easily generalizable outside U.S. system. Conversion to QALY outcome allows conclusions regarding value for money to be made |

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| Foster & Jones (2007) | Conduct disorder | Mostly indicated Fast track | CEA using results from an existing trial | Third-party payer | Only intervention costs included; biggest limitation was that a broader costing perspective not included | Three key outcomes included: cases of conduct disorder avoided, index criminal offenses avoided, and acts of interpersonal violence avoided. Results showed that high willingness-to-pay threshold required for the intervention to be more cost-effective and even more so for high risk | Good | The biggest limitation of this study is the narrow costing perspective, whereby health sector and educational sector costs are not included (there may be important cost-offsets not included in the study). Furthermore, sensitivity testing around the discount rate should have been conducted |
| Mihalopoulos et al. (2007) | Conduct disorder | Universal, selective, indicated Triple P-Positive Parenting Program | CEA and threshold analysis using existing literature (modeling) | Government and limited societal, 26 years | Government costs using Australian and international estimates (cost of conduct disorders) | Assessed using Child Behavior Checklist cut-off and extrapolating to reduction in conduct disorder; intervention found to be dominant (that is, cost saving) | Good | Although the study is of high quality, the extrapolation to diagnostic outcomes is not ideal. Furthermore, cost offsets associated with reduction in conduct disorder are based on an international study with questionable generalizability. Australian context of study makes it useful to Australian decision makers |
| Petrou et al. (2006) | Post-natal depression | Indicated Home-visiting therapist | Concurrent CEA and pragmatic randomized | Public sector (government), 18 months | Although stated that public sector costs were included, exact nature was not specified | Well assessed using standardized diagnostic instruments; no significant differences between groups observed | Good | Limitations and comments similar to those for Lynch et al. (2005) |

*(Continued)*

**Table 1** *(Continued)*

| Paper | Disorder targeted | Intervention[1] | Evaluation type[2] | Perspective and time horizon | Costs[3] | Outcomes and results[4] | Quality[5] | Comment |
|---|---|---|---|---|---|---|---|---|
| Sari et al. (2008) | Adolescent suicide | Selective General education and peer support at university level | CBA framework using existing literature (modeling) | Lifetime benefit (production savings over lifetime) | Unclear what is included in health-related cost offsets (only autopsy is discussed) | Assessed using human capital approach (stream of future earnings) but defined as productivity losses; programs have benefit-to-cost ratios of 2 and 3.7, respectively | Average | Possibly modeled as an add-on to current practice; though not stated, effectiveness not well established, and perspective not clearly stated |
| Smit et al. (2006) | Adult depression | Indicated Brief bibliotherapy | CEA alongside a pragmatic randomized trial | Societal, 1 year | Other nonmed costs not cited (e.g., welfare sector) | Well assessed using standardized diagnostic instruments and validated symptomatic scales; intervention found to be cost saving (borderline significant) | Good | Well-conducted evaluation; however, limited generalizability outside the Dutch system, and short time horizon did not use CUA, so difficult to ascertain value for money |
| Van't Veer-Tazelaar et al. (2010) | Depression and anxiety in later life | Indicated Stepped-care approach including waiting, brief bibliotherapy, problem solving, and referral | CEA alongside a pragmatic randomized trial | Societal, 12 months | Appropriate range of costs, including health service use and carer time. Production costs not included owing to age of participants | Assessed using diagnostic criteria but measured as a disorder-free year—€4367/depression-free year—99% of simulations fell in northeast or southeast quads | Good | Evaluation type makes it difficult to denote value-for-money judgment. Limited generalizability owing to context and short time frame |

| Wiggins et al. (2004) | Postnatal depression | Selective Support health visitor and community group support | CCA alongside randomized trial (3-arm trial) | Health sector and mothers, 18-month horizon | Appropriate range of costs included | Assessed using symptomatic scales of mental health and general health; no differences in outcomes or costs were observed | Good | Diagnostic outcome not assessed although observations of change would be unlikely because no symptomatic differences were observed. Study has limited generalizability |
|---|---|---|---|---|---|---|---|---|
| Zaloshnja et al. (2003) | Suicide | Selective Multifaceted program for Native Americans | CBA and CUA using existing literature (modeling) | Perspective not clear. Lifetime benefit | Perspective not cited, but reasonable costs included | Assessed using existing utility weights and wages; program has a benefit-to-cost ratio of 43 and a cost-per-QALY of U.S. $419 | Average | Possibly modeled as an add-on to current practice but not stated; effectiveness not well established. No sensitivity analysis and very limited generalizability |

[1]Column 3 includes information on the type of intervention that is evaluated using the classification system developed by Mrazek & Haggerty (1994).

[2]Column 4 briefly states the economic evaluation type.

[3]Column 6 includes a brief comment on whether all the relevant costs were captured by the economic evaluation; only important omitted costs are stated.

[4]Column 7 includes a brief comment on how comprehensively outcomes were assessed.

[5]Column 8 summarizes how well the study performed against the Drummond ten-point criteria checklist (Drummond et al. 2005): excellent, 10/10; good, 9–8/10; average, 7–6/10; and poor, 5 and below/10.

Abbreviations: CBA, cost-benefit analysis; CCA, cost consequences analysis; CEA, cost-effectiveness analysis; CUA, cost utility analysis; HMO, health maintenance organization; QALY, quality-adjusted life year.

approaches focus on due process or consensus; and philosophical approaches focus on a priori ethical principles. Although there are merits to these various approaches, there are also important deficiencies. For example, while economics offers an attractive approach based on efficiency (operationalized through incremental analysis), priority-setting approaches that focus only on this criterion have been rejected largely because of the perceived perversities created. This occurs particularly when interventions that are not life saving are given priority over those that are life saving. A well-known example of this was the initial league table of cost-effective interventions developed in the state of Oregon, which was subsequently rejected (Sabik & Lie 2008). In a recent review of priority setting in eight countries, Sabik & Lie (2008) concluded that the priority-setting exercises (mostly based on economic principles) had little impact on service provision and funding.

In developing his approach to priority setting, Carter focused on making economic appraisal more relevant to the needs of decision makers. His work considered the contributions of economic theory, ethics and social justice, empirical evidence, and the practical needs of decision makers (Carter 2001, Carter et al. 2008). Carter developed a 10-point checklist for priority-setting approaches based on explicit consideration of the theoretical, ethical, and practical aspects of the different approaches. Four commonly used models of priority setting were considered: needs-based models (from epidemiology), consensus models (from behavioral science), league tables (from economics), and program budgeting and marginal analysis (from economics). Each model had strengths but was also found to be deficient in some way. For example, needs-based approaches do not provide sufficient information regarding which health services or interventions should be financed. Although it is beyond the scope of this review to detail these approaches, further information is available in Carter et al. (2008).

