Effective Health Care Program

Comparative Effectiveness Review
Number 75

Practice-Based Interventions Addressing Concomitant Depression and Chronic Medical Conditions in the Primary Care Setting

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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The investigators deeply appreciate the considerable support, commitment, and contributions of the EPC team staff at RTI International and the University of North Carolina at Chapel Hill. We express our gratitude to the following individuals for their contributions to this project: Carol Woodell, B.S.P.H., our Project Manager; Meera Viswanathan, Ph.D., Director of the RTI-UNC EPC; Timothy S. Carey, M.D., M.P.H, Director of the Cecil G. Sheps Center for Health Services Research at UNC; Megan Van Noord, M.S.L.S., our EPC Librarian; Carol Offen, editor; and Loraine Monroe, our EPC publications specialist.

Key Informants

Key Informants are the end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the Key Questions for research that will inform health care decisions. The EPC solicits input from Key Informants when developing questions for systematic review or when identifying high priority research gaps and needed new research. Key Informants are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The Task Order Officer and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Technical Experts comprise a multidisciplinary group of clinical, content, and methodologic experts who provide input in defining populations, interventions, comparisons, or outcomes as well as identifying particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicted opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore study questions, design and/or methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor contribute to the writing of the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism

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Potential Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than $10,000. Peer Reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

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Practice-Based Interventions Addressing Concomitant Depression and Chronic Medical Conditions in the Primary Care Setting

Structured Abstract

Objectives: For adults with concomitant depression and chronic medical conditions seen in the primary care setting, to assess the effectiveness of practice-based interventions for improving mental health or medical outcomes.

Data Sources: We searched MEDLINE®, Embase, the Cochrane Library, CINAHL®, and PsycINFO® from inception to December 2011. We identified additional studies from reference lists and technical experts.

Review Methods: Two people independently selected, extracted data from, and rated the quality of relevant trials and systematic reviews. We conducted quantitative analyses for outcomes when feasible and reported all results by medical condition when possible. Two reviewers graded the strength of evidence (SOE) using established criteria.

Results: We included 24 published articles reporting data from 12 studies (9 randomized controlled trials and 3 preplanned subgroup analyses from a tenth trial). Sample sizes ranged from 55 to 1,001, and study duration ranged from 6 to 60 months. Eleven studies were conducted in the United States (1 in Puerto Rico) and 1 in Scotland. All studies characterized their respective intervention as a form of collaborative care compared with usual or enhanced usual care, and generally involved a care manager with physician supervision; we found no studies describing other types of practice-based interventions. Settings of care for included studies, although rarely characterized, included both open and closed systems. All studies specified depression as the targeted mental health condition. Medical conditions included arthritis, cancer, diabetes, heart disease, HIV, and one or more conditions. Our meta-analyses found that intervention recipients achieved greater improvement than controls in depression symptoms, response, remission, and depression-free days (moderate SOE); satisfaction with care (moderate SOE); and mental and physical quality of life (moderate SOE). Few data were available on outcomes for chronic medical conditions, except for diabetes; only one trial used a medical outcome as the primary outcome. Diabetic patients receiving collaborative care exhibited no difference in diabetes control as compared with control groups (change in HbA1c: weighted mean difference 0.13, 95% CI, -0.22 to 0.48 at 6 months; 0.24, 95% CI, -0.14 to 0.62 at 12 months; low SOE).

Conclusions: Collaborative care interventions improved outcomes for depression and quality of life in primary care patients with multiple different medical conditions. Few data were available on medical outcomes, except for HbA1c in diabetes, which showed no difference between treatment and usual care. Future studies should be designed to target a broader range of medical conditions, or clusters of conditions, and should compare variations of practice-based interventions in head-to-head trials.

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Executive Summary

Background

The World Health Organization has identified the integration of mental health into primary care as the most salient means of addressing the burden of mental health conditions, noting its ~~"u~~rgent importance."[1] In the United States, half of the care for common mental health disorders is delivered in general medical settings,[2] emphasizing the vital role that primary care providers play in the diagnosis and treatment of these disorders.

Common mental health conditions, such as depression and anxiety, are found in up to 10 percent of primary care patients,[3] and these conditions often coexist with chronic medical conditions. Accordingly, considerable interest has been expressed in improving the recognition and management of mental health conditions, especially depression, within primary care.[4-6] Specifically, interest is emerging about whether treatment of common mental health conditions in primary care can improve both mental health and chronic medical outcomes. The arena of mental health and primary care is moving from consideration of single conditions and their outcomes to more real-world, complex-care paradigms.[2, 7] However, to date, no synthesis has been done of the evidence on practice-based interventions that accounts for the primary care patient with ~~"m~~ultiple chronic conditions"[8, 9] and examines both mental health and chronic medical outcomes simultaneously.

Despite the prevalence and importance of other mental health conditions (e.g., anxiety disorders, psychotic disorders, substance use disorders) in the primary care setting, our preliminary review of the literature revealed that only depression had the evidence base necessary to support a comparative effectiveness review. Anxiety disorders initially appeared to be adequately represented, but ultimately did not have any studies that met our inclusion criteria.

The purpose of this report, therefore, is to summarize the available evidence about the effectiveness of practice-based interventions aimed at adult primary care patients with concomitant depression and chronic medical diagnoses. We believe this summary will add to the literature by synthesizing data about (1) mental health outcomes among people with defined chronic medical conditions, and (2) chronic medical outcomes among these same people.

Depression and Chronic Medical Conditions

Of all mental health conditions, depression contributes the greatest societal burden as measured by social and economic costs.[10] By 2030, depression itself is projected to be the single leading cause of overall disease burden in high-income countries.[11] Worldwide, depression makes a large contribution to the burden of disease, ranking third worldwide, eighth in low-income countries, and first in middle- and high-income countries.[12] In 2000, the U.S. economic burden of depressive disorders was estimated to be $83.1 billion.[13] More than 30 percent of these costs were attributable to direct medical expenses.[13]

Half of all Americans live with a chronic medical condition.[14] An estimated 23.6 million people (7.8 percent of the U.S. population) have diabetes.[15] Roughly 24 million U.S. adults have chronic obstructive pulmonary disease, and an additional 23 million have asthma.[16] Up to one-quarter of people living with chronic medical conditions have limitations in daily activity.[14] Living with chronic disease also takes a personal and emotional toll on patients and their families because of significant reductions in quality of life.[14]

Chronic medical conditions commonly associated with depression include arthritis, heart disease, diabetes, asthma, lung disease, and cancer [17, 18] (Table A). Depression among people with chronic physical illness has been linked to an increase in use of health care services, disability, and work absenteeism when compared with those without depression, even after controlling for the varying burden of the physical health condition.[19, 20]

Table A. Prevalence of depression in chronic medical conditions

Chronic Condition	Prevalence of Depression
Arthritis	
Rheumatoid arthritis	13%-20%[21, 22]
Osteoarthritis	19.4%[23]
Heart disease	
Post-myocardial infarction	10% to 47%[24]
Coronary artery disease	15%[25] to 23%[26]
Diabetes	11% to 15%[27] (MDD specifically) 17.6%[28] to 31.0%[27] (any depressive disorder)
Pulmonary disease	
Asthma	26.6%[29]
Chronic obstructive pulmonary disease	27.2%[30]
Cancer	9% to 24%[31] (MDD) 20% to 50% [31] (any depressive disorder)

Abbreviations: MDD = major depressive disorder

Treating Depression in Primary Care

Repeated evidence reviews show the benefits of integrated and collaborative care models, as compared with usual care, on the outcomes of depression in the general health setting without consideration of coexisting mental health conditions.[4, 32-34] An emerging literature addresses whether better treatment of depression in primary care can also improve chronic medical outcomes, such as for diabetes.[35-37] A review of similar studies will help address the clinical uncertainty about whether such interventions can make a difference in more than one disease outcome and guide the development of policy decisions about the potential benefit of adopting such guidance.

Scope and Key Questions

Scope of the Review

Two previous reports have particular relevance to this topic: a 2008 Agency for Healthcare Research and Quality (AHRQ) report examining the integration of mental health/substance abuse and primary care[32] and a 2009 National Institute for Health and Clinical Excellence (NICE) guideline for depression in adults with a chronic physical health problem.[33] The AHRQ report required trials to include patients with a mental health condition seen in primary or specialty care, but did not require the presence of a chronic medical condition. The NICE report neither specified primary care as the setting of interest nor examined disease-specific chronic medical outcomes. This review is therefore distinct.

As we conceptualized the approach to this report through the topic nomination and refinement process, preliminary evidence reviews revealed insufficient data about mental health conditions other than depression to substantiate a comparative effectiveness review. We specifically searched for evidence in patients with anxiety, but no studies met final eligibility criteria. The exclusion of mental health conditions other than depression does not reflect a belief

that they are less important, but that the literature is not mature enough to answer the questions set forth.

This review therefore summarizes the body of evidence that examines the effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions in adult primary care patients with depression and chronic medical condition(s) at baseline. The inclusion criteria require a level of depression that exceeds generally accepted cut points for major depression on common instruments but were not necessarily confirmed by gold standard evaluations. We use the term depression throughout the report to reflect this definition. In an effort to address the inherent heterogeneity of complex interventions,[38] this report also compares the specific characteristics of the interventions and the practice settings in which they are delivered.

These results should be of interest to multiple stakeholders, including patients, providers, and policymakers. A family physician nominated this topic because he wanted to know whether concomitantly treating mental health and general health conditions in the primary care setting could improve overall health outcomes. As we move to consider shared savings programs, such as accountable care organizations,[39] and the patient-centered medical home (PCMH),[40] consumers and payers are eager to identify interventions and processes that can streamline care for multiple conditions and improve the quality and efficiency of care. In fact, the PCMH has been defined as being accountable for "meeting the vast majority of each patient's physical and mental health care needs."[41] Numerous barriers, many financial, have hindered implementation of collaborative depression treatment in primary care, despite its considerable evidence base.[4, 42, 43] This report aims to provide new data about the common and costly problem of primary care patients with concomitant depression and chronic medical conditions. Such information can help guide clinical decisionmaking as well as potential reimbursement and coverage strategies.

Population

The focus of this review is on adults with one or more diagnosed chronic medical conditions and a diagnosis of depression, being treated in a primary care setting. An example is patients with diabetes and depression. The inclusion criteria require a level of depression that exceeds generally accepted cut points for major depression on common instruments. The purpose is to include patients with a level of severity known to benefit from treatment and to be associated with poor outcomes.

Interventions

For this review we use the term "practice-based" to define the interventions of interest. This term reflects an explicit effort to be inclusive of a wide range of interventions while also requiring the primary care site to be the nucleus of activity. We acknowledge the crucial role of primary care, where most patients receive care, and from which care can be coordinated.[44]

Practice-based is understood to mean any intervention that (1) targets the care process within a system of care and (2) works to improve depression or both depression and chronic medical conditions. Examples of practice-based interventions that may meet our inclusion criteria include, but are not limited to, coordinated care, integrated care, and collaborative care; they often involve a care manager. Each of these terms has varying, and possibly overlapping, definitions and is not specifically defined for the purposes of this report. In general, we perceive them broadly to mean primary care providers and mental health providers working together to address the comprehensive needs of the patient. Because of the dual focus on (1) concurrent

management of both depression and the chronic medical condition within primary care and (2) systematic changes that can improve the delivery of care (rather than testing specific interventions), we exclude medication-only, device, and psychotherapy-only clinical trials (e.g., efficacy studies comparing a medication with a placebo) from this review. Practice-based interventions can include person-level components such as problem-solving therapy and antidepressant medications, but they must be delivered as part of a broader systematic strategy to improve care.

Comparators

Potential comparators include different combinations, approaches, and modalities of practice-based interventions; they also include usual care, or enhanced usual care, as defined by individual studies.

Outcomes

We focused on five main outcomes: depression (Key Question [KQ] 1), chronic medical (KQ 2), harms of interventions (KQ 3), components of interventions (KQ 4), and characteristics of practice settings in which the interventions occurred (KQ 5). All KQs draw from the same universe of studies, such that KQs 3, 4, and 5 are subsidiary to KQs 1 and 2.

Settings

Settings include traditional primary care (e.g., family medicine, internal medicine, obstetrics/gynecology, and geriatrics) and settings with a primary care–type relationship (e.g., oncology clinics for those with cancer, infectious disease clinics for those with HIV).

Key Questions

- Key Question (KQ) 1a: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on intermediate depression outcomes (e.g., symptom improvement)?
- KQ 1b: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on other mental health outcomes (e.g., depression-related quality of life) and use of mental health-related services?
- KQ 2a: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on intermediate chronic medical outcomes (e.g., hemoglobin [Hb]A1c for patients with diabetes)?
- KQ 2b: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression

or both depression and chronic medical conditions (when compared with similar interventions or usual care) on general and other health outcomes (e.g., diabetes-related morbidity, use of general health-related services, costs)?

- KQ 3: What harms are associated with practice-based interventions for primary care patients with chronic medical conditions and concomitant depression?
- KQ 4: What are the characteristics of the practice-based interventions addressing concomitant depression and chronic medical conditions used in the primary care setting with regard to specific components and/or intensity (e.g., visit frequency, total number of contacts, provider discipline, use of self-management)?
- KQ 5: What are the specific characteristics of the practice setting where the interventions were delivered with regard to such variables as organizational characteristics (e.g., decision support, level of integration, information technology, electronic medical records, presence of mental health services on site, payer and service mix, practice size, and practice location/setting) or the relationship between elements of the system in which the practice operates (e.g., coordination, financing of care, payment arrangements)?

Analytic Framework

We developed an analytic framework to guide the systematic review process (Figure A). KQ 1 addresses the effectiveness of practice-based interventions for improving depression outcomes: KQ 1a addresses intermediate clinical outcomes related to depression, such as symptom response, and KQ 1b addresses other outcomes related to mental health, such as depression-related quality of life, and the use of mental health care services. KQ 2 addresses the effectiveness of practice-based interventions for improving chronic medical condition outcomes: KQ 2a addresses intermediate clinical outcomes, such as pain severity scores for patients with arthritis, and KQ 2b addresses other important chronic medical outcomes, such as disease-related quality of life and the use of general health-related services. KQ 3 addresses the potential harms of practice-based interventions. KQs 4 and 5 assess the characteristics of the interventions and practice settings, respectively.

Methods

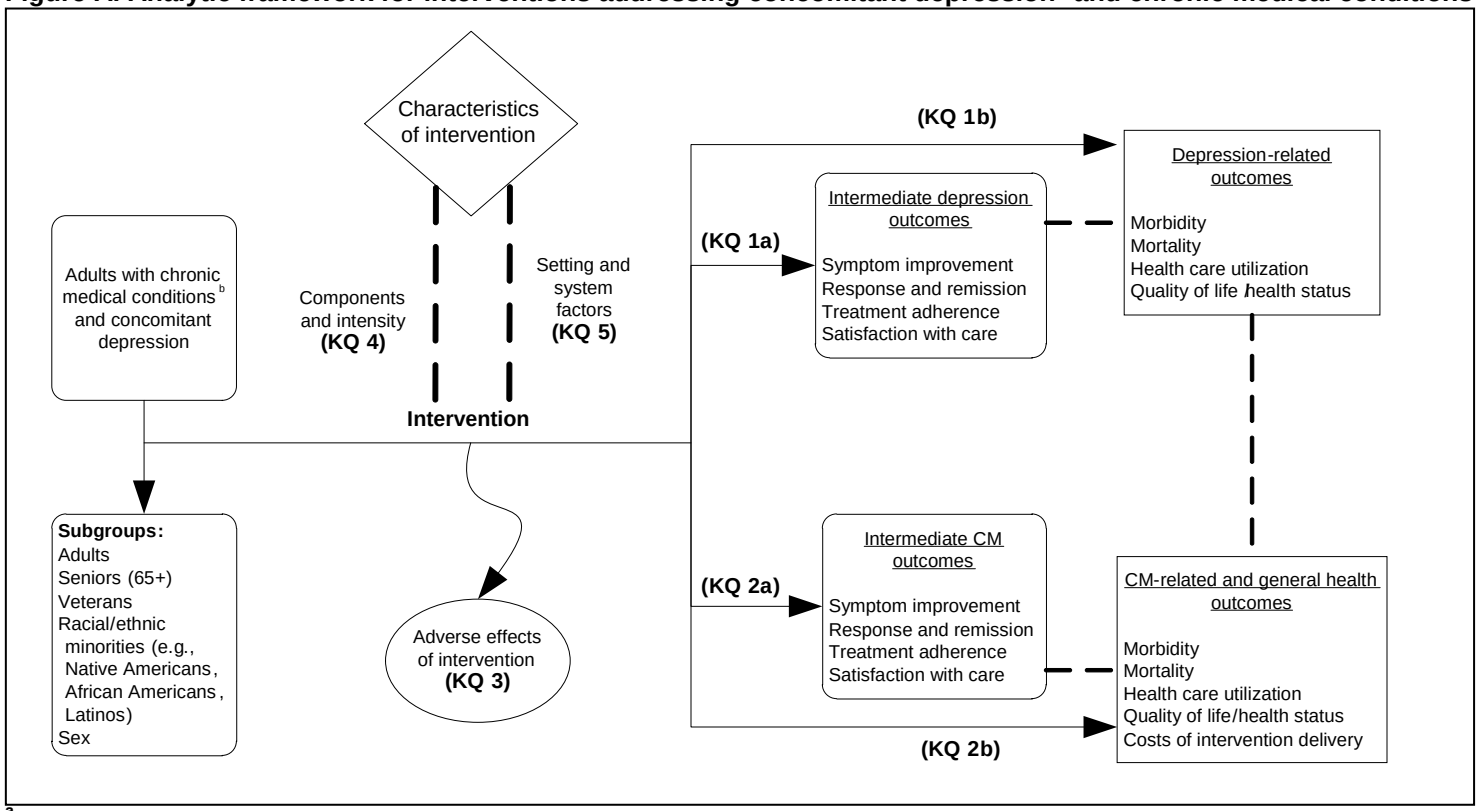
Topic Refinement and Review Protocol

During the topic development and refinement processes, we generated an analytic framework, preliminary Key Questions, and preliminary inclusion/exclusion criteria in the form of PICOTS (Population, Intervention, Comparator, Outcome, Timing, and Setting). We worked with the five Key Informants during the topic refinement and five members of our Technical Expert Panel (one individual participated in both) during the comparative effectiveness review process; they provided input on the scope, process, and reporting methods of the review.

To achieve an appropriate scope for the review, we prioritized conditions and interventions that were most clinically relevant. Preliminary evidence reviews casting a wide net for mental health conditions revealed insufficient data on mental health conditions other than depression and anxiety, and the latter ultimately yielded no qualified studies. We selected the following chronic medical conditions identified as priority conditions by the AHRQ[45] and the Institute of Medicine (IOM):[46] arthritis; diabetes; asthma or chronic obstructive pulmonary disease (COPD); cancer; chronic pain; stroke; HIV/AIDS; heart disease, heart failure, myocardial ischemia,

coronary artery bypass graft, postmyocardial infarction, and coronary artery disease; ~~–c~~omplex" patients with multiple comorbidities; and frailty due to old age.

Figure A. Analytic framework for interventions addressing concomitant depression[a] and chronic medical conditions[b] in primary care



[a] Our original framework and search strategy included both depression and anxiety; because our searches yielded no studies of the latter, we have removed it from this figure for clarity.

[b] Chronic medical conditions are considered broadly and include the AHRQ priority conditions and IOM priority conditions such as diabetes, arthritis, and chronic pain, among others.

Abbreviations: CM = chronic medical; MH = mental health interventions.

We searched MEDLINE®, Embase, the Cochrane Library, CINAHL®, and PsycINFO® from the inception of each database through December 19, 2011. We used Medical Subject Headings (MeSH or MH) as search terms when available or key words when appropriate, focusing on terms to describe the relevant population and the interventions of interest. We reviewed our search strategy with the Technical Expert Panel members and incorporated their input into our search strategy. We limited the electronic searches to English-language publications. The final search strategy is listed in Appendix A in the full report. We manually searched reference lists of pertinent reviews, included trials, and background articles on this topic to look for any relevant citations that might have been missed by our searches.

We developed eligibility (inclusion and exclusion) criteria with respect to patient PICOTS, and study designs and durations for each part of KQs 1 and 2. We included controlled studies of at least 6 months' duration in adults (age 18 or older) with depression and/or anxiety (the only conditions represented in the topic refinement process that would support a comparative effectiveness review) and one or more of the chronic medical conditions listed above. We also searched for systematic reviews of such studies. We chose to exclude studies without comparison groups due to the potential risk of bias in such studies (especially the risk of selection bias and confounding).

Depression and anxiety were defined as threshold-level conditions, meeting criteria for a disorder as determined by valid and reliable measures with established cut points; we excluded subthreshold symptoms and minor depression. Included studies must have used practice-based interventions aimed at improving the mental health condition or both the mental health and chronic medical conditions. A practice-based intervention is one that targets the care process within a system of care. Examples of practice-based interventions include coordinated care, integrated care, and collaborative care. Eligible controls were other practice-based interventions or usual care. All studies eligible for KQ 1 or 2 were eligible for KQs 3, 4, and 5.

Two trained members of the research team independently reviewed all titles and abstracts identified through searches. We retrieved any study that either reviewer marked for possible inclusion for full-text review. Two trained team members then independently reviewed each full-text article for final inclusion or exclusion. If the reviewers disagreed, an experienced team member resolved the conflicts. Appendix B in the full report contains the list of studies that were reviewed at the full-text stage but failed to meet all the inclusion criteria.

For studies that met our inclusion criteria, we abstracted important information into evidence tables. We designed structured data abstraction forms to gather pertinent information from each article. Trained reviewers extracted the relevant data from each included article to put into the evidence tables. A second member of the team reviewed all data abstractions for completeness and accuracy. Data abstraction forms were almost identical to the evidence tables containing abstracted data (Appendix C in the full report).

Quality Assessment of Individual Studies

To assess the quality (internal validity) of studies, we used predefined criteria based on those developed by the U.S. Preventive Services Task Force (ratings: good, fair, poor)[47] and the University of York Centre for Reviews and Dissemination.[48] These criteria assess the adequacy of randomization, allocation concealment, similarity of groups at baseline, masking, attrition, and whether intention-to-treat analysis was used. In general terms, a "good" study has the least risk of bias, and its results are considered valid. A "fair" study is susceptible to some bias but

probably not sufficient to invalidate its results. A "poor" study has significant risk of bias (e.g., stemming from serious errors in design or analysis) that may invalidate its results.

Two independent reviewers assigned quality ratings for each study. Disagreements between the two reviewers were resolved by discussion and consensus or by consulting a third member of the team. We excluded studies rated "poor" from our analyses. Quality assessments of individual studies are located in Appendix D in the full report.

Data Synthesis

The research team determined prioritization and/or categorization of outcomes with suggestions from Technical Expert Panel members. With their participation, we decided that despite the variation and inherent heterogeneity of medical conditions, we would analyze outcomes across conditions to provide a summary effect. We conducted quantitative analyses using meta-analyses of outcomes reported by a sufficient number of studies that were homogeneous enough for us to justify combining their results. When quantitative analyses were not appropriate (e.g., because of heterogeneity, insufficient numbers of similar studies, or insufficiency or variation in outcome reporting), we synthesized the data qualitatively.

We used random-effects models to estimate pooled effects.[49] For continuous outcomes, we used the weighted mean difference as the effect measure; if the measurement scale differed among trials, we calculated the standardized mean difference. For most dichotomous outcomes, we reported risk differences. Sensitivity analyses were conducted for all analyses in which considerable heterogeneity was present (i.e., I^2 statistic greater than 75 percent).

Strength of the Body of Evidence

We graded the strength of evidence based on the guidance established for the Evidence-based Practice Center Program.[50] Developed to grade the overall strength of a body of evidence, this approach incorporates four key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. It also considers other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, strength of association (magnitude of effect), and publication bias. We graded strength of evidence based on our level of confidence that the evidence reflected the true effect of the intervention on the outcome (i.e., how likely further research is to change our confidence in the estimate of effect). Possible grades were "high," "moderate," "low," and "insufficient" (evidence is unavailable or does not permit estimation of an effect).

We graded the strength of evidence for mental health outcomes (KQ 1), chronic medical condition outcomes (KQ 2), and harms (KQ 3). Two reviewers assessed each domain for each key outcome, and differences were resolved by consensus.

Applicability

We assessed applicability of the evidence following guidance from the Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[51] We used the PICOTS framework to explore factors that affect applicability. Some factors identified a priori that may limit the applicability of evidence included the following: ethnicity of enrolled populations, type of practice setting, and the use of interventions that may be difficult to incorporate into routine practice for many providers (e.g., they require substantial resources or time, or they may be

delivered by research staff rather than existing staff in the practice). We also recognized that applicability could be influenced by payer type.

Results

Results are organized by KQ and grouped by medical condition(s) when possible. Our results pertain to the general adult population; no studies that met our inclusion criteria reported on young adults or pregnant women. Regarding older adults, one study selectively recruited for age 60 or older;[52-56] however, participants across all studies in this review tended to be middle aged or older (mean age, 59; range of means, 47 to 72), so we do not report results for older adults separately. Several studies reported on traditionally underrepresented populations, including women,[57-59] Spanish speakers,[57-60] and predominantly African-American male veterans with HIV;[61] we report these results in the context of overall results by medical condition, not in separate categories.

Results of Literature Searches

We ultimately included 24 published articles reporting on 10 randomized, controlled trials. We recorded the reason that each excluded full-text publication did not satisfy the eligibility criteria and compiled a comprehensive list of such studies (Appendix B in the full report). Evidence tables for included studies can be found in Appendix C in the full report.

Description of Included Studies

In the 10 included trials, sample sizes ranged from 55 to 1,001, and study duration ranged from 6 to 60 months. Nine trials were conducted in the United States (one of these in Puerto Rico) and one in Scotland. All included studies characterized their respective intervention as a form of collaborative care, not another form of a practice-based intervention (such as integrated care). Similarly, all included studies specified depression as the targeted mental health condition; no studies specified anxiety as the condition of interest. Five articles[52-56] are secondary analyses from the Improving Mood—Promoting Access to Collaborative Treatment (IMPACT) trial;[5] it tested a collaborative care depression intervention in older adult primary care patients, including preplanned subgroups of patients with arthritis, cancer, and diabetes. For ease of interpretation, we consider each subgroup a unique study in the Results chapter of the full report. Consequently, our results include data from 12 studies (9 stand-alone randomized control trials [RCTs] and 3 IMPACT subgroups). The designated chronic medical conditions included arthritis,[53, 56] cancer,[52, 57, 59, 62] diabetes,[35, 37, 58, 63-66] heart disease,[67] and HIV.[61] Two studies involved patients with one or more active medical conditions.[60, 68]

All KQs draw from the same universe of evidence. Table B summarizes key elements of the trial interventions and shows their quality ratings.

