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Review Article

Indicated preventive interventions for depression in children and adolescents: A meta-analysis and meta-regression

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ABSTRACT

Depression contributes about 2% to the global burden of disease. A first onset of depressive disorder or subsyndromal depressive symptoms is common in adolescence, indicating that early prevention is a priority. However, trials of preventive interventions for depression in youths show conflicting results. This systematic review and meta-analysis investigated the effectiveness of group-based cognitive behavioral therapy (GB-CBT) as a preventive intervention targeting subsyndromal depression in children and adolescents. In addition, the impact of different covariates (type of comparator and use of booster sessions) was assessed. Relevant articles were identified from previous systematic reviews, and supplemented with an electronic search spanning from 01/09/2014 to 28/02/2018. The retrieved articles were assessed for eligibility and risk of bias. Relevant data were extracted. Intervention effectiveness was pooled using a random-effects model and the impact of covariates assessed using meta-regression. 38 eligible articles (34 trials) were obtained. The analysis showed GB-CBT to significantly reduce the incidence (relative risk 0.43, 95% CI 0.21–0.87) and symptoms (Cohen's d -0.22 , 95% CI -0.32 to -0.11) of depression at post-test compared to all controls. Comparisons with passive comparators suggested that the effect decayed over time. However, compared to active controls, a significant intervention effect was evident only after 12 month or more. Our results suggest that the preventive effect of GB-CBT wears off, but still lasts longer than the effect of active comparators. Only a few studies included booster sessions, precluding firm conclusions. Future studies should clarify to what extent maintenance strategies can prolong the preventive effect of GB-CBT.

1. Introduction

Depression is a common disorder with a lifetime prevalence between 10 and 15% (Lepine and Briley, 2011), contributing to 1.84% (1.38%–2.33%) of the total global burden of disease (Disability Adjusted Life Years) (Institute for Health Metrics and Evaluation (IHME), 2016; Whiteford et al., 2013). The disorder is characterized by persistent low mood and loss of interest in previously pleasurable activities (Kasper et al., 2015; American Psychiatric Association, 2013), and is associated with decreased productivity (Lepine and Briley, 2011; Rost et al., 2014), diminished health related quality of life (HRQoL), strains

in relationships, poor educational outcomes, unemployment as well as increased utilization of healthcare services (OECD, 2015), and an increased risk of all-cause mortality (Cuijpers et al., 2014), including suicide (Osby et al., 2001; Wulsin et al., 1999).

A significant proportion (over 25%) report that their first episode occurs during adolescence (Kessler et al., 2005), making this a vulnerable time. A substantial proportion of adolescents also have subsyndromal symptoms and go undiagnosed or unmanaged (Bertha and Balazs, 2013; Cameron et al., 2011). Depression with an adolescent onset is associated with an increased risk of depression in adulthood (Jonsson et al., 2011; Copeland et al., 2013). In addition, there is a large

Abbreviations: GB-CBT, group-based cognitive behavioral therapy; SMD, standardized mean differences; MDD, Major Depressive Disorder; EOI, end of intervention; ES, effect size; RR, relative risk