In light of the deficiencies of existing models of priority setting, a comprehensive model that is based on economic techniques was developed; the model integrated other learning from ethics and empirical experience with priority setting. This model has been refined in Australia since 2001 and is known as the Assessing Cost-Effectiveness (ACE) approach (Carter et al. 2008). The broad-based approach of ACE has considerable appeal, including its focus on methodological rigor, data tractability, and due process considerations. Its foundation is the decision-making school of thought, and it includes cost-utility analysis based on standardized methods (so that results are comparable both within and across diseases). The approach includes other considerations important to decision makers, such as due process and impact on equity. ACE performs well against the criteria developed by Carter (2001) and is summarized in **Figure 1**. It involves stakeholder consultation, usually with decision makers representing various governmental jurisdictions, clinical and topic experts, and other interested
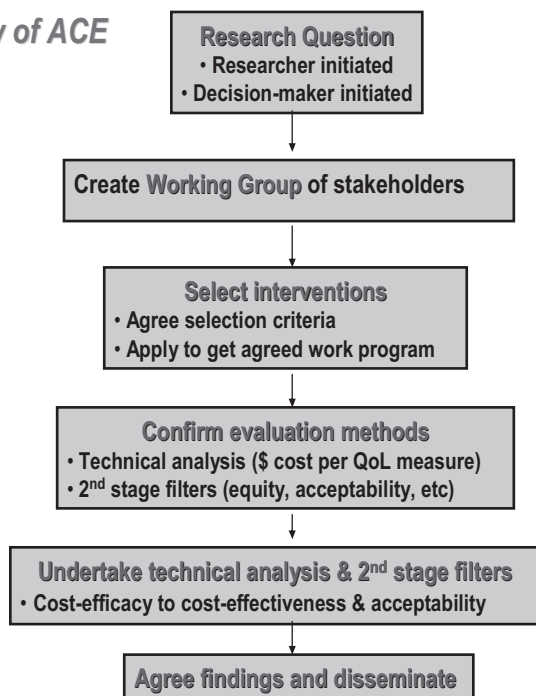


**Figure 1**

Overview of steps in the Assessing Cost-Effectiveness (ACE) approach to priority setting (from Carter et al. 2008, p. 603).

parties, such as nongovernment organizations. Stakeholders and researchers work together to refine the research question and choose interventions for consideration that are useful from a decision-making viewpoint. Other considerations beyond the technical ICERs are included. The unique feature of this approach is that decision makers, key stakeholders, and researchers all work together to ensure that results are as practically useful as possible.

A number of ACE projects have been completed in Australia in the areas of cancer control, mental health treatment, cardiovascular disease, alcohol misuse, and obesity prevention (Carter 2001, Dep. Human Serv. 2006, Vos et al. 2005b). The most recent ACE study, ACE-Prevention, aims to provide decision makers with information regarding the most cost-effective bundle of preventive services for noncommunicable diseases given available resources. This project ran for five years, and the final project report was released in September 2010 (**http://www.sph.uq.edu.au/bodce-ace-prevention**).

Consideration of the prevention of mental disorders was an important part of the ACE-Prevention project. The methods undertaken to evaluate the cost-effectiveness of preventive interventions for mental disorders were similar to all the other interventions.

## General Methodology for ACE-Prevention

The key features of the methods are divided into those pertinent to the study frame and those pertinent to the study design. Together, both these features ensure that the economic methods are rigorous and appropriate to the research question. The following section is sourced from the project protocol (Carter et al. 2005).

## Study Frame

**Interventions chosen for analysis.** The primary criterion for intervention selection was a credible evidence base for intervention efficacy/effectiveness. This evidence was gleaned from the existing literature and was based on quality studies of efficacy and effectiveness that employed sound evaluation techniques to minimize the chance of bias and confounding. Although evidence from a large number of randomized trials is the gold standard, pragmatically, this is not always available for many interventions of interest to policy makers. A framework for evidence classification was developed for the ACE studies and allowed for evidence outside the classic experimental paradigm to be considered and classified (**Table 2**) (Haby et al. 2006).

The second key criterion was that the intervention needed to be of relevance to the policy context. This is a practical consideration because there is little point in evaluating interventions that are of no relevance to the local political scene.

Finally, the interventions needed to have a specifiable intervention pathway—that is, who does what to whom and how often needed to be clear (Drummond et al. 2005). This was essential for interventions to be costed and economically appraised.

**Perspective.** The chosen perspective was the health sector, including important health-related out-of-pocket costs to patients/families. Costs to third-party government payers and individuals are differentially reported. Although a societal perspective is ideal, the data requirements of such a perspective are substantial and rarely properly measured. However, if important nonhealth-sector costs are impacted by the intervention, these were clearly flagged and included in a secondary sensitivity analysis.

**Target population.** The Australian population of 2003 (the study reference year) was the target population. Universal interventions target the entire population or at least major subcategories of the population (e.g., children/adolescents), whereas selective and/or indicated interventions target specific subsections of the population with conditions/risk factors of interest.

**Study boundaries.** Theoretically, all costs and consequences to whomever they accrue should be included in economic evaluations (Drummond et al. 2005). The extent to which

**Table 2   Classifying the strength of the evidence: approach adopted in ACE-Prevention**

| Conventional approach based on epidemiological study design: evidence from Level I–III study designs | Additional categories utilized in the ACE-Prevention study: evidence from Level IV studies, indirect[1] or parallel evidence[2], and/or from epidemiological modeling using a mixture of study designs |
|---|---|
| "Sufficient evidence of effectiveness" <br> Effectiveness is demonstrated by sufficient evidence from well-designed research: <br> (*a*) The effect is unlikely to be due to chance (e.g., $p < 0.05$), and <br> (*b*) the effect is unlikely to be due to bias, e.g., evidence from[3]: <br> –a level I study design; <br> –several good-quality level II studies; or <br> –several high-quality level III-1 or III-2 studies from which effects of bias and confounding can be reasonably excluded on the basis of the design and analysis. | "Likely to be effective" <br> Effectiveness results are based on: <br> (*a*) Sound theoretical rationale and program logic; and <br> (*b*) Level IV studies, indirect evidence[1] or parallel evidence[2] for outcomes; or <br> (*c*) epidemiological modeling to the desired outcome using a mix of evidence types or levels. <br> The effect is unlikely to be due to chance (the final uncertainty interval does not include zero and there is no evidence of systematic bias in the supporting studies). <br> Implementation of this intervention should be accompanied by an appropriate evaluation budget. |
| "Limited evidence of effectiveness" <br> Effectiveness is demonstrated by limited evidence from studies of varying quality: <br> (*a*) The effect is probably not due to chance, e.g., $p < 0.10$, but bias—although not certainly an explanation for the effect—cannot be excluded as a possible explanation; e.g., evidence from[3]: <br> –one level II study of uncertain or indifferent quality; <br> –evidence from one level III-1 or III-2 study of high quality; <br> –evidence from several level III-1 or III-2 studies of insufficiently high quality to rule out bias as a possible explanation; or <br> –evidence from a sizeable number of level III-3 studies that are of good quality and consistent in suggesting an effect. | "May be effective" <br> Effectiveness results are based on: <br> (*a*) Sound theoretical rationale and program logic; or <br> (*b*) Level IV studies, indirect[1] or parallel evidence[2] for outcomes; or <br> (*c*) epidemiological modeling to the desired outcome using a mix of evidence types or levels. <br> The effect is probably not due to chance, but bias—although not certainly an explanation for the effect—cannot be excluded as a possible explanation. <br> The intervention would benefit from further research and/or pilot studies before implementation. |
| "Inconclusive evidence of effectiveness" <br> Inadequate evidence due to insufficient research or research of inadequate quality. <br> No position could be reached on the presence or absence of an effect of the intervention (e.g., no evidence from level I or level II studies; level III studies are available, but they are few and of poor quality). | "No evidence of effectiveness" <br> No position could be reached on the likely credentials of this intervention. Further research may be warranted. |

