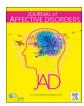
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#### Review article

What are the effects of preventative interventions on major depressive disorder (MDD) in young adults? A systematic review and meta-analysis of randomized controlled trials



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#### ABSTRACT

*Background:* Depression is a prevalent disorder with a peak rate of onset in young adulthood from 18 to 25 years. To date, no review has systematically assessed the effectiveness of programs that aim to reduce depressive symptoms or diagnosis of depression in young adults.

*Method:* A systematic search was performed in Cochrane, PubMed, PsycINFO and EMBASE. We performed a random-effects meta-analysis of the randomized controlled studies that compared an intervention for young adults (aged 18–25) without a diagnosis or history of depression and a control condition. Comparisons between intervention and control group outcomes were carried out at the post-intervention time point. We also compared intervention and control group outcomes at later follow-up time points where data were available.

*Results*: Twenty-six randomized controlled trials among 2865 young adults were included in the analysis. The pooled effect size of the interventions versus control at post-intervention was g = 0.37 (95% CI: 0.28–0.47, NNT = 9) and heterogeneity was moderate  $I^2 = 36$  (95% CI: 11–64). There were no significant effects in terms of the type of delivery, focus of study, type of control, or type of support within the interventions.

Limitations: The authors were unable to assess the effects of interventions on the onset of depression as none of the included studies measured incidence. The risk of bias was high in most studies (81%). Only one study included a follow-up of more than a year. Demographic factors were inconsistently reported in the included articles.

*Conclusion:* While it was not possible to investigate the effects of interventions on depression incidence, some evidence was found for the effectiveness of preventative interventions in reducing depressive symptoms in young adults. Future research should address limitations of the current evidence base to allow stronger conclusions to be drawn.

#### 1. Introduction

Depression is a costly and debilitating condition, which frequently develops during young adulthood (Eaton et al., 2008). Young, or emerging, adulthood is a transitional phase in life between the ages of 18 and 25 years, where a cumulative exposure to risk factors such as instability, finding employment, exploring identity, and enhanced self-focus increases the likelihood of developing mental health problems (Arnett, 2000). Consistent with these factors, the risk of developing major depressive disorder (MDD) for this group is high compared to

other age groups or diagnostic categories. The US National Comorbidity Survey found that the cumulative risk of the development of MDD was at its highest in 18–29-year-old compared to individuals in later life stages (Kessler et al., 2003). These results were replicated by a more recent incidence study on young adults aged 18–23.9 years (N = 816) (Rohde et al., 2013).

Developing depression during young adulthood is linked to poorer outcomes in later life, and early onset of MDD is often found to be predictive of recurrence (Eaton et al., 2008). More broadly, depression during this phase of life is related to lower rates of degree attainment,

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unemployment, and lower income in later life (Fergusson et al., 2007; Wilson et al., 2015; Zisook et al., 2007). Reducing the likelihood of developing depression in the first instance can help prevent recurrence in later life (Burcusa and Iacono, 2007). Whilst treatment is an option to pursue if symptoms worsen, therapeutic resources are by definition scarce, and in the UK, only 59.7% make a full recovery after receiving therapy (Gyani et al., 2013).

While several studies have aimed to reduce the risk of developing MDD in young adults, the majority of studies focussing on preventing MDD have been conducted with child and adolescent populations (Hetrick et al., 2016; Merry et al., 2011; Rasing et al., 2017; Stockings et al., 2016), . Evidence from these studies suggests that strategies for groups with mild to moderate (i.e. subclinical) symptoms of depression (targeted interventions) rather than for groups with none or very low symptoms of depression (universal interventions) tend to be more effective in reducing the risk of developing MDD (Ahlen et al., 2015). A potential explanation for this is that individuals with subclinical depression have an increased risk of developing MDD compared to those with very low, or no symptoms of depression (Karsten et al., 2011). Thus, some preventative efforts have now focussed on reducing subclinical symptoms as a strategy to prevent symptoms from deteriorating and reaching diagnostic thresholds.

Previous research on depression prevention found strongest effects for indicated interventions for cognitive behavioral therapy (CBT) (Ahlen et al., 2015; Hetrick et al., 2016; Horowitz et al., 2007). However, reviews have indicated that interventions compared to inactive controls (where no intervention was provided) displayed stronger effects than those compared to active control groups, such as a placebo control (Davies et al., 2014a). For young adults in higher education, similar results were found (Conley et al., 2015, 2017).

Thus far, only one review has compared the effect of preventative interventions on the incidence of depression in adults and high school students (van Zoonen et al., 2014), although no significant differences were found between these groups. Further sensitivity analysis did not identify any differences in the effectiveness on depression prevention in terms of the number of sessions, whether the intervention was targeted or universal, or the theoretical underpinnings of the intervention. Moreover, the above-described reviews only focused on adults in school settings. Furthermore, the reviews only compared to psychological therapies and did not include comparisons with other interventions focused on improving psychological health and wellbeing for prevention of depression. Thus, to our knowledge, no review has been conducted to assess the effects of interventions that prevent the first onset of MDD or reduce symptoms of depression. The objective of this review is to summarize, evaluate, and assess the quality of evidence and determine whether, compared to control, interventions are more effective at reducing depressive symptomatology either via symptom measurement or diagnosis for young adults with no or subclinical symptoms of depression. The following research questions are addressed:

- (1) Are preventative interventions effective at reducing depressive symptoms or diagnosis of depression in young adults relative to a control group?
- (2) Are there any underlying (study, intervention) factors influencing this effect?

# 2. Methods

# 2.1. Identification and selection of studies

The study protocol was registered on PROSPERO (https://www.crd. york.ac.uk/PROSPERO/display\_record.asp?ID = CRD42016048118.). A comprehensive search of the literature in four bibliographic databases (Cochrane, PsycINFO, EMBASE, PubMed (including Medline)) was performed. No date restrictions were applied in order to maximize recall. Final searches were carried out on 18 December, 2016 and an

update was performed on 15 March, 2018.

