Turning prevention into a challenge

Towards a new integrated model of depression prevention

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Publication date
2021

English Summary

Turning prevention into a challenge: Towards a new integrated model of depression prevention

Common mental health disorders (CMDs), including depressive and anxiety disorders, are prevalent and debilitating conditions, affecting 1 in 5 people each year. While there are effective treatments available, the prevalence of these conditions has not yet decreased in the past years. To further understand how to reduce the impact of common mental health disorders, we can also further explore preventive interventions. Prevention interventions aim to prevent a person from developing a common mental health condition or prevent the relapse of such a condition.

In order to prevent the onset of CMDs, the relative effectiveness of preventive interventions should be studied among high-risk groups. Especially adolescence and young adulthood are important phases, as most CMDs develop by the age of 24. Two possible approaches for preventing CMD onset were explored in Chapters 2 and 3. In Chapter 2, leading interventions to prevent the first onset of depression in young adults were searched systematically, and the effects thereof meta-analysed. We identified 26 manuscripts with 2865 participants in total. We found that mostly Cognitive Behavioural Therapy [CBT] and mindfulness-based interventions delivered in a group or individual setting were effective at reducing depressive symptomatology. However, we were not able to conclude that there was robust long-term effectiveness and that the onset of depression had actually been prevented, neither for universal nor targeted interventions. This aligned with other meta-analyses on onset prevention among adults, where no preventive effect on onset prevention after seven months was realised. Overall, we can conclude that the evidence on onset prevention based on these studies is limited.

Given the aforementioned findings, it is becoming increasingly important to explore what other, perhaps 'out-of-the-box' interventions may be effective in preventing CMDs onset. Beyond individual or group-based interventions as studied in Chapter 2, recent studies have suggested that fostering a strong sense of neighbourhood social connectedness (i.e., having strong connections in the neighbourhood and a lack of latent social conflict) may protect against developing CMD. In Chapter 3, this hypothesis was tested, and it was explored whether for whom and in which way increasing neighbourhood social connection can prevent CMD in adolescents and young adults. Via a rapid systematic review, we sought for experimental or quasi-

experimental studies as well as longitudinal and cross-sectional trials to assess the evidence for neighbourhood social connection as a preventive intervention. There were no experimental or quasi-experimental studies that evaluated the preventive effect, but 11 longitudinal studies were found. The results from these studies indicated that exposure to high neighbourhood social cohesion (including safety, trust, positive social connections, helping others and a lack of crime and violence) was associated with less depressive symptoms and to lesser extent anxiety symptoms in adolescence and young adulthood. The evidence is thus encouraging for neighbourhood social cohesion as a potential preventive intervention for preventing depression and anxiety. Still, more experimental or quasi-experimental studies are needed to assess whether interventions that increase neighbourhood social cohesion are effective at preventing the onset of CMDs in adolescents and young adults. Potential interventions that can be studied further include neighbourhood regeneration programmes which include improving outdoor and community spaces, community-led groups (i.e., volunteering), and creating online spaces for people where young and old can interact which may facilitate offline connection.

One of the features from the onset prevention literature, namely, outcome assessment, was studied in Chapter 4. Outcome assessment affects the conclusions one can make about the effectiveness of preventive interventions. Building on Chapters 2 and 3, where we noted there were few diagnostic outcome assessments for onset prevention, Chapter 4 systematically reviewed which outcome measurement tools were used in onset prevention studies. One hundred and twenty-seven studies measuring the outcomes of onset prevention studies were identified, using 65 different measurement tools. Diagnostic assessments were used in one out of five studies. Symptom measurement for assessing preventive effectiveness may have several limitations. While self-report symptom measurements measure a reduction in symptoms, they cannot determine whether an onset has occurred or not. Hence, it is suggested that future research includes a diagnostic assessment where possible.

