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Review



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ARTICLE INFO

Available online 3 September 2014

Keywords:
Depression
Primary health care
Recurrence
Relapse
Secondary prevention

ABSTRACT

Objective: A systematic review was conducted to assess the efficacy of pharmacological and psychological interventions for preventing relapse or recurrence of depression in adults with depression in primary care.

Method: Papers published from inception to January 28th 2014 were identified searching the electronic databases MEDLINE, EMBASE, PsycINFO, and CENTRAL. Randomized controlled trials of any pharmacological, psychological or psychosocial intervention or combination of interventions delivered in primary care settings were included, with relapse or recurrence of a depressive disorder as a main outcome. The Cochrane Collaboration risk of bias tool was used to assess study quality.

Results: Only three studies with a small number of patients fulfilled the inclusion criteria. None of the three randomized controlled trials included in our review showed a statistically significant superiority of an intervention for the prevention of depression relapse or recurrence.

 $\it Conclusions:$ There is limited evidence to inform relapse or recurrence prevention strategies specifically in primary care.

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Contents

| Introduction | . S17 |
|------------------------------------|-------|
| Methods | . S17 |
| Eligibility criteria | . S17 |
| Information sources | . S17 |
| Search | . S17 |
| Study selection | . S17 |
| Data extraction | . S17 |
| Risk of bias in individual studies | . S17 |
| Data synthesis | . S18 |
| Results | . S18 |
| Risk of bias within studies | . S19 |
| Study outcomes | . S19 |
| Discussion | . S19 |
| Main findings | . S19 |
| Strengths and limitations | . S20 |
| Conclusions | . S20 |
| Conflict of interest statement | . S20 |
| References | . S20 |
| | |

[†] Funding: The project has received funding from a Network for Prevention and Health Promotion in Primary Care (redIAPP, RD12/0005) grant and a research project grant (PI12/01914) from the Instituto de Salud Carlos III (Institute of Health Carlos III) of the Ministry of Economy and Competitiveness (Spain), co-financed with European Union ERDF funds.

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Introduction

Depression is a highly prevalent and disabling disorder and a major public health concern (Kessler et al., 2003). Psychopharmacology, psychotherapy or combined treatments are well supported by evidence in the acute management of the depressive disorders (Stewart et al., 2012; Fournier et al., 2010; Cuijpers et al., 2010; Imel et al., 2008; de Maat et al., 2007). Despite the successful acute treatment of depression, the risk of relapse or recurrence remains very high (Burcusa and Iacono, 2007; Yiend et al., 2009; Harter et al., 2007; Hardeveld et al., 2010; Gopinath et al., 2007). After a first episode of depression the probability of a further episode is approximately 50%; this rises to 70% for two episodes and 90% after a third episode (Burcusa and Iacono, 2007; Kessler et al., 1996). It also appears that with each further episode there is an increase in the severity of depressive symptoms and an increased probability that the symptoms will be resistant to treatment (Kendler et al., 2000). For these reasons it has become increasingly clear that developing interventions for the prevention of relapse or recurrence in specialized mental health care and in primary care is a major concern for longterm management of depressive patients.

It is relevant to differentiate between relapse and recurrence when developing treatment strategies for depression. According to expert consensus (Frank et al., 1991; Rush et al., 2006) the term relapse should be used to describe a re-emergence of symptoms in a patient who has initially responded to treatment but who is not yet in remission. Recurrence is the appearance of a new episode of depression after full remission of a previous episode has been achieved. Despite these operational definitions, the majority of published clinical trials do not precisely define relapse or recurrence. Researchers have conflated relapse and recurrence without making a clear distinction between these terms (Beshai et al., 2011).