Table B. Summary of collaborative care intervention trials

Author/ Trial Name Disease Sample Size	Quality Rating[a]	Intervention Summary	Delivery Method Delivered By Psychiatrist Supervision?
Lin et al., 2003;[56] Lin et al., 2006;[53] Fann et al., 2009;[52] Williams et al., 2004;[55] Katon et al., 2006[54] IMPACT Arthritis, cancer, diabetes[b] 1,001	Fair	Care management based on stepped care treatment algorithm; patient preference for treatment: antidepressants or problem-solving therapy (6–8 sessions); monitoring of treatment response (IMPACT model)	In-person and telephone Depression care specialist (nurse or clinical psychologist) Yes
Dwight-Johnson et al., 2005[57] MODP Cancer 55	Fair	Described as being based on the IMPACT model	In-person and telephone Bilingual cancer depression care specialist (master's level social worker) Yes
Ell et al., 2008;[59] Ell et al., 2011[69] ADAPt-C Cancer 472	Fair	Described as being based on the IMPACT model	In-person and telephone Bilingual cancer depression care specialist (master's level social worker) Yes
Ell et al., 2010;[58] Ell et al., 2011;[70] Hay et al., 2012[71] MDDP Diabetes 387	Fair	Described as being based on the IMPACT model	In-person and telephone Bilingual diabetes depression care specialist (master's level social worker) Yes
Ciechanowski et al., 2006;[37] Katon et al., 2008;[63] Katon et al., 2004;[35] Kinder et al., 2006;[64] Lin et al., 2006;[65] Simon et al., 2007[66] Pathways Diabetes 329	Fair	Described as being based on the IMPACT model	In-person and telephone Depression clinical specialist (nurse) Yes
Katon et al., 2010;[68] Von Korff, 2011;[72] Lin, 2012[73] TEAMcare Diabetes +/- heart disease 214	Fair	Support for self-care of depression (including pharmacotherapy) and individualized goal-setting; treat-to-target program for DM and/or CHD; motivational coaching; maintenance support	In-person and telephone Medically supervised nurse trained in diabetes education Yes

Table B. Summary of collaborative care intervention trials (continued)

Author/ Trial Name Disease	Quality Rating	Intervention Summary	Delivery Method Delivered By Psychiatrist Supervision?
Pyne et al., 2011[61] HITIDES HIV 249	Good	Stepped care approach; education/activation; recommendations for medications and/or mental specialty referral; web-based decision support	Telephone Off-site depression care team: nurse depression care manager, pharmacist, psychiatrist Yes
Rollman et al., 2009[67] Bypassing the Blues Heart disease 302	Good	Education on depression and CHD; support to PCP on antidepressants; referral to mental health specialists as needed; phone monitoring for symptoms	Telephone Nurse care manager Yes
Strong et al., 2008[62 c] SMaRT Oncology 1 Cancer 200	Fair	Manual-based Depression Care for People with Cancer; up to 10 sessions of problem-solving treatment to address coping; progress monitored by telephone; advice on choice of antidepressant if requested	In-person and telephone Nurses with no psychiatry experience Yes
Vera et al., 2010[60] NA ≥1 of the following: diabetes, hypothyroidism, asthma, hypertension, chronic bronchitis, arthritis, heart disease, high cholesterol, stroke 179	Good	Depression education; antidepressant medications and/or 13 sessions of cognitive behavioral therapy	In-person and telephone Master's level counselor or psychologist Yes

[a] These criteria assess for biases, including appropriate masking/blinding, attrition, and intent-to-treat analyses. In general terms, a good study has the least risk of bias, and its results are considered to be valid. A fair study is susceptible to some bias but probably not sufficient to invalidate its results. For detailed quality assessment, see Appendix D in the full report.[b] Although IMPACT is a single randomized, controlled trial, several subgroups, including those with chronic medical conditions, were analyzed. For ease of interpretation throughout this report, we consider each of the three IMPACT subgroups (arthritis, cancer, and diabetes) a separate study.

[c]Study took place in the United Kingdom, where both primary care and mental health specialty services are free at the point of delivery.

Abbreviations: ADAPt-C = Alleviating Depression Among Patients with Cancer; CHD = coronary heart disease; DM = diabetes mellitus; IMPACT = Improving Mood—Promoting Access to Collaborative Treatment; MDDP = Multifaceted Diabetes and Depression Program; PCP = primary care provider.

For IMPACT,[52-56] Bypassing the Blues,[67] Symptom Management Research Trials (SMaRT) Oncology 1,[62] HITIDES (HIV Implementation of Translating Initiatives for Depression into Effective Solutions),[61] the Multifaceted Oncology Depression Program,[57] and Vera et al.,[60] the control condition was usual care, which consisted of informing patients of their depression status and advising them to share this information with their PCP. By contrast, ADAPt-C,[59] Pathways,[35, 37, 63, 64, 66] TEAMcare,[68] and the Multifaceted Diabetes and Depression Program[58] compared collaborative care with enhanced usual care, which extended usual care by including some degree of additional communication between the research staff or diabetes care manager and the patient's PCP and/or family about the patient's depression status.

Key Findings and Strength of Evidence

Key Question 1a: Intermediate Depression Outcomes and Satisfaction With Care

We summarize findings and SOE for this question in Table C. Evidence from 11 studies (9 RCTs and 2 subgroups from IMPACT) indicated that patients receiving a collaborative care intervention had greater improvement in depressive symptoms. Collaborative care interventions were also associated with greater depression treatment response (≥50 percent reduction in symptoms) compared with usual care in nine studies[35, 52, 56-60, 67, 68] (moderate SOE). These results were consistent across medical conditions and reflected clinically meaningful changes on well-accepted measures of depression. The evidence showed that five patients would need to be treated to achieve one more depression response than would be seen with usual care at 6 months, with a number needed to treat (NNT) of six patients at 12 months.

Table C. Summary of results for collaborative care interventions compared with controls for people with depression and one or more chronic medical conditions: intermediate mental health outcomes

Outcome	Summary of Results	Strength of Evidence
Symptom improvement	Greater symptom improvement scores in intervention groups at both 6 months (SMD, 0.45; 95% CI, 0.29 to 0.61; 7 studies) and 12 months (SMD, 0.47; 95% CI, 0.29 to 0.65; 6 studies) compared with control groups. Benefits were sustained through 24 months, but the magnitude of benefit was reduced (WMD, 0.18; 95% CI, 0.10 to 0.26; 3 studies)	Moderate
Depression-free days	More depression-free days at 12 months for those in intervention groups than in usual care groups (5 studies, range of differences between intervention and control groups: 20 to 59 days)	Moderate
Response (≥50% reduction)	Higher rates of depression response in intervention groups than in usual care, based on 10 studies (NNT, 5 at 6 months; NNT, 6 at 12 months) Benefits persisted, but to a lesser degree, at 18 months (RD 0.12; 95% CI, 0.02 to 0.22; 3 studies).	Moderate
Remission	Remission of depression favored intervention over usual care at 6 months and at 12 months based on 5 studies (NNT, 8 at 6 months; NNT, 12.5 at 12 months). Benefits persisted at 18 months, but showed no difference between groups at 24 months.	Moderate
Recurrence	Only 1 study[59, 69] (of patients with cancer) addressed recurrence as an outcome, and showed no difference between groups at 18 or 24 months.	Insufficient
Treatment adherence	Mixed results: 1 study[65] reported significantly greater adherence to antidepressants in the intervention arm at 6 and 12 months; the other[61] reported no difference between groups at 6 and 12 months.	Insufficient
Treatment satisfaction	Greater satisfaction with care for intervention participants than for controls at 12 months (RD, 0.21; 95% CI, 0.11 to 0.30) (4 studies),[a] and this extended to 24 months (RD, 0.14, 95% CI, 0.06 to 0.21) (3 studies)'	Moderate

[a] Results are from meta-analysis of the 4 trials that reported satisfaction for both intervention and control arms. Two additional trials reported treatment satisfaction for the intervention arm, but not the usual care arm.

Abbreviations: CI = confidence interval; NA = not applicable; NNT = number needed to treat; RCT = randomized controlled trial; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference.

Although less frequently measured, patients receiving collaborative care also had more depression-free days (moderate SOE) and higher rates of depression remission (moderate SOE) compared with patients receiving usual care. Intervention patients similarly reported greater satisfaction with care (moderate SOE).

Evidence was insufficient to draw conclusions about adherence to antidepressants based on limited data and variable definitions. Of the two studies that provided adequate data on adherence, one showed significant differences between groups[65] and one did not.[61] We found insufficient data to draw conclusions about recurrence of depression (only one study[59, 69]).

Key Question 1b: Morbidity, Mortality, Quality of Life, Function, and Use

This question looked at other mental health outcomes, including suicide, use of antidepressants, mental health–related quality of life, use of mental health care services, sick days attributable to mental health, and employment stability (Table D). Only one suicide was reported, in the usual care arm of a cancer trial.[62] Meta-analysis from three studies[52, 61, 67] showed no difference in antidepressant use between groups at 6 months; but there was noticeable heterogeneity, with the two studies enrolling subjects with cancer or heart disease both finding a similar increase in antidepressant use, and one study enrolling subjects with HIV finding no difference (Appendix E in the full report). Meta-analysis of five studies[52, 55, 56, 58, 59, 61] showed that the use of antidepressants was greater in collaborative care arms than in control groups across populations with various chronic medical conditions at 12 months, not including the HIV study, which introduced substantial heterogeneity (moderate SOE). Quality of life was measured in several ways but most frequently using the mental component of the Medical Outcomes Study Short-Form (SF-12); the trials showed that collaborative care interventions achieved greater quality of life scores than usual care at 6 and 12 months (moderate SOE). Five studies[35, 52, 53, 58, 59, 69, 70] reported on the use of mental health care services; each showed greater use of any mental health services at 6 or 12 months (or both) by those receiving the collaborative care intervention, and one as-treated sample of patients with cancer[52] showed that this trend persisted at 18, but not 24, months (low SOE). No data were available on sick days or employment stability (insufficient SOE).

Table D. Summary of results for collaborative care interventions compared with controls for people with depression and one or more chronic medical conditions: other mental health outcomes

Outcome	Summary of Results	Strength of Evidence
Suicide	1 study reported 1 suicide in the usual care group	Insufficient
Use of anti-depressants	Greater antidepressant use for collaborative care interventions than for usual care at 12 months (RD, 0.23; 95% CI, 0.15 to 0.30 ; 5 studies[a]), but not 6 months (RD, 0.09; 95% CI, -0.02 to 0.20; 3 studies).	Low
MH-related quality of life	Greater mental health–related quality of life for patients in collaborative care intervention arms than usual care at 6 and 12 months using the mental component of the Medical Outcomes Study Short Form (WMD, 2.98; 95% CI, 1.41 to 4.55 at 12 months; 4 studies)	Moderate
MH care use	Greater use of any mental health services other than or in addition to antidepressants for collaborative care interventions than for usual care at 6 and/or 12 months (40% to 97% vs. 16% to 57% for intervention and control groups, respectively; based on 8 studies)	Low
MH-related sick days	Not reported	Insufficient
MH-related employment stability	Not reported	Insufficient

[a] Results of the meta-analysis excluding the HITIDES data, which was an outlier and accounted for significant heterogeneity (Appendix E in the full report)

Abbreviations: CI = confidence interval; HITIDES = HIV Implementation of Translating Initiatives for Depression into Effective Solutions; MH = mental health; RD = risk difference; WMD = weighted mean difference.

Key Question 2a: Intermediate Chronic Medical Outcomes

For this question, we were interested in the effects of collaborative care interventions on intermediate outcomes for the specified chronic medical condition(s). For most chronic medical

conditions of interest here, we found just one study (Table E). We found multiple studies of people with diabetes and depression.

Table E. Summary of results for collaborative care interventions compared with controls for people with depression and one or more chronic medical conditions: intermediate chronic medical outcomes

General Outcome	Specific Disease-Related Outcome	Summary of Results	Strength of Evidence
Symptom improvement	Arthritis: pain	Insufficient evidence from 1 subgroup analysis to draw conclusions.	Insufficient
	HIV: symptom severity	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
Response	Diabetes: HbA1c	Meta-analysis of 3 studies showed no between-group differences at 6 or 12 months. A single study[70] showed no difference between groups at 18 and 24 months	Low
	Heart disease: ≥10 mmHg decrease in SBP	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
Adherence	Cancer: followed treatment	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
	Diabetes: diet	Not calculated; no between-group difference at any time points in all studies examined.	Moderate
	Diabetes: exercise	3 of 3 trials found no difference between groups at 6 months; of these same trials, 2 of 3 found no difference at 12 months.	Low
	Diabetes: medications	Insufficient evidence from 2 studies to draw conclusions.	Insufficient
	HIV: medications	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
Satisfaction with care	Diabetes, heart disease, or both	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient

Abbreviations: HbA1c = hemoglobin A1c; mmHg = millimeters of mercury; RCT = randomized controlled trial; SBP = systolic blood pressure.

In the HITIDES study of HIV-positive patients, authors reported significant adjusted intervention effects on HIV symptom severity versus controls at 6 months (beta, -0.62; 95% CI, -1.2 to -0.08; p=0.03) but not 12 months (beta, -0.09, 95% CI, -1.58 to 1.40, p=0.88).

HbA1c was reported as a measure of response in four trials of people with diabetes; baseline HbA1c ranged from 7.28 percent to 9.03 percent. Our meta-analyses found no significant differences between intervention and control groups (WMD, 0.13; 95% CI, -0.22 to 0.48 at 6 months, 3 studies); (WMD, 0.24; 95% CI, -0.14 to 0.62 at 12 months, 3 studies); findings were somewhat inconsistent and lacked precision (low SOE). However, the only study to use HbA1c as a predefined outcome measure, the TEAMcare study,[68] reported significant differences in HbA1c. The figures were as follows for intervention versus control groups: 8.14 versus 8.04 at baseline; 7.42 versus 7.87 at 6 months; and 7.33 versus 7.81 at 12 months (overall p<0.001). Ell and colleagues[70] reported 18- and 24-month data on HbA1c, showing no difference between groups, with an overall mean difference at 24 months of 0.23 (95% CI, -0.34 to 0.81).

Three studies reported on adherence to recommended treatment.[55, 65, 68] The patients in the collaborative care intervention were no more likely than controls to adhere to a generally healthy diet (low SOE), and they were no more likely to adhere to an exercise program in two of three studies[55, 65, 68] (low SOE). For rates of adherence to an overall regimen (including oral hypoglycemics, lipid-lowering agents, and angiotensin-converting enzyme inhibitors), evidence was insufficient to draw conclusions. A summary of diabetes self-care based on a measure of overall self-reported adherence was reported by one study, and showed no difference between groups at 12,18, or 24 months.[58, 70] They similarly showed no difference between groups in diabetic complications for these same time frames.

Data were insufficient to draw conclusions about treatment satisfaction with care for chronic medical conditions.

Key Question 2b: General Health Outcomes and Costs

General health outcomes of interest included condition-specific morbidity, mortality, use of health care services, and quality of life. All evidence was insufficient to draw conclusions other than for mortality and quality of life (Table F).

Table F. Strength of evidence for collaborative care interventions for people with depression and one or more chronic medical conditions: KQ 2b, general health outcomes and costs

Outcome	Summary of Results	Strength of Evidence
Condition-specific morbidity	Insufficient evidence from 1 RCT (post-CABG) and 1 subgroup analysis (arthritis) to draw conclusions.	Insufficient
Mortality	Eight studies reported no difference between groups, with few overall events; 6 months: RD, 0.00 (95% CI, -0.02 to 0.02); 12 months: RD, 0.00 (95% CI, -0.02 to 0.01).	Moderate
Health care utilization	Data were insufficient to draw conclusions about use of health care services.	Insufficient
Quality of life	Greater quality of life for those receiving collaborative care at 6 and 12 months, based on several different measures.	Moderate
Cost of intervention	Data were insufficient because of heterogeneity in the ways costs were reported; a crude estimate of the average intervention cost is $705 per patient.	Insufficient

Abbreviations: CABG = coronary artery bypass graft; CI = confidence interval; RCT = randomized controlled trial; RD = risk difference

All but one study[60] reported on mortality, and few deaths were reported overall. Most occurred in studies of people with cancer. Intervention and control patients did not differ in mortality at 6 months (risk difference [RD], 0.00; 95% CI, -0.02 to 0.02; seven studies[52, 55-57, 59, 61, 67, 69]) or 12 months (RD, 0.00; 95% CI, -0.02 to 0.02; seven studies[52, 55, 56, 59, 61, 62, 68, 69]) (moderate SOE).

Patients receiving collaborative care interventions generally experienced better quality of life than control patients at 6 and 12 months, based on several different measures from six studies[52, 56, 57, 59, 61, 69, 72] (moderate SOE).

Key Question 3: Harms

Very few data were reported on harms, leaving insufficient evidence to draw conclusions. Only the TEAMcare study, involving patients with depression, diabetes, and/or heart disease,[68] defined adverse events; the investigators reported higher rates of mild adverse events (e.g., medication side effects) and of moderate adverse events (e.g., falls) in the intervention arm. These could be attributed to increased rates of medication adjustment related to the collaborative care intervention. Additionally, patients in the intervention arm had more frequent contacts with the care manager and thus had more opportunities to report adverse events, so findings might be the result of detection bias.

Key Question 4: Characteristics of Service Interventions

All interventions were described as collaborative care interventions; we found no study with any other types of practice-based interventions that met our inclusion/exclusion criteria.

The summary finding was that collaborative care hinged on the role of care manager, whose training and expertise varied widely. A physician (11 of 12 were psychiatrists) supervised care; a

form of stepped care, patient preferences for treatment, and self-management were central to most interventions.

The TEAMcare study[68] was the most original in its design. Its investigators had a goal not just of reducing depression, but also controlling risk factors for various diseases simultaneously using a nurse to support guideline-concordant care.

Key Question 5: Characteristics of the Practice Setting

Given that characteristics of the practice setting often determine the feasibility of implementing interventions, we were interested in assessing similarities and differences. Eleven of 12 studies were conducted in the United States (1 in Puerto Rico[60]), and 1[62] took place in the United Kingdom. Overall, practice-setting characteristics (e.g., location, practice type and size, open/closed system, level of integration, payer mix and payer type, service mix, information technology) and system characteristics (e.g., financing of care and payment arrangements) were rarely reported.

We categorized the system as open (no membership or eligibility required) in six trials[57-60, 62, 67] and closed in three trials.[35, 37, 61, 63-66, 68] Closed systems were generally self-contained; in this evidence base, they included Group Health Cooperative and the Department of Veterans Affairs (VA) system, in which an array of services was accessible to patients who were members of these organizations. This latter factor may be important for applicability because of the nature of collaborative care and its focus on coordination, which is arguably easier in a closed than an open system of care.

Discussion

Our findings reinforce the evidence for the effectiveness of collaborative care interventions for treating depression in primary care.[34] Moreover, they add a level of detail that had previously not been systematically reviewed. We selected trials that required the diagnosis of one or more chronic medical conditions (rather than generic primary care samples), and we reported on both the depression and the chronic medical outcomes. This review also extended the parameters of primary care to include settings in which certain patients with chronic disease receive the majority of their care. We found that recipients of collaborative care had significantly greater improvement in depression outcomes as compared with patients receiving usual care for people with arthritis, cancer, diabetes, heart disease, and HIV.

Although the relationship between depression and chronic disease is established,[27, 74, 75] the extent to which successful treatment of depression improves chronic medical conditions remains unknown. Our review shows that investigators are beginning to examine these outcomes, particularly in diabetes, although largely as secondary outcomes and with negative or inconclusive data at present. We excluded some relevant studies because of short duration of followup[76] or because the treatment occurred outside the purview of a primary care–like setting.[77-79]However, our inability to answer the basic question posed by a primary care provider —Will treating my patient's depression (with an evidence-based collaborative care program) improve their medical conditions?" was both surprising and disappointing.

One study in the review, TEAMcare,[68] is unique because it identifies markers of disease risk for multiple conditions as primary outcomes. Using a guideline-based —treat-to-target" approach delivered by a medically trained nurse, these investigators targeted patients with poorly controlled diabetes, coronary artery disease, or both and coexisting depression; their goal was to reduce overall risk factors. This approach is a detour from the traditional model, in which the

focus is on collaborative care of depression, presumably in the hope that treating depression will improve overall health. Perhaps partly because of the benefits of having an integrated health care system, TEAMcare recipients showed clear improvements, not only in depression, but also in reducing HbA1c and systolic blood pressure to target goals.

Implementation, Dissemination, and Role of Decisionmakers

Despite evidence for the use of collaborative depression care in primary care settings, and a recommendation from the President's New Freedom Commission on Mental Health,[80] uptake of such interventions has been poor. Although financial and system barriers have been identified,[81] it is still unclear why decisionmakers have not advocated for the dissemination of collaborative depression care. One reason may be that in our current system, primary care providers have little incentive to find and treat mental health problems. Should a model of accountable care[39] be adopted, in which one bundled payment must suffice for the breadth of necessary care, a focus on concomitant mental health conditions will align incentives in a way that gives priority to dissemination of proven programs. Once incented to keep people well, primary care providers may also find new motivation for gaining proficiency in mental health care.[82] Inherent in any new model of payment will be the discussion of both absolute costs and the cost-effectiveness of such interventions—neither of which topics had comprehensive data or were a central focus of this report.

This review adds further evidence supporting the effectiveness of collaborative care interventions. We show that patients with multiple and specific medical conditions can achieve improvement in depression (moderate SOE), satisfaction with care (moderate SOE), and improved mental and physical quality of life (moderate SOE).

Stakeholders for improving the quality of primary care can apply the findings in this review from several perspectives. One way these data might be used and further disseminated is in measuring quality, for instance, to meet new standards for the PCMH.[40]

Applicability

Our findings are generally applicable to primary care patients with depression and at least one chronic medical condition, but they may not apply to patients with multiple chronic conditions. The average age across studies was 59, an age group likely to have chronic disease. For that reason, we cannot speak directly to the relevance of these results to young adults with chronic disease. People of Hispanic origin (predominantly female)[58, 59] and male veterans[61] were represented and appeared to respond similarly across outcomes, but there were too few data to analyze separately. Reported studies used clinically meaningful measures and had study durations (at least 6 months) that provided a real-world context.

Although these trials represented several settings, including primary care–like cancer and HIV clinics, they all had in common a care manager who directed the intervention. The intermediate mental health outcomes achieved might, therefore, apply only to settings that can accommodate and afford to provide such services. Although we did not attempt, as others have, to identify "key ingredients" of collaborative care such as training background of team members,[38] our report suggests that the complexion of teams and their types of training may afford some flexibility.

Limitations of the Comparative Effectiveness Review Process

Outlining the scope of this evidence review posed a challenge in regard to defining the interventions of interest. With involvement from our Key Informants and members of our Technical Expert Panel, we ultimately arrived at the term "practice-based" to differentiate interventions relative to this review from person-level interventions such as medications or stand-alone psychotherapies. We did not find the term "practice-based" in the literature, but we used other eligibility criteria and some known interventions to inform our searches. Even though we also added the terms "collaborative care," "integrated care," and "telemedicine" to guide our search, we may have missed relevant interventions that are not indexed in these categories. However, we included a general intervention term (see Appendix A in the full report) that should have identified studies that were not found using the more specific terms.

We also recognize that limiting the eligibility to trials of patients with clear medical diagnoses may have missed some potentially relevant work. One example is a recent RCT of a novel intervention for patients with anxiety conducted in the primary care setting;[83] the trial did not require a coexisting medical condition.

We chose to exclude studies without comparison groups because of the potential risk of bias in such studies (especially the risk of selection bias and confounding). We recognize that studies without comparison groups can sometimes identify important information, but for the purposes of our questions we generally consider such studies to provide hypothesis-generating information, rather than valid evidence, to answer our questions. The purpose of this review was not to uncover hypothesis-generating information, but rather to find evidence with a sufficiently low risk of bias to provide more definitive answers to the KQs. The number of potential known confounders is substantial for the questions we addressed in this review (and there may always be additional unknown confounders). Thus, we believe that the risk of bias in studies without comparison groups is too high to provide reliable evidence to answer our KQs. Note, however, that important and innovative systems efforts in the fields of mental health and primary care[84] may be overlooked using these methods.

Limitations of the Evidence Base

Few relevant trials reported medical outcomes specifically. We also acknowledge significant heterogeneity among conditions (e.g., cancer differs from diabetes). Only 1 of our 12 studies[68] was specifically designed to answer KQ 2a about intermediate medical outcomes. The remainder aimed to look at mental health outcomes in patients with different medical conditions.

We had no head-to-head trials in our report; this meant that we could make comparisons only with usual or enhanced usual care. We had only one study from outside the United States, highlighting the lack of similar literature from other countries. Although we characterized the interventions' components, we could not evaluate quantitatively the determinants of effectiveness (i.e., "active ingredients"[38]). This was not the intention of the review but highlights the difficulty in synthesizing data on complex interventions.

Remember, too, that studies did not necessarily screen for mental health comorbidities (such as substance abuse), which may have negatively influenced medical outcomes, particularly related to self-care activities. A completely unexplored area is personality disorders, which are pervasive by nature and can prove a barrier to achieving therapeutic goals.[85]

Research Gaps

Depression Treatment and Outcomes of Chronic Disease

Depression can negatively affect general medical illness, but we do not know whether the effective treatment of depression in the primary care setting can alter the course of chronic disease. Is it that treating depression isn't enough to improve medical outcomes, or that we need more innovative interventions that do not just focus on depression? The TEAMcare approach offers an example, in which treatment goals include targets for all relevant diseases and individualized approaches to reach these targets. Designing, implementing, and sustaining such approaches will not be without considerable challenge, and studies will require larger sample sizes, longer time frames, and, optimally, higher levels of joint funding from multiple institutes more used to focusing on one disease.

Our report identified outcomes mostly for single medical conditions, which does not necessarily reflect real-world primary care patients that may have multiple comorbidities. Trials involving other medical conditions not represented here, such as lung disease or pain syndromes, could be informative as an incremental approach, but perhaps what the field needs most to understand is what models of care work best for patients with common clusters of disease in primary care. One possible cluster could be diabetes, hypertension, and obesity, concomitant with depression; this group may be particularly salient given the probable role of vascular disease in late-onset depression.[86, 87] More generally, the bidirectional aspect of depression and medical illness needs further exploration. For example, investigators could usefully explore whether effectively improving vascular risk factors reduces depression.

Other Mental Health Conditions

This report did not identify relevant evidence for practice-based interventions targeting common disorders known to be prevalent and problematic in primary care, including anxiety spectrum, psychotic disorders, substance-use disorders, and cognitive disorders. It is unclear whether interventions for each of these need to be studied in isolation with related medical conditions, or whether perhaps a more broad-based approach might make sense. Instead of the current reductionist approach of screening for one mental health condition at a time, it might be possible to screen broadly[88] and develop and tailor an intervention accordingly, with a core set of features that could be similar to collaborative care. Diagnoses other than depression must be considered.

Head-to-Head Trials

It is noteworthy that we identified no studies of co-location or integrated care in this review, and disappointing that we found no-head-head trials of various approaches. Head-to-head trials of practice-based interventions should be considered; these might include collaborative care versus mental health co-location, or another model of integrated care versus collaborative care. Given the desire to find the active ingredients of practice-based care,[38] we should test variations of existing efficacious models. Certain components of the collaborative care model may be more salient than others, and future studies that explicitly compare intervention components within the collaborative care model may help address this issue. For example, head-to-head comparisons of telephone-based versus face-to-face approaches might be useful. Examining session frequency and/or study intensity (i.e., frequency plus duration) as a predictor of outcome within these two approaches may also prove fruitful.

Exploring the extent to which mental health and physical health outcomes are related to the intervention provider's training is another important issue; that could entail determining whether, for instance, outcomes improve by having a depression care specialist deliver the intervention rather than a provider not trained in mental health.

Answering some of these basic design questions in ways that facilitate comparisons with true interventions, and not simply usual care, will eventually facilitate translation and implementation of these approaches on a broader scale.

Conclusions

In primary care patients with depression and one or more specific chronic medical condition, collaborative care interventions achieved improvement in depression symptoms, response, remission and depression-free days (moderate SOE); satisfaction with care (moderate SOE); and improved mental and physical quality of life (moderate SOE). These improvements were consistent across different common chronic medical conditions. Patients with diabetes receiving collaborative care had no difference in HbA1c (low SOE). To determine the relative benefit of implementing collaborative care programs for depression (or other mental health conditions) on overall health, we need studies designed to measure the effectiveness of practice-based interventions on medical outcomes. Future investigations should compare variations of such interventions in head-to-head trials to discern best models of care. They should also move from addressing single medical conditions to common clusters of disease and, similarly, broaden the net for mental health conditions beyond depression.

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Introduction

Background

The World Health Organization has identified the integration of mental health into primary care as the most salient means of addressing the burden of mental health conditions, noting its "urgent importance."[1] In the United States, half of the care for common mental health disorders is delivered in general medical settings,[2] emphasizing the vital role that primary care providers play in the diagnosis and treatment of these disorders.

Common mental health conditions, such as depression and anxiety, are found in up to 10 percent of primary care patients,[3] and these conditions often coexist with chronic medical conditions. Accordingly, considerable interest has been expressed in improving the recognition and management of mental health conditions, especially depression, within primary care.[4-6] Specifically, interest is emerging about whether treatment of common mental health conditions in primary care can improve both mental health and chronic medical outcomes. The arena of mental health and primary care is moving from consideration of single conditions and their outcomes to more real-world, complex-care paradigms.[2, 7] However, to date, no synthesis of the evidence on practice-based interventions accounts for the primary care patient with "multiple chronic conditions"[8] and examines both mental health and chronic medical outcomes simultaneously.