The search terms were developed together with a health sciences librarian and comprised of four aspects: (1) depression, (2) preventative intervention, (3) age range, and (4) study design. Index terms with free terms using Boolean operators were used. The full search string for PubMed is available in Supplementary Appendix A. Reference lists of previous relevant meta-analyses were also hand-searched, and the references of retrieved relevant articles were reviewed. Inclusion criteria were Randomized Controlled Trials (RCT) that investigated the effect of a preventative intervention on depressive symptoms or incidence of depression. Prevention was defined as a decrease in depressive symptoms or incidence of depression at post-intervention or follow-up (Andrews and Wilkinson, 2002: Pencheon et al., 2013).

Participants with no or subthreshold symptoms of depression and who had no known prior diagnosis were deemed suitable for a preventative intervention. Thus, we only included studies where participants had no or subclinical symptoms of depression, defined by measurement scores on the following questionnaires: Beck Depression Inventory (BDI)- II and I <19 (Beck et al., 1988, 1996 ), Centre for Epidemiological Studies Depression scale (CES-D) < 16 (Eaton et al., 2004), Hamilton Depression Rating Scale < 20 (Hamilton, 1960), Patient Health Questionnaire-9 (PHQ-9) <10 (Kroenke et al., 2001) and Depression, Anxiety and Stress Scale 21 (DASS-21) depression subscale <20 (Lovibond and Lovibond, 1995). Studies with participants who met the diagnostic criteria for depression (DSM-III-R or DSM-IV) before commencement were excluded, as interventions would then be classified as treatment—as opposed to preventative—of depression. Where reported, studies that concerned participants who already received treatment for a mental health problem or had a prior diagnosis of depression were also excluded.

In order to assess the effect of a range of interventions, the inclusion criteria for the interventions were kept broad. Universal and indicated preventative interventions based on psychological therapy or mind-body approaches were included (Andrews and Wilkinson, 2002; Pencheon et al., 2013). Interventions of pharmaceutical nature (i.e. pills, vaccines) were excluded.

As the meta-analysis aimed to study young adults, studies that focused on children, adolescents, and adults > 25 years were excluded. To ensure that most of the participants included in this meta-analysis were aged 18–25 years, we excluded studies where the mean age of the samples was outside the range of 19–24 years and the standard deviation was greater than 1. In cases where the age was unclear, the authors contacted the corresponding author for information.

# 2.2. Data extraction and quality assessment

Covidence (Veritas Health Innovation, 2016) was used for importing studies. Title/abstract screening and full-text extraction were performed by two independent assessors at a time and five assessors in total (AK, JB, AS, VZ and JY) using a standardized form. Disagreements were resolved through discussion and consensus with the lead author. Several subgroups were coded to examine differences in program effectiveness. Two researchers independently coded the classifications according to pre-specified categories and disagreements were resolved by contacting the lead author. Included studies were coded to 'targeted' and 'universal' interventions to assess whether interventions targeted at participants with elevated levels of depression at baseline were more effective compared to studies where participants had low or no symptoms of depression. The authors also coded focus of intervention, this was stated in the primary outcomes section where authors identified which constructs the intervention ought to have an effect on (i.e. general psychological health, stress reduction, anxiety and stress). To code this, two researchers read the intervention description provided in text on the modifiable constructs which the intervention intended to change. If no primary construct was identified, and the aim was to improve overall wellbeing, the intervention was classified as 'psychological health' Other subgroup categories were coded including 'type of guidance', 'theoretical framework', length and setting of intervention. Please see appendix C for an overview of subgroup categories and coding applied to the study and intervention characteristics.

Any missing data were requested from the included study corresponding authors, who were given a two-week time window to respond. The Cochrane risk of bias tool by Higgins et al. (2011) was used to assess the possibility of bias in the included studies. These included the following categories for RCTs: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, and (6) selective reporting. Unclear risk items were classified as high risk of bias. A study with high or unclear risk scores on two or more criteria was defined as a study with high risk of bias, whereas a study with lowrisk scores on five or more criteria was defined as low risk of bias. The outcomes were categorized as "Low risk" of bias or "High risk" of bias. To include risk of bias in the meta-regression analysis, a continuous risk of bias score was calculated for each study. Each high-risk category was scored as 2, each unclear risk category was scored as 1, and each lowrisk category was scored as 0. Therefore, each study could score between 0 (low risk on all categories) and 12 (high risk on all categories). Risk of bias assessment was conducted independently by two reviewers (JB and AK). Inter-rater reliability was calculated using Cohen's kappa for each category of risk of bias.

#### 2.3. Analyses

Comprehensive Meta-Analysis Software package, version 3 (Biostat, Englewood NJ) was used to calculate the pooled effect sizes on postintervention comparisons between intervention and control groups. Hedges' g was used to allow for small sample bias correction when calculating the difference between the intervention and control conditions at post-intervention. If multiple measures of depression were used in a single study, the mean of the effect sizes was calculated. As depression was our primary outcome, only instruments that specifically measured depression were included (e.g., the BDI-II (Beck et al., 1996) or the DASS-21 (Lovibond and Lovibond, 1995) depression subscale). The I<sup>2</sup> statistic and 95% Confidence Intervals (CI) were calculated to assess heterogeneity. NNT was calculated by the Furukawa method (Furukawa and Leucht, 2011). The main analysis used a random-effects model. Subgroup analyses were performed using a mixed effects model, and meta-regression analyses were performed. Duval et al. (2000) trim and fill procedure, the Egger's test (1997) (Egger et al., 1997), and the classic fail-safe N were used to examine publication bias. Subgroup analyses on the risk of bias, prevention type, theoretical framework, type of guidance, length and setting of interventions were also carried Out.