[1]Indirect evidence: information that strongly suggests that the evidence exists (e.g., a high and continued investment in food advertising is indirect evidence that there is positive (but proprietary) evidence that food advertisement increases sales of those products (Swinburn et al. 2005).

[2]Parallel evidence: evidence of intervention effectiveness for another public health issue using similar strategies (e.g., the role of social marketing, regulation, or behavioral change initiatives in tobacco control, sun exposure, speeding, etc.) (Swinburn et al. 2005).

[3]The evidence classifications below are based on those of the Natl. Health Med. Res. Counc. (2000).

I: evidence obtained from a systematic review of all relevant randomized controlled trials.

II: evidence obtained from at least one properly designed randomized controlled trial.

III-1: evidence obtained from well-designed pseudo-randomized controlled trials (alternate allocation or some other method).

III-2: evidence obtained from comparative studies with concurrent controls and allocation not randomized (cohort studies), case-control studies, or interrupted time series with a control group.

III-3: evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.

IV: evidence obtained from either pretest or posttest case series.

Source: Table is based on Haby et al. (2006).

this is pragmatically possible is debatable. Included costs and consequences should be related to the research question and decision context. There is also controversy surrounding the inclusion of some spillover effects (such as production gains and losses or unrelated future healthcare costs) (Drummond et al. 2005, Gold et al. 1996). Therefore, the main analyses in ACE-Prevention included only health gains and costs directly attributable to the intervention and the key recipients of the intervention, although any significant external spillover effects were flagged and included in a secondary sensitivity analysis.

**Time horizon.** The time horizon for modeling the cost-effectiveness of interventions was lifetime (i.e., the lifetime benefits and costs are evaluated). The actual time horizon modeled was shorter for some interventions—for example, where one-off or time-limited interventions were modeled (e.g., a short psychological intervention consisting of a few contacts with a psychologist with only short-term evidence of effectiveness), where benefits decayed over time (that is, the effectiveness of the intervention reduces over time), or for disorders where the lifetime epidemiology is poorly documented.

**Choice of comparators.** Two types of comparators were considered in ACE-Prevention. The first was current practice, which may be an alternative intervention or "do nothing" if the intervention is an add-on to current practice and does not replace another intervention. For combinations of interventions, a null comparator, which was defined as no interventions in place, was also used. The null is important in helping to determine an ideal mix of interventions if one could start from scratch. This type of analysis was introduced by the World Health Organization in its generalized cost-effectiveness methods (Hutubessy et al. 2003).

## The Study Design

**Framework.** The economic framework for the ACE approach was cost-utility analysis, whereby outcomes are valued using generic health outcomes to ensure that comparability across different interventions is possible. The key features of the economic technical analysis are listed below.

**Outcomes.** The chosen outcome for the ACE studies was the DALY. This is consistent with the chosen perspective and theoretical underpinnings of the study (key stakeholders have defined health as the primary outcome). DALYs combine years of life lost due to premature mortality and years of life lived with a disability (determined by multiplying the duration of illness by a disability weight associated with that particular health state—much like QALYs) in the one metric (Murray & Lopez 1996). However, the metric used in the ACE studies, although similar to the burden of disease DALYs, differs. First, in burden of disease, DALYs are descriptive and estimate the disease burden compared to some hypothetical ideal. In the ACE context, population-specific mortality rates are used, which is similar to the derivation of QALYs. Second, any reduction in the morbidity component in DALYs is weighted by disability weights (mortality is not weighted by burden of disease), whereas QALYs tend to use utility weights. It is beyond the scope of this review to discuss the difference between these weights; interested readers are referred to Sassi (2006).

DALYs have been estimated for Australia for each of the major diseases and risk factors for both the general population and the indigenous population. In the Australian context, DALYs provide an existing database, based on consistent methods, to estimate the health gains associated with a large number of potential interventions.

**Intervention effectiveness.** Evidence of intervention effectiveness was usually sourced from the existing literature by systematic review of existing studies. Where possible, meta-analysis was used to synthesize the outcomes into one metric. For the analyses of interventions designed to prevent mental disorders, only studies that measured the impact on diagnosed mental disorders (using one of the standardized psychiatric diagnostic instruments) were included.

**Costs.** A health sector perspective means that all relevant costs and consequences from the health sector perspective must be included in the evaluation, although important costs occurring outside the health sector are flagged and included in a sensitivity analysis. All interventions were costed under steady-state assumptions—that is, they were assumed to be fully implemented and operating in accordance with their efficacy potential. The following costs are included:

- ongoing recruitment (+/− training of providers, dependent on whether providers should be familiar with this as a result of their professional training);
- key intervention elements (e.g., advice, consultations, procedures, change in legislation, etc.);
- monitoring, evaluation, and support if required in routine implementation; and
- downstream cost offsets—health resources not consumed as a consequence of the intervention but that would have been consumed if the intervention did not occur.

Time and travel costs are also included in the evaluations, although the primary results are presented without time and travel costs. Because interventions are assessed in steady state, we assume that trained personnel (with all associated infrastructure) are available to deliver the intervention.

Among excluded costs were:

- costs associated with the research and development of materials used in the intervention;
- costs associated with training the trainer;
- costs associated with the development and education of an adequate provider workforce (e.g., training more psychologists);
- production gains and losses in the general economy;
- the time costs of children; and
- monitoring and evaluation above a routine level.

The valuation of resource use was based on Australian national pricing standards as developed by the Pharmaceutical Benefits Advisory Council (Commonw. Dep. Health Ageing 2002). The use of this manual ensured a consistent approach to pricing across all interventions.

The cost of nonadherence was also included, whereby costs are attributed to people who drop out or do not comply with an intervention (no health benefit is included).