Despite the prevalence and importance of other mental health conditions in the primary care setting, especially anxiety,[9, 10] substance use,[11] and psychotic disorders,[12] our preliminary review of the literature revealed that only depression has the evidence base necessary to meet eligibility criteria for a comparative effectiveness review.

The purpose of this report, therefore, is to summarize the available evidence on the effectiveness of practice-based interventions aimed at adult primary care patients with concomitant depression and chronic medical diagnoses. We believe this will add to the literature by (1) synthesizing data on mental health outcomes among people with defined chronic medical conditions, and (2) synthesizing data on chronic medical outcomes among these same people.

Depression and Chronic Medical Conditions

Of all mental health conditions, depression contributes the greatest societal burden as measured by social and economic costs.[13] Indeed, by 2030, depression itself is projected to be the single leading cause of overall disease burden in high-income countries.[14] Worldwide, depression makes a large contribution to the burden of disease, ranking third worldwide, eighth in low-income countries, and first in middle- and high-income countries.[15] In 2000, the U.S. economic burden of depressive disorders was estimated to be $83.1 billion.[16] More than 30 percent of these costs were attributable to direct medical expenses.[16]

Half of all Americans live with a chronic medical condition.[17] An estimated 23.6 million people (7.8 percent of the U.S. population) have diabetes.[18] Roughly 24 million U.S. adults have chronic obstructive pulmonary disease, and an additional 23 million have asthma.[19] Up to one-quarter of people living with chronic medical conditions have limitations in daily activity.[17] Living with chronic disease also takes a personal and emotional toll on patients and their families, owing to significant reductions in quality of life.[17]

Chronic medical conditions commonly associated with depression include arthritis, heart disease, diabetes, asthma, lung disease, and cancer.[20, 21] (Table 1). Depression among people with chronic physical illness has been linked to an increase in health care utilization, disability, and work absenteeism when compared with those without depression, even after controlling for the varying burden of the physical health condition.[22, 23]

Table 1. Prevalence of depression in chronic medical conditions

Chronic Condition	Prevalence of Depression
Arthritis	
Rheumatoid arthritis	13% to 20%[24, 25]
Osteoarthritis	19.4%[26]
Heart disease	
Post-myocardial infarction	10% to 47%[27]
Coronary artery disease	15%[28] to 23%[29]
Diabetes	11% to 15%[30] (MDD specifically) 17.6%[31] to 31.0%[30] (any depressive disorder)
Pulmonary disease	
Asthma	26.6%[32]
Chronic obstructive pulmonary disease	27.2%[33]
Cancer	9% to 24%[34] (MDD) 20% to 50% [34] (any depressive disorder)

Abbreviations: MDD = major depressive disorder.

Treating Depression in Primary Care

Repeated evidence reviews show the benefits of integrated and collaborative care models, as compared with usual care, on the outcomes of depression in the general health setting without consideration of coexisting mental health conditions.[4, 35-37] An emerging literature addresses whether better treatment of depression in primary care can also improve chronic medical outcomes, such as for diabetes.[38-40] A review of similar studies will help address the clinical uncertainty about whether such interventions can make a difference in more than one disease outcome and inform policy decisions about the potential benefit of adopting such guidance.

Scope and Key Questions

Previous Reports

Two recent reports have particular relevance to this topic: a 2008 Agency for Healthcare Research and Quality (AHRQ) report examining the integration of mental health/substance abuse and primary care[35] and a 2009 National Institute for Health and Clinical Excellence (NICE) guideline for depression in adults with a chronic physical health problem.[36] The AHRQ report required trials to include patients with a mental health condition seen in primary or specialty care, but did not require the presence of a chronic medical condition. The NICE report neither specified primary care as the setting of interest nor examined disease-specific chronic medical outcomes. This review is therefore distinct.

Scope of the Review

As we conceptualized the approach to this report through the topic nomination and refinement process, preliminary evidence reviews revealed insufficient data on mental health conditions other than depression that met all eligibility criteria. We specifically searched for evidence in patients with anxiety, but no studies met final eligibility criteria. The exclusion of

mental health conditions other than depression does not reflect a belief that they are less important, but that the literature is not mature enough to answer the questions set forth.

This review therefore summarizes the body of evidence that examines the effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions in adult primary care patients with depression and chronic medical condition(s) at baseline. The inclusion criteria require a level of depression that exceeds generally accepted cut points for major depression on common instruments, but were not necessarily confirmed by gold standard evaluations. We use the term depression throughout the report to reflect this definition. In an effort to address the inherent heterogeneity of complex interventions,[41] this report also compares the specific characteristics of the interventions and the practice settings in which they are delivered.

These results should be of interest to multiple stakeholders, including patients, providers, and policymakers. A family physician nominated this topic because he wanted to know whether concomitantly treating mental health and general health conditions in the primary care setting could improve overall health outcomes. As we move to consider shared savings programs, such as accountable care organizations,[42] and the patient-centered medical home,[43] consumers and payers are eager to identify interventions and processes that can streamline care for multiple conditions and improve the quality and efficiency of care. In fact, the PCMH has been defined as being accountable for ~~"m~~meeting the vast majority of each patient's physical and mental health care needs." [pcmh.ahrq.gov/portal/server.pt/community/pcmh__home/1483/PCMH_Defining%20the%20PCMH_v2] Numerous barriers, many financial, have hindered implementation of collaborative depression treatment in primary care despite its considerable evidence base.[4, 44, 45] This report aims to provide new data about the common and costly problem of primary care patients with concomitant depression and chronic medical conditions. Understanding how depression care influences a broad range of health outcomes can inform clinical decisionmaking as well as potential reimbursement and coverage strategies.

Population

The focus of this review is on adults with one or more diagnosed chronic medical condition and a diagnosis of depression, being treated in a primary care setting. An example is patients with diabetes and depression. The inclusion criteria require a level of depression that exceeds generally accepted cut points for major depression on common instruments. The purpose is to include patients with a level of severity known to benefit from treatment and to be associated with poor outcomes.

Interventions

For this review we use the term "~~p~~practice-based" to define the interventions of interest. This term reflects an explicit effort to be inclusive of a wide range of interventions while also requiring the primary care site to be the nucleus of activity. Our rationale is to honor the spirit of the original nomination by acknowledging the crucial role of primary care, where most patients receive care, and from which care can be coordinated.[46]

Practice-based is understood to mean any intervention that (1) targets the care process within a system of care and (2) aims to improve depression or both depression and chronic medical conditions. Examples of practice-based interventions include but are not limited to coordinated care, integrated care, and collaborative care; they often involve a care manager. Because of the

dual focus on (1) concurrent management of both depression and the chronic medical condition within primary care and (2) systematic changes that can improve the delivery of care (rather than testing specific interventions), we exclude medication-only, device, and psychotherapy-only clinical trials (e.g., efficacy studies comparing a medication with a placebo) from this review. Practice-based interventions can include person-level components such as problem-solving therapy and antidepressant medications, but they must be delivered as part of a broader systematic strategy to improve care.

Comparators

Potential comparators include different combinations, approaches, and modalities of practice-based interventions. A comparator of usual care, or enhanced usual care, is defined by each study.

Outcomes

We focused on five main outcomes: depression (Key Question [KQ] 1), chronic medical (KQ 2), harms of interventions (KQ 3), components of interventions (KQ 4), and characteristics of practice settings in which the interventions occurred (KQ 5). All KQs draw from the same universe of studies, such that KQs 3, 4, and 5 are subsidiary to KQs 1 and 2.

Settings

Settings include traditional primary care (e.g., family medicine, internal medicine, obstetrics/gynecology, and geriatrics) and settings with a primary care–type relationship (e.g., oncology clinics for those with cancer, infectious disease clinics for those with HIV).

Key Questions

- KQ 1a: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on intermediate depression outcomes (e.g., symptom improvement)?
- KQ 1b: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on other mental health outcomes (e.g., depression-related quality of life) and use of mental health-related services?
- KQ 2a: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on intermediate chronic medical outcomes (e.g., hemoglobin [Hb]A1c for patients with diabetes)?
- KQ 2b: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression

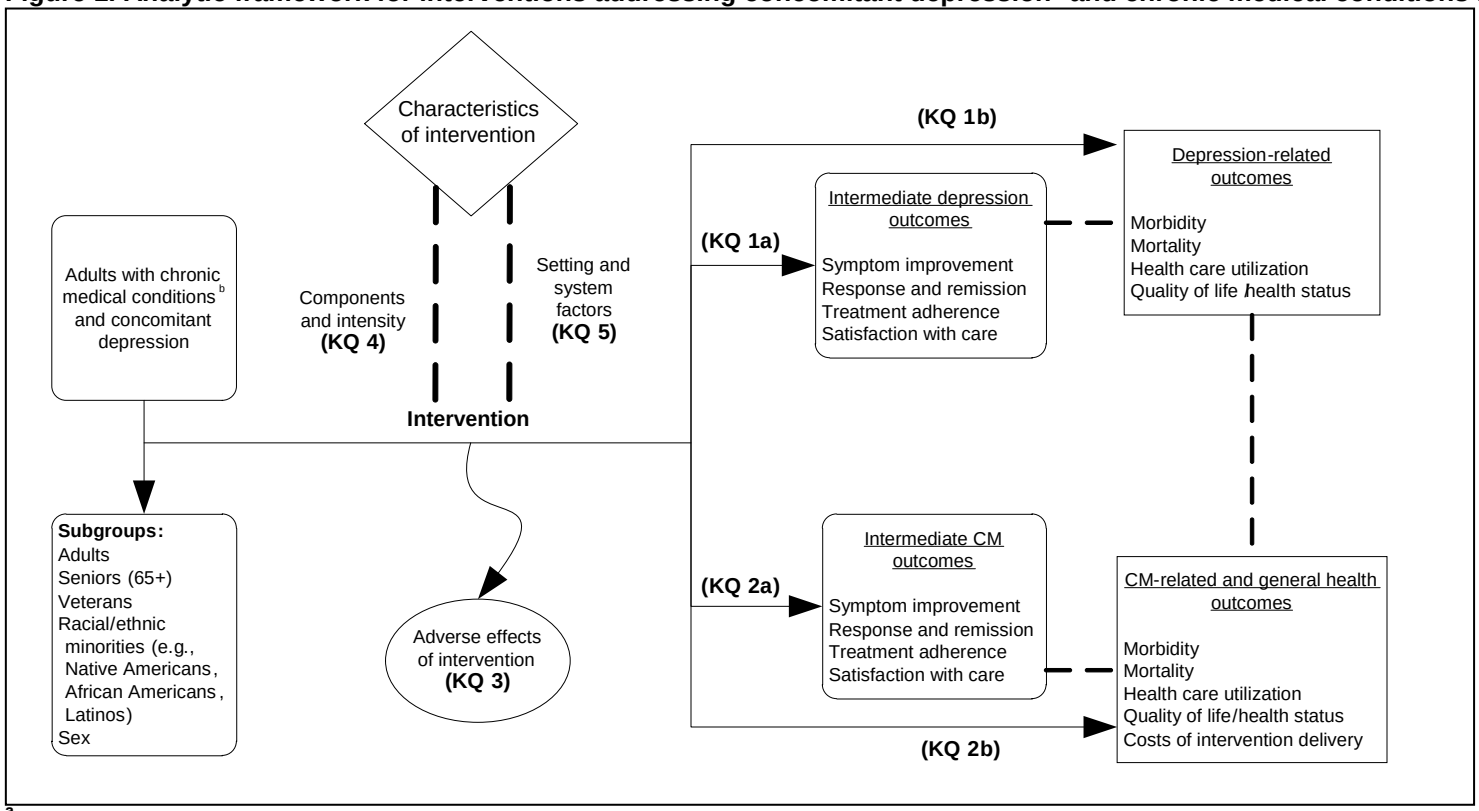
or both depression and chronic medical conditions (when compared with similar interventions or usual care) on general and other health outcomes (e.g., diabetes-related morbidity, general health-related utilization, costs)?

- KQ 3: What harms are associated with practice-based interventions for primary care patients with chronic medical conditions and concomitant depression?
- KQ 4: What are the characteristics of the practice-based interventions addressing concomitant depression and chronic medical conditions used in the primary care setting with regard to specific components and/or intensity (e.g., visit frequency, total number of contacts, provider discipline, use of self-management)?
- KQ 5: What are the specific characteristics of the practice setting where the interventions were delivered with regard to such variables as organizational characteristics (e.g., decision support, level of integration, information technology, electronic medical records, presence of mental health services on site, payer and service mix, practice size, and practice location/setting) or the relationship between elements of the system in which the practice operates (e.g., coordination, financing of care, payment arrangements)?

Analytic Framework

We developed an analytic framework to guide the systematic review process (Figure 1). KQ 1 addresses the effectiveness of practice-based interventions for improving depression outcomes—1a addresses intermediate clinical outcomes related to depression, such as symptom response, and 1b addresses other outcomes related to mental health, such as depression-related quality of life, and mental health care utilization. KQ 2 addresses the effectiveness of practice-based interventions for improving chronic medical condition outcomes—KQ 2a addresses intermediate clinical outcomes, such as pain severity scores for patients with chronic pain, and 2b addresses other important chronic medical outcomes, such as disease-related quality of life, and general health-related utilization. KQ 3 addresses the potential harms of practice-based interventions. KQs 4 and 5 assess the characteristics of the interventions and practice settings, respectively.

Figure 1. Analytic framework for interventions addressing concomitant depression[a] and chronic medical conditions in primary care



[a] Our original framework and search strategy included both depression and anxiety; since our searches yielded no studies of the latter, we have removed it from this figure for clarity.

[b] Chronic medical conditions are considered broadly and include the AHRQ priority conditions and IOM priority conditions, including diabetes, arthritis, and chronic pain, among others.

Abbreviations: CM = chronic medical; MH = mental health.

Methods

The methods for this comparative effectiveness review (CER) follow the methods suggested in the Agency for Healthcare Research and Quality (ARHQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews (www.effectivehealthcare.ahrq.gov/methodsguide.cfm). The main sections in this chapter reflect the elements of the protocol established for this CER; certain methods map to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[47]

Topic Refinement and Review Protocol

During the topic development and refinement processes, we generated an analytic framework, preliminary Key Questions (KQs), and preliminary inclusion/exclusion criteria in the form of PICOTS (Population, Intervention, Comparator, Outcome, Timing, Setting), and study design. The processes were guided by the information provided by the topic nominator, a scan of the literature, methods and content experts, and Key Informants. We worked with five Key Informants during the topic refinement, and five members of our Technical Expert Panel (TEP); (one individual participated in both). Key Informants and TEP members participated in conference calls and discussions through email to review the analytic framework, KQs, and PICOTS at the beginning of the project; TEP members also discussed the preliminary assessment of the literature, including inclusion/exclusion criteria and review of the protocol, and provided input on the information and categories included in evidence tables.

To achieve an appropriate scope for the review, we prioritized conditions and interventions that were most clinically relevant. Preliminary evidence reviews casting a wide net for mental health conditions revealed insufficient data on mental health conditions other than depression and anxiety, and the latter ultimately yielded no qualified studies. With input from our Key Informants, we selected the following chronic medical conditions identified as priority conditions by AHRQ[48] and the Institute of Medicine:[49] arthritis; diabetes; asthma or chronic obstructive pulmonary disease (COPD); cancer; chronic pain; stroke; HIV/AIDS; heart disease, heart failure, myocardial ischemia, coronary artery bypass graft, postmyocardial infarction, and coronary artery disease; "complex" patients with multiple comorbidities; and frailty due to old age.

Our KQs were posted for public comment on AHRQ's Effective Health Care Web site from March 18, 2011, through April 15, 2011; we put them into final form after review of the comments and discussion with the TEP.

Literature Search Strategy

Search Strategy

To identify articles relevant to each KQ, we searched MEDLINE®, Embase®, the Cochrane Library, CINAHL®, and PsycINFO®. The full search strategy is presented in Appendix A. We used Medical Subject Headings (MeSH or MH) as search terms when available or key words when appropriate, focusing on terms to describe the relevant population and the interventions of interest. We reviewed our search strategy with the TEP members and incorporated their input into our search strategy.

We limited the electronic searches to English-language publications (because of time and other resources) and humans. Sources were searched from the inception of each database through May 23, 2011. We used the National Library of Medicine publication type tags to identify reviews, randomized controlled trials, and meta-analyses.

We manually searched reference lists of pertinent reviews, included trials, and background articles on this topic, including the 2008 AHRQ report on integration of care,[35] to look for any relevant citations that might have been missed by our searches. We imported all citations into an electronic database (EndNote® X4). We also searched for unpublished studies relevant to this review using ClinicalTrials.gov and the World Health Organization's International Clinical Trials Registry Platform.

We conducted an updated literature search (of the same databases searched initially) through December 19, 2011. Literature suggested by Peer Reviewers or from the public were investigated and, if appropriate, incorporated into the final review. Appropriateness was determined by the same methods listed above.

Inclusion and Exclusion Criteria

We developed eligibility (inclusion and exclusion) criteria with respect to patient PICOTS, and study designs and durations for each KQ (Table 2). Appendix B contains the list of studies that were reviewed at the full-text stage but failed to meet all inclusion criteria.

Table 2. Study eligibility criteria

Criteria	Definition
Population(s)	Adults (age 18 or older) with depression[a] and one or more of the following chronic medical conditions: arthritis; diabetes; asthma or chronic obstructive pulmonary disease; cancer; chronic pain; stroke; HIV / AIDS; heart disease, heart failure, myocardial ischemia, coronary artery bypass graft, post-myocardial infarction, or coronary artery disease; "complex" patients with multiple comorbidities; and frailty due to old age. The inclusion criteria require a level of depression that exceeds generally accepted cut points for major depression on common instruments, but were not necessarily confirmed by gold standard evaluations. We use the term depression throughout the report to reflect this definition.
Interventions	Practice-based interventions aimed at improving depression or both depression and the chronic medical condition. Practice-based is understood to mean any intervention that (1) targets the care process within a system of care and (2) aims to improve depression or both depression and chronic medical conditions. Examples of practice-based interventions include but are not limited to coordinated care, integrated care, and collaborative care; they often involve a care manager. Each of these terms has varying, and possibly overlapping definitions, and is not specifically defined for the purposes of this report. In general, we perceive them broadly to mean primary care providers and mental health providers working together to address the comprehensive needs of the patient.
Comparators	Different combinations, approaches, and modalities for the above interventions Usual care (as defined by the study, representing, however, a particular practice or setting is providing care for patients who do not receive an intervention)

Table 2. Study eligibility criteria (continued)

Criteria	Definition
Outcomes	Intermediate depression outcomes: • symptom improvement, response rates, and remission and/or recurrence as measured by scores on reliable and valid instruments (to include self-rated instruments) ; • treatment adherence; and • satisfaction with care. Intermediate chronic medical condition outcomes: • symptom improvement, remission, and remediation; • response to treatment (e.g., HbA1c); • treatment adherence; and • satisfaction with care. Other depression–related outcomes: • disease-related mortality, • disease-related morbidity, • disease-related functional status, • mental health–related quality of life, • sick days related to mental health, • mental health care utilization, and • employment stability. Other chronic medical and general health outcomes: • all-cause mortality, • disease-related mortality, • disease-related morbidity, • disease-related functional status, • general health–related quality of life, • disease-specific outcomes, • general health care utilization, • total sick days and sick days due to general health condition, • employment stability, and • costs of intervention delivery. Potential adverse effects of interventions: • adverse effects of pharmacotherapy and • other harms as reported.
Timing	Outcome assessment at least 6 months after randomization (or from receipt of the intervention for nonrandomized controlled trials)
Settings	Traditional primary-care settings; settings with a primary care-type relationship that may be applicable to traditional primary care settings (e.g., infectious disease clinics for people with HIV, oncology clinics for people with cancer). No geographic limits.
Study designs	Randomized controlled trials, nonrandomized trials with concurrent eligible controls, and recent systematic reviews with or without meta-analyses. We chose to exclude studies without comparison groups owing to the potential risk of bias in such studies (especially the risk of selection bias and confounding). No sample size limits.

[a] Our original framework and search strategy included both depression and anxiety; since our searches yielded no studies of the latter, we have removed it from this figure for clarity.
Abbreviations: HbA1c = hemoglobin A1c.

Data Extraction

For studies that met our inclusion criteria, we abstracted important information into evidence tables. We designed and used structured data abstraction forms to gather pertinent information from each article, including characteristics of study populations, settings, interventions,

comparators, study designs, methods, and results. Trained reviewers extracted the relevant data from each included article into the evidence tables. A second member of the team reviewed all data abstractions against the original article for completeness and accuracy. We recorded intention-to-treat results if available. All data abstraction was performed using Microsoft Excel® software. Data abstraction forms were almost identical to the evidence tables containing abstracted data (Appendix C).

Quality Assessment of Individual Studies

To assess the quality (internal validity) of studies, we used predefined criteria based on those developed by the U.S. Preventive Services Task Force (ratings: good, fair, poor)[50] and the University of York Centre for Reviews and Dissemination.[51] These criteria assess for the adequacy of randomization, allocation concealment, similarity of groups at baseline, masking, attrition, and whether intention to treat analysis was used. In general terms, a "good" study has the least risk of bias and its results are considered to be valid. To be rated "good" for the purpose of this review, a study must have fulfilled all or all but one of the following criteria: adequate randomization of patients; adequate allocation concealment; blinded outcome assessors; similar baseline characteristics across treatment arms; overall attrition less than 20 percent; differential attrition less than 15 percent (i.e., there is less than a 15 percentage point difference between attrition in one group and attrition in another); intention-to-treat analysis; and use of equivalent, valid, and reliable outcome measures. A "fair" study is susceptible to some bias but probably not sufficient to invalidate its results. A "poor" study has significant risk of bias (e.g., stemming from serious errors in design or analysis) that may invalidate its results. We gave poor quality ratings to studies that had a fatal flaw (defined as a methodological shortcoming that leads to a very high risk of bias) in one or more categories, and we excluded them from our analyses.

Two independent reviewers assigned quality ratings for each study. Disagreements between the two reviewers were resolved by discussion and consensus or by consulting a third member of the team. Appendix D details the criteria used for evaluating the quality of all included studies as well as comments on the studies rated "poor" and excluded from analysis.

Data Synthesis

Overall Approach

The research team determined prioritization and/or categorization of outcomes with input from TEP members. Quantitative analyses were conducted using meta-analyses of outcomes reported by a sufficient number of studies that were homogeneous enough that combining their results could be justified. To determine whether quantitative analyses were appropriate, we assessed the clinical and methodological heterogeneity of the studies under consideration following established guidance.[52] We did this by qualitatively assessing the PICOTS of the included studies, looking for similarities and differences. When quantitative analyses were not appropriate (e.g., because of heterogeneity, insufficient numbers of similar studies, or insufficiency or variation in outcome reporting), we synthesized the data qualitatively.

Statistical Analyses

We ran meta-analyses for outcomes with sufficient data, including depression symptom improvement, reduction of depression symptoms, remission of depression, mental health

treatment satisfaction, mental health status, prescription antidepressant use, change in hemoglobin A1c (HbA1c), change in physical health status, and all-cause mortality. For continuous outcomes of mean score change between baseline and endpoint, many studies did not report a variance measure of the mean change but did include variance information at baseline and 12 months. In these cases, we assumed a correlation of 0.5 to estimate the mean change variance[53] and conducted sensitivity analyses with assumed correlations of 0.3 and 0.7 to confirm that this assumption did not significantly change our results. However, in cases in which the final mean value was adjusted for baseline via regression or analysis of covariance, we used this endpoint value instead of assuming a correlation because it is the most efficient and least-biased statistic.[54] Separate analyses were run for studies reporting 6- and 12-month outcomes.

We used random-effects models to estimate pooled effects.[55] For continuous outcomes, the effect measure was the weighted mean difference or, if the measurement scale differed among trials, the standardized mean difference was calculated. For most dichotomous outcomes, we report risk differences. For all-cause mortality at 6 or 12 months, the comparison between intervention and control was calculated as a risk ratio. Forest plots graphically summarize results of individual studies and of the pooled analysis (Appendix E).[56]

The chi-squared statistic and the I^2 statistic (the proportion of variation in study estimates attributable to heterogeneity) were calculated to assess heterogeneity in effects between studies.[57, 58] An I^2 from 0 to 40 percent might not be important, 30 to 60 percent may represent moderate heterogeneity, 50 to 90 percent may represent substantial heterogeneity, and ≥75 percent represents considerable heterogeneity.[54] The importance of the observed value of I^2 depends on the magnitude and direction of effects and on the strength of evidence for heterogeneity (e.g., p value from the chi-squared test, or a confidence interval for I^2). Whenever including a meta-analysis with considerable statistical heterogeneity in this report, we provide an explanation for doing so, considering the magnitude and direction of effects.[54] We conducted sensitivity analyses for all analyses where considerable heterogeneity was present (i.e., I^2 statistic greater than 75 percent). Quantitative analyses were conducted using Stata® version 11.1 (StataCorp LP, College Station, TX) and Comprehensive Meta Analysis® version 2.2.055 (BioStat, Inc., Englewood, NJ).

Strength of the Body of Evidence

We graded the strength of evidence based on the guidance established for the Evidence-based Practice Center Program.[59] Developed to grade the overall strength of a body of evidence, this approach incorporates four key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. It also considers other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, strength of association (magnitude of effect), and publication bias.

Table 3 describes the grades of evidence that can be assigned. We graded the strength of evidence for mental health outcomes (KQ 1), chronic medical condition outcomes (KQ 2), and harms (KQ 3). Two reviewers assessed each domain for each key outcome and differences were resolved by consensus.

Table 3. Definitions of the grades of overall strength of evidence

Grade	Definition
High	**High confidence that the evidence reflects the true effect.** Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	**Moderate confidence that the evidence reflects the true effect.** Further research may change our confidence in the estimate of the effect and may change the estimate.
Low	**Low confidence that the evidence reflects the true effect.** Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate.
Insufficient	**Evidence either is unavailable or does not permit estimation of an effect.**

*Owens et al., 2010[59]

Applicability

We assessed applicability of the evidence following guidance from the Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[60] We used the PICOTS framework to explore factors that affect applicability. Some factors identified a priori that may limit the applicability of evidence included the following: ethnicity of enrolled populations, type of practice setting (open vs. closed), and use of interventions that may be difficult to incorporate into routine practice for many providers (e.g., they require substantial resources or time, or they may be delivered by research staff rather than existing staff in the practice).

Peer Review and Public Commentary

Experts in the field and individuals representing stakeholder and user communities were invited to provide external peer review of this CER. They were charged with commenting on the content, structure, and format of the evidence report, providing additional relevant citations, and pointing out issues related to how we conceptualized the topic and analyzed the evidence. Our Peer Reviewers (listed in the front matter) gave us permission to acknowledge their review of the draft. AHRQ staff and an associate editor also provided comments. In addition, the Scientific Resource Center posted the draft report on the AHRQ Web site (effectivehealthcare.ahrq.gov/) for 4 weeks to elicit public comment. We addressed all reviewer comments, revising the text as appropriate, and documented everything in a "disposition of comments report" that will be made available 3 months after the Agency posts the final CER on the AHRQ Web site.

Results

Introduction

This chapter is organized by Key Question (KQ) and grouped by medical condition(s) when possible. Briefly, we wanted to examine the comparative effectiveness of practice-based interventions for primary care patients with concomitant depression and chronic medical conditions; we focused on five main outcomes: mental health (KQ 1), chronic medical (KQ 2), harms of interventions (KQ 3), components of interventions (KQ 4), and characteristics of practice settings in which the interventions occurred (KQ 5). Our results pertain to the general adult population; no studies that met our inclusion criteria reported on young adults or pregnant women. Regarding older adults, one study[61-65] selectively recruited for age 60 or older; however, participants across all studies in this review tended to be middle-aged or older (mean age, 59; range of means, 47 to 72) so we do not report results for older adults separately. Several studies reported on traditionally underrepresented populations, including women,[66-68] Spanish speakers,[66-72] and predominantly African-American male veterans with HIV;[73] we report these results in the context of overall results by medical condition, not in separate categories.