### 3. Results

# 3.1. Selection and inclusion of studies

The literature search resulted in 10,672 articles. After removal of duplicates, 6048 titles and abstracts of studies were screened for eligibility. Fig. 1 displays the PRISMA flowchart, which provides an overview of the selection process. A further fifteen studies were identified through searches of reference lists. In total, 405 full-text articles were retrieved from the literature search that potentially met the inclusion criteria. Of these 378 were excluded, with the majority (N = 163) excluded as the participants were either below (N = 62) or above (N = 101) the pre-specified age criterion. Twenty-six studies were included in the final analysis.

# 3.2. Characteristics of included studies

The 26 studies included a total of 2865 participants who had

completed both baseline and post-intervention measures (not including follow-up) (control N = 1,431, intervention N = 1,434). The average number of participants in the intervention condition was 56 at baseline and 49 at post-intervention. In the control condition, an average of 61 participants completed the baseline test battery, and 55 completed postintervention tests. Twelve studies examined the effects in an a population with heightened risk (targeted prevention) (Aboalshamat et al., 2015; Biggam and Power, 2002; Cui et al., 2016; Day et al., 2013; Ellis et al., 2011; Kang et al., 2009; McGrady et al., 2012; Niles et al., 2014; Rohde et al., 2014, 2016; Seligman et al., 2007; Takagaki et al., 2016) and fourteen in a general young adult population (universal prevention) (Bowden et al., 2010, 2011; Cukrowicz et al., 2007; Dvořáková et al., 2017: Enrique et al., 2017: Frazier et al., 2015: Hazlett-Stevens and Oren, 2016; Houston et al., 2017; Lee and Jung, 2018; Levin et al., 2014; McGrady et al., 2012; Moir et al., 2016; Pratt et al., 2000; Song and Lindquist, 2015; Thomas et al., 2016). Twenty-five studies were conducted with university student populations. Age data was available in most cases (N = 23); the mean age was 19.6 years (SD = 1.40). Studies were carried out in North America (N = 14), Asia (N = 6), Europe (N = 4) and Oceania (N = 2). Thirteen out of 26 studies reported on participants' ethnicity; a commonly reported category was Caucasian in eleven studies, and the average percentage of Caucasian participants was 58.7%. Eleven studies also reported on Asian ethnicity with an average percentage of 30.3%. Other categories (Black American, Hispanic, Native American, and Mixed) were reported infrequently and mostly inconsistently. Twenty-three studies reported on gender, and the average percentage of females in the studies was 68.8%. None of the included studies reported on participants' socioeconomic status.

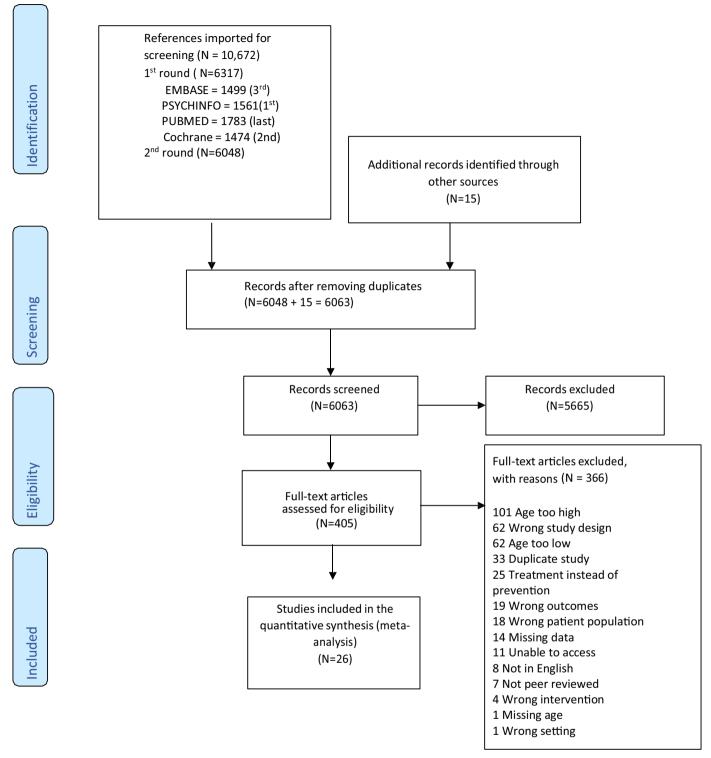
Most of the interventions were based on CBT (N=8) or Mindfulness-Based Stress Reduction (MBSR) (N=8) and were delivered by a professional (N=12). In nine studies, the main intervention was unguided. In six studies a trained non-professional facilitated the intervention (and in one other study, the secondary intervention was delivered by a trained non-professional); in one condition the intervention was led and delivered by peers (e.g. classmates). The delivery method of the interventions varied; in four of the trials, the intervention was delivered face-to-face in a 1:1 manner, and in thirteen the intervention was delivered in a group setting. Seven interventions were provided online, and three were offered in a self-help format (including one study's secondary intervention) e.g. bibliotherapy. Tables 1 and 2 include further selected characteristics of the studies and interventions.

Pre-(T1) and post-intervention (T2) data were available for all 26 studies, but only ten studies provided data at 1–3 months (T3) follow-up, three studies at 4–6 (T4) months follow-up, one study reported on a T5 (6–9) time point, and one study reported on 10–12 months (T6) follow-up. The average length of interventions was 7.3 weeks. Many studies (N=9) reported that the control condition received no additional intervention or support (N=536), four studies indicated that participants in the control condition were directed to literature about mental health or wellbeing (psycho-education) (N=232), eight studies reported a waitlist control condition (N=325), and in five studies, participants received a placebo intervention (N=346). None of the studies measured the incidence (diagnosis) of depression at post-intervention assessment. All outcome measures were scale-based and continuous, with lower scores indicating fewer depressive symptoms.