As described in the introduction, relapse prevention interventions form the second approach explored in this thesis that may reduce the prevalence of CMD. After remission, for patients who respond to treatment, antidepressants are most commonly continued to avoid relapse. In Chapter 5, a systematic review and meta-analysis compared the effectiveness of psychological interventions alone and added to antidepressants on reducing the risk of relapse for (partially) remitted patients with a history of depression. We identified 11 studies (*N*=1,599 patients). We found

that adding a psychological intervention (i.e., CBT, Preventive Cognitive Therapy [PCT], Interpersonal Therapy [IPT]) to antidepressants significantly reduced the risk of relapse compared taking antidepressants alone. It is recommended that clinical guidelines consider including the combination of a psychological intervention and antidepressants for reducing the risk of a future depressive relapse, especially PCT may be a short-term alternative compared to other more long-term psychological interventions such as IPT or CBT. Chapter 5 also found that patients who were tapering antidepressants while receiving a 'top-up' of a psychological intervention did not have an increased risk of relapse, compared to continuing antidepressants alone. This offers alternatives to patients who do wish to taper from long-term antidepressant use and may help the clinical decision-making process.

A second clinical question within depressive relapse prevention is what works for whom. For patients who are on continued long-term antidepressant use, it is not clear for whom it might be possible to taper. Ongoing use is especially recommended for patients who are deemed high risk because of clinical factors such as the number of previous episodes and baseline symptomatology, as well as the severity of the last episode. As suggested by previous research and confirmed in Chapter 5, receiving a psychological intervention while tapering antidepressants does not increase the risk of relapse and may thus be a viable alternative to long-term antidepressant use. The question for which patients to recommend this approach remains unclear. Therefore, in Chapter 6, we conducted an individual participant analysis, where we combined individual participant data of four randomised controlled trials. In this study, we gathered potential predictors of treatment effect, including the number of previous episodes, baseline symptomatology, and assessed whether these predicted which intervention would result in a lower risk of relapse for them over 15 months follow-up. Importantly, we found no evidence to suggest that any of the nine included potential moderators affected the risk of relapse. So, regardless of clinical and other characteristics of the patient associated with poor prognosis, a short psychological intervention (i.e., PCT or Mindfulness-Based Cognitive Therapy [MBCT]) can be a viable alternative to long term use of antidepressants.

In addition to the findings in Chapters 5 and 6, there are other relapse prevention strategies that have been studied meta-analytically, but not yet with an individual patient data meta-analysis. Chapter 7 introduces an individual patient data meta-analysis, which will include predictors and moderators in a wider range of comparisons than included in Chapter 6. This includes studying predictors and

moderators of psychological interventions (delivered either alone or in addition to antidepressants) versus a range of controls (antidepressants, placebo, treatment as usual). By also assessing the effects of these relapse prevention strategies, and what works for whom, further (personalised) clinical recommendations may be made for a broader set of relapse prevention options.

In Chapter 8, a discussion of the main findings and leading approaches for preventing depressive onset and relapse are provided. Based on the current literature available, we conclude that it is not yet possible to confirm whether we can prevent the first onset of depression in the long-term. Resulting from this, we advise a reserved approach towards immediately investing in mental health prevention programmes on a large scale until long-term preventive effects on the onset of CMD are known. Contrasting this to relapse prevention literature, where we found effects for relapse prevention interventions, we propose a tentative integrated model of prevention. If future studies on onset prevention are being conducted, they could incorporate learning from relapse prevention literature where robust effects for short term interventions on preventing depressive relapse were found for psychological interventions added to antidepressants alone. A consideration stemming from this result would be the routine recommendation of combination therapy after (partial) remission (psychological intervention combined with antidepressants) in order to further reduce risk of relapse for patients with MDD. Patients who have a strong wish to seek for an alternative or cannot continue antidepressants could also consider tapering antidepressants with a psychological relapse prevention intervention (i.e., PCT or MBCT), regardless of poor clinical prognosis.

Returning to the model, we recommend to falsify our assumptions of integration of onset and relapse prevention, as well as move towards transdiagnostic validation in other mental health conditions, including anxiety disorders and addiction. The integration between onset and relapse prevention literature will be of importance for future intervention development towards a further reduction of the prevalence of these debilitating conditions and the impact it has on individuals and society.