Results of Literature Searches

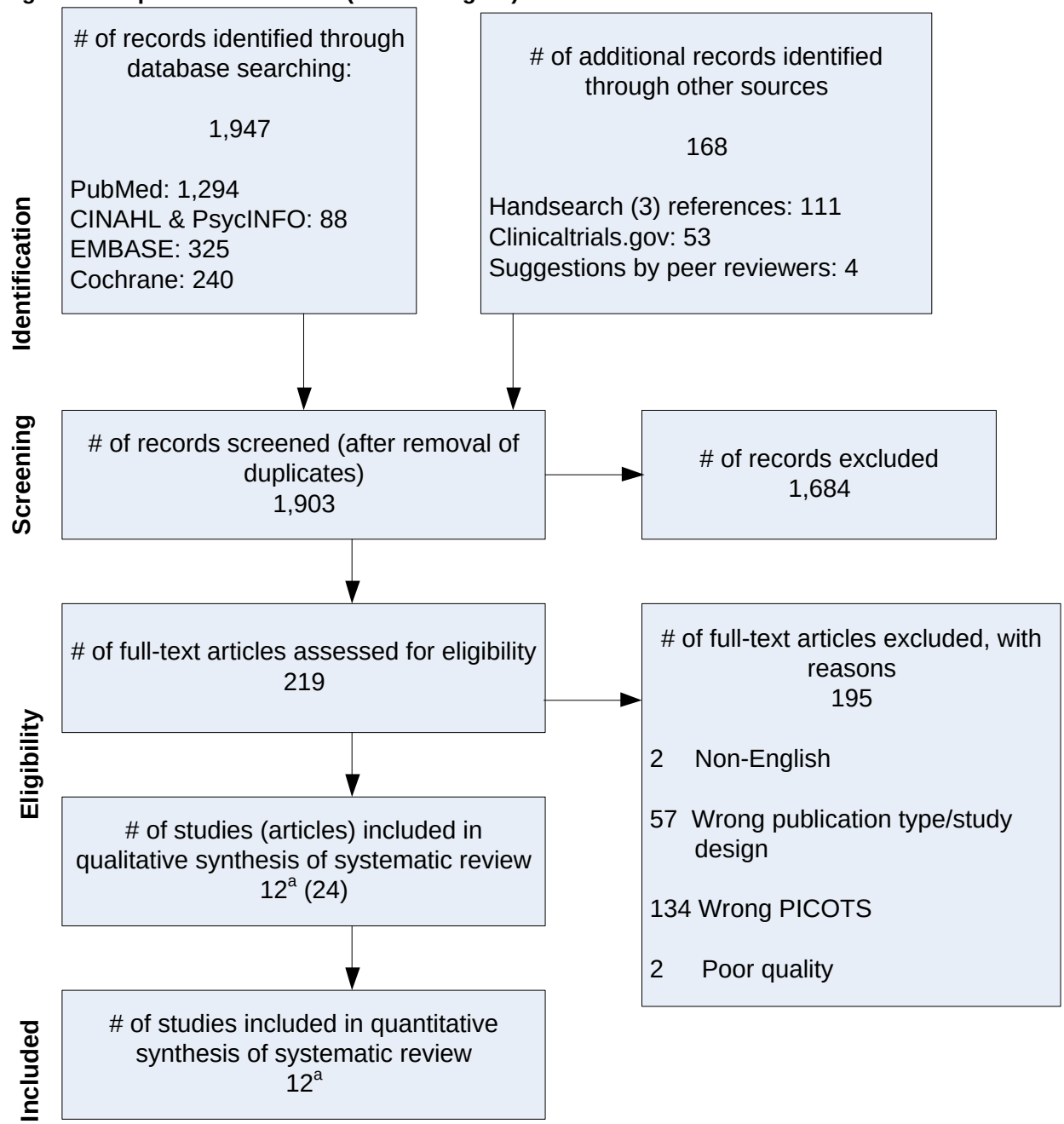
Results of our searches are presented in Figure 2. We ultimately included 24 published articles reporting on 10 randomized controlled trials (RCTs). We recorded the reason that each excluded full-text publication did not satisfy the eligibility criteria and compiled a comprehensive list of such studies (Appendix B). Evidence tables for included studies can be found in Appendix C.

Description of Included Studies

In the 10 included trials, sample sizes ranged from 55 to 1,001, and study duration ranged from 6 to 60 months. Nine trials were conducted in the United States (1 of these in Puerto Rico[72]) and 1 in Scotland.[74] All included studies characterized their respective intervention as a form of collaborative care, not another form of a practice-based intervention (such as integrated care). Similarly, all included studies specified depression as the targeted mental health condition; no studies specified anxiety as the condition of interest. The designated chronic medical conditions included arthritis,[62, 65] cancer,[61, 66, 68, 71, 74] diabetes,[38, 40, 63, 64, 67, 69, 70, 75-78] heart disease,[79] and HIV.[73] Two studies selected patients with one or more active medical conditions.[72, 80, 81]

Five articles[61-65] are secondary analyses from the Improving Mood—Promoting Access to Collaborative Treatment (IMPACT) trial;[5] it tested a collaborative care depression intervention in older adult primary care patients, including preplanned subgroups of patients with arthritis, cancer, and diabetes. For ease of interpretation, we consider each subgroup a unique "study" in the Results chapter. Consequently, our results include data from 12 studies (9 stand-alone RCTs and 3 IMPACT subgroups). Six articles[38, 40, 75-78] are from the Pathways trial, which tested a collaborative care intervention in primary care patients with diabetes and depression. The majority of all studies reported their funding source as the government, and in some cases "multiple sources," including foundations. All studies reported their funding source, and no study identified an industry sponsor.

Figure 2. Disposition of articles (PRISMA figure)



Source: Moher et al., 2009.[47]

[a] This result includes the Improving Mood—Promoting Access to Collaborative Treatment (IMPACT) trial;[5] it tested a collaborative care depression intervention in older adult primary care patients, including preplanned subgroups of patients with arthritis, cancer, and diabetes. For ease of interpretation, we consider each subgroup a unique ~~–s~~tudy" in the Results chapter. Thus, our results include data from 12 studies (9 stand-alone RCTs and 3 IMPACT subgroups).

Abbreviations: CINAHL = Cumulative Index to Nursing and Allied Health Literature; PICOTS = population, intervention, comparator, outcome, timing, setting; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Because all KQs draw from the same universe of evidence, we present the trials in two ways here as context for reading the remainder of results. Tables 4 through 9 display the characteristics of trials for the specific chronic medical conditions. Table 10 summarizes the main elements of the trial interventions and control groups. For IMPACT,[61-65] Bypassing the Blues,[79] Symptom

Management Research Trials (SMaRT) Oncology 1,[74] HITIDES (HIV Implementation of Translating Initiatives for Depression into Effective Solutions),[73] the Multifaceted Oncology Depression Program (MODP),[66] and Vera et al.,[72] the control condition was usual care, which consisted of informing patients of their depression status and advising them to share this information with their primary care provider (PCP). By contrast, ADAPt-C,[68, 71] Pathways,[38, 40, 75, 76, 78] TEAMcare,[80-82] and the Multifaceted Diabetes and Depression Program (MDDP)[67, 69, 70] compared collaborative care with enhanced usual care, which extended usual care by including some degree of additional communication between the research staff or diabetes care manager and the patient's PCP and/or family about the patient's depression status.

Table 4. Characteristics of included trials of patients with arthritis

Author, Year Study Name Country Setting	N Duration (mths)	Mean Age (y)[a]	% Female[a] % Nonwhite[a]	Depression-Related Eligibility Requirement Baseline Depression Score[a,b]	Quality[c]
Lin et al., 2003;[65] Lin et al., 2006[62] IMPACT U.S. PC	1,001 24	72.0[d]	68.3 24	Current DSM-IV diagnosis of MDD and/or dysthymia SCL-20: 1.7	Fair

[a] Overall mean as reported, range of means for treatment groups, or overall mean calculated using mean age from each treatment group.
[b] See Table 11 for depression scale details.
[c] Quality assessment considers potential for biases including appropriate masking/blinding, attrition, and intent-to-treat analyses. In general terms, a "good" study has the least risk of bias and its results are considered to be valid. A "fair" study is susceptible to some bias but probably not sufficient to invalidate its results. For detailed quality assessment, see Appendix D.
[d] The IMPACT trial enrolled only people ≥60 years of age.
Abbreviations: DSM = Diagnostic and Statistical Manual; IMPACT = Improving Mood—Promoting Access to Collaborative Treatment; MDD = major depressive disorder; mths = months; PC = primary care;SCL-20 = Symptom Checklist—depression scale; U.S. = United States; y = years.

Table 5. Characteristics of included trials of patients with cancer

Author, Year Study Name Country Setting	N Duration (mths)	Mean Age (y)[a]	% Female[a] % Nonwhite[a]	Depression-Related Eligibility Requirement Baseline Depression Score[a,b]	Quality[c]
Dwight-Johnson et al., 2005[66] MODP U.S. PC-like	55 8	47.3	NR[d]	Major depression per PHQ-9 or dysthymia per PRIME-MD PHQ-9: 12.6-13.4	Fair
Ell et al., 2008;[68] Ell et al., 2011[71] ADAPt-C U.S. PC-like	472 24	~50[e]	84.5 87.9	PHQ-9 ≥10 or dysthymia per DSM-IV SCI PHQ-9: 13.1	Fair
Fann et al., 2009[61] IMPACT U.S. PC	215 24	71.8[f]	60 25	Major depression or dysthymia per DSM-IV SCI SCL-20: 1.6	Fair
Strong et al., 2008[74] SMaRT Oncology 1 UK PC-like	200 12	56.6	69-72 NR	HADS ≥15 and major depression per DSM-IV SCI and SCL-20 ≥1.75 SCL-20: 2.3-2.4 (median)	Fair

[a] Overall mean as reported, range of means for treatment groups, or overall mean calculated using mean age from each treatment group.
[b] See Table 11 for depression scale details.
[c] Quality assessment considers potential for biases including appropriate masking/blinding, attrition, and intent-to-treat analyses. In general terms, a "good" study has the least risk of bias and its results are considered to be valid. A "fair" study is susceptible to some bias but probably not sufficient to invalidate its results. For detailed quality assessment, see Appendix D.
[d] Race/ethnicity not reported, but 85–96 percent were Spanish-only speakers.
[e] Age only reported as percent ≥50 yrs.
[f] The IMPACT study enrolled only people ≥60 years old.
Abbreviations: ADAPt-C = Alleviating Depression Among Patients with Cancer; DSM = Diagnostic and Statistical Manual; HADS = Hospital Anxiety and Depression Scale; IMPACT = Improving Mood – Promoting Access to Collaborative Treatment; MODP = Multifaceted Oncology Depression Program; mths = months; NR = not reported; PC = primary care; PHQ-9 = Patient Health Questionnaire – depression module; PRIME-MD = Primary Care Evaluation of Mental Disorders; SCI = structured clinical interview; SCL-20 = Symptom Checklist – depression scale; SMaRT = Symptom Management Research Trials; UK = United Kingdom; U.S. = United States; y = years.

Table 6. Characteristics of included trials of patients with diabetes

Author, Year Study Name Country Setting	N Duration (mths)	Mean Age (y)[a]	% Female[a] % Nonwhite[a]	Depression-Related Eligibility Requirement Baseline Depression Score[a,b]	Quality[c]
Ell et al., 2010;[67] Ell et al., 2011;[69] Hay et al., 2012[70] MDDP U.S. PC and PC-like	387 24	NR[d]	79.8-84.5 96.5	PHQ-9 ≥10 SCL-20: 1.4-1.7	Fair
Ciechanowski et al., 2006;[40] Katon et al., 2008;[75] Katon et al., 2004;[38] Kinder et al., 2006;[76] Lin et al., 2006;[77] Simon et al., 2007;[78] Pathways U.S. PC	329 60	58.4	64.8-65.2 19.9-24.8	PHQ-9 ≥10 and SCL-20 ≥1.1 SCL-20: 1.63-1.71	Fair
Williams et al., 2004[64]; Katon et al., 2006[63] IMPACT U.S. PC	417 24	70.2[e]	53-54 35-37	Major depression or dysthymia per DSM-IV SCI SCL-20: 1.67-1.72	Fair

[a] Overall mean as reported, range of means for treatment groups, or overall mean calculated using mean age from each treatment group.
[b] See Table 11 for depression scale details.
[c] Quality assessment considers potential for biases including appropriate masking/blinding, attrition, and intent-to-treat analyses. In general terms, a "good" study has the least risk of bias and its results are considered to be valid. A "fair" study is susceptible to some bias but probably not sufficient to invalidate its results. For detailed quality assessment, see Appendix D.
[d] Age only reported as percent ≥50 yrs; 69 percent-75 percent were ≥50 yrs.
[e] The IMPACT study enrolled only people ≥60 years old.
Abbreviations: DSM = Diagnostic and Statistical Manual; IMPACT = Improving Mood – Promoting Access to Collaborative Treatment; MDDP = Multifaceted Diabetes and Depression Program; mths = months; NR = not reported; PC = primary care; PHQ-9 = Patient Health Questionnaire – depression module; SCI = structured clinical interview; SCL-20 = Symptom Checklist – depression scale; U.S. = United States; y = years.

Table 7. Characteristics of included trials of patients with heart disease

Author, Year Study Name Country Setting	N Duration (mths)	Mean Age (y)[a]	% Female[a] % Nonwhite[a]	Depression-Related Eligibility Requirement Baseline Depression Score[a,b]	Quality[c]
Rollman et al., 2009[79] Bypassing the Blues U.S. Unclear[d]	302 8	64.0	37-46 7-12	PHQ-9 ≥11 PHQ-9: 13.5-13.6 HRSD: 15.9-16.5	Good

[a] Overall mean as reported, range of means for treatment groups, or overall mean calculated using mean age from each treatment group.
[b] See Table 11 for depression scale details.
[c] Quality assessment considers potential for biases including appropriate masking/blinding, attrition, and intent-to-treat analyses. In general terms, a "good" study has the least risk of bias and its results are considered to be valid. A "fair" study is susceptible to some bias but probably not sufficient to invalidate its results. For detailed quality assessment, see Appendix D.
[d] Patients were recruited before hospital discharge; intervention took place over the telephone.
Abbreviations: HRSD = Hamilton Rating Scale for Depression; mths = months; PHQ-9 = Patient Health Questionnaire – depression module; U.S. = United States; y = years.

Table 8. Characteristics of included trials of patients with HIV

Author, Year Study Name Country Setting	N Duration (mths)	Mean Age (y)[a]	% Female[a] % Nonwhite[a]	Depression-Related Eligibility Requirement Baseline Depression Score[a,b]	Quality[c]
Pyne et al., 2011[73] HITIDES U.S. PC-like	276 12	49.8	2.4-3.2 61.6-63.4	PHQ-9 ≥10 PHQ-9: 15.7-16.0 SCL-20: 1.8-1.9	Good

[a] Overall mean as reported, range of means for treatment groups, or overall mean calculated using mean age from each treatment group.
[b] See Table 11 for depression scale details.
[c] Quality assessment considers potential for biases including appropriate masking/blinding, attrition, and intent-to-treat analyses. In general terms, a "good" study has the least risk of bias and its results are considered to be valid. A "fair" study is susceptible to some bias but probably not sufficient to invalidate its results. For detailed quality assessment, see Appendix D.
Abbreviations: HITIDES = HIV Implementation of Translating Initiatives for Depression into Effective Solutions; mths = months; PC = primary care; PHQ-9 = Patient Health Questionnaire – depression module; SCL-20 = Symptom Checklist – depression scale; U.S. = United States; y = years.

Table 9. Characteristics of included trials of patients with multiple conditions

Author, Year Study Name Country Setting	N Duration (mths)	Mean Age (y)[a]	% Female[a] % Nonwhite[a]	Depression-Related Eligibility Requirement Baseline Depression Score[a,b]	Quality[c]
Katon et al., 2010;[80] Von Korff, 2011;[82] Lin, 2012[81] TEAMcare[d] U.S. PC	214 12	56.9	48-56 22-25	PHQ-9 ≥10 PHQ-9: 13.9-14.7 SCL-20: 1.7	Fair
Vera et al., 2010[72] None U.S. (Puerto Rico) PC	179 6	55.2	76 100	PHQ-9 (cutoff NR) and SCL-20 >1.0 SCL-20: 2.2-2.3	Good

[a] Overall mean as reported, range of means for treatment groups, or overall mean calculated using mean age from each treatment group.
[b] See Table 11 for depression scale details.
[c] Quality assessment considers potential for biases including appropriate masking/blinding, attrition, and intent-to-treat analyses. In general terms, a "good" study has the least risk of bias and its results are considered to be valid. A "fair" study is susceptible to some bias but probably not sufficient to invalidate its results. For detailed quality assessment, see Appendix D.
[d] Diabetes and/or heart disease.
Abbreviations: mths = months; PC = primary care; PHQ-9 = Patient Health Questionnaire—depression module; SCL-20 = Symptom Checklist—depression scale; U.S. = United States; y = years.

Table 10. Summary of collaborative care intervention trials

Author/ Trial Name Disease	Intervention Summary	Delivery Method Delivered By Psychiatrist Supervision?	Control Condition[a]
Lin et al., 2003;[65] Lin et al., 2006;[62] Fann et al., 2009;[61] Williams et al., 2004;[64] Katon et al., 2006[63] IMPACT Arthritis, cancer, diabetes	Care management based on stepped care treatment algorithm; patient preference for treatment: antidepressants or problem-solving therapy (6–8 sessions); monitoring of treatment response ("IMPACT model")	In-person and telephone Depression care specialist (nurse or clinical psychologist) Yes	Usual care
Dwight-Johnson et al., 2005[66] MODP Cancer	Described as being based on the IMPACT model	In-person and telephone Bilingual cancer depression care specialist (master's level social worker) Yes	Usual care
Ell et al., 2008;[68] Ell et al., 2011[71] ADAPt-C Cancer	Described as being based on the IMPACT model	In-person and telephone Bilingual cancer depression care specialist (master's level social worker) Yes	Enhanced usual care
Ell et al., 2010;[67] Ell et al., 2011;[69] Hay et al., 2012[70] MDDP Diabetes	Described as being based on the IMPACT model	In-person and telephone Bilingual diabetes depression care specialist (master's level social worker) Yes	Enhanced usual care
Ciechanowski et al., 2006;[40] Katon et al., 2008;[75] Katon et al., 2004;[38] Kinder et al., 2006;[76] Lin et al., 2006;[77] Simon et al., 2007[78] Pathways Diabetes	Described as being based on the IMPACT model	In-person and telephone Depression clinical specialist (nurse) Yes	Enhanced usual care
Katon et al., 2010;[80] Von Korff, 2011;[82] Lin, 2012[81] TEAMcare Diabetes +/- heart disease	Support for self-care of depression (including pharmacotherapy) and individualized goal-setting; treat-to-target program for DM and/or CHD; motivational coaching; maintenance support	In-person and telephone Medically supervised nurse trained in diabetes education Yes	Enhanced usual care

Table 10. Summary of collaborative care intervention trials (continued)

Author/Trial Name Disease	Intervention Summary	Delivery Method Delivered By Psychiatrist Supervision?	Control Condition[a]
Pyne et al., 2011[73] HITIDES HIV	Stepped care approach; education/activation; recommendations for medications and/or mental specialty referral; web-based decision support	Telephone Off-site depression care team: nurse depression care manager, pharmacist, psychiatrist Yes	Usual care
Rollman et al., 2009[79] Bypassing the Blues Heart disease	Education on depression and CHD; support to PCP on antidepressants; referral to mental health specialists as needed; phone monitoring for symptoms	Telephone Nurse care manager Yes	Usual care
Strong et al., 2008[74 c] SMaRT Oncology 1 Cancer	Manual-Based Depression Care for People with Cancer; up to 10 sessions of problem-solving treatment to address coping; progress monitored by telephone; advice on choice of antidepressant if requested	In-person and telephone Nurses with no psychiatry experience Yes	Usual care
Vera et al., 2010[72] NA ≥1 of the following: diabetes, hypothyroidism, asthma, hypertension, chronic bronchitis, arthritis, heart disease, high cholesterol, stroke	Depression education; antidepressant medications and/or 13 sessions of cognitive behavioral therapy	In-person and telephone Master's level counselor or psychologist Yes	Usual care

[a]Specific components of usual care and enhanced usual care are listed in Appendix C.
[b] Though IMPACT is a single randomized, controlled trial, several subgroups, including those with chronic medical conditions, were analyzed. For ease of interpretation throughout this report, we consider each of the three IMPACT subgroups (arthritis, cancer, and diabetes) a separate study.
[c]Study took place in the United Kingdom where both primary care and mental health specialty services are free at the point of delivery.
Abbreviations: ADAPt-C = Alleviating Depression Among Patients with Cancer; CHD = coronary heart disease; DM = diabetes mellitus; IMPACT = Improving Mood—Promoting Access to Collaborative Treatment; MDDP = Multifaceted Diabetes and Depression Program; PCP = primary care provider.

Key Question 1a: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on intermediate depression outcomes (e.g., symptom improvement)?In the key points below, we summarize the main findings by outcome and report the strength of evidence (SOE) for each outcome.

Key Points

- Collaborative care interventions achieved greater depression symptom improvement than usual care (standardized mean difference [SMD], 0.45; 95% CI, 0.29 to 0.61 at 6 months; seven studies; SMD 0.47, 95% CI, 0.29 to 0.65 at 12 months; six studies). Benefits were sustained through 24 months, but the magnitude of benefit was reduced (moderate SOE).
- Collaborative care interventions achieved higher rates of depression response (≥50 percent reduction in symptoms from baseline) than usual care, based on 10 studies (number needed to treat [NNT], 5 at 6 months; NNT, 6 at 12 months). Benefits persisted, but to a lesser degree, at 18 months (moderate SOE).
- Collaborative care interventions resulted in more depression-free days at 12 months than usual care in the five studies that measured the outcome (range of differences between intervention and control groups: 20 to 59 days (moderate SOE).
- Remission of depression favored collaborative care over usual care at 6 months and at 12 months (but less so) based on five studies (NNT, 8 at 6 months; NNT, 12.5 at 12 months). Benefits persisted at 18 months but showed no difference between groups at 24 months (moderate SOE).
- Only one study (of patients with cancer) addressed recurrence as an outcome, and showed no difference between group at 18 or 24 months (insufficient SOE).
- Evidence was insufficient to draw conclusions about the effect of collaborative care interventions on adherence to antidepressants.
- Collaborative care interventions received significantly higher ratings of patient satisfaction than usual care at 12 months as reported in four studies, including patients with diabetes, heart disease, and cancer. Benefits were sustained at 24 months (moderate SOE).

Detailed Synthesis

Depression Symptom Improvement and Treatment Response

All included studies examined depression symptom improvement or depression treatment response (≥50 percent reduction in depression score), or both, at 6 and 12 months; three studies[61, 67, 69, 71] reported on one or both of these outcomes at 18 months, and five studies[61, 63, 64, 69, 71, 78] reported relevant 24-month data. Nine studies[38, 61-65, 67, 72-74, 80] used the Symptom Checklist-20,[83]

two[66, 68] used the Patient Health Questionnaire-9,[84] and one[79] used the Hamilton Rating Scale for Depression[85] (Table 11).

Table 11. Instruments used to measure depressive symptoms, response, and remission

Abbreviated Name	Complete Name of Measure or Instrument	Range of Scores	Improvement Denoted by	Notes
HRSD17[a]	Hamilton Rating Scale for Depression – 17 item	0-52	Decrease	Observer-rated
PHQ-9	Patient Health Questionnaire – 9 item	0-27	Decrease	Self-rated
SCL-20 (HSCL-20)	(Hopkins) Symptom Checklist – 20 item	0.0-4.0	Decrease	Self-rated

[a] Also referred to as the HAM-D[17] and the HDRS.[17]
Abbreviations: HAM-D = Hamilton Rating Scale for Depression; HDRS = Hamilton Depression Rating Scale; HSCL = Hopkins Symptom Checklist; HRSD = Hamilton Rating Scale for Depression; PHQ = Patient Health Questionnaire; SCL = Symptoms Checklist Depression.

Quantitative analyses and strength of evidence data are detailed in Appendix E and Appendix F, respectively.

For the intermediate outcome of improvement in depression symptoms, Table 12 reports results of meta-analyses from 6, 12, and 24 months. Results from studies that used the Symptoms Checklist Depression-20 (SCL-20) are reported using weighted mean differences (WMD). Results that include studies using any measure of depression symptoms are reported using standardized mean difference (SMD) values.

Using the WMD method, patients receiving collaborative care interventions had a 0.38 greater improvement from baseline on the SCL-20 at both 6 and 12 months than those in control groups (five studies[38, 61, 64, 74, 80]). Given that the range of the SCL-20 is 0 to 4 (lower scores meaning less depression), this magnitude of change is generally considered a clinically important difference.[86, 87]

Table 12. Summary of meta-analyses for intermediate outcomes for practice-based interventions aimed at improving depression or both depression and chronic medical conditions compared with controls

Outcome	Timing	N Studies	Statistic	Effect Size	95% CI	I^2
Depression symptoms	6 months	5	WMD	0.38	0.24 to 0.51	66.94
Depression symptoms	6 months	7	SMD	0.45	0.29 to 0.61	64.52
Depression symptoms	12 months	5	WMD	0.38	0.30 to 0.46	1.09
Depression symptoms	12 months	6	SMD	0.47	0.29 to 0.65	68.55
Depression symptoms	24 months	3	WMD	0.18	0.10 to 0.26	0.00
Response[a]	6 months	9	RD	0.20	0.14 to 0.26	54.66
Response[a]	12 months	7	RD	0.17	0.12 to 0.23	50.95
Response[a]	18 months	3	RD	0.12	0.02 to 0.22	53.51
Remission[b]	6 months	3	RD	0.12	0.06 to 0.18	0.00
Remission[b]	12 months	3	RD	0.08	0.02 to 0.14	0.00
Remission[c]	18 months	3	RD	0.08	0.01 to 0.14	0.00
Remission[c]	24 months	3	RD	0.05	-0.02 to 0.11	0.00
Treatment satisfaction	12 months	4	RD	0.21	0.11 to 0.30	69.62
Treatment satisfaction	24 months	3	RD	0.14	0.06 to 0.21	29.65

[a] Response indicated by ≥ 50 percent reduction in symptom score.
[b] Remission indicated by a Symptom Checklist-20 score <0.5.
[c]Remission indicated by a Symptom Checklist-20 score <0.5, or a PHQ-9 <5
Abbreviations: CI = confidence interval; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference.

Using a 50 percent or greater reduction in depression symptom score to indicate response, we pooled data at 6, 12, and 18 months. At 6 months (nine studies[38, 61, 65-68, 72, 79, 80]), 20 percent more patients receiving collaborative care achieved response (50 percent reduction in mental health

score) than did patients in control groups. The TEAMcare study[80] reported a significantly higher percentage difference in those achieving response at 6 months than in those with usual care (0.36; 95% CI, 0.23 to 0.49); a sensitivity analysis removing that study slightly reduced that number to 17 percent more patients achieving response compared with patients in control groups. From these data, we calculated an NNT to achieve response at 12 months of six patients. Despite significantly greater improvement among intervention participants than among controls on measures of depression, a large proportion of patients remained symptomatic. For example, the range among intervention arms of patients reporting response at 6 months (≥50 percent reduction in depression score from baseline) was 37 percent to 59 percent (Appendix E).

For patients with diabetes in the Pathways trial,[38] additional analyses showed that patients with two or more diabetic complications were significantly more likely than usual care patients to experience reductions in depressive symptoms; patients with fewer than two complications showed no difference between arms.[76] When investigators stratified the participants in the Pathways trial by independent versus interactive relationship styles, depression outcomes improved more significantly compared with usual care in patients with an independent attachment style.[40] These isolated analyses lend context for interpreting the findings in patients with diabetes, but they are insufficient to draw quantitative conclusions.