Australian national expenditure costs associated with all the major diseases are used as the valuation of cost offsets (Aust. Inst. Health & Welfare 2005). The advantage of these costs was that they are standardized across all diseases/disorders.

**Discounting.** A 3% discount rate was applied to all costs and consequences. This rate was varied in the sensitivity analysis (0, 5%, 7%).

**Epidemiological models.** Mathematical models were developed to assess the cost-effectiveness of all interventions. The principles underlying all models were that they should be lifetime models capable of capturing all costs and consequences of the intervention accruing over a lifetime; second, they should be population-level models so that total costs and consequences for the 2003 Australian population could be determined. The exact nature of the models varied across diseases/disorders, depending on the available evidence with regard to disease epidemiology and effects of the intervention on subsections of the population. The main modeling techniques used in economic evaluation were Markov models, multistate life tables, and microsimulations. The first two model types appraise, in discrete steps (usually yearly cycles), the probability of average intervention recipients being in various health states (and incurring certain costs), with different probabilities associated with the intervention and comparator case. Microsimulations are best used when there is heterogeneity in treatment response and disease course, although such models require considerable empirical data to be validly populated. Markov models with limited time horizons are the main technique used for the

evaluation of interventions designed to prevent mental disorders. This is because there is little information regarding the longer-term effectiveness of these interventions and details regarding the longer-term epidemiology of many disorders are not available (e.g., duration of symptoms in anxiety disorders).

The burden of disease studies provide a relatively comprehensive set of epidemiological parameters useful for economic modeling, including incidence, remission, prevalence, mortality risks, and duration.

**Uncertainty and sensitivity analysis.** The term uncertainty analysis was used to denote uncertainty in model parameters, whereas the term sensitivity analysis was used to denote value judgments made in the models that can be varied with an alternative judgment (e.g., discount rate, economic perspective). Many economic evaluation texts (e.g., Drummond et al. 2005) use the term sensitivity analysis to refer to both uncertainty and sensitivity analyses. Probabilistic Monte Carlo simulations were used as the main form of uncertainty analysis, whereby model parameters are simultaneously varied using 2,000 iterations (Microsoft Excel add-in software such as @Risk is used to do this). Commonly varied parameters included the efficacy/effectiveness measure, participation rates, and unit costs. Uncertainty ranges for all point estimates were then reported; this is called a 95% uncertainty interval (the upper and lower values of this interval represent the cut-offs in which 95% of iterations lie).

One-way sensitivity analyses were used for discount rate variations and when important effects (either costs or outcomes) have been identified for an intervention.

**Extrapolating treatment effects over time.** It is rare for trials to adopt a lifetime perspective. More commonly, follow-up assessments are made over a limited time frame (rarely more than three years for mental health interventions). Assumptions regarding longer-term effectiveness are inevitably made. However, whether such assumptions can credibly be made

is dependent on the intervention, discussions with technical experts, and a plausible modeling approach. Many of the interventions evaluated for the prevention of mental disorders adopted a shorter time horizon that was consistent with the length of the study follow-up or adopted a decay effect after the first year.

**Reporting.** The reporting of results was standardized across all interventions. The main results included the ICER along with the 95% uncertainty interval (without time and travel costs) of the most likely intervention scenario (usually agreed upon by discussion with experts). This information was graphically displayed in a cost-effectiveness plane or an acceptability curve. A cost-effectiveness plane is a four-figure quadrant of cost differences plotted against benefit differences. The top right quadrant contains the number of iterations (from the uncertainty analysis) in which the intervention is more effective and more costly than the comparator; the bottom right quadrant shows the number of iterations where the intervention is less costly and more effective than the intervention; the bottom left quadrant shows the number of iterations in which the intervention is less costly and less effective than the comparator; and the top left quadrant shows the number of iterations in which the intervention is more costly and less effective than the intervention. An acceptability curve shows the probability of the uncertainty iterations being below different willingness-to-pay thresholds.

In ACE, we have adopted a threshold value-for-money criterion of $50,000 per DALY averted. This threshold is somewhat arbitrary and is considered by the ACE stakeholders, including decision makers, as acceptable. Interventions that save more resources than what they cost (dominant) are denoted excellent value-for-money, interventions with ratios below $10,000 per DALY averted are denoted very good value for money, and interventions with ratios between $10,000 and $50,000 are considered good value for money. Alternative threshold values can be adopted if considered relevant by decision makers.

**Cost-effectiveness plane:** graphical representation of uncertainty in economic evaluations within a two-dimensional, four-quadrant space (cost differences versus benefit differences)

**Threshold value-for-money criterion:** a monetary criterion that is used to denote whether results of an economic evaluation provide value for money

## The Nontechnical Analysis (Second-Stage Filter Considerations)

One of the key features of the ACE approach is the ability to capture a broader range of decision makers' concerns, which technical ICERs cannot easily capture. These considerations have been called second-stage filter considerations and are agreed upon by the steering committee of all ACE projects at the project outset. This ensures that each project is as relevant as possible to the existing decision-making context. Discussion, definition, and finalization of these criteria necessitate input by the committee, ensuring all relevant viewpoints and concerns are captured. Within the ACE-Prevention context, the steering committee agreed to five criteria: strength of evidence, equity, feasibility of implementation and sustainability, acceptability to key stakeholders, and other effects not captured in the technical analysis. Each intervention is qualitatively assessed against the criteria, and results are presented in tabular format. The final row of the table presents a judgment around the policy implications of the technical analysis as well as the second-stage

filter criteria. Even though an intervention may perform very well on the ICER criterion, attention to these second-stage criteria may mean that the intervention is recommended as a pilot rather than initial widespread implementation. **Table 3** is the pro forma of how this information is presented.

## ACE-PREVENTION: THE PREVENTION OF MENTAL DISORDERS

The prevention of mental disorders is an important aspect of the ACE-Prevention project. This section provides a summary of the work undertaken.

Although the primary focus is on the prevention of mental disorders, interventions designed to prevent suicide have also been evaluated within this work program. Reviews of preventive interventions for mental disorders and suicide suggest that there are interventions suitable for evaluation, particularly for adult and childhood depression and suicide. There is some emerging evidence that psychotic disorders may be prevented or at least delayed

**Table 3   Pro forma of the second-stage filter considerations**

| Cost per DALY | Level of evidence | Equity | Feasibility of implementation | Acceptability to stakeholders | Other effects not captured in technical analysis |
|---|---|---|---|---|---|
| Describe intervention Present ICERs and 95% uncertainty interval (with and without time and travel costs) | Judgment made based on quality framework used in this study | Effects of intervention on any special-needs group (indigenous, rural/remote, low SES, non-English speaking background, etc.) | Consider issues with respect to workplace/ training, whether the intervention can be provided under current institutional arrangements and financing mechanisms, and whether the implementation is likely to be easy or hard | Document key issues, particularly for funders, providers, and recipients of intervention | Document any important spillover effects (both positive and negative) attributable to the intervention |
| **Decision points** | Judgment | Judgment | Judgment | Judgment | Judgment |
| **Policy issues** | Overall summary here (e.g., strong economic grounds to accept), but key decision points are (*a*) summary of implications regarding the design (and any need for redesign), (*b*) evaluation, or (*c*) piloting of the intervention. | | | | |

DALY, disability-adjusted life year, ICERs, incremental cost-effectiveness ratios; SES, socioeconomic status.