# 3.3. Risk of bias

The risk of bias was high in most studies (N = 23), with a mean score of 2.6 and a standard deviation of 1.2. In sixteen studies, an adequate sequence generation method was applied. Seventeen out of 26

 $<sup>^{\</sup>rm 1}$  This excludes McGrady et al. (2012) which does not state the number of participants initially allocated to the control condition.



 $Fig. \ 1. \ {\it Flowchart of inclusion of studies (PRISMA flow diagram)} .$ 

studies reported independent allocation condition. All studies had treatment outcomes, and this was interpreted as all studies having unblinded assessors. Eight trials reported an intention to treat analysis. Only three studies were scored as low risk, with no studies meeting all quality criteria. Twenty-two studies reported information on dropout rates, which ranged from 0 to 64%; studies that did not make a reasonable attempt to account for drop-out rates were deemed to have a substantial risk of bias in the outcome incomplete category. The risk of bias in study results is summarized in Table 3. The Cohen's k indicated

that inter-rater reliability between the two reviewers' judgements was high, k = 0.95, p < 0.0005.

# 3.4. Effects of preventative interventions on reducing depression versus control groups

With 26 studies included, 29 comparisons were conducted wherein the intervention group was compared to control group. This resulted in an overall effect size of g = 0.37, NNT was 9, heterogeneity was

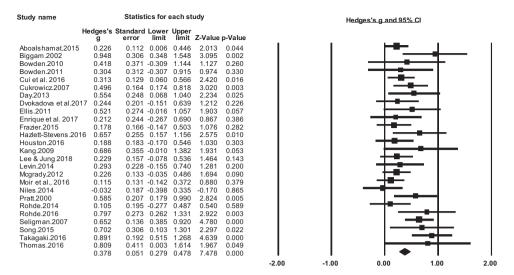


Fig. 2. Forest plot.

moderate  $I^2 = 36\%$  (95% CI: 11–64), (p = 0.000) as can be seen in Table 4. Four studies were excluded from the main analysis as they represented extreme positive outliers (g > 1). With these studies included, the overall effect size rises to g = 0.53, with NNT of 6, and heterogeneity rising to  $I^2 = 74\%$  (95% CI: 67–84). Figure 2 contains the forest plot with individual and overall study effect sizes.

Three studies included more than one intervention group. That is, two preventative interventions were compared to the same control group. Separate analyses were carried out to include only one effect size per study, as including both effect sizes could artificially reduce heterogeneity and inflate effect size. As the interventions could not be categorized into similar groups, a separate analysis with the highest and lowest effect size per intervention in each study was conducted, which resulted in comparable effect sizes of g=0.39 and g=0.37, respectively. The effect size for T2 was g=0.38, NNT = 8 and for T3–T6 g=0.28, NNT = 11.

To assess publication bias, inspections of the funnel and forest plot were conducted, suggesting the possibility of some bias in the data (Appendix B). Following adjustment for publication bias, the effect size changed from 0.37 to 0.29 (95% CI: 0.19–0.40) for seven trimmed studies. Egger's test showed that the funnel plot was asymmetrical, intercept: 1.35; 95% CI: 0.01–2.68, df (27), p=0.05, suggesting that there was some publication bias present in the studies. The classic failsafe N was 693, indicating that 693 studies would need to be added to make the observed test result 'insignificant'.

# 3.5. Subgroup analyses

We carried out several subgroup analyses (Table 4). We did not find a significant association between the following study characteristics and effect size: (i) type of prevention (targeted or universal), (ii) type of support (self-help, peer support, professional, or trained student support), (iii) intervention setting (online, group-based, face to face, self-led) (iv) theoretical framework (CBT, mindfulness, mind-body, or other approaches), (v) the primary focus of the intervention (depression, comorbid depression and anxiety, psychological health, stress reduction), and (vi) the type of control (care as usual, placebo, psychoeducation and wait-list).

### 3.6. Meta-regression analysis

A meta-regression analysis was performed to further investigate the effects of continuous subgroup variables on depression. Predictors in the model were Risk of Bias and Length of Intervention (Table 5). The

regression model explained very little of the total variance (adjusted  $R^2 = 0.00$ ). None of the included variables was significant.

#### 4. Discussion

The results of this meta-analysis indicate that there is a moderate, positive effect of preventative interventions on reducing the symptoms of depression compared to controls. This effect appears to be sustained at longer-term follow-up time points. No data were available on the incidence of depression. Thus, we were unable to report on the prevention of the onset of a depressive episode. Further subgroup analysis did not find significant differences between groups. Meta-regression analyses found that there was no significant association between risk of bias or length of interventions and effect size.

# 4.1. What does this add to our existing knowledge?

This, to our knowledge, is the first study exploring the effect of preventative interventions on depression in young adults, aiming to include also those who are not in university settings. The review confirms several aspects already observed in public mental health literature. In line with prior research, most studies were conducted in university settings. Further to this we did not find any significant subgroup level differences. One interesting trend was that the effect of the intervention was strongest when compared to inactive control, which is in line with prior studies (Christensen et al., 2010; Davies et al., 2014a; van Zoonen et al., 2014). This suggests that non-specific intervention characteristics may partly explain effects found in the intervention.

Similarly, non-significant subgroup effects were found (including the type of prevention, level of support offered, delivery and theory type) in a meta-analysis addressing the effects of psychological interventions on depression incidence in adults (van Zoonen et al., 2014). This is in contrast with prior meta-analyses on children, adolescents, and university students, which found significant subgroup differences for targeted versus universal interventions (Ahlen et al., 2015; Hetrick et al., 2016; Horowitz et al., 2007) and CBT based interventions (Davies et al., 2014a) .The findings may be explained by the differences in the population groups. Furthermore, the moderate degree of heterogeneity in this review may have added challenges in detecting differences between subgroups.