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cost burden associated with depressive disorders (Hu, 2006; Gustavsson et al., 2011). In view of the early occurrence of depressive symptoms and the poor prognosis later in life, prevention has received considerable attention (Cuijpers et al., 2012). Specifically, preventive interventions have shown to be less costly than treatment and have a potential to reduce symptom severity (Hetrick et al., 2015; Garber et al., 2016; Crowe and McKay, 2017; Werner-Seidler et al., 2017; Yang et al., 2017), thus being cost-effective (Mihalopoulos and Vos, 2013). This is especially true for indicated preventive interventions for depression in adolescents (Garber, 2006; Rasing et al., 2017). Indicated preventive interventions are preventive measures targeted to people with symptoms that are either too few or not severe enough to warrant a diagnosis of e.g. Major Depressive Disorder (MDD). Indicated preventive interventions for depression in children and adolescents have demonstrated moderate effects, showing relative risks between 0.29 and 0.78 in comparison to all controls (Horowitz and Garber, 2006; Stice et al., 2009; Stockings et al., 2016). There is a range of indicated preventive interventions based on different theoretical grounds e.g. cognitive behavioral therapy, interpersonal therapy, problem solving based therapy, and psychodynamic therapy approaches. Out of these interventions, group-based cognitive behavioral therapy (GB-CBT) is the one that has been most extensively studied. It has been shown to be effective at reducing depressive symptoms when delivered in routine practice and schools (Hetrick et al., 2015; Rasing et al., 2017; Stockings et al., 2016; Bellón et al., 2015; Mendelson and Eaton, 2018). However, some research in the area has found GB-CBT interventions to have inconsistencies, such as low to no effect and that evidence is insufficient to draw generalizable conclusions on effectiveness (Rasing et al., 2017; Merry and Spence, 2007; Brent et al., 2015; Corrieri et al., 2013; Holmes et al., 2018). Most research has also expressed results as continuous outcome measures e.g. Cohen's d, which are not suitable for assessing cost-effectiveness as compared to relative risks. Relative risks can be directly used in health economics modelling to adjust the transition probabilities from one health state to another as opposed to Cohen's d. Furthermore, the effectiveness estimates are regarded the same irrespective of type of comparator (active or passive controls) and presence or absence of booster sessions, which may limit the clinical relevance of the results since earlier research, Gearing et al., demonstrates this difference for booster sessions (Gearing et al., 2013). These distinctions are relevant from both a clinical and economic perspective. Firstly, it is of importance to know if GB-CBT outperforms interventions based on non-specific components related to provision of support and counselling that might be less costly or more practical to implement. Secondly, it is also essential to ascertain if booster sessions have any additional health benefit since its inclusion increases the costs. In addition, to conduct cost-effectiveness evaluations of GB-CBT interventions for children and adolescents, it would require a more definitive evidence synthesis of the effectiveness. Stockings et al. (2016), and Rasing et al. (2017), published the most recent reviews and meta-analyses on the effects of preventive interventions on depression and anxiety in children and adolescents. Stockings' work focused on all types of preventive interventions while Rasing's work focused on targeted (selective and indicated) CBT based interventions but expressed outcomes as continuous outcomes (Cohen's d) rather than RRs. Both studies did not explore the impact of booster sessions and type of comparator (active or passive).

We hypothesized that GB-CBT indicated preventive interventions for depression in children and adolescents would demonstrate to be effective when compared to passive comparators, but that the results would differ for active comparators. We also presumed that inclusion of booster sessions would improve the results.

The aim of this study was to synthesize evidence on GB-CBT *indicated* preventive interventions for depression in children and adolescents with particular focus on:

1) Addressing the inconsistencies in effectiveness of GB-CBT indicated

interventions for the prevention of depression in children and adolescents.

- 2) The effectiveness of GB-CBT indicated preventive interventions in relation to an *active* or *passive* comparator and the impact of booster sessions on intervention effectiveness.
- 3) Synthesizing and reporting effect sizes in a useful form for inputs in cost-effectiveness assessments and decision-analytic modelling of these interventions.

Addressing the above aims will provide a better base for decision making concerning optimal resource allocation for adoption and implementation of these interventions.

2. Methods

This study was a systematic literature review with a meta-analysis based on the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2011), and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement guidelines (Moher et al., 2009). This work stems from meta-analyses conducted by Stockings et al. (2016), and Rasing et al. (2017), which were assessed to be of good quality according to the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) framework (Shea et al., 2007).

2.1. Eligibility criteria

Eligibility of the studies considered for inclusion in this work was based on their specified characteristics deemed relevant for answering our research question(s). These study characteristics are summarized in the PICOS below:

P (Population): Children/adolescents aged 12–19 years with depressive symptoms or behaviour indicating depression, not high enough to warrant a diagnosis of a depressive disorder.

I (Intervention): GB-CBT indicated preventive interventions with or without booster sessions.

C (Comparator): Active comparator i.e. other specified preventive treatments for depression or an intervention designed to control for non-specific aspects of treatment for depression (e.g. group counselling and bibliotherapy) and passive comparators e.g. waitlist and treatment as usual (assessment only control with the participants free to seek care).

(Outcome): primary outcome: cases of a depressive disorder (dichotomous). Secondary outcome: depressive symptoms over time (continuous).

S (Study design): Randomized controlled trial (RCT).

2.2. Information sources and literature search

Firstly, all the indicated preventive studies included in Stockings' and Rasing's work were reviewed and only those addressing depression prevention using GB-CBT indicated preventive interventions were selected. Thereafter, a literature search was conducted in electronic databases including PubMed, Web of Science, PsycINFO, Medline and the Cochrane Library of Systematic Reviews using a combination of search terms e.g. adolescents, depression, preventive interventions and cognitive behavioral therapy. A search-strategy is presented in the supplementary material (*eSearch strategy (a)*).

The search was limited to English language, and the period 01/09/2014 to 28/02/2018, to supplement the articles investigating indicated preventive interventions already retrieved in the previous meta-analyses. Furthermore, the reference lists of eligible articles were scanned to obtain potentially missed literature.

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