**Supplementary appendix**

This document presents a full description of methods used to model the cost-effectiveness of delivering universal and indicated school-based interventions to prevent the onset of depression in Australian youth aged 11-17 years.

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# Broad overview of the decision analytic model

### Overview

This document seeks to supplement the methods presented in the manuscript entitled, ‘The population cost-effectiveness of delivering universal and indicated school-based interventions to prevent the onset of major depression among youth in Australia’. In this economic evaluation study, we developed a decision-analytic model to calculate the costs and benefits of implementing several interventions to prevent depression in youth, aged 11-17 years old, in the Australian context. The various sections in this document are as follows:

* Section 1 outlines: the approach used to conduct the decision analytic model, the choice of intervention pathways, and the rationale for using various data sources in the model;
* Section 2 provides a detailed description of the meta-analysis of intervention effect sizes;
* Section 3 outlines the process used to calculate the eligible population when implementing intervention pathways in the Australian context;
* Section 4 describes the methods and data used to model health benefits;
* Section 5 describes the methods and data used to conduct the cost analysis of intervention pathways; and
* Section 6 describes the methods and data used to conduct univariate sensitivity analyses described in the main manuscript.

### Analytic scope of the model

The original research question guiding the development of our decision-analytic model was,

‘What is the comparative cost-effectiveness (i.e., value for money) of different interventions for the prevention of depression in Australian youth aged 5-17 years?’

A search of the literature was unable to find a comprehensive randomised control trial (RCT) evaluating the cost-effectiveness of multiple prevention interventions targeting youth in the Australian context. In the absence of a definitive RCT study by which to conduct an accompanying economic evaluation (i.e., trial-based economic evaluation), we developed a decision-analytic model that used, ‘mathematical relationships to define a series of possible consequences that would flow from a set of alternative options being evaluated’ [1]. The decision-analytic model that we developed would apply a systematic approach to decision making under uncertainty; such that it would account for variability and uncertainty associated with accompanying policy decisions [1].

The starting point for the analysis was to identify all evidence-based interventions for the prevention of depression in youth (aged between 5-17 years) that are: (1) suitable for implementation in the Australian context; and (2) have strong evidence of effectiveness. For the purposes of the decision-analytic model, we sought to use the strongest level of evidence designated by the Australian National Health and Medical Research Council (NHMRC) – i.e., systematic reviews of randomised control trials [2]. Briefly, a meta-review was conducted by Stockings et al. [3] which identified all relevant RCT studies on the prevention of depression in youth that have been identified by previous systematic reviews of the literature (including a Cochrane systematic review by Merry et al. [4]). From the meta-review, we identified several intervention types that were suitable for implementation in the Australian context and had multiple RCTs that could be combined in a meta-analysis. These included: (1) universal prevention involving group-based psychological interventions delivered to all participating school students; (2) indicated prevention involving group-based psychological interventions delivered to students with subthreshold depression; and (3) indicated prevention involving self-help bibliotherapy delivered to students with subthreshold depression. Group-based psychological interventions typically involved: a teacher or external facilitator; delivering a series of intervention modules based on psychotherapeutic approaches such as CBT; to a group of students in the classroom setting. By contrast, self-help bibliotherapy involved students reading a book containing adapted psychotherapeutic modules.

Additional studies were found with regards to several selective prevention interventions (e.g., interventions targeting children of parents with a mental illness or interventions targeting children from low socioeconomic backgrounds). However, many of these selective prevention studies were considered too heterogenous to combine in a meta-analysis, or were deemed to have insufficient internal validity (i.e., poor evidence of effectiveness) or external validity (i.e., generalisability to the Australian context).

It should be noted that the inclusion criteria for our meta-analysis encompassed RCTs that reported intervention outcomes as a discrete variable denoting the change in the number of incident cases of major depression following intervention. This was regardless of whether the RCT study evaluated these changes using structured clinical interviews (i.e., the gold standard) or were based on the number of people who scored above an established cut-off on a validated symptom screening scale for depression. The inclusion criteria meant that we excluded all RCTs that reported intervention outcomes as a continuous variable – i.e., changes to the mean (and standard deviation) score on a depression symptom rating scale. The reason why we excluded studies that reported outcomes as a mean score on a depression symptom rating scale was due to the methodological difficulties involved with translating these mean scores into a corresponding number of depressive cases in the sample.

Most interventions identified in the previous meta-review encompassed the age range between 11-17 years. This age range is significant as it was the same age range modelled in the previous economic evaluation study by Mihalopoulos et al. [5] (and from which this cost-effectiveness model is adapted). We conducted a separate meta-analysis to calculate the pooled intervention effect size when limiting the scope of studies to those using an age range of 11-17 years versus an age range of 5-17 years. From this, we found that there were negligible differences when restricting the scope of studies to the ages 11-17 years. As such, we chose to meta-analyse intervention effect sizes for all RCT studies including youth aged 5-17 years; while limiting the scope of our model to ages 11-17 years to maintain consistency with the previous model by Mihalopoulos et al. [5].

Based on the findings outlined above, we refined our original research question to ask,

‘What is the comparative cost-effectiveness (i.e., value for money) of universal and indicated school-based interventions for the prevention of depression in Australian youth aged 11-17 years?’

Most RCT studies identified by the meta-review encompassed preventive interventions that are delivered through a face-to-face modality (e.g., teachers presenting intervention modules didactically in the classroom). There is emerging interest in the use of internet-delivered interventions for the treatment and prevention of depression and other mental disorders (i.e., completing online intervention modules using a computer with access to the internet) [6-8]. As a secondary research question, we sought to compare the cost-effectiveness between preventive interventions (both universal and indicated) that are delivered through either face-to-face or internet-delivered modalities

### Rationale for data sources chosen to model intervention pathways

Our baseline analysis modelled intervention pathways using best available information on costs and benefits from a range of data sources for demography, disease epidemiology and burden, health system costs and cost offsets that best describe services in the Australian context. In the absence of Australia-specific information, we used data from intervention trials (i.e., RCTs on intervention efficacy identified via the previous meta-review) to inform decision modelling. Assumptions were made to fill data gaps for several model parameters which were tested in subsequent univariate sensitivity analyses.

The structure of the decision-analytic model was based on intervention pathways adapted from the intervention literature (i.e., RCT studies for each broad intervention type identified in the previous meta-review). Our model involved a comparative analysis – i.e., it compared the total benefits and costs that would occur in a scenario where an eligible population cohort undertook the intervention versus a scenario where the same cohort does not undertake the intervention. Modelling intervention pathways encompassed three broad components: (1) determining the eligible population who will participate in an intervention; (2) calculating the total health impacts that occur with (and without) the intervention, by simulating how each eligible cohort transitions between different health states over time; and (3) calculating the accompanying costs and cost offsets that result from the intervention pathway.

We briefly discuss the rationale for choosing different data sources in the model with regards to: the eligible population for each intervention pathway (see Table 1); modelling health benefits (see Table 2); costing intervention pathways for universal prevention (see Table 3); and costing intervention pathways for indicated prevention (see Table 4). It should be noted that there were insufficient data to calculate pooled intervention effect sizes for universal and indicated prevention interventions delivered via the internet (see section 2.6). As such, we made a series of assumptions to impute effect sizes which, in turn, relegated this analysis to a separate sensitivity analysis (see section 6.10). We have, for convenience, included a description of cost parameters for internet-delivered prevention in Table 3 and Table 4, though we would point out that these were only used in the sensitivity, and not the baseline, analysis.

Complete methods and data pertaining to each of these modelling components are discussed in more detail in sections 3 to 5.

* + - 1. Rationale and description of various data sources used to determine the eligible population [[1]](#footnote-1)

| Input parameter  *(applicable intervention types)* | Data source and rationale |
| --- | --- |
| 2013 Australian population  *(both universal and indicated)* | The starting population for our model was the 2013 Australian population based on demographic data from the Australian Bureau of Statistics [9]. Population data (by age and sex) are presented in Table 7 for universal prevention and Table 10 for indicated prevention. |
| % of Australian schools that participate in the intervention  *(both universal and indicated)* | Obtaining a reliable estimate on the likely participation rate among Australian schools is problematic (see section 3.2). We were unable to find a reliable data estimate that could be used to accurately predict the number of schools that would participate in a universal and/or indicated psychological prevention intervention if it were to be scaled up nationally. The true coverage rate is dependent on how successful the nationwide implementation of these programs would be (which is a question beyond the scope of our model).  We consequently assumed that all Australian schools (i.e., 100%) would participate in the intervention. We acknowledge that this is practically infeasible. However, assuming 100% school coverage allows us to calculate the potential health benefits and costs that would arise from the full-scale, nationwide implementation of the universal prevention program. Furthermore, changing the value of this parameter will have a negligible effect on the final ICER as both costs and health benefits will be reduced proportionally to each other – e.g., assuming a 50% coverage rate will lead to both a 50% reduction of total DALYs and a 50% reduction in total costs. Likewise, assuming a 25% coverage rate will lead to both a 75% reduction in total DALYs and a 75% reduction in total costs, relative to a 100% coverage rate.  It follows that using a baseline of 100% gives us the option to calculate the total benefits and costs that would occur at any coverage rate less than 100%. All you have to do is multiply the desired coverage rate (e.g., 50%) by the total DALYs and total costs calculated in the baseline model assuming 100% coverage. In any case, the final ICER will remain approximately the same. |
| Screening for students with elevated depressive symptoms  *(indicated only)* | Identifying the eligible population for indicated prevention involves screening students to identify those who have elevated depressive symptoms but do not have a diagnosis of major depression.  The best nationally representative data source on the proportion of students who have elevated depressive symptoms (calculated using the CES-D depression rating symptom scale) was the Child and Adolescent component of the 1997 National Survey of Mental Health and Wellbeing (NSMHWB) [10]. This population representative survey conducted CES-D screening among youth aged 13-17 years to identify those who have clinically significant depressive symptoms (i.e., score above a cut-off of 16). Data for this parameter are presented in Table 8. |
| % of students who have elevated depressive symptoms and agree to undergo further diagnostic testing  *(indicated only)* | Students who are identified as having elevated depressive symptoms need to undertake further diagnostic testing (i.e., a structured clinical interview) to ascertain if their elevated depressive symptoms are due to a diagnosis of major depression (or not). Three RCT studies identified in the previous meta-review of intervention efficacy (included in Table 6) contained data on the proportion of students who are screened using a depression symptom rating scale and subsequently agree to participate in further diagnostic testing. We meta-analysed data from these studies to calculate the pooled proportion of students who agree to participate in further diagnostic testing. The forest plot for this meta-analysis is shown in Figure 12 |
| Identifying students who have elevated depressive symptoms but do not have a diagnosis of major depressive disorder  *(indicated only)* | Of the students who have elevated depressive symptoms and agree to participate in further diagnostic testing, we now calculate what proportion of these have a diagnosis of major depression.  There is additional data from the Child and Adolescent component of the 1997 NSMHWB on the proportion of students who score above the CES-D cut-off and also have a diagnosis of major depression. We are interested in calculating the inverse of this – i.e., determining the number of students who have elevated symptoms but have no diagnosis of depression. Students who fit this criteria were classified as having subthreshold depression. Data for this parameter are presented in Table 9. |
| % of students who agree to participate in the intervention  *(both universal and indicated)* | In the case of universal prevention, six RCT studies identified in the previous meta-review of intervention efficacy (included in Table 5) contained data on the proportion of students who obtain parental consent to participate in the universal prevention intervention. We meta-analysed data from these studies to calculate the pooled proportion of students who agree to participate in the universal psychological intervention. The forest plot for this meta-analysis is shown in Figure 10.  Likewise, five RCT studies identified in the previous meta-review of intervention efficacy (included in Table 6) contained data on the proportion of students who are identified as having subthreshold depression (following screening and further diagnostic testing) and subsequently obtain parental consent to participate in the indicated prevention intervention. We meta-analysed data from these studies to calculate the pooled proportion of students who agree to participate in the indicated psychological intervention. The forest plot for this meta-analysis is shown in Figure 13. |

* + - 1. Rationale and description of various data sources used to model the health impacts that results from intervention and comparator scenarios [[2]](#footnote-2)

| Input parameter  *(applicable intervention types)* | Data source and rationale |
| --- | --- |
| Intervention effect sizes  *(both universal and indicated)* | Information on intervention pathways and intervention efficacy were based on results from the previous meta-review conducted by Stockings et al. [3]. We identified three intervention types that were suitable for implementation in the Australian context and had strong evidence of effectiveness – i.e., universal psychological prevention, indicated psychological prevention and indicated bibliotherapy (N.B. all intervention types involve the face-to-face delivery of intervention material in the classroom by a trained facilitator). For the purposes of the model, we included RCT studies that assessed intervention outcomes in terms of changes to the discrete number of incident cases (i.e., regardless of whether this was measured through structured clinical interviews or cut-offs on a depression symptom rating scale). We excluded studies that measured intervention outcomes in terms of continuous changes in the mean score on a depression symptom rating scale.  The majority of studies reported intervention outcomes at post-intervention and at different follow-up points. We meta-analysed all available RCT studies to calculate pooled intervention effect sizes for each intervention type across four consecutive follow-up periods (i.e., post-intervention, 6-month follow-up, 1-year follow-up and 2-year follow-up). The studies that met inclusion criteria for our decision-analytic model are listed in: Table 5 (for universal prevention); and Table 6 (for indicated prevention). We have listed all relevant study design characteristics in each table and have made a note of the follow-up points in each study for which we had meta-analysable data on intervention outcomes. The results of each meta-analysis by intervention type and follow-up period are presented in sections 2.3 to 2.5.  While conducting the meta-review of intervention efficacy, we found 2 studies examining effect sizes for internet-delivered psychological interventions for the (universal) prevention of depression in youth [11,12]. These 2 studies were, however, excluded as they did not meet inclusion criteria for measuring intervention outcomes as a discrete variable. Given the paucity of data, we opted to model internet-based prevention interventions in the sensitivity analysis by assuming that intervention effect sizes for internet-based preventive interventions are equal to either 100% or 50% of the total effect size of corresponding face-to-face interventions (see section 2.6).  In the baseline models, we used intervention effect sizes that reached the 5% level of significance. Non-significant effect sizes were modelled in a separate sensitivity analysis. |
| Average duration of a major depressive episode  *(both universal and indicated)* | We assumed an average duration of 29.9 weeks, rather than the average duration of 37.7 weeks which was used in the GBD 2013 study. The rationale for this choice was to be consistent with previous studies which examined the burden of disease and cost-effectiveness of depression in Australia (see section 4.2). |
| Incidence of major depression  *(both universal and indicated)* | We obtained population incidence rates for major depression in the 2013 Australian population from the Global Burden of Disease (GBD) 2013 study [13]. These incidence rates were calculated in GBD 2013 by assuming an average disease duration of 37.7 weeks. However, we opted to use an average duration of 29.9 weeks in our model instead (see section 4.2). As such, we adjusted our baseline incidence rates to account for an average duration of 29.9 weeks (see section 4.3 for a description of the methods).  The incidence rates calculated above are applicable to people in the healthy ‘at-risk’ population (i.e., the ‘Healthy population’ health state in the universal prevention model – see Figure 15). Further adjustments were needed to calculate the incidence rate of major depression among youth with subthreshold depression (i.e., the ‘Subthreshold depression’ health state in the indicated prevention model – see Figure 16). Adjustments were made by multiplying baseline population incidence rates taken from GBD 2013 with the incidence rate ratio (IRR) of major depression among youth with subthreshold depression (see section 4.3 and the next parameter below).  Incidence rates for the general Australian population and the subset of youth with subthreshold depression are presented in Table 12. |
| Increased risk of major depression among youth with subthreshold depression  *(indicated only)* | As stated above, baseline population incidence rates were adjusted in the indicated prevention models to calculate the elevated incidence of major depression among youth with subthreshold depression. We conducted a separate meta-review of longitudinal studies that examined the increased risk of major depression among people with subthreshold depression (the findings of this meta-review are yet to be published). From this, we found five studies that could be combined in a meta-analysis to calculate the pooled incidence rate ratio (IRR) of major depression among youth with subthreshold depression relative to the general population. The forest plot for this meta-analysis is presented in Figure 17. |
| Other-cause mortality  *(both universal and indicated)* | Other-cause mortality estimates were based on all-cause mortality estimates derived from deaths data obtained from the Australian Bureau of Statistics [14]. All-cause mortality estimates were converted into other-cause mortality estimates by removing the total number of deaths attributable to suicide as a proxy of deaths attributable to major depression. Suicide data were obtained from the GBD 2013 study [15]. Other-cause mortality estimates are presented by age and sex in Table 13. |
| Case fatality among prevalent cases of major depression  *(both universal and indicated)* | We calculated case fatality rates among people with major depression based on known mathematical relationships between the case fatality rate, other-cause mortality and the relative risk of mortality (see section 4.5). Data on the relative risk of mortality were obtained from a systematic review by Baxter et al. [16]. Case fatality estimates are presented by age and sex in Table 14. |
| Remission of major depression  *(both universal and indicated)* | We calculated remission rates among people with major depression based on known mathematical relationships between remission, case fatality and duration (see section 4.6). |
| Prevalence of major depression  *(universal only)* | Prevalence data were used in the universal prevention model to account for the current prevalence of major depression in the population, prior to the commencement of the intervention. That is, the initial distribution of the eligible population between ‘healthy’ and ‘depressed’ health states at the start of the model time horizon (see state transition diagram in Figure 15). Data on the current prevalence of major depression were obtained from GBD 2013 [13]; with age-sex prevalence estimates shown in Table 15. |
| Disability weight for major depression  *(both universal and indicated)* | We derived a composite disability weight for major depression by calculating the weighted average of GBD 2013 disability weights for mild, moderate and severe depression [17]. The weighted average was based on a severity distribution derived from the GBD study [18]; which calculated the comorbidity-adjusted proportion of mild, moderate and severe depression using validated SF-12 cut-offs from the 1997 National Survey of Mental Health and Wellbeing (NSMHWB) [19].There were several other permutations by which to calculate composite disability weights which we have discussed in section 4.8. Based on this exploratory analysis, we decided to conduct separate sensitivity analyses to test the impact of replacing the baseline disability weight outlined above with: (1) a weighted average disability weight calculated using a severity distribution based on DSM-IV algorithms for the classification of mild, moderate and severe depression in the 1997 NSMHWB; and (2) replacing GBD 2013 disability weights for mild, moderate and severe depression with utility weights sourced from Mohiuddin and Payne [20]. |