We found a higher effect size compared to mean effect sizes found in comparable meta-analyses in children and adolescents, with effects in these studies ranging between d=0.11 (95% CI 0.03–0.20) for universal prevention (Ahlen et al., 2015) and d=-0.21, (95% CI -0.27

Selected characteristics of the included studies.

Study	Region	$N^{\mathrm{a}}$	Mean age, years (SD)	Sample	Conditions	Outcome measure	Follow-up
Aboalshamat et al. (2015)	Asia	323	20.99 (0.83)	Students	Other vs. placebo	DASS-21	5 weeks
Biggam and Power (2002)	Europe	46	19.3 (1.5)	Young offenders	CBT vs. care as usual	HADS	3 months
Bowden et al. (2010)	Europe	32	23 (3.5)	Students	Mind-body vs. placebo	DASS-21	Post intervention test only
Bowden et al. (2011)	Europe	20	18-31 (only range available)	Students	Mind-body vs. placebo	DASS-21	5 weeks
Cui et al. (2016)	Asia	180	19.42 (1.66)	Students	CBT vs. active control vs. wait-list	SDS	6 months
Cukrowicz et al. (2007)	North America	152	19.2 (1.9)	Students	CBT vs. psycho-educative control	BDI	Post intervention test only
Day et al. (2013)	North America	99	23.55 (4.98)	Students	CBT vs. wait-list	DASS-21	Post intervention test only
Dvořáková et al. (2017)	North America	109	18.2 (0.4)	Students	Mindfulness vs. wait-list	РНО	Post intervention test only
Ellis et al. (2011)	Oceania	56	19.67 (1.66)	Students	CBT vs. other vs. CAU	DASS-21	Post intervention test only
Enrique et al. (2017)	Europe	81	23.8 (3.85)	Students	Other vs. placebo	BDI-II	1 and 3 month
Frazier et al. (2015)	North America	257	18-45 (only range available)	Students	Other vs. psycho-educative control	DASS-21	3 weeks
Hazlett-Stevens & Oren, Y. (2016)	North America	89	22.1 (4.7)	Students	Mindfulness-based stress reduction bibliotherapy vs. care as	DASS-21	Post intervention test only
					usual		
Houston et al. (2017)	North America	128	19.98 (1.2)	Students	Other vs. care as usual	CES-D	Post intervention test only
Kang et al. (2009)	Asia	32	22.47 (1.18)	Students	Mindfulness vs. care as usual	BDI	Post intervention test only
Lee and Jung (2018)	North America	206	Control -20.9; intervention	Students	Mindfulness vs. waitlist	QIDS-SR	Post intervention test only
			-20.3				
Levin et al. (2014)	North America	26	19.37 (0.54)	Students	Acceptance and commitment therapy vs. wait-list control	DASS-21	3 weeks
McGrady et al. (2012)	North America	370	23.4	Students	Mindfulness vs. wait-list control	BDI-II	5 months
Moir et al. (2016)	Oceania	275	20.9 (2.9)	Students	Mindfulness vs. care as usual	6-ОНА	6 months
Niles et al. (2014)	North America	116	21.2 (2.89)	Students	Other vs. placebo	DASS-21	Post intervention test only
Pratt et al. (2000)	North America	110	18.6	Students	Other vs. care as usual	CES-D	Post intervention test only
Rohde et al. (2014)	North America	09	19 (0.9)	Students	CBT vs. psycho-education vs. psycho-educative placebo	K-SADS	6 and 12 months
					control		
Rohde et al. (2016)	North America	29	21.8 (2.3)	Students	CBT vs. psycho-education vs. placebo	BDI	Post and 3-month follow-up
Seligman et al. (2007)	North America	227	ı	Students	CBT vs. care as usual	BDI	3- and 6-month follow-up
Song and Lindquist (2015)	Asia	20	19.6 (1.7)	Students	Mindfulness vs. wait list control	DASS-21	Post intervention test only
Takagaki et al. (2016)	Asia	118	18.4 (0.4)	risk Students	Other vs. care as usual	BDI-II (Japanese	Post intervention test only
Thomas et al. (2016)	Asia	24	21 (2.07)	Students	Mindfulness vs. wait list control	adaptation) BDI-II	Post intervention test only

Theory of intervention: ACT = acceptance commitment therapy, CBT = cognitive behavioral therapy, Mind-body,

Mindfulness = Mindfulness-based Stress Reduction, Other = interventions based on other theoretical underpinning, due to low N these were categorized in 'other';

Control group: CAU = care as usual, Placebo, WL = wait-list control;

Measures: BDI = Beck Depression Inventory, BDI-II = Beck Depression Inventory II, CES-D = Center for Epidemiologic Studies Depression Scale, DASS-21 = Depression Anxiety and Stress Scale 21, K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia.

<sup>a</sup> This refers to the *N* at baseline.

