



Evidence Synthesis for Determining the Efficacy of Psychotherapy for Treatment Resistant Depression

EXECUTIVE REPORT

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PREFACE

VA's Health Services Research and Development Service (HSR&D) works to improve the cost, quality, and outcomes of health care for our nation's veterans. Collaborating with VA leaders, managers, and policy makers, HSR&D focuses on important health care topics that are likely to have significant impact on quality improvement efforts. One significant collaborative effort is HSR&D's Evidence-based Synthesis Program (ESP). Through this program, HSR&D provides timely and accurate evidence syntheses on targeted health care topics. These products will be disseminated broadly throughout VA and will: inform VA clinical policy, develop clinical practice guidelines, set directions for future research to address gaps in knowledge, identify the evidence to support VA performance measures, and rationalize drug formulary decisions.

HSR&D provided funding for the two Evidence Based Practice Centers (EPCs) supported by the Agency for Healthcare Research and Quality (AHRQ) that also had an active and publicly acknowledged VA affiliation—Southern California EPC and Portland, OR EPC—so they could develop evidence syntheses on requested topics for dissemination to VA policymakers. A planning committee with representation from HSR&D, Patient Care Services, Office of Quality and Performance, and the VISN Clinical Management Officers, has been established to identify priority topics and to ensure the quality of final reports. Comments on this evidence report are welcome and can be sent to Susan Schiffner, ESP Program Manager, at Susan.Schiffner@va.gov.

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EXECUTIVE SUMMARY

BACKGROUND

Major depressive disorder (MDD) is a prevalent disorder impacting an estimated 13% of the general population, and a third of the veteran population. Of the patients who experience at least one depressive episode, approximately 20% will experience chronic depression and 60-85% will experience recurrence and relapse. Antidepressant medications are the most commonly prescribed treatment modality for MDD and are often the first line of treatment in primary care settings. However, fewer than 50% of patients fully remit after adequate dosage of antidepressant treatment. Treatment options for these “treatment resistant” patients vary but typically involve using other psychoactive medications as augmentation (i.e., addition of another medication) or substitution treatment (i.e., switching medications). Less attention has been paid to using psychotherapy as an augmentation or substitution treatment for treatment resistant patients, despite psychotherapy being associated with clinical improvements in MDD comparable to those achieved with antidepressants. The current review will address the effectiveness of psychotherapeutic approaches as a second step treatment for MDD in patients who do not achieve remission after initial treatment with antidepressants.

Question: In primary care patients with major depressive disorder who do not achieve remission with acute phase antidepressant treatment, is empirically based psychotherapy used as an augmentation or substitution treatment more effective than control for achieving remission?

METHODS

We searched PubMed from 1950-2009 using standard search terms. Titles, abstracts, and articles were reviewed in duplicate. Extant literature was initially screened for relevant systematic reviews. Following this, primary literature was screened for relevant randomized clinical trials comparing medications to psychotherapy in patients with major depressive disorder. Data were extracted in duplicate in articles that were included in this review. We evaluated study quality for the primary literature. All data were summarized in evidence tables and in narrative.

RESULTS

We initially screened 41 systematic reviews, of which 29 were excluded at the title/abstract level and the remaining 12 were excluded after full-text review. For the primary literature, 333 titles were screened, of which 290 were excluded at the title/abstract level and 31 were excluded after full-text review. The remaining 12 articles reflected five unique randomized clinical trials examining the effect of psychotherapy in patients who had shown resistance to antidepressant therapy. Because one of the trials had both “substitution with psychotherapy” and “augmentation with psychotherapy” arms, these were treated as two different studies, resulting in a total of six studies reviewed. A total of 567 patients were evaluated; none of these were recruited from VA clinics. Psychotherapy was examined as an augmentation to antidepressant medication in four studies and as a substitution treatment to replace medication in two studies. The STAR*D trial examined psychotherapy in both conditions. Three studies-including the two STAR*D treatment

arms- were rated as good quality, two studies were rated fair, and one was rated poor. The STAR*D trial used an equipoise stratified randomization design; the remaining four studies were true RCTs. Patients in the comparison groups were on medications in all studies.

A fair quality trial compared psychotherapy as augmentation treatment to medication by randomizing 24 patients to either a 16-session dialectical behavior therapy (DBT) group or to a wait list condition. Participants in the DBT group evidenced significantly more improvement than participants in the wait list condition, both on interviewer rated and self-report measures of depression severity. Interpretation is complicated by control participants being allowed to continue in individual therapy.

Psychotherapy was also examined as an augmentation treatment to medication in a fair quality trial, in which 44 patients were randomized to either 12 sessions of cognitive therapy or to lithium augmentation. Participants in the lithium augmentation condition evidenced significantly more improvement than participants in the cognitive therapy condition on an interviewer rated measure of depression severity, but there were no between-group differences on a self-report measure of depression severity. One limitation was that patients must have partially responded to medication treatment to be eligible for inclusion.

A moderate sized, good quality trial also used psychotherapy to augment antidepressant treatment. In this study, 158 patients were randomized to either 16 sessions of cognitive therapy (CT) or to clinical management with antidepressant medication. Participants in both conditions improved over time but there were no significant differences between the two treatment groups.

The good quality STAR*D trial examined psychotherapy and medication as either augmentation or substitution treatments to initial treatment with citalopram. Sixteen sessions of CT were provided, although only a minority of enrolled participants completed all sessions. Only the portion of results germane to our question was considered for the review, resulting in a sample size of 304 participants. Patients were allowed to refuse randomization to treatment strategies that they found unacceptable, resulting in the two CT conditions having roughly half the number of participants as in the two medication conditions. While participants in all four conditions evidenced improvement over time, there were no significant differences between the conditions. However, participants who had citalopram augmented with another antidepressant did demonstrate quicker benefit than participants who had citalopram augmented with cognitive therapy. This study had excellent ecological validity given that patient preferences were taken into account prior to randomization.

Finally, a poor quality study by Blackburn and Moore (1997), examined psychotherapy as a substitution treatment to replace antidepressant medication. There were 37 patients in this study who were randomized to 27 sessions of psychotherapy over two years or to clinical management with antidepressant medication. While participants in both conditions evidenced clinical improvement over time, there were no significant differences between the two conditions.

SUMMARY

In summary, two good quality, moderate-sized trials showed equal benefit from augmenting antidepressant medication with CT and from active medication management, one fair quality small study showed lithium augmentation to be more beneficial than CT, and one fair quality trial showed short-term benefit from augmentation through 16 sessions of DBT. A moderate-sized, good quality study and a small, poor quality study found equal benefit from substituting CT for antidepressant treatment and from continuing management of depression with medication. There was significant heterogeneity in study designs, sample sizes, and comparator groups, and most studies were underpowered to detect moderate effect sizes. We conclude that current trials do not support favoring psychotherapy over antidepressant medication for mid-life adults with treatment resistant MDD; however, psychotherapy appears to be an equally effective treatment compared to antidepressant medication and is therefore a reasonable treatment option for this demographic. Whether these results are directly applicable to Veterans is uncertain because most study samples were mid-life adults, more than 50% female, and medical and psychiatric co-morbidity was incompletely described. The limited number of studies, mixed effects and uncertain applicability to Veterans suggest a need for additional trials to adequately evaluate the potential treatment benefit of psychotherapy for treatment resistant depression.