(McGorry et al. 2009). There is also some Australian evidence suggesting that childhood anxiety disorders can be prevented (Bayer et al. 2009). Although the existing reviews cover many potential interventions, the list is substantially reduced when the selection criteria for interventions within the current project are applied (particularly the requirement around evidence of effectiveness using diagnostic criteria). There is also a substantial body of literature evaluating interventions designed to prevent behavioral disorders in children (mostly parenting strategies). The main limitation of this literature is the lack of diagnostic outcomes at follow-up. Furthermore, conduct disorder has not been included in the burden of disease studies to date; therefore, many of the parameters required for economic modeling were not available within the time context of the project.

Preventive interventions for adult depression, postnatal depression, childhood/adolescent depression, psychosis, childhood anxiety, and suicide have been evaluated. Interventions for reductions in alcohol and cannabis use have also been evaluated within ACE-Prevention, although they are modeled as risk factor reductions with implications broader than substance abuse (e.g., reductions in cancer and injuries) and thus are not included in the current review. Interested readers are referred to a report detailing the reduction in alcohol use (Doran et al. 2009) and to a PhD thesis detailing the reduction in cannabis use (Tay-Teo 2009).

It is beyond the scope of this article to discuss at length the details of how each of the evaluations was undertaken; rather, a synopsis of this work is provided that focuses on the interventions evaluated and that summarizes results presented. Further information is available from the first author of this review.

## Adult Depression

Only three reviews focused on studies of preventive interventions that diagnostically measured depression at follow-up (Cuijpers et al. 2005, 2007, 2008). The most recent of these evaluated psychological interventions designed to prevent major depressive disorder and included interventions aimed at adults and children. An update of this study was conducted for the purposes of the ACE-Prevention project, which resulted in the inclusion of one additional study (Seligman et al. 2007). Pooling all the studies into an average intervention was not possible because they targeted different groups (e.g., children and adults) and were phenomenologically different. The first intervention modeled had particular merit for Australia because it was set in primary care (primary care serves as the health system gatekeeper in Australia) and involved opportunistic screening of the general population. People who screened positive, that is, showed elevated signs of depressive symptoms, were then referred for further assessment and offered a brief bibliotherapeutic intervention developed in the Netherlands (Willemse et al. 2004). The second intervention consisted of a similar screening process except an average group-based psychological intervention was offered that was based on four studies that were conducted in adult populations (Allart-van Dam et al. 2003, 2007; Munoz et al. 1995; Seligman et al. 1999, 2007).

A five-year Markov model was developed to evaluate the cost-effectiveness of these interventions. This was a variation to the modeling approach adopted by ACE-Prevention because the longer-term epidemiology of depression is not well evaluated (Vos et al. 2004, 2005a). The comparator to both interventions was current practice in Australia. The effectiveness of the brief bibliotherapy intervention was based on the Willemse et al. (2004) trial, and the effectiveness of the more intensive psychological intervention was based on the Cuijpers et al. (2008) meta-analysis (which consisted of more studies with minimal evidence of heterogeneity). A decay function of 50% was built into the effectiveness measure after the first year because the longer-term effectiveness of such interventions is not well investigated, with

limited evidence suggesting effect decay over time. A recent paper describes this work in detail (Mihalopoulos et al. 2011).

## Postnatal Depression

An update of two previous meta-analyses (Cuijpers et al. 2008, Dennis 2005) evaluating interventions designed to prevent postnatal depression (PND) was undertaken. This involved a systematic search for all studies published after the Dennis (2005) review, with an emphasis on studies using standardized diagnostic criteria at baseline and follow-up. Eight studies (Austin et al. 2008; Brugha et al. 2000; Elliott et al. 2000; Gorman 2001; Hagan et al. 2004; Munoz et al. 2007; Priest et al. 2003; Zlotnick et al. 2001, 2006) were used in the final analysis and were similar enough for a generic intervention pathway to be specified and evaluated. The measure of intervention effectiveness from this meta-analysis was used, again with a 50% decay rate after the first year. The intervention consisted of a brief screening contact undertaken during a routine antenatal care visit to ascertain eligibility plus six group-based psychological contacts. The theoretical orientation of the intervention was cognitive behavioral or interpersonal therapy in nature.

The modeling approach used was consistent with the adult depression approach, although variations in the time horizon (to one year) were undertaken as part of a sensitivity analysis.

## Childhood/Adolescent Depression

The main intervention for the prevention of childhood/adolescent depression is based on a meta-analysis of eight studies that all use a brief screening tool (usually within a school setting) designed to identify at-risk children/adolescents (i.e., showing elevated levels of depression) (Arnarson & Craighead 2009; Clarke et al. 1995, 2001; Garber et al. 2009; Gillham et al. 2006; Sheffield et al. 2006; Stice et al. 2008; Young et al. 2006). Students who screen positive are then further assessed to determine intervention eligibility

and are offered up to 12 sessions of group-based psychological therapy (largely cognitive-behavioral in nature).

The recent study by Stice et al. (2008) included a second intervention arm based on a brief bibliotherapeutic intervention. The effectiveness in this study appeared to be similar to the more intensive psychological intervention. However, this is the only study (using a small sample size) that has evaluated such a brief intervention; therefore, results must be cautiously interpreted. The pathway for this intervention is similar to the psychological intervention pathway except that eligible students receive only a therapy manual.

Parenting interventions to prevent childhood/adolescent depression have also been evaluated (either parents diagnosed with depression or parents of recently bereaved children) (e.g., Beardslee et al. 1997, 2007; Sandler et al. 2003; Wolchik et al. 2002). Unfortunately, technical issues with these studies (e.g., "any" mental disorder was the outcome in one of the studies) meant that a meta-analysis was not possible to assess their effectiveness or to even use individually.

As with the previous two depression evaluations, the modeling approach consisted of a five-year time horizon, with many parameters based on the adult model because the literature did not contain sufficient information about childhood/adolescent depression.