We were able to perform meta-analyses on treatment response at 18 months based on three studies[61, 69, 71] (Table 12), revealing a smaller but still significant difference between groups favoring the intervention (NNT=8).

Depression-Free Days

Five studies reported depression-free days.[38, 61-65, 67, 73] The cancer subgroup of IMPACT[61] reported 51 more depression-free days in the intervention patients than in the usual care patients at 12 months (186 vs. 135, p<0.001); in the diabetes subgroup,[63] patients receiving collaborative care had 59 more depression-free days at 1 year than controls (95% CI, 37 to 81). In the Pathways project,[78] patients in the intervention arm had 20 more depression-free days at 12 months than controls (186 vs. 166; 95% CI, -2 to 42). The HIV study[73] reported an adjusted mean difference of 19 days (95% CI, 11 to 28) at 12 months. A study in patients with diabetes[67] reported an estimated difference between groups of 32.6 days (p<0.001).

Remission and Recurrence

6- and 12-Month Data

We pooled data from three studies in meta-analyses of remission of depression in patients with diabetes, HIV, and cancer at 6 and 12 months (Table 12 and Appendix E).[61, 68, 73] Defining remission as SCL-20 <0.5, by 6 months, 12 percent fewer patients in control groups than patients in intervention groups achieved remission (RD, 0.12; 95% CI, 0.06 to 0.18). From this, we calculated an NNT of 8 patients to achieve one remission. Although results continued to favor the intervention group at 12 months, the NNT to achieve one remission was 12.5.

Two additional trials were not amenable to meta-analysis owing to a different definition or measurement of remission. The ADAPt-C study of predominantly female Hispanic patients with cancer used the PHQ-9.[68] Those investigators reported that 70 percent of intervention patients were in remission at 6 months, with remission defined as ~~"n~~o longer had major depression"; conclusions cannot be drawn in the absence of comparator data. In the arthritis subgroup of

IMPACT, Lin and colleagues reported that 24 percent of intervention patients and 38 percent of usual care patients met DSM-IV criteria for depression at 6 months (t, -4.6; p<0.001).[65]

18- and 24-Month Data

Three studies (two in patients with cancer[61, 71] and one in patients with diabetes[69]) were amenable to meta-analyses at 18 and 24 months, based on remission defined as PHQ-9 < 5[69, 71] or HSCL <0.5,[61] revealing that the intervention group was favored by a small but significant margin at 18 but not 24 months (Table 12).

Recurrence

No trial examined recurrence of depression at 6 or 12 months. One study of patients with cancer[71] showed that among patients remitted at 12 months (PHQ-9<5), there was no difference in recurrence between groups at 18 or 24 months (36 percent in the intervention group vs. 39 percent in the control group).

Satisfaction With Treatment

Six studies[38, 61, 67-69, 71, 74, 80] addressed patient satisfaction with depression treatment, although two assessed only the intervention group.[68, 74] The remaining four studies were suitable for meta-analysis at 12 months; all four favored the intervention group across patients with diabetes,[64, 66] diabetes and/or heart disease,[80] and cancer.[61] Our meta-analysis found that 21 percent (95% CI, 0.11 to 0.30) more patients receiving collaborative care than controls were satisfied with treatment (Table 12 and Appendix E). In those trials, treatment satisfaction was defined as follows: care rated "satisfied" to "very satisfied" (MDDP[67, 69]); care rated "moderately satisfied" to "very satisfied" (Pathways[38]); care rated "very satisfied" to "extremely satisfied" (TEAMcare[80]); care rated "very good" or "excellent"[74] and care rated "good" or "excellent" (IMPACT[61]). Meta-analysis of the three studies reporting satisfaction responses at 24 months[61, 69, 71] were suitable for meta-analysis, favoring the intervention (RD 0.14; 95% CI, 0.06 to 0.21).

Treatment Adherence

Two trials[73, 77] reported on the outcome of adherence to antidepressant medications; we could not draw meaningful conclusions from this small amount of evidence. The Pathways study of patients with diabetes showed significantly greater adherence to antidepressants in the collaborative care group, reporting a 6-month adjusted odds ratio (OR) of 2.29 (95% CI, 1.38 to 3.82) and a 12-month adjusted OR of 2.18 (95% CI, 1.32 to 3.62).[38] The HITIDES (HIV)[73] study showed no difference between treatment groups at 6 months, with an OR of 1.65 (95% CI, 0.75 to 3.62). At 12 months, the direction of effect was reversed but remained statistically insignificant (OR, 0.56; 95% CI, 0.20 to 1.57).[73]

We found no other measures of adherence relevant to intermediate mental health outcomes.

Applicability

These findings are generally applicable to primary care patients with depression and at least one chronic medical condition, but they may not apply to patients with medical conditions not addressed in this report. The average age across studies was 59, an age group most likely to have chronic disease; thus, the relevance of these results to either young adults with chronic disease or more elderly patients who may have multiple disorders remains unclear. (IMPACT included only

adults ≥60 years of age, but the average age was 71.[5]) People of Hispanic origin (predominantly female)[66-68] and male veterans[73] were represented and appeared to respond similarly across outcomes, but we had too few data on such patients to analyze separately.

Included trials used clinically meaningful measures and had study durations (at least 6 months) that provided a real-world context. Although these trials represented several types of settings, including primary care–like cancer and HIV clinics, they all had in common a care manager who directed the intervention. The intermediate mental health outcomes achieved here might, therefore, apply only to settings in which such services and personnel can be accommodated and afforded. Similarly, practices that agreed to participate in these trials may reflect a selection bias based on culture and willingness to collaborate.

Key Question 1b: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on other mental health outcomes (e.g., depression-related quality of life) and use of mental health-related services?

In the key points below, we summarize the main findings by outcome and report the SOE for each outcome. For this KQ, outcomes of interest include suicide, use of antidepressants, mental health–related quality of life, use of mental health care, sick days attributable to mental health, and employment stability.

Key Points

- Evidence was insufficient to draw conclusions about suicide; one suicide was reported in a usual care group.
- Collaborative care interventions generally resulted in greater antidepressant use for collaborative care interventions than for usual care at 12 months (RD, 0.23; 95% CI, 0.15 to 0.30; 5 studies), but not 6 months (RD, 0.09; 95% CI, -0.02 to 0.20; 3 studies) (low SOE).
- Patients in collaborative care intervention arms achieved greater mental health–related quality of life than usual care at 6 and 12 months using the mental component of the Medical Outcomes Study Short Form (WMD, 2.98; 95% CI, 1.41 to 4.55 at 12 months; four studies) (moderate SOE).
- Eight studies reported on use of mental health services (other than medication alone); each showed greater use of any services at 6 and/or 12 months (40 percent to 97 percent vs. 16 percent to 57 percent for intervention and control groups, respectively). One as-treated sample of patients with cancer[61] showed that this trend persisted at 18, but not 24 months (low SOE).
- Evidence was insufficient (no data from any trial) on sick days or employment stability.

Detailed Synthesis

Suicide

Two studies reported suicide-related outcomes. Authors of the MODP reported that they were unaware of any attempted or completed suicides in either treatment group.[68] Strong and colleagues reported one suicide in the usual care group.[74] In a second trial, investigators reported that they were unaware of any attempted or completed suicides in either treatment group.[68] Data were too sparse to permit conclusions for this outcome.

Use of Antidepressants

Meta-analysis from three studies[61, 73, 79] showed no difference in antidepressant use between groups at 6 months; but there was moderate heterogeneity (I^2, 55.22), with the two studies enrolling subjects with cancer or heart disease both finding a similar increase in antidepressant use, and one study enrolling subjects with HIV finding no difference (Appendix E).[61, 73, 79] Six studies reported use of antidepressants at 12 months, including additional populations with cancer,[71] diabetes,[67] and arthritis.[64] Our meta-analysis indicated greater use in the intervention arms, but heterogeneity was considerable (I^2, 73.50) (Appendix E). The one study that did not find greater use of antidepressants for those in the intervention group was again the HIV study, HITIDES.[73] Because patients with HIV may differ from patients with other chronic diseases in ways that could affect medication use, we ran a sensitivity analysis, removing the HITIDES results. This analysis resulted in less heterogeneity (I^2, 55.24; RD, 0.23; 95% CI, 0.15 to 0.30) and an overall NNT of 4.5 (Appendix E).

Mental Health–Related Quality of Life

Five studies measured well-being using the mental component of Medical Outcomes Study Short Form.[64, 67, 68, 73, 79] Four studies[64, 67, 68, 73] used the 12-item instrument (Short Form Health Survey [SF-12]); and one used the 36-item (SF-36).[79] We conducted a meta-analysis across conditions, combining studies of patients with depression and one chronic disorder (cancer, diabetes, heart disease, or HIV). Our meta-analysis favored collaborative care interventions over controls at both 6 and 12 months (Table 13 and Appendix E). Only the HIV study did not find a statistically significant difference between intervention and control groups at either time point, but point estimates favored the intervention group.[73]

Table 13. Summary of meta-analyses for other mental health–related outcomes

Outcome	Timing	N Studies	Statistic	Effect Size	95% CI	I^2
Use of antidepressants	6 months	3	Risk difference	0.09	-0.02 to 0.20	54.22
Use of antidepressants	12 months	5a	Risk difference	0.23	0.15 to 0.30	55.24
Self-rated mental health-related QOLb	6 months	4	SMD	0.31	0.16 to 0.45	35.31
Self-rated mental health-related QOLc	6 months	3	WMD	3.62	1.30 to 5.94	61.53
Self-rated mental health-related QOLc	12 months	4	WMD	2.98	1.41 to 4.55	41.77

[a] Results of the meta-analysis that excluded the HIV Implementation of Translating Initiatives for Depression into Effective Solutions (HITIDES) study because of high heterogeneity.
[b] Self-rated mental health was measured with the 12-item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials except Bypassing the Blues, which used the SF-36. The Bypassing the Blues data were from the 8-month endpoint.[c] Self-rated mental health is measured with the 12-item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials.
Abbreviations: CI = confidence interval; QOL = quality of life; SMD = standardized mean difference; WMD = weighted mean difference.

Use of Mental Health Services

Eight studies[38, 61, 62, 65-67, 69, 71, 72, 79] reported use of mental health care services other than antidepressants alone. Ell et al., in their sample of patients with diabetes, showed that intervention patients received any depression treatment more often than controls at 12 and 18 months (83.9 percent vs. 32.5 percent and 45.8 percent vs. 24.1 percent, respectively, both $p<0.001$).[67] In the Puerto Rico trial of patients with one or more medical conditions, significantly more intervention patients received any depression treatment at 6 months (97 percent vs. 57 percent, p not reported).[72] Data from the IMPACT trial showed that patients with arthritis in the intervention group were more likely to receive mental health services at 12 months than patients in the control group (47 percent vs. 16 percent, $p<0.001$);[65] similarly for the sample with cancer,[61] service use favored the intervention group at 6 and 12 months (percentage with any mental health visit in the past 3 months: 40 vs. 15 and 42 vs. 16, respectively, both $p<0.001$), but the difference was no longer statistically significant at 18 months (15 vs. 12, $p=0.56$). The ADAPt-C trial of patients with cancer[71] reported in its as-treated sample that more intervention patients than usual care patients received any depression care at 12 and 18, but not 24, months (Appendix C). The association with more depression treatment in the intervention group was consistent across all trials that reported on this outcome at 6, 12, and 18 months.

Sick Days Related to Mental Health

No data on sick days related to mental health were reported.

Employment Stability

No data on employment stability were reported.

Applicability

We refer to the applicability section in KQ 1a for the same consideration of constraints posed by these types of studies. In general, the results in this section apply to primary care patients with depression and one or more chronic medical conditions, receiving care in a setting where a care manager is available to coordinate care. These results must be considered in the context of heterogeneity across medical conditions and interventions.

Key Question 2a: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar

interventions or usual care) on intermediate chronic medical outcomes (e.g., hemoglobin [Hb]A1c for patients with diabetes)?

For this Key Question, we were interested in the effects of practice-based interventions on medical outcomes related to the specified chronic medical condition(s). Of the trials that met our inclusion criteria, the medical conditions included arthritis, diabetes, cancer, heart disease, HIV, and one or more conditions. Outcomes of interest include symptom improvement, response to treatment, treatment adherence, and satisfaction with care. We summarize the main findings by medical condition and report the strength of evidence (SOE) for each outcome.

Key Points

- Few studies reported specifically on symptom improvement; data were reported for people with arthritis (between group difference at 12 but not 6 months)[62, 65, 67] and HIV (between-group difference at 6 but not 12 months).[73] Evidence was insufficient to reach conclusions for this outcome.
- Hemoglobin A1c (HbA1c) was reported as a measure of response in four studies of patients with diabetes, though only three[64, 67, 80] were reported in a way suitable for meta-analysis. Our meta-analysis found no between-group differences for change in HbA1c at 6 months (weighted mean difference [WMD], 0.13; 95% CI, -0.22 to 0.48; three studies) or 12 months (WMD, 0.24; 95% CI, -0.14 to 0.62; three studies). A single study[69] showed no difference between groups at 18 and 24 months (low SOE).
  - The TEAMcare trial may serve as an exception because of its design and because it was the only study to use HbA1c as a predefined outcome measure;[80] it reported significant differences in HbA1c (intervention vs. control): 8.14 versus 8.04 at baseline; 7.42 versus 7.87 at 6 months; and 7.33 versus 7.81 at 12 months; overall $p<0.001$. At 12 months, 37 intervention patients versus 18 controls achieved a ≥1.0 percent improvement (response) in HbA1c ($p=0.006$).
- Treatment adherence was reported for cancer,[66] diabetes,[64, 77, 80] and HIV,[73] but only diabetes provided data from more than one study.
  - Diabetes and diet: Patients receiving the collaborative care intervention were no more likely than controls to adhere to a generally healthy diet in three of three trials[64, 77, 80](moderate SOE).
  - Diabetes and exercise: Patients receiving the collaborative care intervention were no more likely than controls to adhere to an exercise program in three of three trials at 6 months and two of three trials at 12 months [64, 77, 80] (low SOE).
  - Diabetes and medications: Based on mixed results from three studies,[64, 77, 82] evidence was insufficient to draw a conclusion.
  - A summary score of diabetes self-care and a mean number of diabetic complications were reported by one study[67, 69] and showed no difference between groups for either outcome at 12,18, or 24 months.
- Evidence was insufficient to draw conclusions about treatment satisfaction.

Detailed Synthesis

Symptom Improvement

Arthritis

One study, the IMPACT subgroup analysis of patients with arthritis,[65] reported data on arthritis pain based on a 10-point severity scale (10 being worse). The intervention group reported a lower pain score compared with the control group at 6 months (-0.21; 95% CI, -0.6 to 0.19) and at 12 months (-0.53; 95% CI, -0.92 to -0.14), but arguably did not reflect clinically meaningful change at less than a 1-point difference. In a separate analysis,[62] baseline pain severity showed significant interactions with the intervention on 12-month pain severity (p=0.04), revealing that the intervention was more effective than usual care in decreasing pain severity only in those with lower initial pain severity, but the difference between groups at 12 months was modest (intervention=4.54; control=5.41; change scores from baseline in each group not reported).

Cancer

No trial reported on cancer-related symptom improvement.

Cardiovascular Disease

No trial reported on heart disease–related symptom improvement.

Diabetes

The Ell et al. trial of predominantly Hispanic patients reported directly on diabetes symptoms using the Whitty-9 instrument,[88] but it did not define a clinically meaningful important difference.[67] Intervention patients had a lower symptom score at 6 months (1.65 vs. 1.79, p=0.07), but they were similar to controls at 12 months (1.66 vs. 1.69, p=0.18) and 18 months (1.79 vs. 1.74, p=0.85).

HIV

The HITIDES trial,[73] in a population of predominantly male veterans, used the 20-item Symptoms Distress Module[89] to measure the severity of common HIV symptoms. Bothersome symptoms were defined as scores of three or four on a Likert-type scale, and the total number of bothersome symptoms was reported. After removing 7 depression-related items due to overlap between the Symptoms Distress Module and the SCL-20, the authors reported significant adjusted intervention effects versus controls at 6 months (beta, -0.62; 95% CI, -1.2 to -0.08; p=0.03) but not 12 months (beta, -0.09, 95% CI, -1.58 to 1.40, p=0.88).

Response

Arthritis

No trial reported on response to arthritis treatment, other than the study assessing pain severity described in the previous section on symptoms.

Cancer

No trial reported on cancer response.

Cardiovascular Disease

The TEAMcare trial of patients with depression and diabetes and/or heart disease reported that intervention patients had a greater reduction in low-density lipoprotein (LDL, or "bad" cholesterol) than usual care patients at 12 months (intervention at baseline=107, at 12 months=92; control at baseline=109, at 12 months=101; mean difference at 12 months=-9.1; 95% CI, -17.5 to -0.8).[80] The investigators also reported that intervention patients had a 4.6-point (95% CI, 1.9 to 7.3) greater reduction in systolic blood pressure (SBP) than usual care patients at 12 months (baseline SBP=136 and 132 in the intervention and control groups, respectively). Response was defined as an SBP ≥ 10 mm Hg decrease from baseline. At 12 months, 41 intervention patients and 25 controls achieved response (p=0.016) from an overall sample of 214.

Diabetes

The TEAMcare trial[80] defined response for HbA1c as a reduction of ≥1 percent from baseline.[80] At 12 months, 37 intervention patients and 18 controls achieved response (p=0.006) from an overall sample of 214. They also reported a greater percentage of intervention patients than controls reaching American Diabetes Association guideline targets for HbA1c, LDL, and SBP at 12 months (16.3 vs. 12.5, p not reported).

Our meta-analysis using three of the four trials reporting HbA1c[64, 67, 80] revealed no significant difference between intervention and control groups at 6 and 12 months (Table 14 and Appendix E). Among these, the TEAMcare study[80] was the only study to report statistically significant differences in HbA1c for intervention patients compared with control patients: 8.14 versus 8.04 at baseline; 7.42 versus 7.87 at 6 months; and 7.33 versus 7.81 at 12 months; overall p<0.001.[80] Importantly, the nature and design of this trial differed from others in this comparative effectiveness review because the investigators set out to provide coordinated care management and "treat-to-target" principles for patients with poorly controlled diabetes, coronary heart disease, or both, and coexisting depression. None of the other trials intended to use HbA1c as a primary outcome. We could not include the Pathways study in our meta-analyses because it lacked sufficient data on differences between arms, but the investigators reported no statistically significant group differences at baseline or 6 or 12 months.[38] They did report that HbA1c levels decreased over time across groups: mean=7.99 percent (standard deviation [SD], 1.47 percent) at baseline; mean=7.58 percent (SD, 1.47 percent) at 6 months; and mean=7.64 percent (SD, 1.57 percent) at 12 months.

Ell and colleagues[69] reported 18- and 24-month data on HbA1c, showing no difference between groups, with an overall mean difference at 24 months of 0.23 (95% CI, -0.34 to 0.81).

Table 14. Summary of meta-analyses for intermediate chronic medical outcomes

Outcome	Timing	N Studies	Statistic	Effect Size	95% CI	I^2
Change in HbA1c	6 months	3	WMD	0.13	-0.22 to 0.48	45.52
Change in HbA1c	12 months	3	WMD	0.24	-0.14 to 0.62	67.79

Abbreviations: CI = confidence interval; HbA1c = hemoglobin A1c; WMD = weighted mean difference.

HIV

No trial reported on response.

Treatment Adherence

Arthritis

No trial reported on adherence to arthritis treatment.

Cancer

Of the three included trials involving cancer patients, only the MODP program[66] reported on adherence; the investigators defined this as ~~–c~~ompleting all doctor-recommended treatment or follow-up visits." Intervention patients (89 percent) were more likely than usual care patients (70 percent) to be adherent at 8 months (OR 3.51; 95% CI, 0.82 to 15.03).

Diabetes

Three trials reported in different ways on adherence to diet and exercise,[64, 77, 80] and two reported on adherence to standard diabetes medications[64, 77] (Appendix C). One study reported a summary of diabetes self-care based on a measure of overall self-reported adherence and showed no difference between groups at 12,18, or 24 months.[69] They similarly showed no difference between groups in diabetic complications for the same time frame. Other measures of self-care were reported infrequently (such as foot care) and are detailed in the evidence tables (Appendix C).

Diet

A further analysis from the Pathways study reported the number of days in 1 week that the patient followed a generally healthy diet;[77] by 12 months this outcome had risen by nearly 1 day in both groups (baseline mean 3.7 days/week for both groups). The two groups did not differ at 6 or 12 months (12-month mean 4.5 days/week for both groups). TEAMcare investigators reported the percentage adhering to a general diet plan ≥ 2 days per week; this outcome also showed no statistical difference at 12 months (68 percent intervention vs. 63 percent control, p=0.37).[80] The IMPACT diabetes analysis revealed a similar trend for patients reporting how well they followed their diet plan (ranked from 1 [always] to 5 [never]); scores were 2.57 (intervention) and 2.54 (control) at 12 months (mean adjusted difference -0.26, 95% CI, -0.65 to 0.12).[64]

Exercise

From the Pathways cohort, Lin et al. reported no difference at any time points for the number of days in the last week spent exercising 30 or more minutes (Appendix C) and no significant improvement from baseline in either group (2.6 vs. 2.3 days at baseline; 2.7 vs. 2.6 at 12 months).[77] TEAMcare researchers reported that 54 percent of intervention patients versus 44 percent of controls adhered to a specific exercise routine ≥ 2 days per week (p=0.21).[80] In the IMPACT diabetes sample,[64] patients in the intervention group performed significantly more exercise than those in the control group at 12 months (mean difference 0.50 day; p=0.01).

Medications

The Pathways researchers evaluated a subsample of participants[77] for medication nonadherence to oral hypoglycemic medications, lipid-lowering agents, and angiotensin-converting enzyme inhibitors based on computerized records of pharmacy refills. Baseline and follow-up data revealed rates of nonadherence that ranged from 20 percent to 30 percent overall; these rates did not significantly change, nor did they differ, among treatment groups for lipid-

lowering agents and angiotensin-converting enzyme inhibitors at 12 months (Appendix C). Interestingly, the rate of nonadherence to oral hypoglycemics was significantly higher in the intervention group than the control group at 12 months (28.2 vs. 24 percent, p<0.03).

The IMPACT investigators asked how often participants took their prescribed medications, scored on a scale from 1 [always] to 5 [never].[64] They reported no significant difference over time and no differences between groups at any time points. At 12 months, the scores were 1.16 for the intervention group and 1.19 for the control group.

HIV

The HITIDES study defined patients as adherent to the HIV medication regimen when the number of pills taken over the past 4 days divided by the number prescribed was ≥95 percent.[73] The groups did not differ at either 6 months (74 percent vs. 72 percent, p=0.65) or 12 months (68 percent vs. 64 percent, p=0.89) (Appendix C).

Satisfaction With Care

TEAMcare asked patients about their satisfaction with care of diabetes, heart disease, or both. At 12 months, 86 percent and 70 percent of patients in the intervention and control groups, respectively, reported being satisfied with their care.[80]

Applicability

We refer to the applicability section in KQ 1a for the same consideration of constraints posed by these types of studies, specifically the required presence of a care manager to carry out the intervention. In general, the results in this section apply to a primary care population with depression and one of the chronic medical conditions discussed here, mostly patients with diabetes. Relatively few data were available on outcomes for patients with arthritis, cancer, heart disease, and HIV.

Key Question 2b: Among adults with chronic medical conditions and concomitant depression (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving depression or both depression and chronic medical conditions (when compared with similar interventions or usual care) on general and other health outcomes (e.g., diabetes-related morbidity, use of general health-related services, costs)?

For this Key Question, we were interested in the effects of the collaborative care intervention on general health outcomes and costs of the intervention. General health outcomes of interest include condition-specific morbidity, mortality, health care utilization, and quality of life. We summarize the main findings by outcome and report the strength of evidence for each outcome.

Key Points

- Evidence was insufficient to draw conclusions about morbidity related to the medical condition. In one arthritis study,[62, 65] the intervention group had less arthritis interference (between-group difference -0.56; 95% CI, -0.96 to -0.16 at 6 months, and -0.59; 95% CI, -1.00 to -0.19 at 12 months). In one trial of post–coronary artery bypass graft (CABG)

patients,[79] the intervention group had greater cardiac-related functioning (overall difference 4.6; 95% CI, 1.9 to 7.3; p=0.001; when stratified by sex, significant only in men).

- All but one study[72] reported on mortality. Few deaths were reported overall (most in cancer studies). Intervention and control patients did not differ in mortality at 6 months (risk difference=0.00; 95% CI, -0.02 to 0.02; seven studies) or 12 months (risk difference, -0.00; 95% CI, -0.02 to 0.01; seven studies) (moderate SOE for no difference).
- Evidence was insufficient to draw conclusions about use of health care services. Hospitalizations were reported in two trials. In one of post-CABG patients[79] at 8 months, overall, 33 percent of intervention patients, 32 percent of controls, and 25 percent of a nondepressed comparison group required hospitalization. In a trial of patients with diabetes and/or heart disease,[80] 27 intervention patients versus 23 controls were hospitalized at 12 months.
- Patients receiving the collaborative care intervention generally experienced greater quality of life than control patients at 6 and 12 months, based on several different measures (moderate SOE).
- Six trials, using various methods, reported costs of the intervention. Using a crude measure based on varying factors and time frames, the average cost of the intervention per patient was $705.00. Individual studies measured other aspects of cost that are detailed in Appendix C, but were not amenable to pooling.

Detailed Synthesis

Morbidity Related to Chronic Medical Condition

The IMPACT arthritis subgroup reported on daily pain interference, using a scale ranging from 0=no interference to 10=unable to perform any activities.[62, 65] Intervention patients had significantly less pain interference than control patients at 6 months (4.08 vs. 4.65; between-group difference -0.56; 95% CI, -0.96 to -0.16) and 12 months (4.40 vs. 4.99; between-group difference -0.59; 95% CI, -1.00 to -0.19).

The Bypassing the Blues study[79] used a heart disease–specific measure of physical functioning, the Duke Activity Status Index (DASI);[90] in this, a change of 3 or more points has been considered the minimal clinically important difference.[90, 91] The investigators reported that patients in the collaborative care group had better scores on this measure than controls at 8 months (between-group difference 4.6; 95% CI, 1.9 to 7.3; p=0.001);[79] both arms of the trial showed an overall improvement over time. Analyses by sex showed that the significantly better scores among intervention patients were found only among males (between-group difference for men, 6.1; 95% CI, 2.7 to 9.6; p<0.001; for women, 3.1; 95% CI, -1.1 to 7.3).

The Bypassing the Blues study of post-CABG patients also examined hospitalizations for cardiovascular causes (intervention=85 vs. control=68).[79] Total hospitalizations are reported under health care utilization and in Appendix C.

Mortality

All-cause mortality was reported in 11 of the 12 studies (Appendix C). Unsurprisingly, it was higher among cancer patients than those with other chronic conditions. In 1 small (N=55) 8-month study of cancer patients,[66] no deaths occurred in the intervention arm, and eight patients

(30 percent) in the control arm died (OR 0.04; 95% CI, 0.002 to 0.74). In the other 2 studies of cancer patients,[61, 68] mortality was similar across treatment arms at all time points.

In our meta-analyses, we detected no difference in mortality between groups at 6 months or 12 months (Table 15), with few events overall. The Pathways study[75] reported deaths at 5 years (intervention=10.3 percent vs. control=12.8 percent); these data were not included in the pooled analyses.

Use of Health Care Services

Two studies reported hospitalizations. We reported cardiac-related rehospitalization in the study of post-CABG patients[79] under condition-specific morbidity as noted above. That same study gave the total number of hospitalization in 8 months; overall, 33 percent of intervention patients, 32 percent of controls, and 25 percent of a nondepressed comparison group, required hospitalization. The TEAMcare trial (patients with diabetes and/or heart disease)[80] reported that 27 (25.5 percent) of intervention patients and 23 control patients (21.3 percent) were hospitalized at some point during the previous 12 months.

We found no other reports of nonmental or overall health care utilization.