* + - 1. Rationale and description of various data sources used to conduct the cost analysis of intervention pathways for universal prevention [[3]](#footnote-3)

| Input parameter  *(Step in intervention pathway)* | Data source and rationale |
| --- | --- |
| *Face-to-face delivery of universal psychological prevention*  The intervention pathway for face-to-face delivery of universal psychological prevention involved teachers delivering psychological intervention modules in the classroom during regular school hours. | |
| Total cost of time spent by (salaried) psychologists to train teachers in how to deliver group-based intervention modules for universal prevention  *(Intervention delivery)* | Prior to the delivery of intervention modules, we assumed that a salaried psychologist would be hired to go to each school to train teachers on how they are to deliver intervention modules. The total number of schools to which these psychologists are required to provide training is calculated as: the total number of teachers across Australia in 2013; divided by the average number of teachers per school. The total number of teachers across Australia in 2013 was calculated by dividing the total number of students (using data on the eligible population in section 3.2) by the average number of students per class (using OECD data [21]). The average number of teachers per school was based on data from an ABS survey of schools [22].  The next step was to calculate the total number of psychologist hours required to provide training to all these schools. We sourced available data from RCTs identified in the meta-review of intervention efficacy (included in Table 5) to calculate a pooled estimate of the average time per school spent by a psychologist (or researcher or program facilitator) to train teachers in how to deliver universal intervention modules. There were a total of 5 studies with relevant data (see section 5.2) by which to calculate a pooled estimate of the total number of hours per school spent by a psychologist (or researcher or trained facilitator) training teachers in a group setting.  Multiplying the average number of hours per school by the total number of school across Australia in 2013 resulted in an estimate of the total psychologist hours required to train all teachers across participating Australian schools in 2013 to deliver the universal psychological intervention. Psychologist time was valued using an hourly wage rate calculated using data from the ABS Employee Earnings and Hours survey [23] (including a 30% loading for on-costs). |
| Total cost of time spent by teachers to deliver group-based intervention modules for universal prevention  *(Intervention delivery)* | We calculated total time spent by teachers delivering face-to-face universal intervention modules across Australia in 2013 by calculating the product of: the total number of teachers across Australia in 2013; the average number of group-based intervention modules; and the average duration of each module.  The total number of teachers across Australia in 2013 was based on the estimate calculated in the previous step. We sourced available data from RCTs identified in the meta-review of intervention efficacy (see Table 5) to calculate a pooled estimate of the average number of intervention modules to be offered as part of the face-to-face delivery of universal prevention. There were a total of 9 relevant studies from which to calculate a pooled estimate of the average number of intervention modules (see section 5.2). These same 9 studies also contained relevant data by which to calculate a pooled estimate of the average duration of each group-based intervention module. The aggregate estimate of teacher’s time spent delivering group-based intervention modules was valued using an hourly wage rate calculated using data from the ABS Employee Earnings and Hours survey [23]; which included a 30% loading for on-costs. |
| Total cost offsets resulting from the reduction in prevalent cases of major depression  *(Cost offsets)* | We included the impact of cost offsets in our baseline analysis – i.e., the costs of treating major depression that are averted due to the reduction in prevalent cases of depression (flowing on from reductions in the incidence of major depression). The average cost per prevalent case of depression was calculated using data from the 2010 AIHW disease expenditure report on the combined expenditures attributable to both depression and anxiety disorders [24]; and using comorbidity data sourced from the 2007 NSMHWB to calculate the expenditures attributable to the total envelope of depression, after excluding anxiety disorders [25]. Total cost offsets were enumerated by multiplying the average cost per prevalent case of depression by the total number of prevalent cases calculated by the health benefit model described in section 4.1. |
| *Internet-based delivery of universal psychological prevention*  The internet-based delivery of universal psychological prevention followed a modified intervention pathway to that used for face-to-face delivery. In this case, we assumed that all eligible youth take time in class to complete online modules. During this time, teachers provide basic supervision while children completed self-directed modules on a school computer (i.e., the teacher monitors the class and provides behaviour management when required, but does not actively guide the students through the completion of modules). This unmoderated form of internet-delivery means that teachers do not require additional training to learn how to facilitate the delivery of intervention modules. | |
| Total annual subscription cost for schools to deliver internet-based modules for universal psychological intervention  *(Intervention delivery)* | We were unable to find a comprehensive estimate on the cost of delivering an online universal intervention – i.e., an estimate inclusive of the cost of developing the content, staff, maintaining servers and other IT infrastructure. As such, we calculated a crude estimate of the annual cost per student of delivering internet-based universal prevention using data on annual subscription fees from THIS WAY UP Schools [26]. The total annual subscription cost across all Australian schools in 2013 was calculated by: multiplying the annual subscription fee per student; by the total number of Australian students in 2013 (this was based on estimates for the eligible population in section 3.2). |
| Cost of time spent by teachers supervising students while they complete online intervention modules  *(Intervention delivery)* | We calculated the total time spent by teachers providing basic supervision to students (while completing online intervention modules using class computers) by calculating the product of: the total number of teachers providing basic supervision to classrooms (based on eligible population data in section 3.2); the average number of internet-delivered intervention modules; and the average duration required to complete each module. While conducting the meta-review of intervention efficacy, we found 2 studies examining effect sizes for internet-delivered universal prevention [11,12]. We sourced data from these studies to calculate pooled estimates of the average number and duration of intervention modules (see section 5.3). The aggregate estimate of teacher’s time spent providing classroom supervision was valued using an hourly wage rate calculated using data from the ABS Employee Earnings and Hours survey [23]; which included a 30% loading for on-costs). |
| Total cost offsets resulting from the reduction in prevalent cases of major depression  *(Cost offsets)* | The method used to calculate cost offsets arising from the internet-delivered intervention pathway for universal prevention was similar to that used in the face-to-face intervention pathway (see above). |

* + - 1. Rationale and description of various data sources used to conduct the cost analysis of intervention pathways for indicated prevention [[4]](#footnote-4)

| Input parameter  *(Step in intervention pathway)* | Data source and rationale |
| --- | --- |
| *Face-to-face delivery of indicated psychological prevention*  The intervention pathway for face-to-face delivery of indicated psychological prevention involves three main steps: (1) screening students at participating schools for elevated symptoms of depression using the CES-D; (2) psychologists conducting further diagnostic testing to identify students without a depression diagnosis; and (3) psychologists delivering group-based psychological intervention modules to eligible students. | |
| Total cost of time spent by (salaried) psychologists to train teachers in how to administer the CES-D screening tool  *(Step 1: Screening)* | Teachers require basic training to administer the CES-D screening tool in the classroom. We assumed that a salaried psychologist would be hired to go to each school to train teachers on how to administer the CES-D. The total number of schools to which these psychologists are required to provide training was calculated as: the total number of teachers across Australia in 2013; divided by the average number of teachers per school. The total number of teachers across Australia in 2013 was calculated by dividing the total number of students (using data on the eligible population in section 3.3) by the average number of students per class (using OECD data [21]). The average number of teachers per school was based on data from an ABS survey of schools [22].  The next step was to estimate the total number of psychologist hours required to provide training to all these schools. In the absence of available data we assumed that group-based training of teachers in each school would take 1 hour in total (this is in line with the assumption made for the same parameter in the previous study by Mihalopoulos et al. [5]).  Multiplying the average number of hours per school by the total number of school across Australia in 2013 resulted in an estimate of the total psychologist hours required to train all teachers across participating Australian schools in 2013 to administer the CES-D questionnaire. Psychologist time was valued using an hourly wage rate based on data from the ABS Employee Earnings and Hours survey [23]; which included a 30% loading for on-costs). |
| Total cost of time spent by teachers administering the CES-D questionnaire  *(Step 1: Screening)* | We calculated the total time spent by teachers administering the CES-D questionnaire across Australia in 2013 by multiplying: the total number of teachers across Australia in 2013; by the average time required to complete CES-D questionnaires in the classroom,  The total number of teachers across Australia in 2013 was based on the estimate calculated in the previous screening parameter. In the absence of available data we assumed that the total time required to complete CES-D questionnaires would take 1 hour in total (this is in line with the assumption made for the same parameter in the previous study by Mihalopoulos et al. [5]). The aggregate estimate of teacher’s time spent administering the CES-D was valued using an hourly wage rate based on data from the ABS Employee Earnings and Hours survey [23]; which included a 30% loading for on-costs.  Note that we assumed that CES-D questionnaires would be completed online at no cost (the CES-D questionnaire has no licensing fees). |
| Total cost of time spent by (salaried) psychologists to conduct further diagnostic testing on eligible students using the DISC-IV  *(Step 2: Further diagnostic testing)* | Students who score above a CES-D cut-off of 16 (i.e., those with elevated symptoms of depression) require further diagnostic testing to ascertain whether they have a confirmed diagnosis of major depression or are, alternatively, experiencing subthreshold depressive symptoms. We assumed that eligible students undertook structured clinical interviews with a psychologist using the Diagnostic Interview Schedule for Children (DISC-IV). The DISC-IV was created by the National Institute of Mental Health in the USA and is considered the gold standard for diagnosing mental disorders in children and adolescents (i.e., as defined on the DSM-IV) [27].  We calculated total time spent by (salaried) psychologists conducting structured clinical interviews on eligible students across Australia in 2013 by multiplying: the total number of students eligible for further diagnostic testing; by the average time required to complete the DISC-IV modules for depression diagnosis. Total number of eligible students is based on eligible population calculations outlined in Table 1; while average time required to complete DISC-IV modules is based on estimates from prior studies [28]. Total time spent conducting further testing was valued using an hourly wage rate based on data from the ABS Employee Earnings and Hours survey [23]; which included a 30% loading for on-costs. |
| Total cost of (MBS-funded) psychologists delivering group-based intervention modules for indicated prevention  *(Step 3: Intervention delivery)* | Intervention delivery for the face-to-face delivery of indicated prevention involved: each student attending an initial one-on-one consult with a psychologist to receive an orientation session; followed by delivery of a series of group-based intervention modules by the psychologist to groups of students.  Unlike universal prevention, indicated prevention involved the delivery of group-based intervention modules by a psychologist. The rationale for choosing a psychologist (instead of a trained teacher) was threefold. First, we assumed that youth with subthreshold depressive symptoms are a higher risk group that require monitoring and evaluation by health professionals with some form of clinical training (i.e., a role that teachers may not be equipped to manage). Second, the majority of studies included in the meta-analysis of intervention efficacy for indicated prevention involved a health professional as the chief program facilitator (see Table 6); which is in contrast to the mix of facilitators used in universal prevention studies (see Table 5). Third, this choice was consistent with intervention pathways employed in the previous study by Mihalopoulos et al. [5]).  We costed psychologists using relevant Medicare Benefits Schedule (MBS) items for individual and group-based psychologist consults (see section 5.4). The decision to cost psychologists using MBS items, rather than a corresponding salary/wage, was threefold: (1) the psychologist would notionally have similar levels of clinical training to other MBS funded psychologists (see comment above about the need to sensitively deal with a higher risk group); (2) using MBS items would lead to more conservative estimates; and (3) to maintain consistency with the cost analysis conducted in the previous study by Mihalopoulos et al. [5]). We assumed that all psychologists were fully trained to deliver the intervention.  We assumed that all students would receive an initial one-on-one consult with the psychologist lasting one hour. The students would then receive multiple group-based interventions. The total cost of group-based The total cost of attending group-based intervention sessions with a psychologist was calculated by calculating the product of: the total number of eligible students (based on relevant calculations in section 2.4); the weighted average cost of a group-based session (based on MBS items); and the total number of group-based intervention sessions offered. We sourced available data from RCTs identified in the meta-review of intervention efficacy (see Table 6) to calculate a pooled estimate of the average number of intervention modules to be offered as part of the face-to-face delivery of indicated prevention. There were a total of 9 relevant studies from which to calculate a pooled estimate of the average number of intervention modules (see section 5.2). These same 9 studies also contained relevant data by which to calculate a pooled estimate of the average duration of each group-based intervention module.  We acknowledge that most RCT studies examining the efficacy of indicated prevention in schools involve interventions delivered in the school setting. For the purposes of our cost analysis, we were agnostic as to whether interventions were delivered to a group of students during/after school hours. |
| Total cost offsets resulting from the reduction in prevalent cases of major depression  *(Cost offsets)* | The methods and data used to calculate cost offsets for the face-to-face delivery of indicated prevention was similar to the method used to calculate cost offsets in the face-to-face delivery of universal prevention (see the cost offset parameter in Table 3). |
| *Internet-based delivery of universal psychological prevention*  The internet-based delivery of indicated psychological prevention followed a modified intervention pathway to that used for face-to-face delivery. This pathway involved the same three steps as the face-to-face delivery of indicated prevention: (1) screening for elevated depressive symptoms; (2) further diagnostic testing; and (3) intervention delivery. We assumed that the cost of steps 1 and 2 in the internet-delivered pathway would be identical to the face-to-face pathway. The only difference would be in the third step where intervention delivery occurs through students completing self-directed intervention modules via the internet. As such, we only present the data and rationale for cost parameters related to this intervention delivery step below. | |
| Total annual subscription cost for schools to deliver internet-based modules for indicated psychological intervention  *(Step 3: Intervention delivery)* | We assumed that internet-delivered indicated prevention would occur through students completing self-directed modules, similar in both form and content to universal prevention intervention modules. As in the face-to-face delivery of indicated prevention, we were agnostic to whether students completed these modules in the classroom or in their own time outside of school hours (though we suspect the latter would be preferable for students).  We assumed that the average cost per student would follow a similar pricing structure to that used in the costing of internet-delivered universal prevention (i.e., we costed internet-delivered indicated prevention using the pricing structure from THIS WAY UP Schools). The total annual subscription cost across all Australian schools in 2013 was calculated by: multiplying the annual subscription fee per student; by the total number of Australian students in 2013 (this was based on estimates for the eligible population in section 3.3). |
| Total cost offsets resulting from the reduction in prevalent cases of major depression  *(Cost offsets)* | The method used to calculate cost offsets arising from the internet-delivered intervention pathway for indicated prevention was similar to that used in the face-to-face intervention pathway (see above). |

### Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

| **Section/item** | **Item No** | **Recommendation** | **Reported on page No/ line No** |
| --- | --- | --- | --- |
| **Title and abstract** | | | |
| Title | 1 | Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared. | Page 1 |
| Abstract | 2 | Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions. | Pages 2-3 |
| **Introduction** | | | |
| Background and objectives | 3 | Provide an explicit statement of the broader context for the study. | Lines 97-106 |
| Present the study question and its relevance for health policy or practice decisions. | Lines 106-112  Appendix Section 1.2 |
| **Methods** | | | |
| Target population and subgroups | 4 | Describe characteristics of the base case population and subgroups analysed, including why they were chosen. | Lines 208-227 |
| Setting and location | 5 | State relevant aspects of the system(s) in which the decision(s) need(s) to be made. | Lines 116-128 |
| Study perspective | 6 | Describe the perspective of the study and relate this to the costs being evaluated. | Lines 134-139 |
| Comparators | 7 | Describe the interventions or strategies being compared and state why they were chosen. | Lines 45-47 |
| Time horizon | 8 | State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate. | Lines 45-47 |
| Discount rate | 9 | Report the choice of discount rate(s) used for costs and outcomes and say why appropriate. | Lines 51-54 |
| Choice of health outcomes | 10 | Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed. | Lines 141-144 |
| Measurement of effectiveness | 11a | *Single study-based estimates:*Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data. | Not applicable |
| 11b | *Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data. | Lines 116-192 |
| Measurement and valuation of preference based outcomes | 12 | If applicable, describe the population and methods used to elicit preferences for outcomes. | Not applicable |
| Estimating resources and costs | 13a | *Single study-based economic evaluation:*Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | Not applicable |
| 13b | *Model-based economic evaluation:*Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | Lines 290-313 |
| Currency, price date, and conversion | 14 | Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate. | Lines 146-149 |
| Choice of model | 15 | Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended. | Lines 230-244 |
| Assumptions | 16 | Describe all structural or other assumptions underpinning the decision-analytical model. | Appendix section 1.3 |
| Analytical methods | 17 | Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty. | Lines 315-335  Appendix section 3  Appendix section 4 |
| **Results** | | | |
| Study parameters | 18 | Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended. | Tables 1-2 in the main manuscript |
| Incremental costs and outcomes | 19 | For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios. | Tables 1-2 in the main manuscript |
| Characterising uncertainty | 20a | *Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective). | Not applicable |
| 20b | *Model-based economic evaluation:*Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions. | Tables 1-2 in the main manuscript |
| Characterising heterogeneity | 21 | If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information. | Not applicable |
| **Discussion** | | | |
| Study findings, limitations, generalisability, and current knowledge | 22 | Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge. | Lines 337-492 |
| **Other** | | | |
| Source of funding | 23 | Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support. | Financial support  (see page 27) |
| Conflicts of interest | 24 | Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations. | Conflicts of interest  (see page 28) |

The CHEERS statement checklist format is based on the format of the CONSORT statement checklist

# Analysis of intervention effect sizes

### Overview

This section provides an overview of the methods used to calculate intervention effect sizes for universal psychological intervention, indicated psychological intervention and indicated bibliotherapy. We first provide brief background on a previous meta-review that was conducted to identify all RCT studies examining the efficacy of school-based prevention interventions for children and adolescents. It is from this meta-review that we identified interventions and their accompanying intervention pathways that had: a strong evidence of effectiveness; and were appropriate to the Australian context (see section 1.2 for a full description of the analytic scope of the meta-review as it relates to the development of the decision-analytic model). We then present detailed results of meta-analyses conducted to derive pooled intervention effect sizes for indicated and universal prevention, by follow-up period. These results mostly relate to interventions involving the face-to-face delivery of intervention modules; though a short section has been placed at the end discussing how we approached intervention effect sizes when modelling prevention interventions (universal and indicated) that are delivered via the internet.

### Meta-review of RCT studies

A meta-review was conducted to identify all systematic reviews published between January 1980 and August 2014 examining the efficacy of prevention interventions for depression. The full methods have been presented elsewhere, and are briefly summarised here [3]. A systematic search was conducted to search for all relevant systematic reviews listed in electronics databases: Medline, PsycINFO and the Cochrane Library of Systematic Reviews. Databases were searched using a combination of MeSH terms and text words relating to: depression; prevention; and intervention trials. Reviews were eligible for inclusion if: they employed systematic methods to review the literature; collected data from randomised control trials (RCTs); included studies comparing the efficacy of a prevention intervention relative to no intervention, placebo or usual care; focussed on the prevention of the onset of major depression; and involved youth aged between 5-18 years.

From the systematic reviews, we identified all studies containing data on the efficacy of interventions seeking to prevent depression in children and adolescents. Furthermore, we conducted our own update of these systematic reviews to compile additional studies with more recent information. We extracted outcomes data and important study design characteristics in using standardised data extraction templates generated in Microsoft Excel 2010. Many of the studies identified in the meta-review contained multiple (independent) study arms with extractable data on intervention efficacy – e.g., a study may have compared the efficacy of two active interventions in separate independent samples, in addition to a control group sample. In this study, we represent multiple study arms (a.k.a., intervention arms) within a study using alphabetical letters (a, b, c, etc) following the study author and year.

Our cost-effectiveness models sought to model burden reduction and thus required health outcomes data that was expressed as a change in the discrete number of incident depression cases following intervention, rather than changes to a continuous mean score of on a depression symptom rating scale. As stated in section 1.2, we included RCT studies that measured intervention outcomes using structured clinical interviews to identify people with a diagnosis of major depression (e.g., DICA-IV or K-SADS). In addition, we included studies that used depression symptom rating scales if they reported outcomes as a discrete variable (i.e., counting the number of people who score above a pre-determined cut-off score on the scale); while excluding studies that reported outcomes as a continuous variable (i.e., a mean and standard deviation on a depression symptom rating scale). Overall, our search found 33 studies with outcomes data on discrete cases of depression incidence across multiple follow-up points over time. These were broadly grouped into indicated (N = 15), selective (N = 6) and universal (N = 11) prevention.

All 11 universal prevention studies involved the delivery of intervention modules to classrooms of school children. It follows that all universal prevention studies were eligible for inclusion in the meta-analysis, as shown in Table 5. We did, however, exclude two studies from the final meta-analysis as they were deemed outliers with unreasonably high incidence proportions in both intervention and control groups when compared to other universal populations [29,30]. For example, the incidence proportion reported by Stallard and Buck [30], was >70% of each respective sample; which is unreasonable for a universal intervention that supposedly targets people in the healthy population (other studies reported incidence proportions <50%). In summary, we found 9 studies containing 12 separate study arms with extractable data on the efficacy of universal prevention.

In the case of selective prevention, there were 5 studies encompassing several at-risk groups, including: children of divorced parents [31]; children of parents with mental illness [32,33]; socially disadvantaged children [34]; and primiparous adolescent girls [35]. Of the 6 selective prevention studies, only 1 examined the efficacy of selective prevention in a school setting – i.e., selective prevention targeting Chinese school children who have depressive symptoms a history of family conflict. It follows that there too few studies to model the population cost-effectiveness of selective prevention in all subgroups (including school-based interventions) in the Australian context (see section 1.2 for a description of the inclusion criteria for the decision-analytic model).

A total of 7 indicated prevention studies were considered out of scope (i.e., low strength of evidence and/or not appropriate for the Australian context) as they: delivered the intervention to youth outside the primary/secondary school setting (i.e., primary care clinics) [36]; targeted non-student populations (i.e., university students, pregnant mothers and children of parents with a mental illness) [37-41]; or targeted both students and parents rather than students alone [42]. This left 8 remaining studies on indicated prevention encompassing 11 separate study arms with extractable data on the efficacy of indicated prevention (see Table 6). Of these, 9 involved an indicated psychological intervention while 2 involved bibliotherapy (see ‘intervention description’ in Table 6).

Table 5 and Table 6 collate the 17 studies identified in the previous meta-review. These 17 studies encompass 26 (independent) study arms for which we could extract relevant data on intervention outcomes. Study characteristics that are presented include: the study author and year; country; sample size; age range; and a brief description of the intervention. We found that the chief program facilitator (i.e., person responsible for delivering intervention modules to students) was an even mix between teachers and health professionals in the case of universal prevention. By contrast, health professionals were unanimously the chief program facilitator for indicated prevention.

The majority of universal and indicated prevention studies used control groups involving waitlist control, treatment-as-usual or no intervention. Very few (i.e., 2 of 26 study arms) used an attention control group, which is the recommended method for placebo control in psychological trials. We have listed the follow-up points (i.e., post-intervention, 6 months, 1 year and 2 years) for which data could be extracted and used in subsequent meta-analyses, across each intervention arm.

The diagnostic criteria used to measure intervention outcomes (i.e., reductions in the discrete number of depression cases) are also listed. These intervention measures broadly identify depression cases by using either: (1) structured clinical interviews; or (2) cut-offs on a depression symptom rating scale. In this column, depression symptom rating scales are denoted by an inequality to right of the scale that indicates the cut-off score used to identify depression cases (e.g., CIS-R ≥12). In the case of universal prevention (see Table 5), approximately half of the study arms use depression symptom rating scales, with the remainder using structured clinical interviews. In the case of indicated prevention (see Table 6), all of the study arms (except one) use structured clinical interviews.

We used the Cochrane Collaboration’s Risk of Bias tool to evaluate the level of risk across 7 potential sources of bias[[5]](#footnote-5) (i.e., low, unclear or high). Each qualitative level of risk was allocated a quantitative score: 3 for ‘low risk’; 2 for ‘unclear risk’; and 1 for ‘high risk’. An aggregate risk of bias score was calculated for each intervention arm by summing the quantitative level of risk scores across the 7 sources of bias. This led to an aggregate risk of bias score out of 21 which is shown in Table 5 and Table 6. In addition to this, we recorded when the study used an intention-to-treat analysis (which was used to conduct univariate sensitivity analyses later on in section 6.7).

The following sections present the results of meta-analyses conducted to calculate pooled effect sizes across the different study arms collated for universal psychological, indicated psychological and indicated bibliotherapy interventions. Extracted data were meta-analysed using the ‘quality effects’ (QE) model – which gives greater weight to studies that have a lower risk of bias (based on the aggregate risk of bias score calculated above) [43]. All meta-analyses were conducted using MetaXL 3.0 (Epigear International, Sunrise Beach, Australia; available at: <http://www.epigear.com/>).

* + - 1. Study design characteristics of independent RCT study arms identified by meta-review that examined the efficacy of school-based universal prevention interventions delivered to students

| Study arm | Country | Sample size | Age range | Included in meta-analysis? | Intervention description | Chief program facilitator | Control group | Data available for these follow-up points | Diagnostic criteria a | Risk of bias score ( /21) | ITT used? | Source |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Bond 2004 | Australia | 2,678 | 13-14 | Yes | The Gatehouse Project | Teacher | NI | PI; 1y; 2y | CIS-R ≥12 | 16 | Yes | [44] |
| Cardemil 2002a | USA | 49 | Yr 5-6 | Yes | Penn Resiliency Program (PRP). Latino sample. | H Prof | NI | PI; 6m; 1y; 2y | CDI ≥20 | 12 | NR | [45] |
| Cardemil 2002b | USA | 103 | Yr 5-6 | Yes | Penn Resiliency Program (PRP). African American sample. | H Prof | NI | PI; 6m; 1y; 2y | CDI ≥20 | 12 | NR | [45] |
| Gillham 2012a | USA | 408 | 10-15 | Yes | Penn Resiliency Program (PRP) | Teacher + H Prof | TAU | 6m | DICA-IV | 16 | Yes | [46] |
| Gillham 2012b | USA | 408 | 10-15 | Yes | Penn Resiliency Program (PRP). | Teacher + H Prof | TAU | 6m | DICA-IV | 16 | Yes | [46] |
| Lowry-Webster 2001 | Australia | 594 | 10-13 | Yes | FRIENDS for children | Teacher | WC | 1y | ADIS-C | 13 | No | [47] |
| Quayle 2001 | Australia | 47 | 11-12 | Yes | The Optimism Program adapted from the Penn Prevention Program | H Prof | WC + TAU | 6m | CDI >13 | 14 | NR | [48] |
| Rivet 2005 | Mauritius | 160 | 12-16 | Yes | Resourceful Adolescent Program (RAP-A). | Teacher | TAU | PI; 6m | NR | 13 | NR | [49] |
| Rooney 2006 | Australia | 136 | 8-9 | Yes | Positive Thinking Program (PTP). | H Prof | TAU | PI; 6m; 2y | DICA-IV | 12 | No | [50] |
| Rooney 2013 | Australia | 910 | 8-10 | Yes | The Aussie Optimism: Positive Thinking Skills Program (AOP: PTS). | Teacher | TAU | PI; 6m; 2y | DICA-IV | 15 | NR | [51] |
| Shatte 1997a | USA | 102 | 12-14 | Yes | Penn Optimism Program (POP). | H Prof | NI | PI; 6m; 1y | CDI >12 | 14 | Yes | [52] |
| Shatte 1997b | USA | 97 | 12-14 | Yes | Penn Enhancement Program (PEP) | H Prof | NI | PI; 6m; 1y | CDI >12 | 14 | Yes | [52] |
| Lock 2003 | Australia | 977 | 9-16 | No b | FRIENDS | Teacher | MC | PI; 1y | ADIS-C-IV | 13 | NR | [29] |
| Stallard 2012a | UK | 1,064 | Yr 8-11 | No c | Resourceful Adolescent Program (RAP) | Teacher | AC | 6m; 1y | SMFQ ≥5 | 18 | NR | [30] |
| Stallard 2012b | UK | 1,064 | Yr 8-11 | No c | Resourceful Adolescent Program (RAP) | Teacher | TAU | 6m; 1y | SMFQ ≥5 | 18 | NR | [30] |

***Abbreviations:*** *1y – 1 year; 2y – 2 years; 6m – 6 months; AC – Attention Control; ADIS-C – Anxiety Disorders Interview Schedule for Children; CDI – Children's Depression Inventory; CIS-R – Clinical Interview Schedule-Revised; DICA-IV – Diagnostic Interview for Children and Adolescents-IV; H Prof – Health Professional; ITT – Intention-to-treat; MC – Matched control; NI – No intervention; NR – Not reported; PI – Post-intervention; SMFQ – Short Mood and Feelings Questionnaire; TAU – Treatment-as-usual; WC – Waitlist control; Yr – Year.*

*a Depression symptom rating scales are denoted by an inequality to right of the scale, which indicates the cut-off score used to identify depression cases (e.g., CIS-R ≥12).*

*b Lock 2003 was excluded from the meta-analysis as an outlier as it reported unreasonably high incidence outcomes in both intervention and control groups.*

*c Stallard 2012a & b were excluded from the meta-analysis as outliers. Incidence outcomes were much higher than what would reasonably be expected in a universal sample (e.g., the incidence proportion in the control group is >75%).*

* + - 1. Study design characteristics of independent RCT study arms identified by meta-review that examine the efficacy of school-based indicated prevention interventions delivered to students with subthreshold depression

| Study arm | Country | Sample size | Age range | Included in meta-analysis? | Intervention description | Chief program facilitator | Control group | Data available for these follow-up points | Diagnostic criteria a | Risk of bias score ( /21) | ITT used? | Source |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Arnarson 2009 | Iceland | 171 | 14-15 | Yes | Psychological prevention with student manuals, handouts, posters, videos and a relaxation tape | H Prof | TAU | PI; 6m; 1y | CAS | 16 | Yes | [53] |
| Clarke 1995 | US | 150 | NR | Yes | Coping With Stress (CWS) | H Prof | TAU | PI; 6m; 1y | K-SADS | 14 | Yes | [54] |
| Gillham 1995b(i) | US | 108 | Yr 5-6 | Yes | Cognitive and social problem-solving group | H Prof | WC | PI; 6m | CDI ≥15 | 12 | NR | [55] |
| Manassis 2010 | Canada | 148 | Yr 3-5 | Yes | The Feelings Club: a manualised CBT-based program | H Prof | AC | PI; 1y | ADIS-C | 16 | NR | [56] |
| Rohde 2013a | US | 378 | 13-19 | Yes | Bibliotherapy: students given "Feeling Good" book by David Burns | H Prof | TAU | 6m | K-SADS | 16 | Yes | [57] |
| Rohde 2013b | US | 378 | 13-19 | Yes | CBT-based group therapy delivered at school after regular school hours in single sex classes | H Prof | TAU | 6m | K-SADS | 14 | Yes | [57] |
| Sheffield 2006b | Australia | 739 | NR | Yes | CBT-based program that teaches interpersonal skills (e.g. assertion, conflict resolution, negotiation) | H Prof | TAU | 1y | ADIS-C | 15 | NR | [58] |
| Stice 2008a | US | 341 | 14-19 | Yes | CBT-based program with applied and interactive learning, homework tasks to apply skills in daily life | H Prof | NI | 6m; 2y | K-SADS | 17 | Yes | [59] |
| Stice 2008b | US | 341 | 14-19 | Yes | Supportive-expressive program that sought to establish rapport, provide support, help identify and express feelings; but did not focus on specific skills. | H Prof | NI | 6m; 2y | K-SADS | 17 | Yes | [59] |
| Stice 2008c | US | 341 | 14-19 | Yes | Bibliotherapy: students given "Feeling Good" book by David Burns | H Prof | NI | 6m; 2y | K-SADS | 17 | Yes | [59] |
| Young 2006 | US | 41 | 11-16 | Yes | Teen Talk: program based on Interpersonal Psychotherapy Adolescent Skills Training (IPT-AST) | H Prof | TAU | PI; 6m | K-SADS-PL | 19 | Yes | [60] |

***Abbreviations:*** *1y – 1 year; 2y – 2 years; 6m – 6 months; AC – Attention Control; ADIS-C – Anxiety Disorders Interview Schedule for Children; CAS – Child Assessment Schedule; CDI – Children's Depression Inventory; H Prof – Health Professional; ITT – Intention-to-treat; K-SADS – Kiddie Schedule for Affective Disorders and Schizophrenia; K-SADS-PL – Kiddie SADS Present and Lifetime Version; NI – No intervention; NR – Not reported; PI – Post-intervention; TAU – Treatment-as-usual; Yr – Year.*

*a Depression symptom rating scales are denoted by an inequality to right of the scale, which indicates the cut-off score used to identify depression cases (e.g., CDI ≥15).*

### Intervention effect sizes for universal psychological intervention

We calculated effect sizes (expressed as a risk ratio) for universal prevention in schools, across four consecutive follow-up points using available data from the RCT study arms listed in Table 5 (see column titled ‘Data available for these follow-up points’). The pooled effect sizes were:

Post-treatment. RR = 0.81 (95% CI: 0.48 - 1.38) based on 8 study arms [44,45,49-52].