## Psychosis

There is a small literature evaluating the merit of treating youth judged to be at ultra-high risk of psychosis to prevent the advent of a psychotic disorder. Australian research has developed a method of identifying such young people (McGorry et al. 2002a). McGorry and colleagues (McGorry et al. 2002b, Yung et al. 2007) evaluated a specific preventive intervention comprising pharmacotherapy (low-dose risperidone), cognitive therapy, and supportive psychotherapy as required. Morrison and colleagues (Morrison et al. 2004, 2007) evaluated a cognitive therapy–based intervention, and

McGlashan et al. (2006) compared olanzapine to placebo. All interventions were different in nature. We modeled the McGorry et al. (2002b) intervention because it contained the major elements of each of the existing interventions and was the most representative, though the pooled measure of effectiveness from all three studies was used. The costs of this intervention have also been evaluated and published (Phillips et al. 2009) and are representative of Australian costs.

Because the evidence base surrounding such interventions is suggestive of a delay to psychosis progression, rather than prevention, a one-year model was used to assess the cost-effectiveness.

## Childhood Anxiety

Recent evidence from Australia suggests that interventions for parents of inhibited preschoolers may prevent the onset of anxiety disorders (Dadds et al. 1997, Kennedy et al. 2009, Rapee et al. 2005). The intervention by Rapee et al. (2005) was modeled for ACE-Prevention because it had good evidence of effectiveness that appears to be sustained over time. In this intervention, children are screened for an inhibited temperament within a preschool setting using a brief screening questionnaire. The parents of children who meet the criteria for screening are subsequently offered a six-session parenting program.

A three-year Markov model was developed to assess the cost-effectiveness of this intervention because recent longer-term evidence of effect (up to three years) is available (Rapee et al. 2011). Second, similar to the other interventions, epidemiological estimates are limited for anxiety disorders in young children.

## Suicide

Although suicide is not a formally diagnosed mental disorder, the risk of suicide is considerably higher in those with mental disorders (Harris & Barraclough 1998). It is argued that the appropriate recognition and treatment of mental disorders (particularly depression and schizophrenia) may be the most effective way of reducing suicide (Mann et al. 2005). The impact of this is covered under other work within the ACE-Prevention and ACE-Mental Health projects (Vos et al. 2005b), particularly for interventions pertinent to major depression (both prevention and treatment). The suite of suicide-prevention interventions evaluated within the ACE-Prevention context targets those who attempt suicide (regardless of whether they have a mental illness).

The choice of interventions was based on a review of the existing literature. A comprehensive systematic review of all interventions was not feasible because the suicide literature is large. Instead, we started with existing recent reviews (Beautrais et al. 2007, Guo et al. 2003, Hawton et al. 1999, Hepp et al. 2004, Mann et al. 2005). These reviews report good evidence associated with reduced access to means and raising awareness and screening for mental disorders, as well as some specific interventions that have occurred in military settings (which have very limited generalizability to routine healthcare settings). There is also emerging evidence for indicated interventions, particularly targeting people who have deliberately self-harmed. The following four interventions were evaluated:

1. Problem-solving therapy after deliberate self-harm;

2. Emergency contact cards after deliberate self-harm;

3. Reduced access to means—gun ownership legislation with an associated gun buy-back scheme; and

4. Responsible media reporting of suicide via active dissemination of responsible media reporting guidelines and education of media professions (e.g., the Mindframe National Media Initiative in Australia; **http://www.mindframe-media.info/**).

A full economic evaluation was conducted only on interventions 1 and 3. A meta-analysis found intervention 2 to be ineffective, and a threshold analysis was conducted on

intervention 4 because a quantitative measure of effectiveness was not available.

A lifetime Markov model on the numbers of people who deliberately self-harm was constructed to assess the cost-effectiveness of the above interventions, with reductions in episodes of deliberate self-harm as the key measure of benefit.

## Results

The advantage of a project such as ACE-Prevention is that economic and epidemiological methods are standardized as far as possible, evaluation principles are clearly specified, and best available evidence is utilized. Recommendations regarding the relative cost-effectiveness of different interventions are therefore far less subject to methodological confounding. **Table 4** contains the cost-effectiveness results of the 11 preventive interventions for mental disorders, along with brief comments about the most important second-stage filter considerations. Most interventions fall below the "$50,000-per-DALY-prevented" value for money criterion and represent either "excellent" or "very good" value for money. Only two interventions are not cost-effective: the gun legislation and buy-back scheme for the reduction of suicide and emergency contact cards for the reduction of episodes of deliberate self-harm. Three interventions have very high probabilities of being cost-effective and are based on sufficient levels of evidence: problem-solving therapy intervention for deliberate self-harm, screening and psychological treatment for childhood/adolescent depression, and screening and parenting intervention to reduce childhood anxiety. Although treatment for youth at ultra-high risk of psychosis has a high probability of being cost-effective, it is based on "likely" evidence of effectiveness. The three adult depression (including PND) interventions are also cost-effective although they are based on credentials of effectiveness that are less strong. Responsible media reporting is likely to be "very cost-effective"; however, the evidence

of effectiveness was based on a single ecological study.

Scatter plots are another way of graphically demonstrating the uncertainty associated with the ICER calculations. As an example, **Figure 2** is the scatter plot of the adult depression interventions. It shows that in 18% of uncertainty simulations, the brief bibliotherapy intervention is not cost-effective; in comparison, only 4% of the uncertainty iterations for the group-based intervention are cost-ineffective. However, the median ICER for brief bibliotherapy was $8,600 per DALY averted (deemed very good value for money) compared to $23,000 per DALY averted for the group-based psychological intervention (good value for money).

## Other Second-Stage Filter Considerations

Although the results presented in **Table 4** may be compelling, the cost-effective interventions cannot be adopted in an uncritical fashion because there are important second-stage filter considerations. For example, the evidence base upon which each intervention is modeled differs widely. The evidence base for problem-solving therapy to reduce deliberate self-harm/suicide has been classified as "sufficient," whereas the evidence base for treatment of youth at ultra-high risk is classified as "limited." Similarly, the evidence base for psychological therapy to prevent childhood/adolescent depression is considered "sufficient," whereas the evidence base for responsible media reporting is classified as "likely." Second, the impact of sensitivity testing of the results varies across the interventions. For example, extensive sensitivity testing of the bibliotherapy intervention to reduce adult depression showed that the results were robust, whereas the intervention for youth at ultra-high risk was more sensitive to model assumptions (particularly around the size of cost offsets). Third, many of these interventions are ideally delivered by psychologists who currently are not publicly funded to provide such interventions within the Australian context (e.g., public financing

of psychological therapy is largely restricted to the treatment of diagnosed disorders). Fourth, there may be important acceptability considerations for many of these interventions, particularly around screening of children for mental health problems. Last, there may be important flow-on effects that have not been captured in these initial analyses and that may contribute to the altered cost-effectiveness of the interventions. Screening for symptoms of depression, for example, is likely to detect untreated disorders and provide a mechanism for these people to access treatment.

## CONCLUSIONS

### Policy Recommendations

The ACE-Prevention project has demonstrated that a number of preventive interventions for mental disorders are cost-effective, have good evidence of effectiveness, and certainly need to be considered in any package of health-promotion and illness-prevention initiatives.