Table 15. Summary of meta-analyses for general health outcomes

Outcome	Timing	N Studies	Statistic	Effect Size	95% CI	I^2
All cause mortality	6 months	7	RD	0.00	-0.02 to 0.02	62.9
All cause mortality	12 months	7	RD	0.00	-0.02 to 0.01	0.00
Self-rated physical health	6 months	4	SMD	0.19	0.08 to 0.31	0.00
Self-rated physical health	6 months	3	WMD	2.12	0.75 to 3.49	0.00
Self-rated physical health	12 months	3	WMD	1.25	-0.45 to 2.95	27.21
Functional impairment[a]	12 months	4	WMD	0.93	0.68 to 1.19	0.00

Abbreviations: CI = confidence interval; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference.

[a] Sheehan Disability Scale of Functional Impairment[92]

Physical Health Quality of Life

Five studies[64, 67, 68, 73, 79] measured self-reported quality of life using the physical component of SF-12[64, 67, 68, 73] or 36 (SF-36).[79] We conducted meta-analyses for these outcomes, using WMD where measures were similar (all SF-12), and SMD to include the trial using the SF-36, at 6 and 12 months (Table 15). Our findings show that patients in the collaborative care groups had higher self-rated physical health status than controls at 6 months. At 12 months the WMD did not show a difference between groups (1.25; 95% CI, -0.45 to 2.95; three studies). Ell and colleagues[69] similarly showed no difference between groups at 18 and 24 months. For context, 3 points is suggested as the minimally important clinical difference on the SF-36.[93]

Four studies[61, 65, 67, 80] used the Sheehan Disability Scale of Functional Impairment[92], which asks the extent to which health interferes with work, family, or social life on a 0–10 scale (0= not at all; 10 = unable to carry on activities). A meta-analysis of these data at the 12-month time point showed a difference in means that favored the intervention group (0.93; 95% CI, 0.68 to 1.19).

Similar to the more condition-specific DASI reported under morbidity outcomes above, the post-CABG study showed no between-group difference overall at 8 months on the SF-36 (1.6; 95% CI, -0.5 to 3.8).[79] When the analyses were done by sex, men in the intervention group had significantly higher scores than men in the control group (3.6; 95% CI, 0.8 to 6.3).

The HIV study also collected the Quality of Well-Being Self-Administered Scale (QWB-SA), which ranges from death (0.0) to perfect health (1.0); the investigators reported no between-group differences at 6 months (-0.03; 95% CI, -0.01 to 0.06) or 12 months (-0.01; 95% CI, -0.05 to 0.03).[73]

Williams et al., in their sample of patients with diabetes,[64] used a self-rated measure of health-related functioning (0=no problem to 10=unable to function). They showed that intervention patients reported significantly better functioning than controls at 6 months (4.37 vs. 4.63) and 12 months (3.91 vs. 4.90).

The arthritis subgroup analysis from IMPACT reported self-rated general health status on a scale ranging from 1 (excellent) to 5 (poor).[62, 65] The investigators showed that intervention participants gave a significantly better rating than controls at 12 months (3.3 vs. 3.6, $p<0.001$). The same study also asked participants to rate their overall quality of life in the past month on a scale of 0 to 10 (zero=your situation is about as bad as dying); this measure also favored the intervention group at 12 months (6.4 vs. 6.0, $p=0.005$). The same scale was reported in the IMPACT cancer cohort;[61] intervention patients gave better scores than controls at 12 months (6.7 vs. 6.0, $p=0.04$) but not 6 months (6.3 vs. 5.7, $p=0.86$).

Despite negative results in the HIV study, the general trends (including meta-analysis at 6 months with HIV included) across studies and measures suggest that patients receiving the collaborative care intervention experienced greater quality of life than control patients at both 6 and 12 months.

Costs of Intervention

Table 16 details costs of interventions in the trials that reported them. In some cases, the costs are per person or per service; in others, they are combined or total costs. Some investigators reported intervention (total) costs over a specified time period; others did not. Using a crude estimate because of such heterogeneity, for the six trials that reported data, the average cost of the intervention per patient was $705.00 Individual studies measured other aspects of cost that are detailed in Appendix C, but were not amenable to pooling.

Table 16. Costs of interventions

Author, Year Study Name Chronic Condition Quality	Costs
Ell et al., 2008[68] ADAPt-C Cancer Fair	$524 per intervention patient over 12 months[a]
Strong et al., 2008[74] SMaRT Oncology 1 Cancer Fair	$523 per patient over the 6-month intervention period[b]
Ell et al., 2010[67] MDDP Diabetes Fair	$820 per patient over the 12-month intervention period[c]
Katon et al., 2008[75] Pathways Diabetes Fair	$543 per patient from baseline through 12 months[d]
Katon et al., 2006[63] IMPACT (secondary analyses) Diabetes Fair	$597 per patient over 24 months[e]
Katon et al., 2010[80] TEAMcare Diabetes and/or heart disease Fair	$1,224 per patient over the 12-month intervention period[f]

[a] Inclusive of costs for intervention provider and patient navigation services, telephone and in-person supervision, evaluation and prescription by study psychiatrist, and intervention materials.
[b] Direct cost of nurse time + psychiatrist time, exclusive of nurse training and screening time.
[c] Assumptions: $71 per 90-minute visit, $35 per 45-minute telephone followup, $10 per 10- to 15-minute patient navigation call, $10 for relaxation tape, $136 for interventionist communication with PCP, $21 for clinical supervision. A later publication[70] calculated average cost per patient to be $515.
[d] Unspecified ~~"in~~intervention visit" costs; assumptions: $79 per 30-minute in-person nurse visit, $31 for each 10- to 15-minute telephone contact, $57 for supervision and information system support.
[e] Inclusive of in-person and telephone contacts, overhead costs, supervision, and intervention materials.
[f] Inclusive of nurse contacts, physician supervision, and information systems support; mean of 10.0 in-person and 10.8 telephone visits; assumptions: $79 per 30-minute in-person nurse visit, $31 per 10- to 15-minute telephone nurse contact, $100 fixed costs per patient for supervision and information systems support.
Abbreviations: ADAPt-C = Alleviating Depression Among Patients with Cancer; CI = confidence interval; IMPACT = Improving Mood—Promoting Access to Collaborative Treatment; SD = standard deviation; SMaRT = Symptom Management Research Trials.

Applicability

We refer to the applicability section in KQ 1a for the same consideration of constraints posed by these types of studies, specifically the required presence of a care manager to carry out the intervention. In general, the results in this section apply to a primary care population with depression and one of the chronic medical conditions discussed here. Some data were available on outcomes for patients with arthritis, cancer, diabetes, heart disease, and HIV, but they were too sparse to generalize to the population level based on condition. These studies did, however, include patients with significant medical morbidity, and as such they reflect real-world circumstances.

Key Question 3: What harms are associated with practice-based interventions for primary care patients with chronic medical conditions and concomitant depression?

All the studies that met our eligibility criteria characterized their intervention as a form of collaborative care. We examined the body of evidence for any reported adverse events (AEs), but we recognized that potential harms reported as a direct effect of this type of intervention are rare.

Key Points

- Very few data on harms were reported.
- The trial that specifically reported AEs,[80] such as medication side effects or emergency room visits for chest pain or neurologic symptoms, found overall rates to be higher among intervention patients than controls.
- More frequent medication adjustments and monitoring of self-reported patient outcomes in the collaborative care arm may have contributed to the higher reported rate of AEs in that single trial.

Detailed Synthesis

We reported deaths and hospitalizations in KQs 1 and 2. One trial, in patients with depression and diabetes and/or heart disease,[80] considered the following to be mild and moderate AEs: falls, medication side effects, extremely high laboratory values, and emergency room visits for chest pain or neurologic symptoms. Mild and moderate AEs were self-reported, and the severity was based on a study clinician's judgment. Two patients (1.9 percent) in the collaborative care arm experienced at least one mild AE; no patient in the control arm had any mild AE. At least one moderate AE was experienced by 17 percent of intervention patients and 3 percent of control patients.

The higher rate of mild and moderate AEs in the intervention arm may be attributable to increased rates of medication adjustment. Additionally, patients in the intervention arm had more frequent contacts with the care manager and thus had more opportunities to report adverse events, so findings might be the result of detection bias.

Applicability

Given the factors related to applicability noted in KQs 1 and 2, these results must be considered in the context of heterogeneity across medical conditions and interventions. Collaborative care is a complex intervention, and harms of the intervention itself may be difficult to assess. These results may also not apply to patients with fewer symptoms of depression.

Key Question 4: What are the characteristics of the practice-based interventions addressing concomitant depression and chronic medical conditions used in the primary care setting with regard to specific components and/or intensity (e.g., visit frequency, total number of contacts, provider discipline, use of self-management)?

This question was addressed in the context of studies that met criteria for KQs 1 and 2. The populations for the included studies all identified depression as the mental health condition. All

interventions were described as collaborative care interventions; we found no studies with other types of practice-based interventions meeting our inclusion/exclusion criteria. The purpose of this key question is to compare and contrast characteristics of the collaborative care intervention.

Key Points

- Components of the Intervention
  - Team Composition. Care teams were diverse and included various combinations of nurses (6 studies), psychologists or counselors (3 studies), social workers (3 studies), supervising psychiatrists (11 studies), independent physicians (4 studies), and a pharmacist (1 study).
  - Main Intervention Provider. The collaborative care intervention was typically delivered by a care manager alone or in concert with another member of the research team. In most cases the care manager was a nurse (six studies), a master's or doctoral-level psychologist or counselor (three studies), or a social worker (three studies); most had received formal depression care training that focused on diagnosis, pharmacotherapy, and problem-solving treatment.
  - Approach and Mode of Delivery. Across studies, the collaborative care intervention incorporated some degree of personalized care, usually in the early stages of the intervention, along with some combination of telephone alone or telephone plus face-to-face sessions. Care often was implemented using a stepped approach, allowing for patient preferences and following established guidelines.
  - Self-management. The collaborative care intervention typically featured some degree of self-management education and monitoring.
- Intensity of the Intervention
  - Session Frequency. After an initial information and education session, care providers talked with or met participants face-to-face for multiple sessions across a period of time ranging from weeks to months. The number of sessions depended sometimes on the study design and sometimes on the pace at which the individual patient responded to treatment. Two studies were solely telephone based.
  - Session Duration. Across studies that reported session duration, the initial information/education session was typically longer than follow-up sessions. The latter varied in length from 5 to 45 minutes.

Detailed Synthesis

Data were abstracted from all twelve studies to address this key question.[38, 40, 61-68, 72-80] Components of the interventions that differed across studies included the composition of the treatment team members, type of provider who delivered the intervention, mode of delivery of the intervention, and the intensity (frequency and duration) of treatment sessions. All studies had in common some degree of personalizing the intervention for the individual patient and use of a stepped care approach, although the specific nature of the stepped care approach differed in complexity and evidence base across studies.

Also common across studies were other core components, many of which were based on the model of the IMPACT trial. These components included (1) a depression care specialist or manager who was typically responsible for patient education, brief problem-solving counseling, symptom monitoring, and follow-up telephone calls to facilitate relapse prevention; (2) a

consulting psychiatrist on the collaborative care team who supervised the care manager and communicated directly with primary care providers of patients who did not respond adequately to treatment; and (3) use of a validated instrument to document change in depressive symptoms over the course of treatment. We could not develop any summary statistics relevant to this question or grade strength of evidence.

Some similarities as well as differences emerged across studies in terms of how and by whom the intervention was delivered (Table 17). In Bypassing the Blues,[79] HITIDES,[73] Pathways,[38, 40, 75-78] SMaRT Oncology 1,[74] and TEAMcare,[80] the collaborative care intervention was delivered by a nurse, who was described as being part of the research staff with the exception of one study in which the nurse's relation to the study team was unclear.[74] In the remaining studies, the intervention was delivered by a trained counselor;[72] a social worker;[66-68] or, using a hybrid approach (IMPACT), either a nurse or psychologist.[61-65] In the majority of studies the nurse,[38, 40, 73, 75-78] social worker,[66, 67] or psychologist[61-63, 65] was a formally trained depression care specialist.

The individual responsible for providing direct patient management (e.g., the depression care specialist) was part of a larger care team. This team included a psychiatrist in all studies, as well as another physician in some trials.[38, 40, 61-65, 75-80] One trial was unique in including a pharmacist as part of the supervisory team.[73]

All trials provided some degree of personalized care, usually during the initial stages of treatment planning; all typically had a structure that included multiple contacts between the care team provider and the patient. Early in treatment, the intervention was personalized by allowing the patient some degree of autonomy in selecting to begin treatment with medication, psychotherapy, or both. Thereafter, treatment recommendations were adjusted according to a patient's symptom response, including increasing the medication dose or contact with the care provider (or both). Two trials relied solely on telephone contact to deliver the intervention;[73, 79] the others used some combination of weekly,[66] twice per month,[38, 40, 73, 75-80] or variable frequency[61-65, 67, 68, 72, 74] face-to-face sessions and follow-up telephone calls. The Pathways[38, 40, 75, 76, 78] and IMPACT[61-65] trials described the initial information and education session as lasting 1 hour, whereas other studies were less descriptive. Session length varied from 5 minutes[61-63, 65] to 30 minutes[38, 40, 75, 76, 78] to 45 minutes[61-63, 65, 74] or was unspecified.[66, 68, 72, 73, 79, 80]

The actual number of treatment sessions differed considerably across trials. In one case it was capped at 10.[74] In the others, it varied over a predetermined length of followup according to the patients' needs (i.e., if response to treatment was unsatisfactory, more frequent followup sessions were allowed).[38, 40, 61-63, 65, 68, 75, 76, 78-80]

Self-management training and reinforcement were integral to the collaborative care interventions. For example, patients received advice and skill-building opportunities regarding sleep hygiene, appropriate levels of physical activity or other pleasant life events, healthy nutrition, and tobacco and alcohol use;[38, 40, 75, 76, 78, 79] scheduling pleasant life events;[61-65] coping behaviors;[74] and medication adherence.[80] In some instances, these behaviors and activities were tracked during the trial and included as study outcomes.

Table 17. Summary of service-level characteristics of included studies

	ADAPt-C[68]	Bypassing the Blues[79]	HITIDES[73]	IMPACT[61-65]	MDDP[67]	MODP[66]	Pathways[38, 40, 75-78]	SMaRT Oncology 1[74]	TEAMcare[80]	Vera et al.[72]
Care provider										
Nurse		X	X	X			X	X	X	
Psychologist/counselor				X					X	X
Social worker	X				X	X				
Supervisory team										
Psychiatrist	X	X	X	X	X	X	X	X		X
Physician		X		X			X		X	
Pharmacist			X							
Stepped approach										
IMPACT algorithm				X						
Modified IMPACT	X				X	X	X			
Other		X	X						X	X
None								X		
Self-management										
Pleasant life events	X	X	X	X			X			
Healthy lifestyle		X	X		X		X			
Coping					X			X		
Medication/treatment adherence	X				X	X			X	

Abbreviations: ADAPt-C = Alleviating Depression Among Patients with Cancer; HITIDES = HIV Implementation of Translating Initiatives for Depression into Effective Solutions; IMPACT = Improving Mood—Promoting Access to Collaborative Treatment; MDDP = Multifaceted Diabetes and Depression Program; MODP = Multifaceted Oncology Depression Program; SMaRT = Symptom Management Research Trials.

Applicability

The majority of trials hired research staff, many with special training in depression or diabetes care, to work directly with patients. For that reason, these findings may not generalize to settings that do not have (or cannot afford) a care manager. This limitation may be most relevant to community health centers and departments and small specialty practices (e.g., obstetrics and gynecology). This collection of trials focused on five major concomitant medical conditions: arthritis, cancer, diabetes, heart disease, and HIV. Missing from this literature are studies that focused on patients with chronic pulmonary disease, chronic pain, or stroke or on the frail elderly. Four trials focused almost exclusively on Hispanic or Latino participants,[66-68, 72] whereas other trials had percentages of minority participants that were reflective of their presence in the general U.S. population.[38, 40, 61-65, 73, 75, 76, 78, 80] No studies, however, were designed a priori to evaluate racial or ethnic differences in outcomes or in acceptability of, or barriers to, treatment. Thus, specific applicability to racial or ethnic subgroups is unclear.

Key Question 5: What are the specific characteristics of the practice setting where the interventions were delivered with regard to such variables as organizational characteristics (e.g., decision support, level of integration, information technology, electronic medical records, presence of mental health services on site, payer and service mix, practice size, and practice location/setting) or the relationship between elements of the system in which the practice operates (e.g., coordination, financing of care, payment arrangements)?

Key Points

- Overall, practice setting characteristics (e.g., geographic location, practice type and size, open/closed system, level of integration, payer mix and payer type, service mix, information technology) and system characteristics (e.g., financing of care and payment arrangements) were rarely reported.
- Nine trials were conducted in the United States (one in Puerto Rico) and one in the United Kingdom (Scotland).
- None of the trials explicitly reported on whether it was conducted in an open (no membership or eligibility required) or closed system, although the IMPACT trial[61-65] was conducted in a mix of systems that included primary care clinics in a large health maintenance organization (HMO) as well as the Department of Veterans Affairs (VA) system. Three studies were presumed to be conducted in closed systems.[38, 40, 73, 75-78, 80] Closed systems included Group Health Cooperative and the VA system.

Detailed Synthesis

Characteristics of the Practice Setting

Geographic Location

Eleven studies were conducted in the United States (one in Puerto Rico[72]);[38, 40, 61-68, 72, 73, 75-80] one trial was conducted in the United Kingdom.[74]

No trial explicitly reported whether the practice setting was urban, rural, or mixed. Three could be presumed to be urban based on information provided in the articles,[66-68] and one could be presumed as mixed setting based on information provided by authors.[72] The IMPACT trial subgroup analyses[61-65] were presumed to be mixed setting based on information provided in an article by Unutzer and colleagues.[5] For the remaining four trials, rural versus urban setting was not noted clearly nor could be inferred based on information in the articles.[38, 40, 67, 73-78, 80] One trial was telephone delivered;[79] hence, urban or rural setting was not deemed relevant for reporting.

Practice Type and Size

Eleven of the 12 studies were conducted in primary care or primary care–like settings. Intervention was conducted by telephone in 2 trials.[73, 79]

The majority of trials did not report practice size, and, when they did, the reporting was inconsistent. One trial was conducted in a cancer center that served 1.5 million people.[74] Another trial reported HMO size (500,000) and number of patients (9,063) that met case identification based on the HMO's population-based diabetes registry, but it did not mention practice size.[38, 40, 75-78]

Open Versus Closed System

System was categorized as open (no membership or eligibility required) in six trials,[66-68, 72, 74, 79] and three were perceived to be closed.[38, 40, 73, 75-78, 80] Closed systems were generally self-contained; in this evidence base, they included Group Health Cooperative and the VA system, in which an array of services was accessible to patients who were members of these organizations. The IMPACT trial subgroup analyses[61-65] enrolled patients from a mix of settings, including some perceived as closed, such as a large HMO.[5] None of the trials explicitly reported on this variable.

Level of Integration: Presence of Mental Health Services On-Site

We defined the level of integration by whether mental health services were available on-site (see Appendix C for trial-specific data), because these trials did not give other descriptors of integration. On-site mental health providers in primary care clinics were described in four trials.[38, 40, 66, 68, 74-78] One trial reported that part-time registered nurses with experience in diabetes education collaborated with primary care providers to implement the intervention.[80] One trial reported that mental health providers for primary care–like settings were located off-site,[73] and another noted that the study team—including care managers, mental health specialist, and psychiatrist—was separate from the primary care practice.[72] For the IMPACT trial subgroup analyses,[5, 61-65] we could infer that depression care managers (nurses) were physically present in three primary care clinics; in another three clinics, some mental health care practitioner was

available on-site whereas in the rest of 12 clinics, none were present on-site. Two trials did not report any information regarding the location of mental health services.[67, 79]

Payer Mix and Payer Type

We defined payer mix as the type of insurance plan. Payer mix or type was not reported for four trials.[66, 68, 72, 79] Two trials described participants as members of Group Health Cooperative, a mixed-model prepaid health plan.[38, 40, 75-78, 80] One group reported that participants were either enrolled in Medicaid/Medicare, a county-funded program, or had no health insurance.[67] In one trial, all participants were covered by VA benefits.[73] For the IMPACT trial subgroups,[61-65] based on information provided in an article by Unutzer and colleagues,[5] a considerable majority of patients had Medicare coverage (77%) and prescription drug coverage (90%). This trial was conducted in 18 primary care clinics, which included patients from 9 HMO/Independent Provider Association practices, 3 VA practices, 5 academic group-practice practices, and 1 private group practice.

Service Mix

Service mix referred to the types of services available at each intervention site. No trial reported service mix.

Information Technology

We defined information technology (IT) to include electronic medical records (EMRs) and how well they were integrated for the intervention and decision support. Decision support included computer-based prompts and/or algorithm triggers related to the disease of interest used as part of the intervention.

Included trials gave limited descriptions of whether and how they used information technology. Half of the trials did not mention health IT or EMRs.[66-68, 72, 74] Another four trials mentioned health IT or EMR,[38, 40, 61-65, 73, 75-78, 80] but two of these did not describe in detail the specific IT features that the intervention employed. See Appendix C for trial-specific details on use of information technology for concomitant care interventions in these four trials. Finally, although one trial[79] did not report use of IT system or EMRs for delivery of concomitant care, it did report that data and safety monitoring was done electronically. The EMR was searched for an increase of 25 percent or more in a Hamilton Rating Scale for Depression (HRSD) score; this triggered a written letter to the treating physician and an offer to identify local mental health specialists and provide additional treatment advice.

Relationship Between Elements of the System in Which the Practice Operates

Financing of Care

Financing of care was not reported for six studies.[38, 40, 61-65, 67, 73, 75-80] Two trials[66, 72] reported that the study itself covered treatment costs, including medication and therapy. One trial reported that participants were reimbursed for time spent completing outcome interviews and for transportation and copays for antidepressant medications if applicable.[68] One trial reported that medical treatments for patients were financed through the U.K. (Scotland) National Health Service.[74]

Payment Arrangements

Payment arrangements include financial arrangements between primary care providers and mental health providers and may include financial resource sharing or incentives. No trial described payment arrangements.

Applicability

These findings generally apply to patients with depression and one or more medical conditions who are receiving care in settings that provide care management. Most trials occurred in the United States, so findings cannot be extended to other countries in general. Even though the systems of care were not well characterized, they likely differed considerably. How such infrastructure influences the delivery of collaborative care is not clear from our findings, and results should be considered with that in mind.

Discussion

In this report, we aimed to address the following overarching question: Among adults with chronic medical conditions and a concomitant mental health condition (such as patients with diabetes and depression) treated in the primary care setting, what is the comparative effectiveness of practice-based interventions aimed at improving the mental health condition or both the mental health and chronic medical conditions?

We broadly defined the scope of our review to include real-world scenarios and patients with clear diagnoses, representing common primary care populations. However, although studies we identified involved several coexisting medical conditions, included studies involved only a single mental health condition, depression. The variety of interventions was similarly limited. Indeed, despite an effort informed by our Technical Expert Panel to be inclusive of practice-based interventions (such as integrated care or telemedicine), the studies in our final analysis all defined their intervention as a form of collaborative care. No study compared its intervention with another intervention; rather, all did comparisons only with usual or enhanced usual care. Therefore, this discussion is based on a body of evidence comparing the effectiveness of collaborative care interventions with usual care for primary care patients with depression and one or more chronic medical conditions, and does not include any head-to-head trials.

Inclusive of a broad range of chronic medical conditions that the Agency for Healthcare Research and Quality (AHRQ) and the Institute of Medicine (IOM) have identified as being of high priority for research, we identified studies on arthritis, cancer, diabetes, heart disease, HIV, and one or more conditions. Nine studies were primary randomized controlled trials (RCTs); three studies were condition-specific subgroup analyses of a separate RCT, with the most data available on patients with diabetes. All trials except one[80] were designed to measure mental health–related outcomes, rather than medical outcomes, as the primary outcome.

Our review focuses on five main groups of outcomes: mental health outcomes (KQ 1), chronic disease medical outcomes (KQ 2), harms of interventions (KQ 3), components of interventions (KQ 4), and characteristics of practice settings in which the interventions occurred (KQ 5).

Key Findings and Strength of Evidence

Key Question 1a: Intermediate Mental Health Outcomes and Satisfaction With Care

We summarize findings and strength of evidence (SOE) for this question in Table 18. Evidence from 11 studies indicated that patients receiving a collaborative care intervention had greater improvement in depressive symptoms. Collaborative care interventions were also associated with greater depression treatment response (≥50 percent reduction in symptoms) than for those receiving usual care in 9 studies (moderate SOE). These results were consistent across medical conditions and reflect clinically meaningful changes on well-accepted measures of depression. The evidence showed that five patients would need to be treated to achieve one more depression response than would be seen with usual care at 6 months, with a number needed to treat [NNT] of six patients at 12 months. Benefits persisted, but to a lesser degree, at 18 months.

Table 18. Summary of results for collaborative care interventions compared with controls for people with depression and one or more chronic medical conditions: intermediate mental health outcomes

Outcome	Summary of Results	Strength of Evidence
Symptom improvement	Greater symptom improvement scores in intervention groups at both 6 months (SMD, 0.45; 95% CI, 0.29 to 0.61; 7 studies) and 12 months (SMD, 0.47; 95% CI, 0.29 to 0.65; 6 studies) compared with control groups. Benefits were sustained through 24 months, but the magnitude of benefit was reduced (WMD, 0.18; 95% CI, 0.10 to 0.16; 3 studies).	Moderate
Depression-free days	More depression-free days at 12 months for those in intervention groups than usual care groups (5 studies, range of differences between intervention and control groups: 20 to 59 days).	Moderate
Response (≥50% reduction)	Higher rates of depression response in intervention groups than usual care, based on 10 studies(NNT, 5 at 6 months; NNT, 6 at 12 months). Benefits persisted, but to a lesser degree, at 18 months (RD 0.12; 95% CI, 0.02 to 0.22; 3 studies).	Moderate
Remission	Remission of depression favored intervention over usual care at 6 months and at 12 months based on 3 RCTs and 2 RCT subgroup analyses (NNT, 8 at 6 months; NNT, 12.5 at 12 months). Benefits persisted at 18 months, but showed no difference between groups at 24 months.	Moderate
Recurrence	Only 1 study (of patients with cancer) addressed recurrence as an outcome, and showed no difference between groups at 18 or 24 months.	Insufficient
Treatment adherence	Mixed results: 1 trial reported significantly greater adherence to antidepressants in the intervention arm at 6 and 12 months; the other reported no difference between groups at 6 and 12 months.	Insufficient
Treatment satisfaction	Greater satisfaction with care for intervention participants than controls at 12 months (RD, 0.21 (95% CI, 0.11 to 0.30; 4 studies)[a]; . Benefits were sustained at 24 months (RD, 0.14; 95% CI, 0.06 to 0.21; 3 studies).	Moderate

[a] Results are from meta-analysis of the 4 trials that reported satisfaction for both intervention and control arms. Two additional trials reported treatment satisfaction for the intervention arm but not the usual care arm.
Abbreviations: CI = confidence interval; NA = not applicable; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference.

Although less frequently measured, patients receiving collaborative care also had more depression-free days (moderate SOE) and higher rates of depression remission (moderate SOE) compared with patients receiving usual care. Intervention patients similarly reported greater satisfaction with care (moderate SOE).

Evidence was insufficient to draw conclusions about adherence to antidepressants based on limited data and variable definitions. Of the two studies that provided adequate data on adherence, one showed significant differences between groups[77] and one did not[73]. We found insufficient data to draw conclusions about recurrence of depression (only one study[68, 71]).