6 months follow-up. RR = 0.59 (95% CI: 0.43 - 0.80) based on 10 study arms [45,46,48-52].

1 year follow-up. RR = 0.99 (95% CI: 0.77 - 1.27) based on 6 study arms [44,45,47,52].

2 years follow-up. RR = 1.03 (95% CI: 0.81 - 1.31) based on 5 study arms [44,45,50,51].

The inclusion criteria for our baseline decision-analytic model (see section 1.2) encompassed intervention effect sizes that reached a 5% level of significance. From the results above, we found that only the intervention effect size at 6 months follow-up was statistically significant. As such, the impact of universal prevention interventions on the incidence of depression in the population would only apply to the period between 6-months to 1-year; with a null effect size (RR = 1.0) being applied to all remaining time points in the model time horizon (i.e., between 0-6 months and between 1-10 years). Forest plots of the pooled intervention effect sizes are provided below in Figures 1 to 4.

* + - * 1. Forest plot of independent study arms used to calculate the effect size of universal psychological intervention at post-intervention



* + - * 1. Forest plot of independent study arms used to calculate the effect size of universal psychological intervention at 6 months follow-up



* + - * 1. Forest plot of independent study arms used to calculate the effect size of universal psychological intervention at 1 year follow-up



* + - * 1. Forest plot of independent study arms used to calculate the effect size of universal psychological intervention at 2 years follow-up



### Intervention effect sizes for indicated psychological intervention

We calculated effect sizes (expressed as a risk ratio) for indicated prevention in schools, across four consecutive follow-up points using available data from RCT studies listed in Table 6 (see column titled ‘Data available for these follow-up points’). The pooled effect sizes were:

Post-treatment. RR = 0.32 (95% CI: 0.14 - 0.73) based on 5 study arms [53-56,60].

6 months follow-up. RR = 0.34 (95% CI: 0.20 - 0.59) based on 7 study arms [53-55,57,59,60].

1 year follow-up. RR = 0.71 (95% CI: 0.35 - 1.43) based on 4 study arms [53,54,56,58].

2 years follow-up. RR = 0.74 (95% CI: 0.41 - 1.36) based on 2 study arms [59].

As stated previously, the inclusion criteria for our baseline decision-analytic model encompassed intervention effect sizes that reached a 5% level of significance. From the results above, we found that intervention effect sizes at post-treatment and 6 months follow-up were statistically significant. As such, the impact of indicated prevention interventions on the incidence of depression in the population would only apply to the period between 0-months to 1-year; with a null effect size (RR = 1.0) being applied to all remaining time points in the model time horizon (i.e., between 1-10 years). Forest plots of the pooled intervention effect sizes are provided below in Figures 5 to 8.

* + - * 1. Forest plot of independent study arms used to calculate the effect size of indicated psychological intervention at post-intervention



* + - * 1. Forest plot of independent study arms used to calculate the effect size of indicated psychological intervention at 6-9 months follow-up



* + - * 1. Forest plot of independent study arms used to calculate the effect size of indicated psychological intervention at 12 months follow-up



* + - * 1. Forest plot of independent study arms used to calculate the effect size of indicated psychological intervention at 18-24 months follow-up



### Intervention effect sizes for indicated bibliotherapy intervention

We were only able to find two independent study arms providing data on the efficacy of indicated bibliotherapy intervention. The forest plot of these studies is shown below. We did not model the cost-effectiveness of bibliotherapy in the baseline analysis as the effect size for indicated bibliotherapy did not reach statistical significance. Indeed, there is a high risk that the intervention does not work. The cost-effectiveness of bibliotherapy was, however, modelled in a subsequent sensitivity analysis (see section 6.5).

* + - * 1. Forest plot of independent study arms used to calculate the effect size of indicated bibliotherapy intervention at 6-9 months follow-up



### Intervention effect sizes for universal and indicated prevention interventions delivered via the internet

One of the aims of our study was to compare the cost-effectiveness of prevention interventions delivered using either face-to-face or internet-based modalities. While conducting the meta-review, however, we excluded 2 studies which examined the efficacy of internet-delivered (universal) psychological interventions [11,12]. These 2 studies were the only RCTs for which we had data on likely intervention pathways for internet-delivered (universal) psychological prevention in schools. That being said, they did not fit the inclusion criteria for our model (refer to section 1.2) which sought studies reporting intervention outcomes in terms of discrete numbers of incident depression cases (these 2 studies reported changes to mean scores on a depression rating scale). The content of internet-delivered intervention modules for universal prevention involved comparable psychotherapeutic content as contained in their face-to-face counterparts. Furthermore, previous studies have demonstrated that internet-based treatment interventions have comparable intervention efficacy to face-to-face psychological treatments [6,61,62]. Given the paucity of data, we opted to model intervention effect sizes for internet-delivered prevention (both universal and indicated) by assuming that the effect size of internet-delivered prevention interventions is equal to some proportion of the effect size of face-to-face interventions. Given the heroic nature of this assumption, we excluded the modelling of internet-delivered prevention from the baseline analysis – choosing instead to model these in separate sensitivity analyses (see section 6.10). For convenience, we have detailed the parameters for the cost analysis of internet-delivered prevention interventions (see sections 5.3 and 5.5) alongside the cost parameters of face-to-face delivery (see section 5.2 and 5.4) We modelled the cost-effectiveness of internet-delivered prevention interventions (universal and indicated) by assuming that effect sizes were equal to either 100% or 50% of the total effect size for face-to-face interventions.

# Identification of the eligible population

### Overview

This section provides further detail on the calculation of the eligible population for universal and indicated prevention interventions. In the case of universal prevention, the eligible population for face-to-face and internet-based delivery was identical. Likewise, the eligible population for indicated prevention was identical regardless of whether the intervention was delivered face-to-face, via the internet or through bibliotherapy. The section starts by providing qualitative descriptions of the intervention pathways for both indicated and universal prevention. Flow charts illustrating these descriptions are also presented, alongside a breakdown of the eligible population by age and sex. Several meta-analyses were conducted to generate pooled parameters to be used in the calculation of the eligible population for both universal and indicated prevention. Extracted data were meta-analysed using the ‘inverse variance heterogeneity’ (IVhet) model – which calculates an estimator under the fixed effect model assumption with a quasi-likelihood based variance structure [63]. All meta-analyses were conducted using MetaXL 3.0, an Excel add-in developed by EpiGear International Pty Ltd [64].

### Eligible population for universal prevention

The eligible population for universal prevention includes all youth aged 11-17 year in the Australian population regardless of underlying risk factors. As part of this process, we accounted for the likelihood of attrition as reported for intervention pathways described in meta-analysed RCT studies (see Table 1). Steps to identify the eligible population are shown in shown in Figure 11, which include:

Step 1 – 2013 Australian population. Start with the 2013 Australian population aged 11-17 years. This was N = 1,982,563 based on data obtained from the Australian Bureau of Statistics [9].

Step 2 – School participation rate. Not all schools will realistically participate in the population delivery of universal prevention. In the absence of hard data, the previous cost-effectiveness study by Mihalopoulos et al. [5] assumed a 60% school participation rate. By comparison, ~66% of secondary schools participated in the MindMatters program, while 17.1% (600/3500) of invited schools participated in Climate Schools Australia (both of which involve mental health initiatives in schools). We obtained feedback from a Technical Advisory Panel (TAP) of prevention experts who noted that the estimate of 66% was likely an overestimate. Given we did not anticipate the school participation rate to affect the resulting cost-effectiveness ratios, we assumed that 100% of schools would participate in the baseline analysis and tested the effect of assuming 50% in a univariate sensitivity analysis (see Table 1 for a more detailed rationale).

Step 3 – Student participation rate. Not all students will participate in the universal prevention intervention. Six RCT studies identified in the previous meta-review of intervention efficacy (included in Table 5) contained data on the proportion of students who obtain parental consent to participate in the universal prevention intervention (see Figure 10). We meta-analysed data from these studies to calculate the pooled proportion of students who agree to participate in the universal psychological intervention. Based on this, we found that 78.6% (95% CI: 63.5 - 91.9) of students agree to participate in the intervention [29,44,46-48,51].

Final estimate. We calculated the eligible population to be N = 1,558,171 which is 78.6% of the initial 2013 Australian population. That is, after accounting for attrition, we expect 78.6% of the 2013 Australian population aged 11-17 years to participate in universal prevention (see Figure 11 and Table 7).

* + - * 1. Forest plot of studies used to calculate the proportion of students who agree to participate in universal prevention



* + - * 1. Flow chart of process used to calculate the eligible population for universal prevention



* + - 1. Table outlining the age-sex breakdown of the eligible population for universal prevention

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Step 1 –**  **2013 Australian population** | | **Step 2 –**  **Total students in participating schools** | | **Step 3 –**  **Students who agree to participate in the intervention** | |
| **Age** | **Male** | **Female** | **Male** | **Female** | **Male** | **Female** |
| **11** | 141,765 | 135,008 | 141,765 | 135,008 | 111,418 | 106,108 |
| **12** | 144,086 | 136,569 | 144,086 | 136,569 | 113,243 | 107,335 |
| **13** | 143,945 | 137,504 | 143,945 | 137,504 | 113,132 | 108,070 |
| **14** | 144,530 | 137,639 | 144,530 | 137,639 | 113,592 | 108,176 |
| **15** | 145,409 | 137,479 | 145,409 | 137,479 | 114,282 | 108,050 |
| **16** | 147,554 | 140,199 | 147,554 | 140,199 | 115,968 | 110,188 |
| **17** | 149,706 | 141,170 | 149,706 | 141,170 | 117,660 | 110,951 |
| **Total** | 1,016,995 | 965,568 | 1,016,995 | 965,568 | 799,295 | 758,876 |

### Eligible population for indicated prevention

The eligible population for indicated prevention includes all youth aged 11-17 years in the Australian population who are identified as having subthreshold depressive symptoms. As part of this process, we accounted for the likelihood of attrition as reported for intervention pathways described in meta-analysed RCT studies (see Table 1). Steps to identify the eligible population are shown in Figure 14, which include:

Step 1 – 2013 Australian population. Start with the 2013 Australian population aged 11-17 years. This was N = 1,982,563 based on data obtained from the Australian Bureau of Statistics.

Step 2 – School participation rate. We assumed a 100% school participation rate similar to that chosen for the universal prevention intervention. See description of this parameter in section 3.2 and Table 1.

Step 3 – Screening for depressive symptoms. We assumed that the CES-D screening tool would be distributed in classrooms across all participating schools to identify students with clinically relevant depressive symptoms. The child and adolescent component of the 1997 National Survey of Mental Health and Wellbeing found that 20.6% of youth aged 13-17 years had a CES-D score above the cut-off of 16 [10]. The age-sex breakdown of these estimates is provided below. We assumed that youth aged 11-12 years had an identical proportion to those aged 13 years (i.e., 12.4% and 18.6% for males and females respectively) due to 13-year-olds being the lowest age group captured by the survey.

* + - 1. Age-sex breakdown of the proportion of youth aged 13-17 years who have a CES-D score above a cut-off of 16

|  |  |  |
| --- | --- | --- |
| **Age** | **Male** | **Female** |
| 13 | 12.4% | 18.6% |
| 14 | 13.6% | 29.0% |
| 15 | 17.6% | 34.8% |
| 16 | 17.2% | 29.4% |
| 17 | 23.4% | 31.5% |

Step 4 – Further diagnostic testing. All students who tested positive for elevated depressive symptoms on the CES-D were referred to a (salaried) psychologist for further diagnostic testing using a structured clinical interview (i.e., the Diagnostic Interview Schedule for Children or DISC-IV) to ascertain whether they had a depressive disorder diagnosis. Three RCT studies identified in the previous meta-review of intervention efficacy (included in Table 6) contained data on the proportion of students who are screened using a depression symptom rating scale and subsequently agree to participate in further diagnostic testing. We meta-analysed data from these studies to calculate the pooled proportion of students who agree to participate in further diagnostic testing (see Figure 12). From this, we found that 45.2% (95% CI: 41.7 - 48.7) of participants who screen positive on the CES-D also obtain parental consent for further diagnostic testing [53,54,60].

* + - * 1. Forest plot of studies used to calculate the proportion of students who participate in a diagnostic interview following CES-D screening



Step 5 – No current diagnosis of depression. Participating youth who have depressive symptoms but no diagnosis of depression are considered to have subthreshold depressive symptoms and are thus eligible to participate in the indicated prevention intervention. Here we assume that the DISC-IV has perfect (100%) sensitivity and specificity to identify current cases of major depression, given that it is widely considered the gold standard diagnostic instrument for mental disorders in children and adolescent [27]. Data from the 1997 NSMHWB indicates that 95.0% of youth aged 13-17 years had no current diagnosis of major depression given that they also had a CES-D score above the cut-off score of 16 (see Table 9). Once again, we assumed that youth aged 11-12 years had an identical proportion to those aged 13 years

* + - 1. Age-sex breakdown of the proportion of youth aged-13-17 years who have no diagnosis of major depression, given a CES-D score above the cut-off of 16

|  |  |  |
| --- | --- | --- |
| **Age** | **Male** | **Female** |
| 13 | 100.0% | 95.5% |
| 14 | 95.6% | 93.9% |
| 15 | 95.6% | 94.1% |
| 16 | 94.4% | 96.4% |
| 17 | 93.4% | 94.5% |

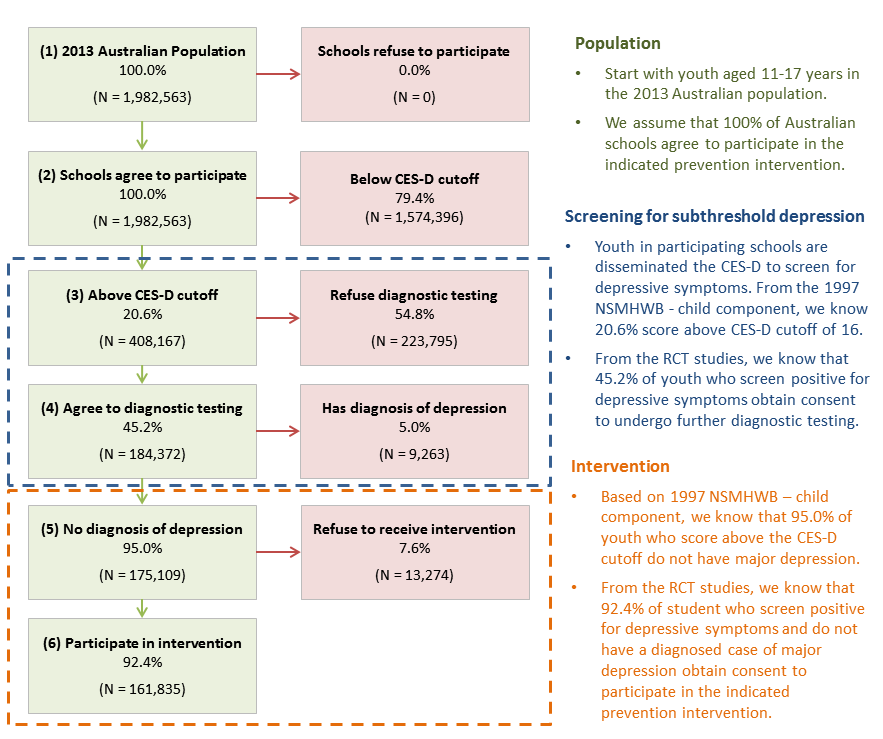
Step 6 – Student participation rate. Not all students who are identified as having subthreshold depression will participate in the indicated prevention intervention. In the absence of better data, we identified five RCT studies from the previous meta-review of intervention efficacy (included in Table 6) which contained data on the proportion of students who were identified as having subthreshold depression (following screening and further diagnostic testing) and subsequently obtain parental consent to participate in the indicated prevention intervention. We meta-analysed data from these studies to calculate the pooled proportion of students who agree to participate in the indicated psychological intervention (see Figure 13). From this we found that 92.4% (95% CI: 86.6 – 97.3) of participants who complete the screening process for subthreshold depression subsequently agreed to participate in the intervention [53,54,57,59,60].