Table 2 Intervention characte

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Study	Label and content	Theoretical classification	Prevention type	Focus	Guidance	Delivery
Aboalshamat et al. (2015)	How to be an ultra super student: a self-development program focusing on improving psychological health and academic performance, administered through lectures a booklet, and audio CDs.	Other	Targeted	Psychological health	Professional	1:1
Biggam and Power (2002)	A problem-solving skills training program was conducted in small groups of 4–6 inmates in five 90-min sessions. Sessions were conducted by the lead researchers, which involved instruction, active discussions, reflective listening, and group exercises.	СВТ	Targeted	Psychological health	Professional	Group
Bowden et al. (2010)	Reiki: a combination of Relix techniques and symbols were used to induce a hyprotic/relaxation state, with each of the 10 sessions lasting 30 min	Mind- body	Universal	Psychological health	Professional	1:1
Bowden et al. (2011)	Section matters of min.  Reiki: a combination of Relix techniques and symbols were used to induce a hypotic/relaxation state, with each of the 6 sessions laxing 30 min.	Mind- Body	Universal	Psychological Health	Professional	1:1
Cui et al. (2016)	A group cognitive-behavioral program for college students at risk of depression. Students attended weekly sessions, which included weekly goal setting, relaxation techniques and homework tasks, and followed Oei's (2012) GCBT manual for depression.	TWCBT	Targeted	Depression	Professional	Group
Cukrowicz et al. (2007)	Cognitive-Behavioral Analysis System of Psychotherapy (CBASP): a single 2-h long computer-based study session was conducted to provide information on depression and anxiety and the principals of GBT and CBASP. Participants were then given related worksheets to complete throughout the R-week moream with email reminders.	CBT	Universal	Anxiety- depression	Self-help	Online
Day et al. (2013)	An internet-based guided self-help program was provided on the basis of CBT for the management of anxiety, depression, and stress. Advice was also offered through email or phone calls	CBT	Targeted	Psychological health	Trained student	Online
Dvořáková et al. (2017)	protocoms: Mindfulness via the L2B program was administered to students in 8 sessions delivered over 6 weeks. The key goals of the program include enhancing students' emotion regulation skills and introducing simple mindfulness techniques so that students may better manage stressful simple mindfulness.	Mindfulness	Universal	Psychological health	Trained facilitator	Group
Ellis et al. (2011)	MoodGVM: a self-help internet-based intervention was administered in three 60-min sessions based on the principals of CBT.  MoodGarden: a peer-support internet-based intervention consisting information and self-management techniques for anxiety and depression was administered in three 60-minute	CBT and other	Targeted	Depression	Self-help + Peer support	Online
Enrique et al. (2017)	A positive psychological intervention (best possible self, BPS) based on positive future thinking was administered to students. Participants were asked to visualize their BPS each day using a Positive Technology Application in order to impact on levels for positive and analysive expectations. Secondary outroones included demessive symptoms.	Other	Universal	Psychological health	Self-help	Online
Frazier et al. (2015)	An Internet-based stress management program was administered over a two-week period, focusing on increasing perceived control over stressful events. The program consisted of video and text-based stress-management instructions and completing logs for stressful	Other	Universal	Stress reduction	Self-help	Online
Hazlett-Stevens & Oren, Y. (2016)	Windfuness-based stress reduction (MBSR) bibliotherapy: a self-help MBSR program was administered through a workbook that participants read over a 10-week period. In week 10, participants engaged in mindfulness-based practices using audio instructions provided along with the workbook	Mindfulness	Universal	Stress reduction	Self-help	Self-help
Houston et al. (2017)	rest the warsoom. Resilience and Coping Intervention (RCI): A group-based intervention designed for children and young people was administered, which involved identifying thoughts, feelings, and coping strategies related to a stressful event.	Other	Universal	Psychological health	Professional	Group
Kang et al. (2009)	A group-based stress coping program based on mindfulness, self-reflection, and physical stretching was administered via voice recorded files and an instructor's manual over 8 weekly sessions.	Mindfulness	Targeted	Stress reduction	Professional	Group
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Study	Label and content	Theoretical classification	Prevention type	Focus	Guidance	Delivery
Lee and Jung (2018)	A mental health app, DeStressify, which was initially developed for teachers, organisations and the general public was provided to students, who were instructed to engage with 5 days a week over 4 weeks. The app delivers mindfulness-based exercises through audio, video and teach flow	Mindfulness	Universal	Stress reduction	Self-help	Online
Levin et al. (2014)	and text nices.  Acceptance and Commitment Therapy (ACT): The internet-based ACT program was administered through multimedia loscons and sundementary tailored emails.	Other	Universal	Anxiety-depression	Self-help	Online
McGrady et al. (2012)	wanning care transfer interince a resonal and supprendingly and the service contains.  A group-based stress management and wellness program was offered in 8 sessions, which included breathing, imagery, mindfulness, coping, nutrition, and life balance exercises.  Sections involved brief presentations worksheets and relaxation practice.	Mindfulness	Universal	Psychological health	Professional	Group
Moir et al. (2016)	A peer-led program where students underwent training to become peer leaders, and subsequently provided support to their peers and offered teaching in mindfulness meditation. Peer leaders also organized two social events, and encouraged their peers to understo have a meditation and their peers to understo have a meditation.	Mindfulness	Universal	Psychological health	Peer-leaders	Group
Niles et al. (2014)	intertake notice practice.  Expressive Writing: Participants were instructed to write about the traumatic or stressful events they experienced, for 20 min. Four sessions were conducted over 8 weeks in a private laboratory, and the session consisted of audio instructions followed by a pen-and-paper-based writing rest.	Other	Targeted	Stress reduction	Self-help	Self-help
Pratt et al. (2000)	Social support discussion groups lead by student facilitators were designed for first-year Social support discussion and semi-structured exercises focusing on improving the transition into student life. The groups met 9 times, starting out as weekly sessions then as historyla coecing the Teach between 75 and 85 min	Other	Universal	Psychological health Trained student	Trained student	Group
Rohde et al. (2014)	Cognitive-behavioral (CB) group: 6 weekly sessions lasting 1 h were conducted in group settings to lower the risk of depression through thought identification, cognitive restructuring, and increased involvement in pleasant activities. Bibliotherapy: principals from the CB approach for preventing and lowering negative mood were administered through a self-help book written at a high-school reading level. Two reminder calls were	CBT	Targeted	Depression	Trained student	Group + Self-help
Rohde et al. (2016)	Ghange Ahead group: 6 weekly sessions lasting 1 h in groups of 6–8 students were change Ahead group: 6 weekly sessions lasting 1 h in groups of 6–8 students were administered. The intervention contained elements of the CB approach, modified to use cognitive dissonance approaches, such as publicly committing towards making a change, followed by home amorphic committees.	CBT	Targeted	Depression	Trained student	Group
Seligman et al. (2007)	A group-based workshop was conducted every week for 8 weeks in groups of 10–12, using CB principals to reduce the risk of depression. Homework assignments were also given between acceptance.	CBT	Targeted	Anxiety-depression	Professional	Group
Song and Lindquist (2015)	Detweet incernings.  MBSR: a trained instructor led the group sessions for 2 h every week for 8 weeks using the principles of MBSR to halv with demoscion, anyiety, and cross	Mindfulness	Universal	Psychological health	Professional	Group
Takagaki et al. (2016)	principles of mison to net with uspression, anxiety, and suess.  Behavioral activation: 5 weekly, 60-min short sessions used the behavioural activation principles of a CBT program to increase access to positive reinforcement activities and reduce the risk of depression. Groups consisted of up to 3 participants, and a behavioral	Other	Targeted	Depression	Professional	1:1
Thomas et al. (2016)	activation workbook was also provided along with homework assignments.  MBSR: 10 weekly 50-min sessions were led by the first and second authors of the paper using the principles of MBSR. Participants were also given weekly homework assignments.	Mindfulness	Universal	Stress reduction	Professional	Group