Problem-solving therapy for people who deliberately self-harm and screening children/adolescents for symptoms of depression with subsequent provision of psychological therapy deserve special mention. Both are well evaluated and, importantly, have evidence of both efficacy and effectiveness—that is, evidence that they work under routine health-service conditions as well as in controlled experimental conditions. Hence both are recommended for widespread adoption.

The parenting intervention for childhood anxiety prevention is also very cost-effective, although the evidence base—classified as "sufficient" because it is a high-quality randomized trial—is an efficacy study, and the effect in routine health-service provision needs to be demonstrated.

Also recommended for adoption are a number of other cost-effective preventive interventions for mental disorders (e.g., screening for minor depression in adults for the prevention of depression and PND and treatment for youth

at ultra-high risk of psychosis), although these interventions would need to be accompanied by rigorous evaluation to expand the evidence base. We recommend that funding continue for the Australian media initiative to promote responsible reporting of suicide, even though the evidence base is "likely." This is a low-cost intervention, and very few suicides would need to be averted to make it cost-effective.

### Strengths and Limitations of the ACE-Prevention Approach for Mental Disorders

The ACE-Prevention study is a significant development that more than doubles the cost-effectiveness evidence base for health promotion in Australia. Important limitations of the ACE approach serve to highlight the difficulty of undertaking comparative economic evaluations for healthcare priority setting within local contexts. It is fortunate that there are key national databases in Australia upon which to base such economic analyses; an important one is the National Survey of Mental Health and Well Being (Aust. Bur. Stat. 1998, 2008). However, such databases cannot provide researchers with all the information required to undertake comprehensive economic analyses. Therefore, other sources of information are required that are sometimes not evidence based. For example, it is difficult to know how many general practitioners or schools would be willing to provide screening to identify people at risk of developing a mental disorder. We make educated estimates, but they are nevertheless only estimates. The paucity of epidemiological information for many mental disorders is particularly striking. Although there are longitudinal community surveys of the key mental disorders in the literature, these studies do not provide all the necessary information required for economic modeling; a common limitation is the duration of active symptomatology over time. This has meant that shorter modeling time frames have been undertaken for many of the interventions designed to prevent mental disorders.

**Table 4  Results: incremental cost-effectiveness ratio (ICER), number of disability-adjusted life years (DALYs) averted, intervention costs and healthcare cost savings, strength of evidence, and major issues identified in the second-stage filter analysis**

| Topic area | Intervention | ICER | | | DALYs averted | Intervention costs (millions of dollars) | Cost-offsets (millions of dollars) | Proportion of uncertainty iterations falling below $50,000 per DALY-averted threshold | Strength of evidence | Major second-stage filter issues |
| | | Median | Lower uncertainty interval[1] | Upper uncertainty interval[1] | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Adult depression | Screening and bibliotherapy for prevention of adult depression | 8,600 | — | — | 2,600 | 37 | -27 | 82% | Likely | General practitioner willingness to screen |
| Adult depression | Screening and group psychological treatment for prevention of adult depression | 20,000 | 12,000 | 66,000 | 1,700 | 38 | -11 | 96% | Likely | |
| Postnatal depression | Screening and psychological treatment for prevention of postpartum depression | 15,000 | — | — | 370 | 6.9 | -6 | 76%–87%[2] | Limited | Feasibility of antenatal screening |
| Childhood and adolescent depression | Screening and psychological intervention for the prevention of childhood/adolescent depression | 5,400 | 1,400 | 32,000 | 5,800 | 48 | -4 | 98% | Sufficient | Feasibility and acceptability in school setting and treatment of children without full-blown disorder |
| Childhood and adolescent depression | Screening and bibliotherapy for the prevention of childhood/adolescent depression | 180 | — | — | 5,800 | 3.6 | -0.8 | —[3] | Limited | |

| | Intervention | | | | | | | | Evidence | |
|---|---|---|---|---|---|---|---|---|---|---|
| Self-harm/suicide | Problem-solving therapy for reduction of deliberate self-harm (suicide) | Dominant | Dominant | Dominant | 260 | 4.0 | -16 | 100% | Sufficient | Workforce availability to provide intervention |
| Self-harm/suicide | Emergency contact cards for the reduction of deliberate self-harm (suicide) | — | — | — | — | — | — | — | No evidence of effectiveness | |
| Self-harm/suicide | Gun ownership legislation and gun buy-back scheme for reduction in suicide | 53,000 | 38,000 | 68,000 | 11,000 | 560 | -5.5 | 40% | May be effective | |
| Self-harm/suicide | Responsible media reporting for reduction of suicide | 170 | — | — | 1,400 | 1.0 | — | —[4] | Likely (ecological evidence) | |
| Psychosis | Treatment for individuals at ultra-high risk for psychosis | Dominant | Dominant | Dominant | 180 | 8.4 | — | 96% | Likely | Workforce availability and treatment fidelity outside Orygen Youth Health in Australia |
| Anxiety | Parenting intervention for prevention of childhood anxiety disorders | 7,000 | 2,600 | 20,000 | 390 | 4.0 | -1.2 | 100% | Sufficient | Feasibility and acceptability of screening in preschool setting |

[1] No uncertainty interval is presented for some of the interventions because the simulation results include negative ICERs, which cannot be meaningfully interpreted within an interval range. The point-estimate median values are based on the full 2,000 uncertainty iterations.

[2] Note that two methods were used to estimate health improvement for postnatal depression. The second method was more conservative than the first (though the first method is more comparable to the other depression evaluations and is reported in the cost/DALY column). The probability of 76% refers to the second, more conservative method of modeling, and 87% refers to the first method. Please refer to the postnatal depression briefing paper (Mihalopoulos 2009) for further information regarding these methods.

[3] Uncertainty calculations were not conducted for this intervention because it was included as a comparative intervention. It is not a likely contender for routine service implementation at this stage given the very scant evidence upon which the ICER calculations are based.

[4] Uncertainty was not conducted for this intervention because the analysis was primarily a threshold analysis, and the scant evidence of effectiveness is based on one ecological study.