* + - * 1. Forest plot of studies used to calculate the proportion of students who agree to participate in indicated prevention following the diagnostic interview



Final estimate. We calculated the final eligible population to be N = 161,835 which is 8.2% of the initial 2013 Australian population. That is, after accounting for attrition, we expect 8.2% of the Australian population aged 11-17 years to participate in the indicated prevention intervention (see Figure 14 and Table 10).

* + - * 1. Flow chart of process used to calculate the eligible population for indicated prevention



* + - 1. Table outlining the age-sex breakdown of the eligible population for indicated prevention

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Step 1**  **2013 Australian population** | | **Step 2**  **Total students in participating schools who are administered the CES-D screening test** | | **Step 3**  **Students who score above CES-D cut-off** | | **Step 4**  **Students who score above the CES-D cut-off and agree to further diagnostic testing** | | **Step 5**  **Students who do not have depression, but score above the CES-D cut-off** | | **Step 6**  **Students with subthreshold depression who agree to participate in the intervention** | |
| **Age** | **Male** | **Female** | **Male** | **Female** | **Male** | **Female** | **Male** | **Female** | **Male** | **Female** | **Male** | **Female** |
| **11** | 141,765 | 135,008 | 141,765 | 135,008 | 17,513 | 25,083 | 7,911 | 11,330 | 7,911 | 10,759 | 7,311 | 9,943 |
| **12** | 144,086 | 136,569 | 144,086 | 136,569 | 17,800 | 25,373 | 8,040 | 11,461 | 8,040 | 10,883 | 7,431 | 10,058 |
| **13** | 143,945 | 137,504 | 143,945 | 137,504 | 17,782 | 25,547 | 8,032 | 11,540 | 8,032 | 10,958 | 7,423 | 10,127 |
| **14** | 144,530 | 137,639 | 144,530 | 137,639 | 19,663 | 39,916 | 8,882 | 18,031 | 8,442 | 16,803 | 7,802 | 15,529 |
| **15** | 145,409 | 137,479 | 145,409 | 137,479 | 25,589 | 47,870 | 11,559 | 21,623 | 10,993 | 20,185 | 10,160 | 18,655 |
| **16** | 147,554 | 140,199 | 147,554 | 140,199 | 25,317 | 41,206 | 11,436 | 18,613 | 10,719 | 17,867 | 9,906 | 16,513 |
| **17** | 149,706 | 141,170 | 149,706 | 141,170 | 35,052 | 44,455 | 15,833 | 20,081 | 14,663 | 18,855 | 13,551 | 17,426 |
| **Total** | 1,016,995 | 965,568 | 1,016,995 | 965,568 | 158,715 | 249,452 | 71,693 | 112,679 | 68,800 | 106,310 | 63,584 | 98,251 |

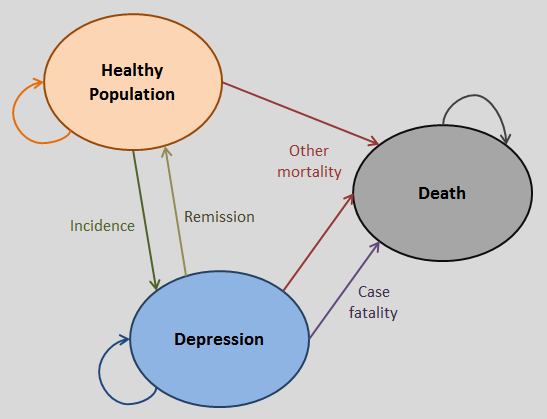
# Modelling health benefits

### Description of the model

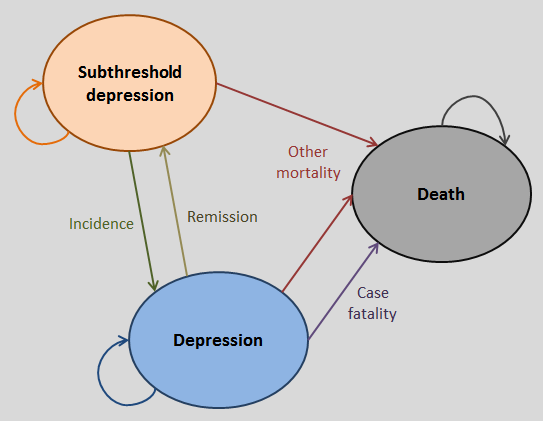
We constructed a multiple cohort Markov model to calculate the health outcomes resulting from the delivery of (universal and indicated) interventions to prevent the incidence of major depression in the eligible population. Model cohorts were based on the eligible 2013 Australian population aged 11-17 years, partitioned by sex and single-year age group (see the final columns of Table 7 and Table 10). Each age-sex cohort was modelled over a 10-year time horizon to provide sufficient time to simulate the full population health impact of prevention [65].

The Markov model was based on DisMod 2 – a simple incidence-prevalence-mortality (IPM) model – that simulated how model cohorts would transition between three health states (i.e., healthy, diseased and dead) [66]. For universal prevention, we assumed that the eligible population encompassed all healthy youth aged 11-17 years in the general population (see Figure 15). The majority of people in the eligible age-sex cohorts began the model in the ‘Well population’ health state at baseline; with a minority of people in the diseased health state (which was calculated based on the current prevalence of major depression in that age-sex cohort). The subsequent year-to-year transitions between health states over the 10-year time horizon corresponded with conventional epidemiological parameters, as denoted in Figure 15. In the case of indicated prevention, the eligible population encompassed all children and adolescents with subthreshold depression (see Figure 16). The model was executed under ‘steady state’ conditions – i.e., we assumed that trained staff and necessary infrastructure were available to deliver all interventions, which operate in accordance with their effectiveness potential (as denoted by the meta-analysis of RCT studies calculating pooled intervention effect sizes) [67,68].

* + - * 1. State transition diagram outlining the epidemiological transitions between three health states for universal prevention



* + - * 1. State transition diagram outlining the epidemiological transitions between three health states for indicated prevention



The model assessed the comparative health benefits (i.e., DALYs averted) arising from changes in the epidemiological profile of an age-sex cohort over time under two opposing scenarios: (1) an ‘intervention’ scenario, where the eligible population participates in the proposed intervention; and (2) a ‘partial null’ comparator scenario, where the eligible population receives neither the proposed intervention nor any established prevention services currently being delivered by the education/health sector [65]. The partial null is qualitatively different from a ‘treatment as usual’ comparator, which models the epidemiological profile of an age-sex cohort under a scenario where they receive existing prevention services currently being delivered in the population. Due to the lack of data on the existing coverage of prevention interventions being delivered in Australian schools, we assumed that no interventions were currently in place. No back-calculation was thus required to calculate the partial null incidence that would occur if the health impact of all existing prevention interventions were removed. In turn, the partial null equated to a ‘no intervention’ scenario.

Our model calculated the total life years lived under the intervention and comparator scenarios, whereby the impact of prevention involved reductions in the current incidence of major depression – i.e., multiplying population incidence rates with the risk ratio of intervention efficacy at applicable time points over the 10-year time horizon. As stated in sections 2.3 to 2.6, intervention effect sizes were applied over the follow-up time periods for which we obtained statistically significant risk ratios in the baseline analysis (with a null effect size of RR = 1.0 being applied to all remaining time periods). Mitigating the number of healthy (or subthreshold) people who transition to the depressed health state over the 10-year time horizon would lead to fewer prevalent cases of major depression over time, such that the 10-year cumulative prevalence of major depression is lower in the intervention population relative to the comparator. The reduction in prevalent cases would lead to fewer prevalent years lived with disability, in addition to a greater number of life years lived in the intervention population via a reduction in excess deaths attributable to major depression. The joint effect of these morbidity and mortality impacts would, in turn, lead to a greater number of DALYs – as calculated using the formula presented in Equation (1).

|  |  |
| --- | --- |
|  | () |

|  |  |
| --- | --- |
| Where: | *LY* is total number of life years lived by a population cohort in a single year |
|  | *Prev t* is the prevalence of major depression at year t; |
|  | *DW* is the disability weight of major depression taken from GBD 2013; and |
|  | *t* denotes the year in the model time horizon (between 0 to 10 years) |

The comparative difference in the total DALYs calculated for intervention and comparator scenarios respectively, is the total DALYs averted[[6]](#footnote-6) by an intervention. In summary, health benefits were measured as the incremental DALYs averted that occur between intervention and comparator scenarios, for each age-sex cohort simulated in the model. The following sections describe the derivation of input epidemiological parameters used in the multiple cohort Markov model outlined above: disease duration; incidence; case fatality; remission; other mortality; and the disability weight.

### Duration parameter

Previous Australian studies on the national burden of depression and the cost-effectiveness of depression treatments have assumed that a prevalent case of depression has an average duration of 29.9 weeks (including two weeks minimum duration) [5,69]. This figure was based on natural history models synthesising data from four longitudinal studies of major depression in community-based samples [70-73]. By contrast, the GBD 2013 study calculated an average duration of 37.7 week [18,74]. This figure was based on a natural history model which used similar methods and identical data sources to the 29.9 weeks duration figure, in addition to data from the Dutch NEMESIS study [75]. Our models assumed an average duration of 29.9 weeks for depression to be consistent with previous burden of disease and cost-effectiveness studies on depression. This, in turn, necessitated the adjustment of incidence rates obtained from the GBD 2013 study so that they would reflect a duration of 29.9 weeks, rather than 37.7 weeks. This process is outlined in the following section outlining the derivation of incidence parameters.

### Incidence parameter

We obtained male and female incidence rates from the GBD 2013 study for the Australian population, aged 11-27 years[[7]](#footnote-7) [13]. As stated previously, we adjusted GBD 2013 incidence rates so that they would reflect an average duration of 29.9 weeks. To do this, we first assumed that prevalence was constant between 29.9 weeks prevalence estimates and 37.7 week prevalence estimates. Second, we employed the epidemiological relationship where prevalence is the product of incidence times duration. Solving these equations led to:

|  |  |
| --- | --- |
|  | () |

Re-arranging Equation (2), in turn, led to:

|  |  |
| --- | --- |
|  | () |

Where Equation (3) calculates the incidence of depression resulting from a 29.9 weeks duration by multiplying the incidence associated with a 37.7 weeks duration with the ratio of duration estimates.

Incidence rates for the indicated prevention models required additional adjustments to reflect the higher incidence risk that would occur among youth with subthreshold depression. We conducted a separate meta-review (unpublished) which found three systematic reviews that examined longitudinal community-based studies with data on the risk of major depression among children and adolescents with subthreshold depression (relative to those in the general population) [76-78]. Table 11 presents all studies with extractable data on the incidence rate ratio (IRR) of major depression among youth with subthreshold depression relative to the general population. Extracted data were meta-analysed using the ‘inverse variance heterogeneity’ (IVhet) model – which calculates an estimator under the fixed effect model assumption with a quasi-likelihood based variance structure [63]. All meta-analyses were conducted using MetaXL 3.0 (Epigear International, Sunrise Beach, Australia; available at: <http://www.epigear.com/>). We calculated an IRR of 2.56 (95% CI: 1.02 - 6.43), as depicted by the Forest plot in Figure 17. The incidence of major depression among the subthreshold population was calculated by multiplying the GBD 2013 incidence (which is reflective of the general population) by the IRR calculated above. Table 12 presents the incidence rates of depression among: (1) the general Australian population aged 11-27 years after adjusting for an average duration of 26.7 weeks; and (2) the corresponding population sub-group with subthreshold depression.

* + - 1. Community-based studies containing data on the incidence rate ratio of major depression in children and adolescents with subthreshold depression

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Study name | Source | Cohort name | Case definition of subthreshold depression | Previous cases of MDD excluded? | Recency of subthreshold depression |
| Fergusson 2005 | [79] | Christchurch Health and Development Study (CHDP) | I. Meeting criteria for minor depression | Not reported | Current |
| Johnson 2009 | [80] | Children in the Community Study (CICS) | I. Meeting criteria for minor depression | Not reported | Past year |
| Shankman 2009 | [81] | Oregon Adolescent Depression Project (OADP) | I. Meeting criteria for minor depression | Yes | Current |
| Oldehinkel 1999 | [82] | Early Development Stages of Psycho-pathology (EDSP) study | I. Meeting criteria for minor depression | Yes | Past year |
| Jonsson 2011 | [83] | Unspecified Uppsala cohort | IV. Elevated scores of depression on a self-reported measure. | Not reported | Current |

*MDD – major depressive disorder*

* + - * 1. Forest plot showing the increased risk of later onset major depression in subthreshold depressive cases relative to the non-depressed population



* + - 1. Incidence rates for the 2013 Australian population categorised by population type, age and sex

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Age  (years) |  | General Australian population | | |  | Australian population with subthreshold depression | | |
|  | **Male** |  | **Female** |  | **Male** |  | **Female** |
| 11 |  | 0.036 |  | 0.058 |  | 0.093 |  | 0.149 |
| 12 |  | 0.042 |  | 0.069 |  | 0.106 |  | 0.176 |
| 13 |  | 0.047 |  | 0.080 |  | 0.121 |  | 0.205 |
| 14 |  | 0.054 |  | 0.093 |  | 0.137 |  | 0.237 |
| 15 |  | 0.060 |  | 0.105 |  | 0.153 |  | 0.270 |
| 16 |  | 0.066 |  | 0.118 |  | 0.168 |  | 0.301 |
| 17 |  | 0.071 |  | 0.129 |  | 0.182 |  | 0.330 |
| 18 |  | 0.076 |  | 0.139 |  | 0.195 |  | 0.356 |
| 19 |  | 0.080 |  | 0.147 |  | 0.206 |  | 0.376 |
| 20 |  | 0.084 |  | 0.153 |  | 0.215 |  | 0.392 |
| 21 |  | 0.087 |  | 0.157 |  | 0.221 |  | 0.403 |
| 22 |  | 0.089 |  | 0.160 |  | 0.226 |  | 0.409 |
| 23 |  | 0.090 |  | 0.161 |  | 0.230 |  | 0.412 |
| 24 |  | 0.090 |  | 0.161 |  | 0.231 |  | 0.411 |
| 25 |  | 0.091 |  | 0.159 |  | 0.232 |  | 0.407 |
| 26 |  | 0.091 |  | 0.157 |  | 0.232 |  | 0.401 |
| 27 |  | 0.091 |  | 0.155 |  | 0.231 |  | 0.396 |

### Other-cause mortality parameter

Other-cause mortality estimates were based on all-cause mortality estimates derived from deaths data obtained from the Australian Bureau of Statistics [14]. These estimates were adjusted by removing the number of deaths attributable to suicide – a leading cause of death among youth where depression is a leading risk factor [18]. Suicide death estimates were sourced from GBD 2013 by using self-harm cause of death estimates as a proxy [15]. Age-sex estimates for other mortality are shown in Table 13.

* + - 1. Other-cause mortality for the 2013 Australian population by age and sex

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age (years) |  | General Australian population | | |
|  | **Male** |  | **Female** |
| 11 |  | 0.00009 |  | 0.00007 |
| 12 |  | 0.00011 |  | 0.00008 |
| 13 |  | 0.00016 |  | 0.00010 |
| 14 |  | 0.00022 |  | 0.00013 |
| 15 |  | 0.00028 |  | 0.00016 |
| 16 |  | 0.00034 |  | 0.00019 |
| 17 |  | 0.00040 |  | 0.00021 |
| 18 |  | 0.00045 |  | 0.00023 |
| 19 |  | 0.00049 |  | 0.00024 |
| 20 |  | 0.00051 |  | 0.00024 |
| 21 |  | 0.00054 |  | 0.00025 |
| 22 |  | 0.00056 |  | 0.00025 |
| 23 |  | 0.00058 |  | 0.00025 |
| 24 |  | 0.00061 |  | 0.00025 |
| 25 |  | 0.00063 |  | 0.00026 |
| 26 |  | 0.00064 |  | 0.00026 |
| 27 |  | 0.00065 |  | 0.00026 |

### Case fatality parameter

We calculated the case fatality rate by rearranging the following equation used to calculate the relative risk of mortality for people with depression:

|  |  |
| --- | --- |
|  | () |

Where: RR is the relative risk of mortality; M is the mortality rate for the total population; and CFR is the case fatality rate among people with major depression. Re-arranging Equation (4) gives:

|  |  |
| --- | --- |
|  | () |

Based on Equation (5), we calculated age- and sex-specific case fatality rates by: using mortality rate data (described in section 4.4); and applying a RR of mortality estimate of 1.9 (95% CI: 1.6 - 2.2), which was taken from a previous study [16]. Table 14 presents the final case fatality rate estimates by age and sex.