Theory of intervention: CBT = cognitive behavioral therapy, Mind-body = Reiki, Mindfulness = Mindfulness. Based stress reduction, Other = interventions based on other theoretical underpinning, due to low N these were categorized in 'other'.

Table 3
Risk of bias summary<sup>a</sup>.

-	Sequence	Allocation	Blindingpps	Blindingass	Outcome Incomp	Selreport	RoBtotal	RoBstatus
Aboalshamat et al. (2015)	-	_	+	+	_	+	3	High
Biggam and Power (2002)	+	+	+	+	_	_	4	High
Bowden et al. (2011)	+	_	_	+	_	_	2	High
Cui et al. (2016)	+	+	+	+	_	+	5	High
Cukrowicz et al. (2007)	+	+	_	+	_	_	3	High
Day et al. (2013)	_	_	_	+	_	_	1	Low
Dvořáková et al. (2017)	_	_	+	+	_	+	3	High
Enrique et al. (2017)	_	_	_	+	+	+	3	High
Frazier et al. (2015)	_	_	_	+	_	_	1	Low
Hazlett-Stevens & Oren, Y. (2016)	_	_	+	+	_	_	2	High
Houston et al. (2017)	_	_	+	+	+	_	3	High
Kang et al. (2009)	_	_	+	+	+	+	4	High
Lee and Jung (2018)	-	-	+	+	+	+	4	High
Levin et al. (2014)	+	+	+	+	-	_	4	High
McGrady et al. (2012)	-	_	+	+	-	_	2	High
Moir et al. (2016)	+	+	+	+	+	+	6	High
Pratt et al. (2000)	_	_	+	+	_	_	2	High
Rohde et al. (2016)	_	_	_	+	_	+	2	High
Seligman et al. (2007)	+	+	+	+	_	_	4	High
Song and Lindquist (2015	+	+	+	+	-	-	4	High
Takagaki et al. (2016)	-	_	_	+	-	+	2	High
Thomas et al. (2016)	+	+	+	+	_	_	4	High
Bowden et al. (2010)	_	_	_	+	_	_	1	Low
Ellis et al. (2011)	+	+	+	+	_	_	4	High
Rohde et al. (2014)	-	_	_	+	+	+	3	High
Niles et al. (2014)	-	-	+	+	-	-	2	High

 $<sup>^{\</sup>rm a}$  Scoring of studies: += high/ unclear risk score, -= low risk score.

**Table 4**Effects of preventative intervention on depression in young people compared to control with Hedges g.

		N comparison	g	95% CI	$I^2$	95% CI	$P^a$	NNT
All studies		34	0.53	0.39-0.67	74	64–81	0.00*	6
Extreme outliers excluded		29	0.37	0.28-0.47	36	0-59	0.00*	9
Highest ES		26	0.39	0.29-0.50	39	3-62	0.00*	8
Lowest ES		26	0.37	0.27-0.48	41	5-63	0.02*	9
Follow up	T2	26	0.38	0.28 - 0.47	39	2-62	0.00*	8
	T3-T6 combined	11	0.28	0.10 - 0.46	59	19-79	0.00*	11
Subgroup analysis								
Type of prevention	Targeted	12	0.45	0.27 - 0.63	60	24-79		7
	Universal	14	0.31	0.20 - 0.42	0	0-55	0.18	11
Theory	CBT	9	0.53	0.38-0.68	6	0-75		6
	Mindfulness	8	0.31	0.15-0.47	22	n/a		11
	Mind-body	2	0.35	0.12 - 0.82	0	0 - 64		9
	Other	10	0.30	0.13-0.47	48	0-67	0.13	11
Format	Online	8	0.33	0.18-0.48	0	0–68		10
	Face to Face	4	0.46	0.09-0.84	67	3-89		8
	Group	14	0.41	0.26-0.56	46	0-71		8
	Individual self help	3	0.23	-0.19 - 0.65	58	n/a	0.75	15
Support type	Professional	14	0.46	0.32-0.65	49	4-73		7
	Trained facilitator	6	0.46	0.25-0.66	4	0–76		7
	Peer support	1	0.12	0.14-0.37	0	n/a		30
	Unguided/self-led	9	0.27	0.13-0.40	0	0-65	0.06	12
Focus	Depression prevention	6	0.54	0.24-0.83	51	0-82		6
	Anxiety and depression prevention	3	0.54	0.35 - 0.72	0	0-90		6
	Stress reduction	6	0.31	0.07-0.54	40	0–76		11
	Psychological health	12	0.30	0.18-0.42	12	0-52	0.11	11
Control type	Care as usual	9	0.54	0.33-0.76	60	16-81		6
	Wait-list	8	0.32	0.18-0.45	0	0-68		10
	Placebo	5	0.19	0.02-0.35	0	0-79		18
	Psychoeducation	4	0.38	0.11-0.65	43	0-81	0.07	8

<sup>&</sup>lt;sup>a</sup> \* p value < 0.05.