—, parameter was not estimated for the intervention
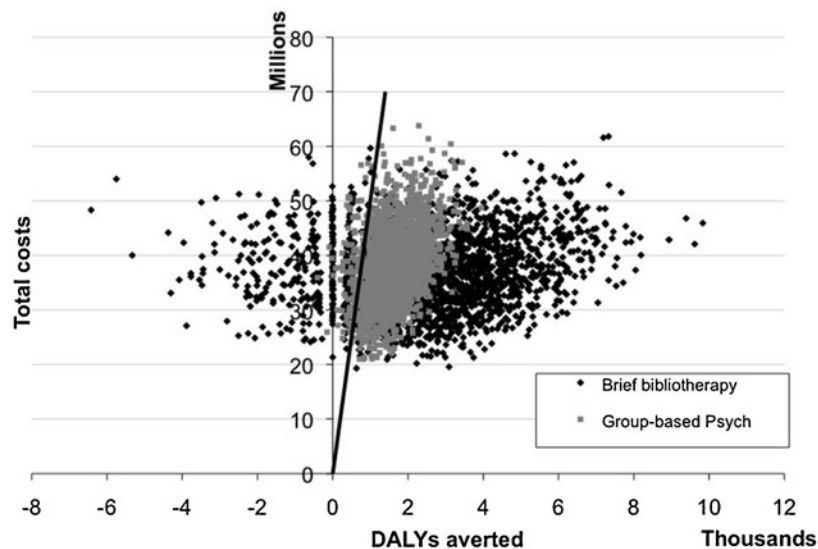
Notes: This diagram represents the top 2 quadrants of a cost-effectiveness plane with the right quadrant showing that the intervention is more costly and more effective and the left quadrant showing that the intervention is more costly and less effective (lose:lose quadrant). The black line represent the $50,000/DALY threshold with iterations to the right falling below this threshold and iterations to the left falling above the threshold.

### Figure 2

Scatter plot of 2,000 uncertainty iterations with $50,000-per-DALY threshold cut-off (source: Mihalopoulos et al. 2011).

The Australian Burden of Disease studies provide a strong epidemiologic database for many analyses because a consistent approach to epidemiologic parameters such as incidence, prevalence, and mortality has been undertaken in these studies. However, the burden-of-disease studies are also susceptible to literature gaps, which vary across the various diseases and disorders. Notably, there is very little information regarding anxiety disorders in younger children. Furthermore, although the disability weight for most diseases/disorders within the ACE framework are sourced from the burden-of-disease studies, the way they are derived is not entirely consistent across all areas, and certainly there is little variation in weights used within diseases/disorders (for example, the same weight is used for depression in children and adults; Begg et al. 2007). This is problematic for disorders that affect children and adults, who may differentially experience and weight the problems associated with such

disorders. The burden-of-disease estimates are also not comprehensive—there are currently no estimates for conduct disorder, for example. This is unfortunate because there is currently reasonable evidence suggesting that parenting interventions such as the Australian Triple P-Positive Parenting Program can provide good value for money in reducing conduct disorders (Mihalopoulos et al. 2007).

Although consistency in assessing costs is paramount in the ACE approach, this may have differential impacts across the different diseases/disorders, particularly with the adoption of a health sector perspective. Mental disorders in particular are likely to incur costs in sectors outside the health sector, such as the welfare or judicial sectors. Such costs are not present in the database used to estimate the cost off-sets associated with the prevention of the various diseases/disorders (Aust. Inst. Health & Welfare 2005). This means that the estimates of cost offsets used in ACE underrepresented

the true cost savings associated with such disorders. However, the extent to which preventive interventions really affect such costs is an empirical issue, and very few economic evaluations undertaken alongside the trials of such interventions measure such consequences. For example, the study by Foster & Jones (2007) of the Fast Track intervention to reduce problematic behaviors in children, including conduct disorder, did not include judicial cost offsets, which have been shown to be a substantial cost component associated with conduct disorder (Scott et al. 2001). It is imperative that future research into preventive interventions for mental disorders includes such costs to ensure that the true impact of these interventions is captured.

In addition, the time frame of the efficacy/effectiveness studies upon which these analyses are based is short. This is not unique to the mental disorder interventions; however, it means that the true impact of the interventions cannot be accurately determined because assumptions around the longer-term effectiveness are inevitably made.

## Final Thoughts

The ACE approach is not unique to the Australian context. It can be adapted for use in other healthcare contexts. For example, the approach is being used in the United States to evaluate obesity-prevention interventions, and a new study will commence soon in New Zealand to evaluate cancer control interventions and prevention of other lifestyle diseases.

It has also been used in developing countries to evaluate healthcare priorities (an example is the SPICE project in Thailand, which has included mental health interventions). The Australian ACE team has successfully translated the methods to these settings by training local evaluators and providing ongoing input. Importantly, the ACE approach should not simply constitute one-off projects. The science of healthcare provision is not static but rather evolving, and the cost-effectiveness of interventions can change markedly as new interventions and evidence emerge. It is hoped that such methods continue to be used in mental healthcare for both preventive and treatment intervention options.

Last, whether studies such as ACE-Prevention meet their key purpose—to be useful to decision makers within the health policy context—remains to be seen. Certainly within Australia, the commissioning of ACE studies by government (over and above studies funded by competitive research grants) is encouraging. It is also incumbent on researchers to make their work available and understandable to decision makers. With this in mind, the ACE-Prevention team has been undertaking "road shows," where it has presented results to government departments in Australia and New Zealand to maximize dissemination and knowledge transfer. There is strong interest at present in the final report of the ACE-Prevention study (released in September 2010). We remain optimistic that our efforts at dissemination will bear fruit and that our results will impact health policy and funding decisions and will improve healthcare practice.

## SUMMARY POINTS

1. A number of effective interventions/programs are designed to prevent mental disorders. However, deciding which interventions should be funded is not straightforward because healthcare resources are limited, and there are many competing demands.

2. Assessing Cost-Effectiveness (ACE) is an innovative priority-setting approach based on economic principles developed in Australia to assist with the difficult task of allocating healthcare resources. ACE combines technical rigor in economic appraisal with implementation analysis to ensure that results are comparable and relevant for decision makers.

3. ACE-Prevention is the most recent ACE study within Australia and included, among the 150 interventions evaluated, 11 preventive interventions for mental disorders and suicide.

4. Interventions designed to prevent adult and childhood depression, suicide, and childhood anxiety provide very good value for money. Problem-solving therapy for people who deliberately self-harm and treatment for youth who are at ultra-high risk for psychosis save more resources than they cost. Interventions that are less cost effective include tightened gun-ownership legislation plus a gun-buyback scheme to reduce gun-related suicides, and emergency cards for people who deliberately self-harm (which have no evidence of effectiveness).

5. The quality of evidence upon which the evaluations are based needs to be considered before recommendations for widespread adoption or further evaluation can be made (e.g., most studies have short-term follow-up). Furthermore, issues such as the acceptability and feasibility of the interventions within individual contexts need to be considered before recommendations for widespread adoption are made.

6. The ACE approach could be applied to preventive interventions for mental disorders, although important gaps in the epidemiological information available for many of the disorders evaluated meant that some of the preferred modeling methods of ACE could not be realized (particularly a lifetime modeling approach).

7. The ACE methodology can be applied in different healthcare contexts, including but not limited to mental healthcare sectors. Appropriate modification to account for different health system designs and issues, such as data tractability and comparability, needs to be considered to ensure that the approach remains robust.

## DISCLOSURE STATEMENT

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Errata

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