* + - 1. Case fatality rates for the 2013 Australian population by age and sex

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age (years) |  | Australian subpopulation with depression | | |
|  | **Male** |  | **Female** |
| 11 |  | 0.00008 |  | 0.00007 |
| 12 |  | 0.00010 |  | 0.00007 |
| 13 |  | 0.00014 |  | 0.00009 |
| 14 |  | 0.00020 |  | 0.00012 |
| 15 |  | 0.00026 |  | 0.00015 |
| 16 |  | 0.00032 |  | 0.00017 |
| 17 |  | 0.00038 |  | 0.00020 |
| 18 |  | 0.00042 |  | 0.00021 |
| 19 |  | 0.00046 |  | 0.00022 |
| 20 |  | 0.00048 |  | 0.00022 |
| 21 |  | 0.00050 |  | 0.00023 |
| 22 |  | 0.00052 |  | 0.00023 |
| 23 |  | 0.00055 |  | 0.00023 |
| 24 |  | 0.00057 |  | 0.00023 |
| 25 |  | 0.00058 |  | 0.00024 |
| 26 |  | 0.00060 |  | 0.00024 |
| 27 |  | 0.00061 |  | 0.00024 |

### Remission parameter

In our models, the remission rate was calculated by using the following equation, which relies on the duration and case fatality estimates calculated in sections 4.2 and 4.5:

|  |  |
| --- | --- |
|  | () |

### Prevalence parameter

Prevalence data were used in the universal prevention models to account for the current prevalence of major depression in the population prior to the commencement of the intervention. That is, the initial distribution of the eligible population in the ‘healthy’ and ‘depressed’ health states was based on the prevalence in each corresponding age-sex cohort. Data on the current prevalence of major depression were obtained from GBD 2013 [13]; with age-sex prevalence estimates shown in Table 15.

* + - 1. Prevalence estimates for the 2013 Australian population by age and sex

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age (years) |  | General Australian population | | |
|  | **Male** |  | **Female** |
| 11 |  | 0.01710 |  | 0.02684 |
| 12 |  | 0.01982 |  | 0.03175 |
| 13 |  | 0.02271 |  | 0.03717 |
| 14 |  | 0.02574 |  | 0.04302 |
| 15 |  | 0.02881 |  | 0.04906 |
| 16 |  | 0.03185 |  | 0.05505 |
| 17 |  | 0.03476 |  | 0.06076 |
| 18 |  | 0.03746 |  | 0.06596 |
| 19 |  | 0.03989 |  | 0.07048 |
| 20 |  | 0.04200 |  | 0.07426 |
| 21 |  | 0.04375 |  | 0.07719 |
| 22 |  | 0.04510 |  | 0.07922 |
| 23 |  | 0.04601 |  | 0.08027 |
| 24 |  | 0.04651 |  | 0.08042 |
| 25 |  | 0.04671 |  | 0.07992 |
| 26 |  | 0.04673 |  | 0.07902 |
| 27 |  | 0.04668 |  | 0.07798 |

### Disability weight

We derived a composite disability weight for major depression by calculating the weighted average of GBD 2013 disability weights for mild, moderate and severe depression [17]. The weighted average was based on a severity distribution derived from the GBD study [18]; which calculated the comorbidity-adjusted proportion of mild, moderate and severe depression using validated SF-12 cut-offs from the 1997 National Survey of Mental Health and Wellbeing (NSMHWB) [19]. Severity distributions were based on: cross-walks of SF-12 scores taken from the 1997 National Survey of Mental Health and Wellbeing (NSMHWB) which were mapped to GBD 2013 disability weights [18]; and a random effects meta-regression which made adjustments to resulting severity proportions after removing the effects of disease comorbidity [19]. The comorbidity-adjusted severity proportions for mild, moderate and severe depression are shown in Table 16. It should be noted that an asymptomatic severity group arose following adjustment for the impacts of disease comorbidity on SF-12 scores. However, we omitted the asymptomatic group from our calculation of the composite disability weight as asymptomatic cases are considered out of scope from a treatment perspective. Data on the relative proportion for each severity level was normalised so that the sum of proportions for mild, moderate and severe depression would sum to one (after excluding the asymptomatic group). We used Ersatz to resample collected data using a Dirichlet distribution implemented via a series of conditional beta distributions; which produced a disability weight of 0.256 (95% CI: 0.195 - 0.324).

We tested the impact of calculating composite disability weights for depression using two alternative sets of disability weights: (1) GBD 2010 disability weights for mild, moderate and severe depression [84]; and (2) a corresponding set of Dutch disability weights used by previous burden of disease and cost-effectiveness studies in Australia [85]. We found that the divergence between the GBD 2013 composite disability weight and the composite disability weights calculated using either GBD 2010 data or Dutch disability weight data was immaterial (see Table 16) and did not warrant further investigation in the cost-effectiveness model as a separate sensitivity analysis. By contrast, separate univariate sensitivity analyses were required when using Standard Gamble and EQ-5D utility weights for mild, moderate and severe depression, which were obtained from a systematic review by Mohiuddin and Payne [20]. Using the GBD 2013 severity distribution reported in Table 16, we calculated the composite utility weights for the Standard Gamble and EQ-5D to be 0.604 (95% CI: 0.353 - 0.817) and 0.499 (95% CI: 0.266 - 0.720), respectively.

As stated in the manuscript, an alternative method for calculating the weighted average disability weight would be to use a severity distribution derived from the 1997 NSMHWB based on DSM-IV algorithms of depression severity. Unlike the severity distribution used in the GBD study, these distributions are not adjusted for comorbidity. Table 17 shows the data by which to calculate composite disability weights when using the severity distribution based on DSM-IV algorithms of depression severity. It follows that composite disability weights calculated using this severity distribution are approximately 1.6 times greater than corresponding disability weights calculated using the GBD 2013 severity distribution (see Table 17); which can have a potentially large impact on the final cost-effectiveness results. It is for this reason that we conducted a separate sensitivity analysis which used the composite disability weight calculated based on the severity distribution derived from DSM-IV algorithms of depression severity. Composite Standard Gamble and EQ-5D utility weights calculated using the severity distribution derived from DSM-IV algorithms were 0.489 (95% CI: 0.220 - 0.773) and 0.419 (95% CI: 0.229 - 0.613), respectively.

* + - 1. Data used to calculate composite disability weights for major depression when using the severity distribution from the GBD 2013 study

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Level of severity | GBD 2013 Severity distribution (95% CI) | GBD 2013 Disability weights (95% CI) | GBD 2010 Disability weights (95% CI) | Dutch Disability weights (95% CI) |
| Mild | 68.5%  (59.7% - 76.3%) | 0.145  (0.099 - 0.209) | 0.159  (0.107 - 0.223) | 0.14  (0.086 – 0.194) |
| Moderate | 19.2%  (14.3% - 24.7%) | 0.396  (0.267 - 0.531) | 0.406  (0.276 - 0.551) | 0.35  (0.272 – 0.425) |
| Severe | 12.2%  (5.1% - 21.5%) | 0.658  (0.477 - 0.807) | 0.655  (0.469 - 0.816) | 0.76  (0.556 – 0.971) |
| Weighted average | N/A | 0.256  (0.195 – 0.324) | 0.267  (0.204 – 0.335) | 0.258  (0.195 - 0.331) |

***Abbreviations:*** *95% CI – 95% confidence interval; GBD – Global Burden of Disease; N/A – Not applicable*

* + - 1. Data used to calculate composite disability weights for major depression when using the severity distribution based on DSM-IV algorithms of depression severity from the 1997 NSMHWB

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Level of severity | DSM-IV algorithms Severity distribution (95% CI) | GBD 2013 Disability weights (95% CI) | GBD 2010 Disability weights (95% CI) | Dutch Disability weights (95% CI) |
| Mild | 27.0%  (22.1% - 32.1%) | 0.145  (0.099 - 0.209) | 0.159  (0.107 - 0.223) | 0.14  (0.086 – 0.194) |
| Moderate | 42.5%  (38.1% - 47.1%) | 0.396  (0.267 - 0.531) | 0.406  (0.276 - 0.551) | 0.35  (0.272 – 0.425) |
| Severe | 30.4%  (26.5% - 34.6%) | 0.658  (0.477 - 0.807) | 0.655  (0.469 - 0.816) | 0.76  (0.556 – 0.971) |
| Weighted average | N/A | 0.407  (0.324 - 0.485) | 0.414  (0.333 - 0.495) | 0.418  (0.338 - 0.488) |

***Abbreviations:*** *95% CI – 95% confidence interval; DSM-IV – Diagnostic and Statistical Manual of Mental Disorders (4th edition); GBD – Global Burden of Disease; N/A – Not applicable*

# Cost analysis

### Overview

This section outlines the steps used to conduct the cost analysis of intervention pathways for universal psychological intervention and indicated psychological intervention using either face-to-face or internet-based delivery; as well as indicated bibliotherapy, which was analysed in a subsequent sensitivity analysis.

### Cost analysis of face-to-face universal psychological intervention

The intervention pathway for face-to-face delivery of universal psychological prevention involved teachers delivering psychological intervention modules in class during regular school hours. Table 3 provides a brief description of the rationale behind data and assumption used to cost intervention pathways for universal prevention. This section provides further details on how we costed the intervention pathway for the face-to-face delivery of universal psychological prevention via teachers in schools. Table 18 presents a summary of the different cost items associated with the face-to-face delivery of universal prevention. The total cost of each cost item is (broadly speaking) the product of unit cost, quantity and (when applicable) time. Resource use parameters and unit costs that were used to enumerate these cost items are presented in Table 2 of the main manuscript. A detailed summary of the method used to cost the intervention pathway for face-to-face delivery of universal psychological intervention is provided below.

* + - 1. Cost items for face-to-face delivery of universal psychological intervention

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cost item** | **Unit Cost** | **Quantity** | **Time (hrs)** | **Total** |
| **A. Intervention delivery** |  |  |  |  |
| Training teachers to deliver intervention | $ 42.33 | 2,060 | 17.2 | $ 1,500,048 |
| Teachers deliver group-based intervention | $ 45.26 | 675,230 | 1.2 | $ 35,653,709 |
|  |  |  |  |  |

Intervention delivery.

1. Training teachers to deliver the intervention. Prior to the delivery of intervention modules, we assumed that a salaried psychologist would be hired to go to each school to train teachers on how they are to deliver intervention modules. The total number of schools to which these psychologists are required to provide training is calculated as: the total number of teachers across Australia in 2013; divided by the average number of teachers per school. From the eligible population calculations in section 3.2 we know that 1,558,171 students aged 11-17 years will participate in the intervention. If the average number of Australian students per class is 23, based on OECD data [21], then there will be a total of 67,523 teachers. We know from ABS data that there are 33 teachers per school [22]. This results in a salaried psychologist having to provide teacher training to 2,060 schools. The average time required to train teachers (per school) was based on data from 5 RCT studies identified from our meta-review of intervention efficacy (see Table 19) [46,47,49,51,58]. The mean and standard deviation (hereafter ‘Std Dev’) of these data points was calculated to be 17.2 hours and 13.5 hours, respectively. Multiplying the average number of hours per school by the total number of schools across Australia in 2013 resulted in an estimate of the total psychologist hours required to train all teachers across participating Australian schools in 2013 to deliver the universal psychological intervention. Psychologist time was valued using an hourly wage rate of $42.33, which was calculated using data from the ABS Employee Earnings and Hours survey [23] and included a 30% loading for on-costs.
   * + 1. Resource use parameters extracted from 9 RCT studies included in the meta-analysis of intervention efficacy for universal psychological prevention

|  |  |  |  |
| --- | --- | --- | --- |
| **Study name (N = 9)** | **Time required to train teachers to deliver the intervention (hours)** | **Number of intervention sessions**  **(count)** | **Length of intervention sessions  (hours)** |
| Bond 2004 | - | 10 | 0.75 |
| Cardemil 2002a & b | - | 12 | 1.50 |
| Gillham 2012a & b | 6 | 10 | 1.50 |
| Lowry-Webster 2001 | 16 | 10 | 1.25 |
| Quayle 2001 | - | 8 | 0.67 |
| Rivet 2005 | 16 | 11 | 0.83 |
| Rooney 2006 | - | 8 | 1.00 |
| Rooney 2013 | 8 | 10 | 1.00 |
| Shatte 1997a & b | 40 | 12 | 2.00 |

1. Teachers deliver the group-based intervention modules. We calculated total time spent by teachers delivering face-to-face universal intervention modules across Australia in 2013 by calculating the product of: the total number of teachers across Australia in 2013; the average number of group-based intervention modules; and the average duration of each module. The total number of teachers across Australia in 2013 was based on the estimate calculated in the previous step (i.e., 67,523 teachers). We calculated the average number of group-based intervention modules offered based on data from the 9 RCT studies (see Table 19) included in our meta-analysis of intervention efficacy for universal prevention (Mean = 10.1, Std Dev = 1.5) [44-52]. Note, in the model we rounded the average number of intervention modules to the nearest whole number (i.e., 10 sessions). These same 9 studies also contained relevant data by which to calculate a pooled estimate of the average duration of each group-based intervention module (Mean = 1.2 hours, Std Dev = 0.4 hours) [44-52]. The aggregate estimate of teacher’s time spent delivering group-based intervention modules was valued using an hourly wage rate of $45.26, which was calculated using data from the ABS Employee Earnings and Hours survey [23] and included a 30% loading for on-costs.

### Cost analysis of internet-delivered universal psychological intervention

Internet-delivered universal psychological intervention followed a modified intervention pathway to that used for face-to-face delivery. In this case, we assumed that all children and adolescents take time in class to complete online intervention modules. During this time, teachers provide basic supervision while children completed self-directed modules on a school computer (i.e., the teacher monitors the class and provides behaviour management when required, but does not actively guide the students through the completion of modules). This unmoderated form of internet-delivery meant that teachers did not require additional training to learn how to facilitate the delivery of intervention modules. Table 20 presents a summary of the different cost items associated with the internet-based delivery of universal prevention. The total cost of each cost item is (broadly speaking) the product of unit cost, quantity and (when applicable) time. Resource use parameters and unit costs that were used to enumerate these cost items are presented in Table 2 of the main manuscript. A detailed summary of the method used to cost the intervention pathway for face-to-face delivery of universal psychological intervention is provided below.

* + - 1. Cost items for internet-delivery of universal psychological intervention

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cost item** | **Unit Cost** | **Quantity** | **Time (hrs)** | **Total** |
| **A. Intervention delivery** |  |  |  |  |
| Annual subscription to ThisWayUp | $ 10.87 | 1,558,171 | N/A | $ 16,936,644 |
| Teacher supervision | $ 45.26 | 405,138 | 0.8 | $ 13,752,145 |
|  |  |  |  |  |

Intervention delivery.

1. Total annual subscription cost of internet-based intervention. We were unable to find a comprehensive estimate on the cost of delivering an online universal intervention – i.e., an estimate inclusive of the cost of developing the content, staff, maintaining servers and other IT infrastructure. As such, we calculated a crude estimate of the annual cost per student of delivering internet-based universal prevention using data on annual subscription fees from THIS WAY UP Schools [26]. This internet-delivered program has been designed to prevent the onset of depression among students and charges each participating school an annual subscription fee based on the number of students who access the program[[8]](#footnote-8). From this, we calculated that the annual cost per student would be $10.87. From the meta-review of intervention efficacy we found 2 RCT studies [11,12] pertaining to the internet-based delivery of universal prevention (see section 2.6). It should be noted that the cost profile outlined above relates to the unmoderated internet-based delivery of universal psychological prevention. Online psychological interventions are conventionally delivered through either unmoderated modalities (i.e., self-help) or clinician-moderated modalities (i.e., self-directed treatment with periodic monitoring by a health professional or clinician; which can improve adherence to the internet-delivered psychological intervention). In the sensitivity analysis, we examined the cost-effectiveness of internet-based delivery of universal prevention by assuming either unmoderated or clinician-moderated internet delivery. Examining the latter simply involved substituting the unmoderated cost outlined above (i.e., $10.87 per student) with the corresponding cost associated with clinician-moderated internet delivery. This was calculated to be $223 per person (see section 6.10).
2. Cost of teachers providing basic supervision. We calculated the total time spent by teachers providing basic supervision to students (while completing online intervention modules using class computers) by calculating the product of: the total number of classes requiring teacher supervision (i.e., 67,523); the average number of internet-delivered intervention modules; and the average duration required to complete each module. From the meta-review of intervention efficacy, we found 2 studies (see Table 21) examining the efficacy of internet-delivered universal prevention [11,12]. We obtained data from these studies to calculate the average number of internet-delivered sessions (Mean = 5.5, Std Dev = 0.7) and the average duration of sessions (Mean = 0.8 hours, Std Dev = 0.4 hours). Note, in the model we rounded the average number of internet-delivered sessions to the nearest whole number (i.e., 6 sessions). The aggregate estimate of teacher’s time spent providing classroom supervision was valued using an hourly wage rate calculated using data from the ABS Employee Earnings and Hours survey [23]) which included a 30% loading for on-costs.
   * + 1. Resource use parameters extracted from 2 RCT studies included in the meta-analysis of intervention efficacy for universal psychological prevention

|  |  |  |
| --- | --- | --- |
| **Study name (N = 2)** | **Number of intervention sessions (count)** | **Length of intervention sessions  (hours)** |
| Calear 2009 | 5 | 0.50 |
| Wong 2014 | 6 | 1.00 |

### Cost analysis of face-to-face indicated psychological intervention

The intervention pathway for face-to-face delivery of indicated psychological prevention involved three main steps: (i) screening students at participating schools for elevated symptoms of depression using the CES-D; (ii) psychologists conducting further diagnostic testing to identify students without a depression diagnosis; and (iii) psychologists delivering group-based psychological intervention modules to eligible students. Table 4 provides a brief description of the rationale behind data and assumption used to cost intervention pathways for the face-to-face delivery of indicated prevention. This section provides further details on how we costed the intervention pathway for the face-to-face delivery of indicated psychological prevention via (MBS-funded) psychologists. Table 22 presents a summary of the different cost items associated with the face-to-face delivery of indicated prevention. The total cost of each cost item is (broadly speaking) the product of unit cost, quantity and (when applicable) time. Resource use parameters and unit costs that were used to enumerate these cost items are presented in Table 2 of the main manuscript. A detailed summary of the method used to cost the intervention pathway for face-to-face delivery of indicated psychological intervention is provided below.