Key Question 1b: Morbidity, Mortality, Quality of Life, Function, and Utilization

This question looked at other mental health outcomes, including suicide, use of antidepressants, mental health–related quality of life, use of mental health care services, sick days related to mental health, and employment stability (Table 19). Only one suicide was reported, in the usual care arm of a cancer trial.[74] In a second trial, investigators reported that they were unaware of any attempted or completed suicides in either treatment group.[68] Meta-analyses from three studies[61, 73, 79] at 6 months showed no difference in antidepressant use between groups, with a clear outlier in the HIV study (see Appendix E). Five studies[61, 64, 65, 67, 68, 73] at 12 months showed that the use of antidepressants was greater in collaborative care arms than in control groups across populations with various chronic medical conditions; we removed

the HIV study in sensitivity analysis (low SOE). Quality of life was measured in several ways but most frequently using the mental component of the Medical Outcomes Study Short-Form (SF-12), showing that collaborative care interventions achieved greater quality of life scores than usual care at 6 and 12 months (moderate SOE). Five studies[38, 61, 62, 67-69, 71] reported on mental health care utilization; each showed greater use of any mental health services at 6 or 12 months (or both) by those receiving the collaborative care intervention, and one as-treated sample of patients with cancer[61] showed that this trend persisted at 18, but not 24 months (low SOE). No data were available on sick days or employment stability (insufficient SOE).

Table 19. Summary of results for collaborative care interventions compared with controls for people with depression and one or more chronic medical conditions: other mental health outcomes

Outcome	Summary of Results	Strength of Evidence
Suicide	One study reported one suicide in the usual care group.	Insufficient
Use of anti-depressants	Greater antidepressant use for collaborative care interventions than for usual care at 12 months (RD, 0.23; 95% CI, 0.15 to 0.30; 5 studies[a]), but not 6 months (RD, 0.09; 95% CI, -0.02 to 0.20; 3 studies).	Low
MH-related quality of life	Greater mental health–related quality of life for patients in collaborative care intervention arms than usual care at 6 and 12 months using the mental component of the Medical Outcomes Study Short Form (WMD, 2.98; 95% CI, 1.41 to 4.56 at 12 months; 4 studies).	Moderate
MH care utilization	Greater use of any mental health services for collaborative care interventions than for usual care at 6 and/or 12 months (42% to 97% vs. 16% to 57% for intervention and control groups, respectively; based on 8studies).	Low
MH-related sick days	Not reported	Insufficient
MH-related employment stability	Not reported	Insufficient

[a] Results of the meta-analysis excluding the HITIDES data

Abbreviations: CI = confidence interval; HITIDES = HIV Implementation of Translating Initiatives for Depression; MH = mental health; mths = months; NA = not applicable; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference.

Key Question 2a: Intermediate Chronic Medical Outcomes

For this question, we were interested in the effects of collaborative care interventions on intermediate outcomes for the specified chronic medical condition(s). For most chronic medical conditions of interest here, we found just one study (Table 20). We found multiple studies of people with diabetes and depression.

HbA1c was reported as a measure of response in four studies of people with diabetes; baseline HbA1c ranged from 7.28 percent to 9.03 percent. Our meta-analyses found no significant differences between intervention and control groups (weighted mean difference [WMD], 0.13; 95% CI, -0.55 to 0.41 at 6 months; three studies; WMD, 0.24; 95% CI, -0.14 to 0.62 at 12 months; three studies). In the single study that measured it (Ell 2011), the finding of no difference between groups persisted at 18 and 24 months (moderate SOE). However, the only study to use HbA1c as a predefined outcome measure, the TEAMcare study,[80] reported significant differences in HbA1c. The figures were as follows for intervention versus control groups: 8.14 versus 8.04 at baseline; 7.42 versus 7.87 at 6 months; and 7.33 versus 7.81 at 12 months (overall $p<0.001$). Ell and colleagues[69] reported 18- and 24-month data on HbA1c,

showing no difference between groups, with an overall mean difference at 24 months of 0.23 (95% CI, -0.34 to 0.81).

Three studies reported on adherence to recommended treatment.[64, 77, 80] Patients in the collaborative care intervention were no more likely than controls to adhere to a generally healthy diet (moderate SOE), and they were no more likely to adhere to an exercise program in two of three studies[64, 77, 80] (low SOE). For rates of adherence to an overall regimen (including oral hypoglycemics, lipid-lowering agents, and angiotensin-converting enzyme inhibitors), evidence was insufficient to draw conclusions. A summary of diabetes self-care based on a measure of overall self-reported adherence was reported by one study, and showed no difference between groups at 12,18, or 24 months.[67, 69] They similarly showed no difference between groups in diabetic complications for these same time frames.

Data were insufficient to draw conclusions about treatment satisfaction with care for chronic medical conditions.

Table 20. Summary of results for collaborative care interventions compared with controls for people with depression and one or more chronic medical conditions: intermediate chronic medical outcomes

Outcome	Summary of Results	Strength of Evidence
Symptom improvement		
Arthritis: pain	Insufficient evidence from 1 subgroup analysis to draw conclusions.	Insufficient
HIV: symptom severity	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
Response		
Diabetes: HbA1c	Meta-analysis of 4 studies showed no between-group differences at 6 or 12 months. A single study[69] showed no difference between groups at 18 and 24 months.	Moderate
Heart disease: ≥10 mmHg decrease in SBP	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
Adherence		
Cancer: followed treatment	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
Diabetes: diet	Not calculated; no between-group difference at any time points in all studies examined.	Moderate
Diabetes: exercise	3 of 3 trials found no difference between groups at 6 months; of these same trials, 2 of 3 found no difference at 12 months.	Low
Diabetes: medications	Insufficient evidence from 2 studies to draw conclusions.	Insufficient
HIV: medications	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient
Satisfaction with care		
Diabetes, heart disease, or both	Insufficient evidence from 1 RCT to draw conclusions.	Insufficient

Abbreviations: CI = confidence interval; mmHg = millimeters of mercury; OR = odds ratio; RCT = randomized controlled trial; SBP = systolic blood pressure; WMD = weighted mean difference.

Key Question 2b: General Health Outcomes and Costs

General health outcomes of interest included condition-specific morbidity, mortality, health care utilization, and quality of life. All evidence was insufficient to draw conclusions other than for mortality and quality of life (Table 21).

All but one study[72] reported on mortality and few deaths were reported overall. Most were in studies of people with cancer. Intervention and control patients did not differ in mortality at 6

months (risk difference [RD], 0.00; 95% CI, -0.02 to 0.02; seven studies) or 12 months (RD, 0.00; 95% CI, -0.02 to 0.01; seven studies) (moderate SOE). Patients receiving collaborative care interventions generally experienced greater quality of life than control patients at 6 and 12 months, based on several different measures from six studies (moderate SOE).

Table 21. Strength of evidence for collaborative care interventions for people with depression and one or more chronic medical conditions: KQ 2b, general health outcomes and costs

Outcome	Summary of Results	Strength of Evidence
Condition-specific morbidity	Insufficient evidence from 1 RCT (post-CABG) and 1 subgroup analysis (arthritis) to draw conclusions.	Insufficient
Mortality	8 studies reported no difference between groups, with few overall events; 6 months: RD, 0.00 (95% CI, -0.02 to 0.02); 12 months: RD, 0.00 (95% CI, -0.02 to 0.01).	Moderate
Health care utilization	Data were insufficient to draw conclusions about use of health care services.	Insufficient
Quality of life	Greater quality of life for those receiving collaborative care at 6 and 12 months, based on several different measures.	Moderate
Cost of intervention	Data were insufficient because of heterogeneity in the ways in which cost was reported. Using a crude estimate because of such heterogeneity, for the 6 trials that reported data, the average cost of the intervention per patient was $705.00. Individual studies measured other aspects of cost that are detailed in Appendix C, but were not amenable to pooling.	Insufficient

Abbreviations: CABG = coronary artery bypass graft; CI = confidence interval; RCT = randomized controlled trial; RD = risk difference.

Key Question 3: Harms

Very few data were reported on harms, leaving insufficient evidence to draw conclusions. Only the TEAMcare study, in patients with depression, diabetes, and/or heart disease,[80] defined adverse events (AEs); the investigators reported higher rates of mild AEs (e.g., medication side effects) and of moderate AEs (e.g., falls) in the intervention arm. These could be attributed to increased rates of medication adjustment related to the collaborative care intervention. Additionally, patients in the intervention arm had more frequent contacts with the care manager and thus had more opportunities to report AEs, so findings might be the result of detection bias.

Key Question 4: Characteristics of Service Interventions

All interventions were described as collaborative care interventions; we found no study with any other types of practice-based interventions that met our inclusion/exclusion criteria.

The summary finding was that collaborative care hinged on the role of care manager, whose training and expertise varied widely. A physician (11 of 12 were psychiatrists) supervised care; a form of stepped care, patient preferences for treatment, and self-management were central to most interventions. Table 17 (in the Results chapter presentation above for KQ 4) shows the detailed comparisons.

The TEAMcare study[80] was the most original in its design. Its investigators had a goal not just of reducing depression, but also controlling risk factors for various diseases simultaneously using a nurse to support guideline-concordant care.

Key Question 5: Characteristics of the Practice Setting

Given that characteristics of the practice setting often determine the feasibility of implementing interventions, we were interested in assessing similarities and differences. Eleven

of 12 studies were conducted in the United States (1 of those in Puerto Rico); 1[74] took place in the United Kingdom. Overall, practice setting characteristics (e.g., location, practice type and size, open/closed system, level of integration, payer mix and payer type, service mix, information technology) and system characteristics (e.g., financing of care and payment arrangements) were rarely reported. We categorized the system as open (no membership or eligibility required) in 6 trials [66-68, 72, 74, 79] and closed in 3 trials.[38, 40, 73, 75-78, 80] Closed systems were generally self-contained; in this evidence base, they included Group Health Cooperative and the VA system, where an array of services was accessible to patients who were members of these organizations. This latter factor may be important for applicability because of the nature of collaborative care and its focus on coordination, which is arguably easier in a closed than in an open system of care.

Findings in Relationship to What Is Already Known

Our findings reinforce the evidence for the effectiveness of collaborative care interventions for treating depression in primary care.[37] Moreover, they add a level of detail that had previously not been systematically reviewed. We selected trials that required the diagnosis of one or more chronic medical conditions (rather than generic primary care samples), and we reported on both the depression and the chronic medical outcomes. This review also extended the parameters of primary care to include settings in which certain patients with chronic disease receive the majority of their care. We found that recipients of collaborative care had significantly greater improvement in depression outcomes as compared with patients receiving usual care, for people with arthritis, cancer, diabetes, heart disease, and HIV.

Although the relationship between depression and chronic disease is established,[30, 94, 95] the extent to which successful treatment of depression improves chronic medical conditions remains unknown. Our review shows that investigators are beginning to examine these outcomes, particularly in diabetes, although largely as secondary outcomes and with negative or inconclusive data at present. We excluded some relevant studies because of short duration of followup[96] or because the treatment occurred outside the purview of a primary care–like setting.[97-99] However, our inability to answer the basic question posed by a primary care provider ―Will treating my patient's depression (with an evidence-based collaborative care program) improve their medical conditions?" was both surprising and disappointing.

One study in the review, TEAMcare,[80] is an exception because it identified markers of disease risk for multiple conditions as primary outcomes. Using a guideline-based ―treat-to-target" approach delivered by a medically trained nurse, these investigators targeted patients with poorly controlled diabetes, coronary artery disease, or both and coexisting depression; their aim was to reduce overall risk factors. This approach is a detour from the traditional model, in which the focus is on collaborative care of depression, presumably in the hope that treating depression will improve overall health. Perhaps partly because of the benefits of having an integrated health care system, TEAMcare recipients showed clear improvements not only in depression, but also in reducing HbA1c and systolic blood pressure to target goals.

Implementation, Dissemination, and Role of Decisionmakers

Despite evidence for the use of collaborative depression care in primary care settings, and a recommendation from the President's New Freedom Commission on Mental Health,[100] uptake of such interventions has been poor. Although financial and system barriers have been identified,[101] it is still unclear why decisionmakers have not advocated for the dissemination of collaborative depression care. One reason may be that in our current system, primary care providers have little

incentive to find and treat mental health problems. Should a model of accountable care[42] be adopted, in which one bundled payment must suffice for the breadth of necessary care, a focus on concomitant mental health conditions will align incentives in a way that gives priority to dissemination of proven programs. Once incentivized to keep people well, primary care providers may also find new motivation for gaining proficiency in mental health care.[102] Inherent in any new model of payment will be the discussion of both absolute costs and the cost-effectiveness of such interventions—neither of which topics had comprehensive data or were a central focus of this report.

This review adds further evidence supporting the effectiveness of collaborative care interventions. We show that patients with multiple and specific medical conditions can achieve improvement in depression (moderate SOE), satisfaction with care (moderate SOE), and mental and physical quality of life (moderate SOE).

Stakeholders for improving the quality of primary care can apply the findings in this review from several perspectives. One way these data might be used and further disseminated is in measuring quality, for instance, to meet new standards for the Patient-Centered Medical Home.[43]

Applicability

Our findings are generally applicable to primary care patients with depression and at least one chronic medical condition, but they may not apply to patients with multiple chronic conditions. The average age across studies was 59, an age group likely to have chronic disease. For that reason, we cannot speak directly to the relevance of these results to young adults with chronic disease. People of Hispanic origin (predominantly female)[66-68] and male veterans[73] were represented and appeared to respond similarly across outcomes, but there were too few data to analyze separately. Reported studies used clinically meaningful measures and had study durations (at least 6 months) that provided a real-world context.

Although these trials represented several settings, including primary care–like cancer and HIV clinics, they all had in common a care manager who directed the intervention. The intermediate mental health outcomes achieved might, therefore, apply only to settings that can accommodate and afford to provide such services. Although we did not attempt, as others have, to identify "key ingredients" of collaborative care such as training background of team members,[41] our report suggests that the complexion of teams and their types of training may afford some flexibility.

Limitations of the Comparative Effectiveness Review Process

Outlining the scope of this evidence review posed a challenge in regard to defining the interventions of interest. With input from our Key Informants and members of our Technical Expert Panel, we ultimately arrived at the term "practice-based" to differentiate interventions relative to this review from person-level interventions such as medications or stand-alone psychotherapies. We did not find the term practice-based in the literature, but we used other eligibility criteria and some known interventions to inform our searches. Even though we also added the terms "collaborative care," "integrated care," and "telemedicine" to guide our search, we may have missed relevant interventions that are not indexed in these categories. However, we included a general intervention term (see Appendix A) that should have identified studies that were not found using the more specific terms.

We also recognize that limiting the eligibility to trials of patients with clear medical diagnoses may have missed some potentially relevant work. One example is a recent RCT of a

novel intervention for patients with anxiety conducted in the primary care setting;[103] the trial did not require a coexisting medical condition.

We chose to exclude studies without comparison groups because of the potential risk of bias in such studies (especially the risk of selection bias and confounding). We recognize that studies without comparison groups can sometimes identify important information, but for the purposes of our questions we generally consider such studies to provide hypothesis-generating information, rather than valid evidence to answer our questions. The purpose of this review was not to uncover hypothesis-generating information, but rather to find evidence with sufficiently low risk of bias to provide more definitive answers to the KQs. The number of potential known confounders is substantial for the questions we addressed in this review (and there may always be additional unknown confounders). Thus, we believe that the risk of bias in studies without comparison groups is too high to provide reliable evidence to answer our KQs. Note, however, that important and innovative systems efforts in the fields of mental health and primary care[104] may be overlooked using these methods.

Limitations of the Evidence Base

Few relevant trials reported medical outcomes specifically. We also acknowledge significant heterogeneity among conditions (e.g., cancer is different from diabetes). Only 1 of our 12 studies[80] was specifically designed to answer KQ 2a about intermediate medical outcomes. The remainder aimed to look at mental health outcomes in patients with different medical conditions.

We had no head-to-head trials in our report; this meant that we could make comparisons only with usual or enhanced usual care. We had only one study from outside the United States, highlighting the lack of similar literature from other countries. Although we characterized the components of the interventions, we could not evaluate quantitatively the determinants of effectiveness (i.e., ~~"a~~ctive ingredients"[41]). This was not the intention of the review but highlights the difficulty in synthesizing data on complex interventions.

Also, note that studies did not necessarily screen for mental health comorbidities (such as substance abuse), which may have negatively influenced medical outcomes, particularly related to self-care activities. A completely unexplored area is personality disorders, which are pervasive by nature and can prove a barrier to achieving therapeutic goals.[105]

Research Gaps

Depression Treatment and Outcomes of Chronic Disease

Depression can negatively affect general medical illness, but we do not know whether the effective treatment of depression in the primary care setting can alter the course of chronic disease. Is it that treating depression isn't enough to improve medical outcomes, or that we need more innovative interventions that do not just focus on depression? The TEAMcare approach offers an example, in which treatment goals included targets for all relevant diseases and individualized approaches to reach these targets. Designing, implementing, and sustaining such approaches will not be without considerable challenge, and studies will require larger sample sizes, longer time frames, and, optimally, higher levels of joint funding from multiple institutes more used to focusing on one disease.

Our report identified outcomes mostly for single medical conditions, which does not necessarily reflect real-world primary care patients that may have multiple comorbidities. Trials involving other medical conditions not represented here, such as lung disease or pain syndromes,

could be informative as an incremental approach, but perhaps what the field needs most to understand is what models of care work best for patients with common clusters of disease in primary care. One possible cluster could be diabetes, hypertension, and obesity, concomitant with depression; this group may be particularly salient given the probable role of vascular disease in late-onset depression.[106, 107] More generally, the bidirectional aspect of depression and medical illness needs further exploration. For example, investigators could usefully explore whether effectively improving vascular risk factors reduces depression.

Other Mental Health Conditions

This report did not identify relevant evidence for practice-based interventions targeting common disorders known to be prevalent and problematic in primary care, including anxiety spectrum, psychotic disorders, substance disorders, and cognitive disorders. It is unclear whether interventions for each of these needs to be studied in isolation with related medical conditions, or perhaps a more broad-based approach might make sense. Instead of the current reductionist approach of screening for one mental health condition at a time, it might be possible to screen broadly[108] and develop and tailor an intervention accordingly, with a core set of features that could be adapted as necessary. Psychotic disorders such as schizophrenia deserve special attention owing to the significant early mortality seen in this group,[109] although many patients with such disorders do not come to primary care. Reverse ~~–e~~o-location,"[110] in which a primary care doctor comes to a mental health setting, may be a preferred arrangement and should be explored. Such studies should focus on prevention and early intervention for medical conditions, to help discern whether downstream morbidity can be avoided.

Head-to-Head Trials

It is noteworthy that we identified no studies of co-location or integrated care in this review, and disappointing that we found no-head-head trials of various approaches. Head-to-head trials of practice-based interventions should be considered; these might include collaborative care versus mental health co-location, or another model of integrated care versus collaborative care. Given the desire to find the active ingredients of practice-based care,[41] we should test variations of existing efficacious models. Certain components of the collaborative care model may be more salient than others, and future studies that explicitly compare intervention components within the collaborative care model may help address this issue. For example, head-to-head comparisons of telephone-based versus face-to-face approaches might be useful. Examining session frequency and/or study intensity (i.e., frequency plus duration) as a predictor of outcome within these two approaches may also prove fruitful.

Exploring the extent to which mental health and physical health outcomes are related to the intervention provider's training is another important issue; that could entail determining whether, for instance, outcomes improve by having a depression care specialist deliver the intervention rather than a provider not trained in mental health.

Answering some of these basic design questions in ways that facilitate comparisons with true interventions, and not simply usual care, will eventually facilitate translation and implementation of these approaches on a broader scale.

Conclusions

In primary care patients with depression and one or more specific chronic medical condition, collaborative care interventions achieved improvement in depression symptoms, response,

remission, and depression-free days (moderate SOE); satisfaction with care (moderate SOE); and mental and physical quality of life (moderate SOE). These improvements were consistent across different common chronic medical conditions. Patients with diabetes receiving collaborative care had no difference in HbA1c (low SOE). To determine the relative benefit of implementing collaborative care programs for depression (or other mental health conditions) on overall health, we need studies designed to measure the effectiveness of practice-based interventions on medical outcomes. Future investigations should compare variations of such interventions in head-to-head trials to discern best models of care. They should also move from addressing single medical conditions to common clusters of disease and, similarly, broaden the net for mental health conditions beyond depression.

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Appendix A. Search Strategy

Initial Searches performed 23 May 2011

MEDLINE®:

Search	Most Recent Queries	Result
#1	Search "depressive disorder"[MeSH Terms] OR "depressive disorder"[tiab] OR "depression"[MeSH Terms]	127175
#2	Search "anxiety disorders"[MeSH Terms] OR "anxiety disorders"[tiab] OR "anxiety disorder"[tiab] OR "anxiety"[MeSH Terms]	101286
#3	Search #1 OR #2	203606
#4	Search #3 Limits: Humans, English	164381
#5	Search "arthritis"[MeSH Terms]	177086
#6	Search #4 AND #5	853
#7	Search "diabetes mellitus"[MeSH Terms] OR "diabetes"[tiab]	354545
#8	Search #4 AND #7	2313
#9	Search (chronic[tiab] AND "pain"[MeSH Terms]) OR "chronic pain"[tiab]	35695
#10	Search #4 AND #9	1988
#11	Search "cancer"[tiab]	813675
#12	Search #4 AND #11	4187
#13	Search "asthma"[MeSH Terms] OR "asthma"[tiab] OR "pulmonary disease, chronic obstructive"[MeSH Terms] OR “chronic obstructive pulmonary disease”[tiab] OR "COPD"[tiab]	142817
#14	Search #4 AND #13	1190
#15	Search "stroke"[MeSH Terms]	63078
#16	Search #4 AND #15	1050
#17	Search "HIV"[MeSH Terms]	69536
#18	Search #4 AND #17	111
#19	Search "heart failure"[MeSH Terms] OR "heart failure"[tiab]	113507
#20	Search #4 AND #19	669
#21	Search "myocardial ischaemia"[tiab] OR "myocardial ischemia"[MeSH Terms] OR "myocardial ischemia"[tiab]	320571
#22	Search #4 AND #21	2328
#23	Search "coronary artery bypass"[tiab] OR "CABG"[tiab]	28137
#24	Search #4 AND #23	246
#25	Search "status post" AND myocardial	29
#26	Search #4 AND #25	2
#27	Search "frail elderly"[MeSH Terms] OR "frail elderly"[All Fields]	5867
#28	Search #4 AND #27	280
#29	Search complex patient*	890
#30	Search #4 AND #29	10
#31	Search #6 OR #8 OR #10 OR #12 OR #14 OR #16 OR #18 OR #20 OR #22 OR #24 OR #26 OR #28 OR #30	14022
#32	Search "Intervention Studies"[MeSH Terms] OR intervention*[tiab]	409254
#33	Search "collaborative care"[tiab]	642
#34	Search "integrated treatment"[tiab] OR "clinical integration"[tiab] OR "integrated services"[tiab] OR "integrated care"[tiab] OR "integrated health care"[tiab]	2743
#35	Search "integrated"[tiab] and "behavioral model"[tiab]	16
#36	Search "service coordination"	105
#37	Search "chronic disease management"	711
#38	Search "coordinated care"	447
#39	Search #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38	412959
#40	Search #31 AND #39	2206

Search	Most Recent Queries	Result
#41	Search ("Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[MeSH]) OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	446111
#42	Search #40 AND #41	598
#43	Search "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields]	47698
#44	Search #40 AND #43	39
#45	Search "review"[Publication Type] OR "review literature as topic"[MeSH Terms] OR "systematic review"[All Fields]	1604853
#46	Search #40 AND #45	379
#47	Search "Comparative Study"[Publication Type]	1512315
#48	Search #40 AND #47	234
#49	Search #42 OR #44 OR #46 OR #48"	1078
#51	Search #40 Limits: Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comparative Study, Evaluation Studies, Multicenter Study	870
#52	Search #49 OR #51	1235

Cochrane Library:

ID	Search	Hits
#1	"depressive disorder"[MeSH Terms] OR "depressive disorder"[tiab] OR "depression"[MeSH Terms]	27842
#2	"anxiety disorders"[MeSH Terms] OR "anxiety disorders"[tiab] OR "anxiety disorder"[tiab] OR "anxiety"[MeSH Terms]	17159
#3	(#1 OR #2)	38401
#4	"arthritis"[MeSH Terms]	8026
#5	"diabetes mellitus"[MeSH Terms] OR "diabetes"[tiab]	21190
#6	(chronic[tiab] AND "pain"[MeSH Terms]) OR "chronic pain"[tiab]	7478
#7	"cancer"[tiab]	63095
#8	"asthma"[MeSH Terms] OR "asthma"[tiab] OR "pulmonary disease, chronic obstructive"[MeSH Terms] OR "chronic obstructive pulmonary disease"[tiab] OR "COPD"[tiab]	26210
#9	"stroke"[MeSH Terms]	25211
#10	"HIV"[MeSH Terms]	9517
#11	"heart failure"[MeSH Terms] OR "heart failure"[tiab]	9329
#12	"myocardial ischaemia"[tiab] OR "myocardial ischemia"[MeSH Terms] OR "myocardial ischemia"[tiab]	2932
#13	"coronary artery bypass"[tiab] OR "CABG"[tiab]	6474
#14	"status post" AND myocardial	5
#15	"frail elderly"[MeSH Terms] OR "frail elderly"[All Fields]	605
#16	(#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)	168623
#17	(#3 AND #16)	5834
#18	"Intervention Studies"[MeSH Terms]	2571
#19	"collaborative care"[tiab]	194
#20	"integrated treatment"[tiab] OR "clinical integration"[tiab] OR "integrated services"[tiab] OR "integrated care"[tiab] OR "integrated health care"[tiab]	291
#21	"integrated"[tiab] and "behavioral model"[tiab]	0
#22	"service coordination"	6
#23	"chronic disease management"	79
#24	"coordinated care"	43
#25	(#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24)	3145
#26	(#17 AND #25)	209
#27	("Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[MeSH]) OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	341441

ID	Search	Hits
#28	"meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields]	17038
#29	"review"[Publication Type] OR "review literature as topic"[MeSH Terms] OR "systematic review"[All Fields]	94139
#30	"Comparative Study"[Publication Type]	135576
#31	(#27 OR #28 OR #29 OR #30)	438947
#32	(#26 AND #31)	204
#33	"Humans"[MeSH]	424963
#34	(#32 AND #33)	175

EMBASE:

ID	Search	Results
1	'anxiety disorder'/exp OR 'anxiety'/exp OR 'depression'/exp	382806
2	'arthritis'/exp OR 'diabetes mellitus'/exp OR 'chronic pain'/exp OR 'neoplasm'/exp OR 'asthma'/exp OR 'chronic obstructive lung disease'/exp OR 'stroke'/exp OR 'human immunodeficiency virus'/exp OR 'heart failure'/exp OR 'heart muscle ischemia'/exp OR 'coronary artery bypass graft'/exp OR 'frail elderly'/exp OR 'complex patient' OR ('status post' AND myocardial)	4346558
3	#1 AND #2	43721
4	'intervention study'/exp OR 'collaborative care' OR 'integrated treatment' OR 'clinical integration' OR 'integrated services' OR 'integrated health care' OR 'integrated care' OR 'integrated behavioral model' OR 'patient care planning'/exp	43591
5	#3 AND #4	354
6	#5 AND [humans]/lim AND [english]/lim AND ([embase]/lim OR [embase classic]/lim)	250

PsycINFO & CINAHL:

#	Query	Last Run Via	Results
S1	(MH "Anxiety+") OR (MH "Anxiety Disorders+") OR (MH "Depression+") OR "depressive disorder"	Interface - EBSCOhost Search Screen - Advanced Search Database - PsycINFO;CINAHL with Full Text	60953
S2	(MH "Arthritis+") OR (MH "Chronic Pain") OR (MH "Neoplasms+") OR (MH "Diabetes Mellitus+") OR (MH "Asthma+") OR (MH "Pulmonary Disease, Chronic Obstructive+") OR (MH "Stroke") OR (MH "Human Immunodeficiency Virus+") OR (MH "Heart Failure+") OR (MH "Myocardial Ischemia+") OR (MH "Coronary Artery Bypass+") OR (MH "Frail Elderly") OR "frail elderly" OR “complex patient”	Interface - EBSCOhost Search Screen - Advanced Search Database - PsycINFO;CINAHL with Full Text	305296
S3	S1 and S2	Interface - EBSCOhost	6787