-0.15) for psychological prevention of depression in children and adolescents (Hetrick et al., 2016). Our large effect size may be explained by the fact that the level of intensity and approach in our studies may have mirrored treatment more than prevention.

As symptom levels in the included studies were self-reported and not independently verified by a clinician, some of the participants may have had depression at the time of the study, which could also be

related to finding a larger effect size for the interventions.

### 4.2. Implications for research and practice

Our results suggest that, compared to control, people who partake in preventative interventions have lower depressive symptoms post intervention, providing some optimism for future practice. The data do

**Table 5**Standardized regression coefficients of moderators: multivariate meta-regression analyses.

	Coef.	95% CI	$P^a$	
Intercept Risk of bias (continuous) Length (continuous)	0.45	0.24	0.66	0.001
	-0.00	-0.04	0.04	0.35
	-0.00	-0.02	0.01	0.55

<sup>&</sup>lt;sup>a</sup> \* if *p* value < 0.05.

not allow us to comment on the prevention of onset, as none of the studies reported on the incidence. Interestingly, results show that prior findings from meta-analyses of studies on children and adolescents cannot be directly generalized to young adult populations. The higher prevalence of depressive symptoms in young adulthood as well as the different settings in which these interventions are delivered (university vs. school) may impact the size of observed effects. Further research is needed to assess the trends found in our analysis, and future practice should take care to account and adapt for the differences in these populations.

No significant differences were found for other moderators, including the length of intervention, delivery type, and support type. However, the NNTs showed that various study characteristics might lead to more favourable results of depression outcomes compared to others. Studies that focused solely on depression prevention, targeted prevention, online delivery, and "other" (non-mindfulness, mind-body, or CBT-based interventions) had the lowest NNT and strongest effect sizes. Future research, with long term follow up (12 months) is needed to investigate the long-term effects of such interventions.

This study also found that risk factors for depression including age, socio-economic status, and previous diagnosis of depression were inconsistently reported across studies. Future research would, therefore, benefit from reporting the participant demographics and study moderators. Individual Participant Data analysis, which is a technique that utilizes data from study participants instead of aggregate data from participants, could be applied to assess this further.

To allow for generalisation of these findings outside a university setting, the study of a more heterogeneous young adult population is needed. Not all 18–25-year olds pursue higher education, and the likelihood of a young person starting higher education by the age of 30 years in 2015/2016 was 49% (Department of Education UK, 2017). For example, further research could be conducted in vocational colleges, work places or apprenticeship schemes for young adults.

We propose the following guidelines for future research to effectively assess the benefits of interventions on public mental health. Firstly, studies should include measurement of the incidence of depression at baseline and follow-up and include follow-up measurements at one to two years to assess the full preventative effects of interventions. Secondly, they should consistently report on the demographic factors (age, gender, ethnicity, socio-economic status) of their participants to assess the differential impact of interventions on subgroups. Third, further research should direct attention to the use of interventions on non-student samples. This will aid in determining their generalizability to other communities and settings.

# 4.3. Limitations

Several limitations should be considered when interpreting this review and its findings. With regards to our methodology, we only considered four main databases and thus may have missed studies from other databases such as CINAHL or ERIC, though we expect this would only identify a small number (if any) of additional records.

The current review attempted to produce evidence of the highest quality by only including RCTs. However, the overall study quality was low and the risk of bias was high in the majority of the included studies (21/26). Further to this, all but one study took place in a university setting, and most participants were Caucasian, female students. These two factors limit the generalizability of these findings to other population groups, such as college students or young adults who are not enrolled in higher education.

While we excluded studies where it was reported that participants had a history of depression, some participants may have still had prior diagnoses of depression. It is therefore possible that some of the participants may have already had depression before participating in the study. Finally, we were not able to comment on the long-term effect of these interventions, as only eight studies reported a 1–3-month follow-up after the intervention. Most importantly, no incidence measures were taken at these time points. Thus, it is not possible to estimate whether these interventions and approaches in the analysis directly affected the prevalence of depression and whether they are truly preventative in the long-term.

#### 5. Conclusion

Whilst this review provides a certain optimism in public health efforts to reduce the incidence of depression, it appears that it is too early to conclude that the currently available interventions can help prevent the incidence of depression in young adulthood. However, compared to control, the interventions included did have an effect on depressive symptoms. Which is an important modifiable risk factor for developing MDD. Future research requires several improvements—both in methodology and scope—to adequately assess the evidence base for depression prevention in this age range. These would include incorporating measurement of incidence, clearer reporting on MDD history, inclusion of longer-term outcomes, research conducted in different settings outside the university, and consistent reporting on demographic variables.

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# Contributors

J.B. conducted the searches, extracted the studies and conducted the analyses. A.K. carried out the extraction of the studies, prepared the tables and reviewed drafts of the manuscript. E.K. and MB reviewed and supported with the meta-analysis. J.B. wrote the manuscript with support from E.K. M.B. C.B. and P.C. P.C. reviewed and oversaw the review from the instigation until final preparation of the manuscript. Both P.C. and C.B. supervised the project.

# Conflict of interest statement

None.

# Disclaimer

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript: Pim Cuijpers, Josefien Breedvelt, Antonis Kousoulis, Claudi

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#### Supplementary materials

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