* + - 1. Cost items for face-to-face delivery of indicated psychological intervention

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cost item** | **Unit Cost** | **Quantity** | **Time (hrs)** | **Total** |
| **A. Screening** |  |  |  |  |
| Training teachers to conduct screening | $ 42.33 | 2,621 | 1.0 | $ 110,966 |
| Teachers disseminate CES-D in class | $ 45.26 | 85,914 | 1.0 | $ 3,888,389 |
|  |  |  |  |  |
| **B. Further diagnostic testing** |  |  |  |  |
| Interview w/ school psychologist | $ 42.33 | 184,372 | 0.5 | $ 4,119,069 |
|  |  |  |  |  |
| **C. Intervention delivery** |  |  |  |  |
| Initial consult | $ 120.40 | 161,835 | 1.0 | $ 19,485,376 |
| Group-based intervention | $ 30.13 | 1,618,353 | 1.2 | $ 48,767,923 |
|  |  |  |  |  |

Screening for students with elevated symptoms of depression.

1. Training teachers to administer the CES-D screening tool. Teachers require basic training to administer the CES-D screening tool in the classroom. We assumed that a salaried psychologist would be hired to go to each school to train teachers on how to administer the CES-D. The total number of schools to which these psychologists are required to provide training was calculated as: the total number of teachers across Australia in 2013; divided by the average number of teachers per school. From the eligible population calculations (see section 3.3) we know that 1,982,563 students aged 11-17 years agree to screening. If the average no. of Australian students per class is 23, based on OECD data [21], then there will be a total of 85,914 teachers. We know from ABS data that there are 33 teachers per school [22]. This leads to a salaried psychologist having to provide basic training to 2,621 schools. The next step was to estimate the total number of psychologist hours required to provide training to all these schools. In the absence of available data we assumed that group-based training of teachers in each school would take 1 hour in total (this was in line with the assumption made for the same parameter in the previous study by Mihalopoulos et al. [5]). Multiplying the average number of hours per school by the total number of school across Australia in 2013 resulted in an estimate of the total psychologist hours required to train all teachers across participating Australian schools in 2013 to administer the CES-D questionnaire. Psychologist time was valued based on an hourly wage rate of $42.33, calculated using data from the ABS Employee Earnings and Hours survey [23] which included a 30% loading for on-costs.
2. Cost of time related to teacher’s administering the CES-D. We calculated the total time spent by teachers administering the CES-D questionnaire across Australia in 2013 by multiplying: the total number of teachers across Australia in 2013; by the average time required to complete CES-D questionnaires in the classroom. The total number of teachers across Australia in 2013 was based on the estimate calculated in the previous screening parameter. Overall, 85,914 teachers were responsible for administering the CES-D screening tool to students in their classrooms. In the absence of available data we assumed that the total time required to complete CES-D questionnaires would take 1 hour in total (this is in line with the assumption made for the same parameter in the previous study by Mihalopoulos et al. [5]). The aggregate estimate of teacher’s time spent administering the CES-D was valued using an hourly wage rate of $45.26, calculated using data from the ABS Employee Earnings and Hours survey [23] which included a 30% loading for on-costs. Note that while there are a total of 1,982,563 students who will fill out the CES-D questionnaire, we assumed that CES-D questionnaires were both completed and processed electronically at no cost (the CES-D has no licensing fees associated with its use).

Further diagnostic testing.

1. Total cost of psychologist time spent providing diagnostic testing. Students who score above a CES-D cut-off of 16 (i.e., those with elevated symptoms of depression) require further diagnostic testing to ascertain whether they have a diagnosis of major depression or are, alternatively, experiencing subthreshold depressive symptoms. We calculated total time spent by (salaried) psychologists conducting further diagnostic testing on eligible students across Australia in 2013 by multiplying: the total number of students eligible for further diagnostic testing; by the average time required to complete the DISC-IV modules for depression diagnosis. The total number of eligible students was based on eligible population calculations outlined in section 3.3, which found that 184,372 students consent to further diagnostic testing. The average time required to complete DISC-IV modules was based on estimates from a prior validation study [28]. According to this data source, the full administration of the DISC-IV takes 70-80 minutes and that 2 out of 6 modules relate to depression and anxiety (i.e., 75 mins \* 0.333 = 25 mins, or 0.5 hrs). Based on these calculations, we determined that the average administration time for the DISC-IV would be approximately 25 minutes (range: 23 - 27). Total time spent conducting further testing was valued using an hourly wage rate for psychologists of $42.33 based on data from the ABS Employee Earnings and Hours survey [23]) which included a 30% loading for on-costs.

Intervention delivery.

1. Total cost of individual and group-based consultations with a psychologist. Intervention delivery for the face-to-face delivery of indicated prevention involved: each student attending an initial one-on-one consult with the psychologist to receive an orientation session; followed by delivery of a series of group-based intervention modules by the psychologist to groups of students. We costed psychologists using relevant Medicare Benefits Schedule (MBS) items for individual and group-based psychologist consults, respectively (see Table 4 for the rationale). We calculated the weighted average unit cost for a consult with an MBS funded psychologist (individual and group-based) by weighting individual MBS item fees for each consult type by the relative number of consults recorded in Australia during 2013. The item numbers and accompanying fees for individual and group-based consults are shown in Table 23. We obtained data on the total number of consults that were recorded against each MBS item from Medicare Australia Statistics [86]. Based on previous eligible population calculations (see section 3.3), we estimated that 161,835 of eligible students attended a single one-on-one consult with the psychologist costing a weighted average of $120.40 (we also assumed that this would last for 1 hour in duration). The total cost of attending group-based intervention sessions with a psychologist was calculated by calculating the product of: the total number of eligible students (i.e., 161,835); the weighted average cost of a group-based session; and the total number of group-based intervention sessions offered. The weighted average cost of group-based sessions was calculated to be $30.13 per session. We calculated the average number of group-based intervention sessions offered based on data from the 8 RCT studies (see Table 24) included in our meta-analysis of intervention efficacy for indicated prevention (Mean = 10.4, Std Dev = 3.5) [53-60]. Note, in the model we rounded the average number of intervention sessions to the nearest whole number (i.e., 10 sessions). These same 8 studies also contained relevant data by which to calculate a pooled estimate of the average duration of each group-based intervention session (Mean = 1.2 hours, Std Dev = 0.4 hours) [53-60].
   * + 1. Cost of single and group-based consults with an MBS-funded psychologist

|  |  |  |
| --- | --- | --- |
| **Cost of single psychologist** | | |
| *MBS item no.* | *No. of consults* | *Fee* |
| 80010 | 1,561,368 | $ 146.45 |
| 80110 | 1,969,233 | $ 99.75 |
|  | | |
| *Weighted average* | | $ 120.40 |

|  |  |  |
| --- | --- | --- |
| **Cost of group therapy service** | | |
| *MBS item no.* | *No. of consults* | *Fee* |
| 80020 | 11,995 | $ 37.20 |
| 80120 | 18,093 | $ 25.45 |
|  | | |
| *Weighted average* | | $ 30.13 |

* + - 1. Resource use parameters extracted from 8 RCT studies included in the meta-analysis of intervention efficacy for indicated psychological prevention

|  |  |  |
| --- | --- | --- |
| **Study name (N = 8)** | **Number of intervention sessions (count)** | **Length of intervention sessions  (hours)** |
| Arnarson 2009 | 14 | 0.75 |
| Clarke 1995 | 15 | 0.75 |
| Manassis 2010 | 12 | 1.00 |
| Gillham 1995b(i) | 12 | 2.00 |
| Rohde 2013b | 6 | 1.00 |
| Sheffield 2006b | 8 | 1.50 |
| Stice 2008a & b | 6 | 1.00 |
| Young 2006 | 10 | 1.50 |

### Cost analysis of internet-delivered indicated psychological intervention

The internet-based delivery of indicated psychological prevention followed a modified intervention pathway to that used for face-to-face delivery. This pathway involved the same three steps as the face-to-face delivery of indicated prevention: (1) screening for elevated depressive symptoms; (2) further diagnostic testing; and (3) intervention delivery. We assumed that the cost of steps 1 and 2 in the internet-delivered pathway would be identical to the face-to-face pathway. The only difference would be in the third step where intervention delivery occurs through students completing self-directed intervention modules via the internet. Table 23 presents a summary of the different cost items associated with the internet-based delivery of indicated prevention. Like internet-delivered universal prevention (see section 5.3), we assumed that internet-delivered indicated prevention would involve students completing self-directed modules through either unmoderated or clinician-moderated modalities. The resource use parameters and average cost per person were: $10.87 per person for unmoderated internet-delivery; and $223 per person for clinician-moderated internet-delivery.

* + - 1. Cost items for internet-delivery of indicated psychological intervention

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cost item** | **Unit Cost** | **Quantity** | **Time (hrs)** | **Total** |
| **A. Screening** |  |  |  |  |
| Training teachers to conduct screening | $ 42.33 | 2,621 | 1.0 | $ 110,966 |
| Teachers disseminate CES-D in class | $ 45.26 | 85,914 | 1.0 | $ 3,888,389 |
|  |  |  |  |  |
| **B. Further diagnostic testing** |  |  |  |  |
| Interview w/ school psychologist | $ 42.33 | 184,372 | 0.5 | $ 4,119,069 |
|  |  |  |  |  |
| **C. Intervention delivery** |  |  |  |  |
| Annual subscription to ThisWayUp | $ 10.87 | 161,835 | 0.8 | $ 1,759,079 |
|  |  |  |  |  |

### Cost offsets

Our baseline analysis included the impact of cost offsets – i.e., the costs of treating major depression that are averted due to the prevention of incident cases. The average annual cost of treating a prevalent case of depression was calculated by: taking data from a 2010 AIHW disease expenditure report on the combined expenditures attributable to both depression and anxiety [24]; and using comorbidity data sourced from the 2007 NSMHWB to calculate the expenditures attributable to the total envelope of depression [25]. From this, we calculated the average annual cost offset for a treated case of depression to be $1,182 (SE: 104).

# Sensitivity analysis

### Overview

This section provides detailed methods outlining the methods used to conduct a series of univariate sensitivity analyses to evaluate the impact of: excluding cost offsets (section 6.2); including time and travel costs (section 6.3); assuming a school participation rate of 50%, instead of 100% (section 6.4); modelling non-significant intervention effect sizes and extrapolating an exponential decay rate over time (section 6.5); modelling effect sizes based on RCTs using structured clinical interviews (section 6.6); modelling effect sizes based on RCTs that use ITT analysis (section 6.7); using a weighted average disability weight based on an alternative severity distribution derived from DSM-IV algorithms for mild, moderate and severe depression (section 6.8); using pooled standard gamble and EQ-5D utility weights (section 6.9); modelling internet-delivered intervention pathways (section 6.10); and applying different discount rates to costs and benefits (section 6.11). When modelling internet-delivered intervention pathways, we conducted an additional threshold analysis to test the impact of: (1) varying the relative efficacy of universal and indicated prevention when assuming unmoderated and clinician-moderated internet-delivery pathways; and (2) changing the average intervention cost of indicated and universal internet prevention when adopting an effect size of 100% and 50% relative to face-to-face intervention. These are also presented in section 6.10, alongside the methods for modelling internet-delivered prevention interventions (universal and indicated).

### Sensitivity analysis excluding cost offsets

This sensitivity analysis involved the omission of cost offsets from the calculation of net intervention costs – leading to a higher ICER due to higher incremental costs in the numerator (see section 5.6 for an overview of cost offsets).

### Sensitivity analysis including time and travel costs

We excluded the estimation of patient time and travel costs from the baseline analysis. In the context of this study, patient time and travel costs would encompass the costs of parent who are required to transport their children to and from intervention sessions. In the case of universal prevention (face-to-face and internet-delivered) there are no additional costs associated with transporting/supervising children over and above what would usually occur during a school day. It is for this reason that patient time and travel costs were not applicable in the case of universal prevention (both face-to-face and internet-delivered). By contrast, the intervention pathway for the face-to-face delivery of indicated prevention involved additional trips for: (1) further diagnostic testing; and (2) intervention delivery – i.e., an initial psychologist consult and a series of group-based intervention sessions. The internet-based delivery of indicated prevention also included time and travel costs associated with further diagnostic testing, but not intervention delivery.

We used time and travel costs obtained from a previous analysis by Vos et al. [67]. The average time cost per hour and the average travel cost per trip was, respectively, AU$17.44 and AU$9.96 – expressed in 2003 Australian dollars. We used Australian health price deflators from the AIHW to convert these costs into 2013 Australian dollars [87]. It follows that the average time cost (per hour) was AU$24.67, while the average travel cost (per trip) was AU$9.96.

To calculate travel costs, we assumed that each consultation with a psychologist necessitated two trips (signifying a return trip going to and from the psychologist’s location). Using the relevant quantities presented in Table 22, we calculated travel costs for the face-to-face delivery of indicated prevention to be $39,124,480 – i.e., $9.96 per trip multiplied by 2 trips and the sum of all consultations (184,372 for further diagnostic testing, 161,835 for the initial intervention consult and 1,618,353 for group-based intervention sessions). Likewise, using the relevant quantities presented in Table 25, we calculated travel costs for the internet-based delivery of indicated prevention to be $3,671,800 – i.e., 2 trips multplied by 184,372 consults for further diagnostic testing.

To calculate time costs, we calculated the product of each type of psychologist consultation and the average time estimated for each consult. Using data from Table 22, we calculated time costs for the face-to-face delivery of indicated prevention to be $52,966,806 – i.e., (184,372 × 0.5 hrs) + (161,835 × 1 hr) + (1,618,353 × 1.2 hrs). Likewise, using data from Table 25, we calculated time costs for the internet-based delivery of indicated prevention to be $2,400,347 – i.e., (184,372 × 0.5 hrs).

### Sensitivity analysis assuming a school participation rate of 50%, instead of 100%

Obtaining a reliable estimate on the likely participation rate among Australian schools was problematic (see section 3.2). We were unable to find a reliable data estimate that could be used to accurately predict the number of schools that would participate in a universal and/or indicated psychological prevention intervention if it were to be scaled up nationally. The true coverage rate would be dependent on how successful the nationwide implementation of these programs turned out (which is a question beyond the scope of our model). We consequently assumed in the baseline analysis that all Australian schools (i.e., 100%) would participate in the intervention. While we acknowledge that this assumption is practically infeasible in real life, assuming 100% school coverage would allow us to calculate the potential health benefits and costs that would arise from the full-scale, nationwide implementation of the universal prevention program. Furthermore, we anticipated that changing the value of this parameter would have a negligible effect on the final ICER as both costs and health benefits would be reduced proportionally to each other – e.g., assuming a 50% coverage rate will lead to both a 50% reduction of total DALYs and a 50% reduction in total costs. Likewise, assuming a 25% coverage rate will lead to both a 75% reduction in total DALYs and a 75% reduction in total costs, relative to a 100% coverage rate. In any case, the final ICER will remain approximately the same.

We tested the aforementioned hypothesis by conducting a sensitivity analysis where we assumed a 50% coverage rate in place of the initial 100% estimate.