Prevention of depression has emerged as a scientific and clinical challenge of great public significance (Muñoz et al., 2012). This has included the prevention of depressive relapse or recurrence and protection from the medical, psychosocial and economic consequences of the future episodes of depression (Reynolds, 2009). Strategies for reducing relapse can be divided into the type of treatment offered (pharmacological, psychological, combination) and when that treatment is delivered (during the acute phase, after the acute phase). There is evidence that psychological treatments, such as cognitive-behavioral therapy, delivered during the acute phase have effects that endure beyond the end of it to reduce subsequent rates of relapse (Vittengl et al., 2007). In contrast, acute-phase antidepressant medication does not confer a benefit in terms of subsequent relapse if the use of medication stops at the end of the acute phase (Thase, 2006). There is, though, evidence that the continued use of antidepressants after the end of acute phase treatment does reduce the likelihood of relapse (Geddes et al., 2003). In addition, continuation-phase CBT and other approaches specifically designed to be delivered after the end of the acute phase of treatment, such as mindfulness-based cognitive therapy (MBCT), also reduce the rate of relapse (Piet and Hougaard, 2011; Vittengl et al., 2007).

Increasingly, the responsibility for initial diagnosis and long-term follow-up of mental illnesses is falling on primary care services, the patient's first point of contact with the health system in the majority of the European countries (Murphy et al., 2000). Around one out of every three primary care patients presents with clinical problems related to mental health difficulties, though the figures range from 26% to 60% (Ansseau et al., 2004; Norton et al., 2007; Roca et al., 2009). While there is evidence that both pharmacological and psychological treatments can be effective in reducing relapse, the majority of the trials were performed in secondary care settings. It is difficult to generalize from such settings to primary care. There are, for example, likely to be differences between the two populations in terms of the likelihood of a relapse and the likelihood of responding to a relapse-focused treatment.

Although there have been improvements in the clinical skills of primary care physicians to detect and treat depression, there is still a long way to go in preventing relapse and recurrence of this disabling disorder and much effort must be made to improve the early identification of depressive patients at risk. We have not found a published meta-analysis or systematic review focused on prevention of relapse or recurrence of depression in primary care settings. The aim of this review is to assess the efficacy of existing pharmacological and psychological interventions for preventing relapse or recurrence of depression in adults with depression in primary care.

Methods

Eligibility criteria

Studies that met the following inclusion criteria were included:

Participants: Studies of adult participants (aged 18+) who had an episode of depression or received treatment for depression. Studies of people diagnosed with bipolar disorder were excluded.

Interventions: Any pharmacological, psychological or psychosocial intervention or combination of interventions delivered in primary care settings. Interventions delivered during the acute phase or a continuation phase were eligible for inclusion, but are considered separately in the analysis.

Comparator/control: Control conditions such as treatment as usual, waiting list or placebo.

Outcomes: Relapse or recurrence of a depressive disorder.

Study design: Randomized controlled trials (RCTs).

Information sources

The primary electronic databases searched were MEDLINE/PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE and PsycINFO (searched from inception to 28 January 2014). References of included studies were examined to identify other potentially eligible studies.

Search

Searches comprised a combination of subject terms selected from the controlled vocabulary with free-text terms. These terms were developed to capture the concepts of relapse, depression, randomized trials and primary care and were combined using the Boolean AND.

Study selection

Three authors independently examined the titles and abstracts of all retrieved citations against the pre-specified inclusion criteria outlined above. The full text of articles passing this first sift were retrieved and examined independently by two authors against the pre-specified inclusion criteria. Disagreements were resolved through consensus and, if consensus could not be reached, discussion with an additional reviewer.

The study selection process with the number of studies included and excluded at each stage of the review is documented, detailing the reasons for exclusion, using a PRISMA flowchart diagram (Fig. 1).

Data extraction

Two reviewers independently extracted data from the included studies. Disagreements were resolved through the same approach as described above. For each study, authors extracted the following details: study design, intervention and control group, sample characteristics, length of follow-up, outcome (including data needed to calculate effect sizes), and study quality.

Risk of bias in individual studies

The Cochrane Collaboration risk of bias tool (Higgins et al., 2011) was used to assess study quality. Two authors independently rated these criteria and disagreements were resolved as described above.

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