### Sensitivity analysis modelling non-significant intervention effect sizes and extrapolating an exponential decay rate over time

Our baseline analysis modelled effect sizes that reached the 5% significance level. As a sensitivity analysis, we tested the effect of both including non-significant effect sizes, in addition to continuing to model effect sizes into the long-term by assuming an exponential decay rate. The rationale for the exponential decay rate was the observation that effect sizes gradually attenuate over time (an exponential decay rate assumes a rapid initial decay that becomes less rapid over time). In the case of indicated psychological intervention, the effect sizes decay progressively from RR=0.31 post-intervention to RR=0.74 at 2-years follow up. We fit an exponential decay function to the pooled effect size data to calculate the annual effect size over a 10-year time horizon, where the effect size approaches the null (i.e., RR=1.0). In this case, the method of least squares was used to calculate the parameters of the exponential decay function that best fit the data on the pooled effect size at each follow-up point. We assumed that uncertainty around years 3-10 would have an identical standard error to that of the pooled effect size calculated at year 2. In the case of universal prevention the effect size attenuates completely by 1-year follow up. As such, we assumed that universal prevention would have a null effect size (i.e., RR = 1.0) from year 2 onwards. In the case of indicated bibliotherapy (which had only one pooled effect size), we used data on the proportional decay rate observed in the indicated psychological intervention scenario and superimposed it on to the single pooled effect size, to model a decay function over time. Figure 18 and Figure 19 show the extrapolated effect sizes that were calculated for indicated psychological intervention and indicated bibliotherapy, respectively.

* + - * 1. Plot of extrapolated effect sizes for indicated psychological intervention
        2. Plot of extrapolated effect sizes for indicated bibliotherapy intervention

The costing of intervention pathways for universal and indicated prevention (both face-to-face and internet-based delivery) have been outlined in sections 5.2 to 5.5. In the case of the intervention pathway for indicated bibliotherapy, we assumed identical intervention pathways and costs in relation to the two intervention stages involving screening and further diagnostic testing (see Table 22). By contrast, intervention delivery (i.e., third intervention stage) differed in that eligible students were disseminated a book containing psychotherapeutic modules that are similar to those taught in the face-to-face psychological intervention and which students can complete in their own time. We assumed that this book was the ‘The Feeling Good Book’ by David Byrne which has a recommended retail price (RRP) of AU$24.14. This book was disseminated to all eligible students for indicated prevention (i.e., a total of 161,835 students).

### Sensitivity analysis modelling effect sizes based on RCTs using structured clinical interviews

In the baseline analysis, we pooled intervention effect sizes using studies that reported intervention outcomes as a discrete variable denoting changes to the number of incident cases of diagnosed depression following an intervention. These studies encompassed one of two methods for measuring discrete cases of depression: (1) structured clinical interviews; and (2) scoring above a cut-off score on a depression symptom rating scale. Inclusion of studies measuring discrete health outcomes using depression symptom rating scales is, however, controversial as there are concerns regarding the validity, reliability and diagnostic utility of these scales with regards to the diagnosis of depression cases [88].

We conducted a sensitivity analysis to test the impact of only including RCT studies that use structured clinical interviews in effect size calculations. The pooled effect sizes for study arms using structured clinical interviews (see Table 5 and Table 6 for the list of studies) are shown in Table 26 for universal psychological prevention and Table 27 for indicated psychological prevention. In the meta-analysis of universal prevention studies, we observed that intervention effect sizes based on studies using structured clinical interviews are larger (i.e., further away from the null of RR = 1.0) than studies using cut-offs on a depression symptom rating scale to identify depression outcomes. In the meta-analysis of indicated prevention studies, there was only one study arm (out of 8) that measured depression outcomes using a cut-off on a depression symptom rating scale. As such, we were unable to draw direct comparisons between pooled intervention effect sizes using the structured clinical interview and those using depression symptom rating scales. As shown in Table 27, pooled intervention effect sizes are fairly similar to those used in the baseline analysis (see section 2.4). The pooled intervention effect sizes calculated in this sensitivity analysis, support the argument that the effect sizes used in the baseline analysis are conservative – i.e., are not biased such that we are using inflated effect sizes that, in turn, lead to more favourable cost-effectiveness results. Note that we only modelled effect sizes that reached the 5% level of significance (as in the baseline analysis).

* + - 1. Pooled effect sizes for universal psychological intervention when limiting the scope of studies to those using structured clinical interviews

|  |  |  |  |
| --- | --- | --- | --- |
| Follow-up | Effect Size | Lower 95% CI | Upper 95% CI |
| PSYCH, Post-treatment (2 study arms) | 0.20 | 0.05 | 0.77 |
| PSYCH, 6-9 months (4 study arms) | 0.48 | 0.19 | 1.20 |
| PSYCH, 12 months (1 study arm) | 0.71 | 0.07 | 7.72 |
| PSYCH, 18-24 months (2 study arms) | 1.24 | 0.18 | 8.54 |

* + - 1. Pooled effect sizes for indicated psychological intervention when limiting the scope of studies to those using structured clinical interviews

|  |  |  |  |
| --- | --- | --- | --- |
| Follow-up | Effect Size | Lower 95% CI | Upper 95% CI |
| PSYCH, Post-treatment (4 study arms) | 0.32 | 0.13 | 0.81 |
| PSYCH, 6-9 months (6 study arms) | 0.35 | 0.20 | 0.61 |
| PSYCH, 12 months (4 study arms) | 0.71 | 0.35 | 1.43 |
| PSYCH, 18-24 months (2 study arms) | 0.74 | 0.41 | 1.36 |

### Sensitivity analysis modelling effect sizes based on RCTs that use ITT analysis

In the baseline analysis, we assumed that all pooled intervention effect sizes used in the baseline model (see section 2) used an intention-to-treat (ITT) approach, such that they (implicitly) incorporated the impact of non-adherence (i.e., non-compliance and loss to follow-up). However, there were several universal and indicated RCT studies that: did not use an ITT analysis; or failed to report its use in the study design (implying that it wasn’t implemented). We investigated the impact of the baseline intervention adherence assumption by conducting separate sensitivity analyses to test the effect of only including studies using an ITT analysis in effect size calculations. The pooled effect sizes for study arms using an ITT approach (see Table 5 and Table 6 for the list of studies) are shown in Table 28 for universal psychological prevention and Table 29 for indicated psychological prevention. In the meta-analysis of universal prevention studies, we observed that intervention effect sizes for studies using an ITT analysis tended towards the null (i.e., they are closer to RR = 1.0) than studies that do not use /report using an ITT analysis. In the meta-analysis of indicated prevention studies, we found that pooled intervention effect sizes calculated based on studies using an intention-to-treat approach were fairly similar to the pooled intervention effect sizes calculate when including both studies that do and do not use an intention-to-treat analysis (see section 2.4). The pooled intervention effect sizes calculated in this sensitivity analysis support the argument that effect sizes used in the baseline analysis are conservative – i.e., are not biased such that we are using inflated effect sizes that, in turn, lead to more favourable cost-effectiveness results. Note that we only modelled effect sizes that reached the 5% level of significance (as in the baseline analysis).

* + - 1. Pooled effect sizes for universal psychological intervention when limiting the scope of studies to those using an intention-to-treat approach

|  |  |  |  |
| --- | --- | --- | --- |
| Follow-up | Effect Size | Lower 95% CI | Upper 95% CI |
| PSYCH, Post-treatment (3 study arms) | 0.90 | 0.66 | 1.24 |
| PSYCH, 6-9 months (4 study arms) | 0.61 | 0.40 | 0.92 |
| PSYCH, 12 months (3 study arms) | 0.99 | 0.70 | 1.42 |
| PSYCH, 18-24 months (1 study arms) | 1.04 | 0.81 | 1.36 |

* + - 1. Pooled effect sizes for indicated psychological intervention when limiting the scope of studies to those using an intention-to-treat approach

|  |  |  |  |
| --- | --- | --- | --- |
| Follow-up | Effect Size | Lower 95% CI | Upper 95% CI |
| PSYCH, Post-treatment (3 study arms) | 0.31 | 0.12 | 0.81 |
| PSYCH, 6-9 months (6 study arms) | 0.35 | 0.20 | 0.61 |
| PSYCH, 12 months (2 study arms) | 0.45 | 0.14 | 1.48 |
| PSYCH, 18-24 months (2 study arms) | 0.74 | 0.41 | 1.36 |

### Sensitivity analysis using a weighted average disability weight based on an alternative severity distribution derived from DSM-IV algorithms for mild, moderate and severe depression

In the baseline analysis, we calculated a disability weight for major depression that was the weighted average of GBD 2013 disability weights for mild, moderate and severe depression. We weighted each of these weights by using a severity distribution (i.e., the proportion of mild, moderate and severe depression) taken from a previous GBD study [18]. In section 4.8, we described an alternative severity distribution by which to calculate the weighted average of GBD 2013 disability weights for mild, moderate and severe depression. This involved using a severity distribution derived from the 1997 National Survey of Mental Health and Wellbeing (NSMHWB), which is based on DSM-IV algorithms for the classification of mild, moderate and severe depression. Unlike the severity distribution used in the GBD study, this severity distribution was not adjusted for comorbidity (see section 4.8). The disability weight for depression that was calculated using the severity distribution based on DSM-IV algorithms was 0.407 (95% CI: 0.324 - 0.485). This was approximately 1.6 times larger than the disability weight of 0.256 (95% CI: 0.195 – 0.324) which was calculated using the severity distribution from the GBD study.

### Sensitivity analysis using pooled standard gamble and EQ-5D utility weights in place of pooled GBD 2013 disability weights for major depression

We also calculated a composite utility weight for major depression by calculating the weighted average of utility weights for mild, moderate and severe depression. The individual weights for mild, moderate and severe depression were obtained from a systematic review by Mohiuddin and Payne [20]. In this study, the authors calculated pooled utility weights by meta-analysing studies involving: the direct valuation of health preferences (e.g., standard gamble, time trade-off and person trade-off methodologies); and the indirect valuation of health preferences using multi-attribute utility instruments (e.g., EQ-5D, SF-6D and the AQoL-8D). They found that Standard Gamble was the most commonly used direct valuation method, while the EQ-5D was the most common indirect valuation method. The study authors, in turn, conducted a meta-analysis to calculated pooled utility weights for the Standard Gamble and EQ-5D approaches. Using the GBD 2013 severity distribution reported in Table 16, we calculated the composite utility weights for the Standard Gamble and EQ-5D to be 0.604 (95% CI: 0.353 - 0.817) and 0.499 (95% CI: 0.266 - 0.720), respectively. It should be noted that our model used disability weights, which are a measure of health loss; as opposed utility weights, which are a measure of health gain [65]. To convert the composite utility weight from a measure of health gain to a measure of health loss (as is required in our model), we used the formula: DW = 1 – UW. Where DW is the disability weight and UW is the utility weight. We substituted these converted utility weights into our model (i.e., assigned them to people in our model who become depressed – see section 4.1) to test the impact of modelling health benefits using the Standard Gamble and EQ-5D approaches.

### Sensitivity analysis modelling internet-delivered intervention pathways

As stated in section 2.6, we were unable to identify any relevant RCT studies involving internet-delivered prevention interventions (universal and indicated), which met the inclusion criteria for our model. As such, we chose to impute intervention effect sizes for internet-delivered prevention interventions (universal and indicated) by assuming that their effect sizes were equal to some proportion of the pooled intervention effect sizes calculated for face-to-face prevention interventions. Given the heroic nature of this assumption, we relegated this investigation to a separate sensitivity analysis. Detailed intervention pathways and their accompanying costs are described in detail in: section 5.3 for internet-delivered universal prevention; and section 5.5 for internet-delivered indicated prevention.

In the sensitivity analysis, we examined the cost-effectiveness of internet-delivered prevention by assuming that the effect size was either 100% or 50% of the pooled intervention effect size for corresponding face-to-face intervention delivery (both universal and indicated). Additionally, we calculated the cost-effectiveness of internet-delivered prevention by changing the cost profile to account for either unmoderated or clinician-moderated intervention delivery. Online psychological interventions are conventionally delivered through either unmoderated modalities (i.e., self-help) or clinician-moderated modalities (i.e., self-directed treatment with periodic monitoring by a health professional or clinician; which can improve adherence to the internet-delivered psychological intervention). In sections 5.3 and 5.5, we outlined the cost of internet-delivered psychological intervention (both universal and indicated) assuming a cost profile associated with unmoderated self-help, which amounts to an average intervention cost of $10.87 per person (adapted from annual subscription fees sourced from THIS WAY UP Schools). We were unable to find a definitive estimate on the average cost per person of clinician-moderated online prevention. The next best estimate was to assume that the average cost per person would range between $55 and $391. The $55 estimate was based on a one-off registration fee paid prior to receiving clinician-moderated treatment from the THIS WAY UP program provided by CRUfAD [26]. This fee represents the lower bound given that is insufficient to cover the full costs of the intervention, but is required to incentivize adherence (i.e., participants are more likely to complete modules if money has been paid). The $391 estimate is the annual cost per person for adults receiving clinician-moderated treatment at the MindSpot clinic (taken from an unpublished cost-effectiveness study) [89]. The mid-point estimate for this range is $223 per person – i.e., $223 pays for the 161,835 eligible participants to access intervention modules during the year. By comparison, this is lower than the cost of paying for the face-to-face intervention delivered by psychologists who are costed based on relevant MBS items (i.e., $422 per person).

We built upon the internet-based intervention models outlined above by conducting a threshold analysis that tested the impact of: (1) varying the imputed effect size for internet delivered prevention so that it lies between 0% and 100% of corresponding effect size for face-to-face prevention; and (2) varying the cost per person of annual subscription fee. These threshold analyses would enable us to explore the cost-effectiveness of internet-delivered universal and indicated prevention across different ranges of efficacy and cost. An exploratory analysis of this nature is vital given the large uncertainty surrounding the (emerging) policy decision of whether it is worthwhile to allocate money to internet-delivered interventions for the prevention of depression. The threshold analysis will thus enable us to explore the limits at which internet-delivered prevention is no longer deemed cost-effective.

In the first threshold analysis, we tested the impact of varying imputed effect sizes under two different costing scenarios: (1) unmoderated intervention delivery; and (2) clinician-moderated intervention delivery. In the second threshold analysis, we tested the impact of varying the annual subscription cost of internet-delivered prevention under two different efficacy scenarios: (1) the efficacy of internet-delivered prevention is equal to 100% of the corresponding efficacy of face-to-face prevention; and (2) the efficacy of internet-delivered prevention is equal to 50% of the corresponding efficacy of face-to-face prevention.

### Sensitivity analysis applying different discount rates to costs and benefits

Our baseline analysis used discount rates of 3% which were applied equally to both costs and health benefits. We tested the impact of applying different discount rates (0% and 6%) to health benefits when holding the discount rate for costs constant (i.e., at 3%). Likewise, we tested the impact of applying different discount rates (0% and 6%) to costs when holding the discount rate for health benefits constant (i.e., at 3%).

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1. Refer to Figure 11 and Figure 14 for flow charts mapping how the eligible population is calculated for intervention pathways relating to universal and indicated prevention, respectively. [↑](#footnote-ref-1)
2. Refer to Figure 15 and Figure 16 for state transition diagrams outlining how the health benefit model simulates the movement of population cohorts between three health states over time for intervention pathways relating to universal and indicated prevention, respectively. [↑](#footnote-ref-2)
3. Refer to Figure 11 for a flow chart mapping how the eligible population is calculated for the intervention pathway of universal prevention. Further detailed methods on the derivation of costs are presented in section 5.2. [↑](#footnote-ref-3)
4. Refer to Figure 14 for a flow chart mapping how the eligible population is calculated for the intervention pathway of indicated prevention. Further detailed methods on the derivation of costs are presented in section 5.5. [↑](#footnote-ref-4)
5. A description of the 7 sources of bias evaluated by the Risk of Bias tool are provided in: <http://handbook.cochrane.org/chapter_8/table_8_5_a_the_cochrane_collaborations_tool_for_assessing.htm> [↑](#footnote-ref-5)
6. The concept of DALYs averted, as used in economic evaluation studies, holds a different qualitative interpretation to DALYs, as used in conventional burden of disease studies. In the former, DALYs averted are a measure of health gain with a similar interpretation to quality-adjusted life years (QALYs) – i.e., a greater number of DALYs averted denotes a greater health gain. By contrast, DALYs used in burden of disease studies denote a measure of health loss where a larger number of DALYs denotes a greater disease burden. [↑](#footnote-ref-6)
7. We modelled age-sex cohorts between the ages 11-17 years over a 10-year time horizon, which meant that a 17-year cohort would be aged 27 years by the end of the 10-year period. Hence, we required age-specific incidence data between 11-27 years. [↑](#footnote-ref-7)
8. Please refer to the following website for a schedule of annual subscription fees: . <https://schools.thiswayup.org.au/index.php/homepage/payOnline> [↑](#footnote-ref-8)