#	Query	Last Run Via	Results
		Search Screen - Advanced Search Database - PsycINFO;CINAHL with Full Text	
S4	"intervention studies" OR "collaborative care" OR "integrated treatment" OR "clinical integration" OR "integrated services" OR (MH "Health Care Delivery, Integrated") OR (MH "Integrative Medicine") OR "integrated care" OR "integrated behavioral model" OR "integratd health care" OR (MH "Patient Care")	Interface - EBSCOhost Search Screen - Advanced Search Database - PsycINFO;CINAHL with Full Text	17848
S5	S3 and S4	Interface - EBSCOhost Search Screen - Advanced Search Database - PsycINFO;CINAHL with Full Text	83

Total number of records before duplicates removed: 1743

Search of clinicaltrials.gov performed 13 December 2011:

Collaborative care | interventional studies | "Anxiety Disorders"	**16**
Collaborative care | interventional studies | "Depression"	59
Integrated treatment | interventional studies | "Depression"	6
Clinical integration| interventional studies | "Depression"	0
Integrated services | interventional studies | "Depression"	3
Integrated care | interventional studies | "Depression"	1
Integrated health care | interventional studies | "Depression"	0
Integrated | interventional studies | "Depression"	37
Behavioral model| interventional studies | "Depression"	0
Service coordination | interventional studies | "Depression"	0
Chronic disease management | interventional studies | "Depression"	0
Coordinated care | interventional studies | "Depression"	1
Total, including duplicates	123
Total, minus duplicates	100

The following update searches were performed on 19 December 2011

MEDLINE®:

Search	Query	Items found
#1	Search "depressive disorder"[MeSH Terms] OR "depressive disorder"[tiab] OR "depression"[MeSH Terms]	131868
#2	Search "anxiety disorders"[MeSH Terms] OR "anxiety disorders"[tiab] OR "anxiety disorder"[tiab] OR "anxiety"[MeSH Terms]	105172
#3	Search #1 OR #2	210976
#4	Search #3 Limits: Humans, English	170496
#5	Search "arthritis"[MeSH Terms]	181036
#6	Search #4 AND #5	892
#7	Search "diabetes mellitus"[MeSH Terms] OR "diabetes"[tiab]	368549

Search	Query	Items found
#8	Search #4 AND #7	2457
#9	Search (chronic[tiab] AND "pain"[MeSH Terms]) OR "chronic pain"[tiab]	37227
#10	Search #4 AND #9	2091
#11	Search "cancer"[tiab]	852198
#12	Search #4 AND #11	4434
#13	Search "asthma"[MeSH Terms] OR "asthma"[tiab] OR "pulmonary disease, chronic obstructive"[MeSH Terms] OR “chronic obstructive pulmonary disease”[tiab] OR "COPD"[tiab]	147430
#14	Search #4 AND #13	1254
#15	Search "stroke"[MeSH Terms]	66379
#16	Search #4 AND #15	1111
#17	Search "HIV"[MeSH Terms]	71832
#18	Search #4 AND #17	113
#19	Search "heart failure"[MeSH Terms] OR "heart failure"[tiab]	117943
#20	Search #4 AND #19	706
#21	Search "myocardial ischaemia"[tiab] OR "myocardial ischemia"[MeSH Terms] OR "myocardial ischemia"[tiab]	327670
#22	Search #4 AND #21	2431
#23	Search "coronary artery bypass"[tiab] OR "CABG"[tiab]	29033
#24	Search #4 AND #23	261
#25	Search "status post" AND myocardial	31
#26	Search #4 AND #25	2
#27	Search "frail elderly"[MeSH Terms] OR "frail elderly"[All Fields]	6165
#28	Search #4 AND #27	289
#29	Search complex patient*	964
#30	Search #4 AND #29	12
#31	Search #6 OR #8 OR #10 OR #12 OR #14 OR #16 OR #18 OR #20 OR #22 OR #24 OR #26 OR #28 OR #30	14766
#32	Search "Intervention Studies"[MeSH Terms] OR intervention*[tiab]	433876
#33	Search "collaborative care"[tiab]	712
#34	Search "integrated treatment"[tiab] OR "clinical integration"[tiab] OR "integrated services"[tiab] OR "integrated care"[tiab] OR "integrated health care"[tiab]	2927
#35	Search "integrated"[tiab] and "behavioral model"[tiab]	17
#36	Search "service coordination"	109
#37	Search "chronic disease management"	778
#38	Search "coordinated care"	479
#39	Search #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38	437827
#40	Search #31 AND #39	2373
#41	Search ("Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[MeSH]) OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	463648
#42	Search #40 AND #41	645
#43	Search "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields]	51984
#44	Search #40 AND #43	48
#45	Search "review"[Publication Type] OR "review literature as topic"[MeSH Terms] OR "systematic review"[All Fields]	1655861
#46	Search #40 AND #45	404
#47	Search "Comparative Study"[Publication Type]	1545102
#48	Search #40 AND #47	241
#49	Search #42 OR #44 OR #46 OR #48	1152
#50	Search #40 Limits: Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comparative Study, Evaluation Studies, Multicenter Study	932
#51	Search #49 OR #50	1320
#52	Search ("2011/03/01"[Date - Entrez] : "3000"[Date - Entrez]) AND #51	59

Cochrane Library:

ID	Search	Hits
#1	"depressive disorder"[MeSH Terms] OR "depressive disorder"[tiab] OR "depression"[MeSH Terms]	28481
#2	"anxiety disorders"[MeSH Terms] OR "anxiety disorders"[tiab] OR "anxiety disorder"[tiab] OR "anxiety"[MeSH Terms]	17664
#3	(#1 OR #2)	39261
#4	"arthritis"[MeSH Terms]	8019
#5	"diabetes mellitus"[MeSH Terms] OR "diabetes"[tiab]	21797
#6	(chronic[tiab] AND "pain"[MeSH Terms]) OR "chronic pain"[tiab]	7913
#7	"cancer"[tiab]	63979
#8	"asthma"[MeSH Terms] OR "asthma"[tiab] OR "pulmonary disease, chronic obstructive"[MeSH Terms] OR "chronic obstructive pulmonary disease"[tiab] OR "COPD"[tiab]	26579
#9	"stroke"[MeSH Terms]	25845
#10	"HIV"[MeSH Terms]	9681
#11	"heart failure"[MeSH Terms] OR "heart failure"[tiab]	9484
#12	"myocardial ischaemia"[tiab] OR "myocardial ischemia"[MeSH Terms] OR "myocardial ischemia"[tiab]	2952
#13	"coronary artery bypass"[tiab] OR "CABG"[tiab]	6519
#14	"status post" AND myocardial	7
#15	"frail elderly"[MeSH Terms] OR "frail elderly"[All Fields]	588
#16	(#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)	170814
#17	(#3 AND #16)	6180
#18	"Intervention Studies"[MeSH Terms]	2728
#19	"collaborative care"[tiab]	218
#20	"integrated treatment"[tiab] OR "clinical integration"[tiab] OR "integrated services"[tiab] OR "integrated care"[tiab] OR "integrated health care"[tiab]	323
#21	"integrated"[tiab] and "behavioral model"[tiab]	1
#22	"service coordination"	7
#23	"chronic disease management"	96
#24	"coordinated care"	51
#25	(#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24)	3353
#26	(#17 AND #25)	280
#27	("Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[MeSH]) OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	350583
#28	"meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields]	18223
#29	"review"[Publication Type] OR "review literature as topic"[MeSH Terms] OR "systematic review"[All Fields]	100203
#30	"Comparative Study"[Publication Type]	138150
#31	(#27 OR #28 OR #29 OR #30)	452959
#32	(#26 AND #31)	274
#33	"Humans"[MeSH]	419855
#34	(#32 AND #33)	245
#35	(#34), in 2011	65

EMBASE:

ID	Search	Results
1	'anxiety disorder'/exp OR 'anxiety'/exp OR 'depression'/exp	404,850
2	'arthritis'/exp OR 'diabetes mellitus'/exp OR 'chronic pain'/exp OR 'neoplasm'/exp OR 'asthma'/exp OR 'chronic obstructive lung disease'/exp OR 'stroke'/exp OR 'human immunodeficiency virus'/exp OR 'heart failure'/exp OR 'heart muscle ischemia'/exp OR 'coronary artery bypass graft'/exp OR 'frail elderly'/exp OR 'complex patient' OR ('status post' AND myocardial)	4,581,284
3	#1 AND #2	47,583
4	'intervention study'/exp OR 'collaborative care' OR 'integrated treatment' OR 'clinical integration' OR 'integrated services' OR 'integrated health care' OR 'integrated care' OR 'integrated behavioral model' OR 'patient care planning'/exp	46,634
5	#3 AND #4	423
6	#5 AND [humans]/lim AND [english]/lim AND ([embase]/lim OR [embase classic]/lim) AND [1-3-2011]/sd NOT [31-12-2011]/sd	75

PsycINFO & CINAHL:

#	Query	Results
S1	(MH "Anxiety+") OR (MH "Anxiety Disorders+") OR (MH "Depression+") OR "depressive disorder"	65947
S2	(MH "Arthritis+") OR (MH "Chronic Pain") OR (MH "Neoplasms+") OR (MH "Diabetes Mellitus+") OR (MH "Asthma+") OR (MH "Pulmonary Disease, Chronic Obstructive+") OR (MH "Stroke") OR (MH "Human Immunodeficiency Virus+") OR (MH "Heart Failure+") OR (MH "Myocardial Ischemia+") OR (MH "Coronary Artery Bypass+") OR (MH "Frail Elderly") OR "frail elderly" OR “complex patient”	327543
S3	S1 and S2	7365
S4	"intervention studies" OR "collaborative care" OR "integrated treatment" OR "clinical integration" OR "integrated services" OR (MH "Health Care Delivery, Integrated") OR (MH "Integrative Medicine") OR "integrated care" OR "integrated behavioral model" OR "integratd health care" OR (MH "Patient Care")	19346
S5	S3 and S4 Limiters - Published Date from: 20110301-20120131	5

Total number of records before duplicates removed: 204

Handsearches of the following references yielded 111 additional records:

Bower P, Gilbody S, Richards D, et al. Collaborative care for depression in primary care. Making sense of a complex intervention: systematic review and meta-regression (Structured abstract). British Journal of Psychiatry. 2006(6):484-93. PMID: DARE-12006008459.

Katon WJ, Seelig M. Population-based care of depression: team care approaches to improving outcomes. J Occup Environ Med. 2008 Apr;50(4):459-67. PMID: 18404019.

van der Feltz-Cornelis CM, Nuyen J, Stoop C, et al. Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes mellitus: a systematic review and meta-analysis. Gen Hosp Psychiatry. 2010 Jul-Aug;32(4):380-95. PMID: 20633742.

Peer Reviewers suggested the following additional references:

Bogner HR, Morales KH, de Vries HF, Cappola AR. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. Ann Fam Med 2012, 10(1):15-22.

Lin EH, Von Korff M, Ciechanowski P, et al. Treatment adjustment and medication adherence for complex patients with diabetes, heart disease, and depression: a randomized controlled trial. Ann Fam Med 2012, 10(1):6-14.

Rollman BL and Belnap BH. The Bypassing the Blues trial: Collaborative care for post-CABG depression and implications for future research. Cleveland Clinic J Med 2011, 78 (Suppl 1): S4-S12.

Boult C, Reider L, Leff B, Frick KD, Boyd CM, Wolff JL, Frey K et al. The effect of guided care teams on the use of health services: results from a cluster-randomized controlled trial. Arch Intern Med 2011, 171(5):460-6

Total references from main and update searches, handsearches and Peer Reviewer suggestions, and the clinicaltrials.gov search, minus duplicates = 1,903

In response to Peer Reviewer comments, we performed two supplemental searches, each using a different intervention term.

In the first, we searched for any of the following (combined with our non-intervention search terms:

- "Decision Support Systems, Clinical"[MeSH]
- "Registry"[MeSH]
- "decision support" (anywhere in record)

- reminder system(s) (anywhere in record)
- "patient care management" (anywhere in record)

Those searches yielded 45 citations of which 15 had been identified during our review. The remaining 30 abstracts were reviewed and none met our inclusion criteria.

Second, we performed a search using "disease management" rather than "chronic disease management," and the additional yield was 66 abstracts. Upon review, none of those met all of our inclusion criteria.

Appendix B. Excluded Studies

Wrong language

Boni F, Corsonello A, Panuccio D. COPD and depression/anxiety ORIGINAL (NON-ENGLISH) TITLE BPCO e depressione/ansia. Italian Journal of Medicine. 2011 March;5(1 SUPPL. 1):S81-S90. PMID: 2011174126.

Hermanns N. Structured depression management in the therapy of comorbid depressive disorders in the case of diabetes ORIGINAL (NON-ENGLISH) TITLE Strukturiertes Depressionsmanagement in der Therapie komorbider depressiver Storungen bei Diabetes. Diabetologe. 2010 June;6(4):297-8. PMID: 2010481602.

Wrong publication type or study design

Adili F, Larijani B, Haghighatpanah M. Diabetic patients: Psychological aspects. Ann N Y Acad Sci. 2006 Nov;1084:329-49. PMID: 17151313.

Agius M, Zaman R, Klepacka K. Developing guidelines for the treatment of resistant unipolar depression across primary and secondary care. Journal of Cancer Education. 2009 2009;24 SUPPL. 1:S428-S9.

Anderson D, Horton C, O'Toole ML, et al. Integrating depression care with diabetes care in real-world settings: lessons from the Robert Wood Johnson Foundation Diabetes Initiative. Diabetes Spectrum. 2007 2007 Winter;20(1):10-6. PMID: 2009536867. Language: English. Entry Date: 20070511. Publication Type: journal article.

Antoni MH, Lutgendorf SK, Cole SW, et al. The influence of bio-behavioural factors on tumour biology: pathways and mechanisms. Nat Rev Cancer. 2006 Mar;6(3):240-8. PMID: 16498446.

Bartels SJ. Caring for the whole person: Integrated health care for older adults with severe mental illness and medical comorbidity. Journal of the American Geriatrics Society. 2004 December;52(SUPPL. 12):S249-S57. PMID: 2005542928 MEDLINE PMID 15541165 (www.ncbi.nlm.nih.gov/pubmed/15541165).

Bland P. Is collaborative care best for depression in chronic disease? The Practitioner. 2011 Jan;255(1736):5.

Block SD. Diagnosis and treatment of depression in patients with advanced illness. Epidemiol Psichiatr Soc. 2010 Apr-Jun;19(2):103-9. PMID: 20815292.

Bloom JR, Kessler L. Risk and timing of counseling and support interventions for younger women with breast cancer. J Natl Cancer Inst Monogr. 1994(16):199-206. PMID: 7999465.

Carlsen K, Jensen AB, Jacobsen E, et al. Psychosocial aspects of lung cancer. Lung Cancer. 2005 Mar;47(3):293-300. PMID: 15713512.

Carlson LE, Bultz BD. Benefits of psychosocial oncology care: improved quality of life and medical cost offset. Health Qual Life Outcomes. 2003;1:8. PMID: 12756059.

Carney RM, Blumenthal JA, Catellier D, et al. Depression as a risk factor for mortality after acute myocardial infarction. Am J Cardiol. 2003 Dec 1;92(11):1277-81. PMID: 14636903.

Chan R, Webster J, Bennett L. Effects and feasibility of a multi-disciplinary orientation program for newly registered cancer patients: design of a randomised controlled trial. BMC Health Serv Res. 2009;9:203. PMID: 19906312.

Cheok F, Schrader G, Banham D, et al. Identification, course, and treatment of depression after admission for a cardiac condition: rationale and patient characteristics for the Identifying Depression As a Comorbid Condition (IDACC) project. Am Heart J. 2003 Dec;146(6):978-84. PMID: 14660988.

Cole SA, Farber NC, Weiner JS, et al. Double-disease management or one care manager for two chronic conditions: pilot feasibility study of nurse telephonic disease management for depression and congestive heart failure. Dis Manag. 2006 Oct;9(5):266-76. PMID: 17044760.

Davidson MB, Echeverry D. Collaborative care for depression and chronic illnesses. N Engl J Med. 2011 Mar 31;364(13):1278; author reply -9. PMID: 21449795.

de Ridder D, Schreurs K. Developing interventions for chronically ill patients: is coping a helpful concept? (Structured abstract). Clinical Psychology Review; 2001. p. 205-40.

Dickens C, McGowan L, Percival C, et al. Depression is a risk factor for mortality after myocardial infarction: fact or artifact? J Am Coll Cardiol. 2007 May 8;49(18):1834-40. PMID: 17481442.

Dobscha SK, Corson K, Leibowitz RQ, et al. Rationale, design, and baseline findings from a randomized trial of collaborative care for chronic musculoskeletal pain in primary care. Pain Med. 2008 Nov;9(8):1050-64. PMID: 18565008.

Echols MR, Jiang W. Clinical trial evidence for treatment of depression in heart failure. Heart Fail Clin. 2011 Jan;7(1):81-8. PMID: 21109211.

Egede LE. Disease-focused or integrated treatment: diabetes and depression. Med Clin North Am. 2006 Jul;90(4):627-46. PMID: 16843766.

Ell K, Aranda MP, Xie B, et al. Collaborative depression treatment in older and younger adults with physical illness: Pooled comparative analysis of three randomized clinical trials. American Journal of Geriatric Psychiatry. 2010 June;18(6):520-30. PMID: 2010302204.

Ell K, Quon B, Quinn DI, et al. Improving treatment of depression among low-income patients with cancer: the design of the ADAPt-C study. Gen Hosp Psychiatry. 2007 May-Jun;29(3):223-31. PMID: 17484939.

Fenton WS, Stover ES. Mood disorders: cardiovascular and diabetes comorbidity. Curr Opin Psychiatry. 2006 Jul;19(4):421-7. PMID: 16721175.

Gallagher R. Telephone-delivered collaborative care for post-CABG depression is more effective than usual care for improving quality of life related to mental health. Evidence-Based Nursing. 2010;13(2):37-.

Ganz P. Institute of medicine report: Recognizing psychological health needs to treat the whole patient. Journal of Oncology Practice. 2008;4(3):128-30.

George PP, Molina JAD, Cheah J, et al. The evolving role of the community pharmacist in chronic disease management - A literature review. Annals of the Academy of Medicine Singapore. 2010 November;39(11):861-7. PMID: 2010697627 MEDLINE PMID 21165527 (www.ncbi.nlm.nih.gov/pubmed/21165527).

Georgiades A, Zucker N, Friedman KE, et al. Changes in depressive symptoms and glycemic control in diabetes mellitus. Psychosom Med. 2007 Apr;69(3):235-41. PMID: 17420441.

Handford C, Tynan A-M, Rackal Julia M, et al. Setting and organization of care for persons living with HIV/AIDS. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2006.

Harris M, Smith B, Veale A. Printed patient education interventions to facilitate shared management of chronic disease: a literature review (Structured abstract). Internal Medicine Journal; 2005. p. 711-6.

Heron KE, Smyth JM. Ecological momentary interventions: incorporating mobile technology into psychosocial and health behaviour treatments. Br J Health Psychol. 2010 Feb;15(Pt 1):1-39. PMID: 19646331.

Johri M, Beland F, Bergman H. International experiments in integrated care for the elderly: a synthesis of the evidence (Structured abstract). International Journal of Geriatric Psychiatry. 2003(3):222-35. PMID: DARE-12003000785.

Katon WJ, Seelig M. Population-based care of depression: team care approaches to improving outcomes. J Occup Environ Med. 2008 Apr;50(4):459-67. PMID: 18404019.

Konstam V, Moser DK, De Jong MJ. Depression and anxiety in heart failure. J Card Fail. 2005 Aug;11(6):455-63. PMID: 16105637.

Krumholz HM, Currie PM, Riegel B, et al. A taxonomy for disease management: a scientific statement from the American Heart Association Disease Management Taxonomy Writing Group. Circulation. 2006;114(13):1432-45. PMID: 2009299317. Corporate Author: American Heart Association. Disease Management Taxonomy Writing Group. Language: English. Entry Date: 20070831. Revision Date: 20101231. Publication Type: journal article.

Mast BT, Vedrody S. Poststroke depression: a biopsychosocial approach. Curr Psychiatry Rep. 2006 Feb;8(1):25-33. PMID: 16513040.

McGregor M, Lin EH, Katon WJ. TEAMcare: an integrated multicondition collaborative care program for chronic illnesses and depression. J Ambul Care Manage. 2011 Apr-Jun;34(2):152-62. PMID: 21415613.

Newport DJ, Nemeroff CB. Assessment and treatment of depression in the cancer patient. J Psychosom Res. 1998 Sep;45(3):215-37. PMID: 9776368.

Opolski M, Wilson I. Asthma and depression: A pragmatic review of the literature and recommendations for future research. Clinical Practice and Epidemiology in Mental Health. 2005;1(18)PMID: 2006590236.

Patel KJ, Dwamena F. Impact of collaborative care management of depression among patients with cancer. Journal of Clinical Oncology. 2009 1;27(10):1730. PMID: 2009162444 MEDLINE PMID 19255305 (www.ncbi.nlm.nih.gov/pubmed/19255305).

Peters-Klimm F, Muller-Tasch T, Schellberg D, et al. Rationale, design and conduct of a randomised controlled trial evaluating a primary care-based complex intervention to improve the quality of life of heart failure patients: HICMan (Heidelberg Integrated Case Management). BMC Cardiovasc Disord. 2007;7:25. PMID: 17716364.

Pirl WF. Evidence report on the occurrence, assessment, and treatment of depression in cancer patients. J Natl Cancer Inst Monogr. 2004(32):32-9. PMID: 15263039.

Price J. Collaborative care improves health outcomes in older people with depression and arthritis. Evidence-Based Mental Health. 2004;7(2):45-.

Rollman BL, Herbeck Belnap B. The Bypassing the Blues trial: collaborative care for post-CABG depression and implications for future research. Cleve Clin J Med. 2011 Aug;78 Suppl 1:S4-12. PMID: 21972329.

Ross L, Boesen EH, Dalton SO, et al. Mind and cancer: does psychosocial intervention improve survival and psychological well-being? Eur J Cancer. 2002 Jul;38(11):1447-57. PMID: 12110489.

Schrader GD, Cheok F, Beltrame JF. Collaborative care for post-CABG depression. JAMA: Journal of the American Medical Association. 2010;303(13):1252-3.

Sharpe M, Strong V, Allen K, et al. Management of major depression in outpatients attending a cancer centre: a preliminary evaluation of a multicomponent cancer nurse-delivered intervention. Br J Cancer. 2004 Jan 26;90(2):310-3. PMID: 14735169.

Shemesh E, Koren-Michowitz M, Yehuda R, et al. Symptoms of posttraumatic stress disorder in patients who have had a myocardial infarction. Psychosomatics. 2006 May-Jun;47(3):231-9. PMID: 16684940.

Thomas SA. Care management for poststroke depression. Stroke. 2007 March;38(3):850-1. PMID: 2007175951 MEDLINE PMID 17303770 (www.ncbi.nlm.nih.gov/pubmed/17303770).

Tully PJ. Randomised controlled trial: telephone-delivered collaborative care for post-CABG depression is more effective than usual care for improving mental-health-related quality of life. Evidence Based Medicine. 2010;15(2):57-8. PMID: 2010667904. Language: English. Entry Date: 20100709. Revision Date: 20100709. Publication Type: journal article.

Van Der Feltz-Cornelis C. Treatment of depression and diabetes when co-morbid. European Psychiatry. 2010;25(1):2010-02.

Vieweg WV, Julius DA, Fernandez A, et al. Treatment of depression in patients with coronary heart disease. Am J Med. 2006 Jul;119(7):567-73. PMID: 16828625.

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Poor quality

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Appendix C. Evidence Tables

Evidence Table 1. Characteristics of included studies[a]

Author, Year Trial Name Country Funding Source	Sample Sizes	Study Design Level of Randomization	Study Setting	Study Duration, Mths
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	Randomized & analyzed: Overall: 55 G1: 28 G2: 27	RCT Patient	Primary care-like (oncology clinics)	8
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	Randomized: Overall: 472 G1: 242 G2: 230 Analyzed 6 mths: G1: 166 G2: 152 12 mths: G1: 144 G2: 114 24 mths: G1: 111 G2: 109	RCT Patient	Primary care-like (oncology clinic)	24

Evidence Table 1. Characteristics of included studies[a] (continued)

Author, Year Trial Name Country Funding Source	Sample Sizes	Study Design Level of Randomization	Study Setting	Study Duration, Mths
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	Randomized: Overall: 387 G1: 193 G2: 194 Analyzed 6 mths G1:151 G2:152 12 mths G1: 142 G2: 139 18 mths G1: 144 G2: 137 24 mths G1: 138 G2: 126	RCT Patient	1 traditional primary care; 1 primary care-referred (diabetes clinic)	24
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	Randomized: Overall: 329 G1: 165 G2: 164 Analyzed: varied by outcome	RCT Patient	Traditional primary care	60 total

Evidence Table 1. Characteristics of included studies[a] (continued)

Author, Year Trial Name Country Funding Source	Sample Sizes	Study Design Level of Randomization	Study Setting	Study Duration, Mths
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	Randomized: Overall: 214 G1: 106 G2: 108 Analyzed Baseline G1: 105 G2: 106 Analyzed (by outcome) *Depression:* 6 mths G1: 97 G2: 96 12 mths G1: 94 G2: 92 *HbA1c:* 6 mths G1: 99 G2: 95 12 mths G1: 101 G2: 97 *SBP:* 6 mths G1:103 G2:102 12 mths G1: 101 G2: 101 *LDL cholesterol:* @ 12 mths only G1: 98 G2: 90	RCT Patient	Traditional primary care (GroupHealth)	12

Evidence Table 1. Characteristics of included studies[a] (continued)

Author, Year Trial Name Country Funding Source	Sample Sizes	Study Design Level of Randomization	Study Setting	Study Duration, Mths
Pyne, 2011[16] HITIDES US Government	Randomized: Overall: 276 G1: 138 G2: 138 Analyzed: G1: 123 G2: 126	RCT Patient	Primary care-like (HIV clinic)	12
Rollman, 2009[17] Bypassing the Blues US Government	Randomized & analyzed: Overall: 302 G1: 150 G2: 152	RCT Patient	Unclear; telephone-based	8
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	Randomized: Overall: 200 G1: 101 G2: 99 Analyzed: G1: 98 G2:99	RCT Patient	Primary care-like (oncology clinics)	12
Vera, 2010[19] NA Puerto Rico Government	Randomized & analyzed: Overall: 179 G1: 89 G2: 90	RCT Patient	Traditional primary care	6

Evidence Table 1. Characteristics of included studies[a] (continued)

Author, Year Trial Name Country Funding Source	Sample Sizes	Study Design Level of Randomization	Study Setting	Study Duration, Mths
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	Randomized: Overall: 1,001 G1: 506 G2: 495 Analyzed 6 mths G1: 498 G2: 489 12 mths G1: 484 G2: 480	RCT Patient	Traditional primary care	24
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	Randomized: Overall: 215 G1: 112 G2: 103 Analyzed 6 mths: G1: 107 G2: 100 12 / 18 / 24 mths: G1: 101 G2: 94 18 mths: G1: 99 G2: 90 24 mths: G1: 97 G2: 86	RCT patient	Traditional primary care	24

Evidence Table 1. Characteristics of included studies[a] (continued)

Author, Year Trial Name Country Funding Source	Sample Sizes	Study Design Level of Randomization	Study Setting	Study Duration, Mths
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	Randomized: Overall: 417 G1: 205 G2: 212 Analyzed 6 mths: G1: 201 G2: 202 12 mths: G1: 193 G2: 200	RCT Patient	Traditional primary care	24

aG1 = intervention arm; G2 = control arm

Abbreviations: HbA1c = hemoglobin A1c; LDL = low density lipoprotein; mths = months; RCT = randomized controlled trial; SB =, systolic blood pressure; US = United States

Evidence Table 2. Characteristics of study populations[a]

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	Depression MDD: PHQ-9 (cutoff NR); 3 items from PRIME-MD to assess dysthymia or persistent depressive symptoms at both baseline and 1 month later	Cancer Women ≥ 3 months past initial diagnosis with cervical cancer or stage I-IV breast cancer receiving care in outpatient breast and gynecology clinics	Overall: NR G1: 47.7 (11.9) G2: 46.8 (10.8) 96% of G1 and 85% of G2 were Spanish-only speakers. 100	PHQ-9, mean (SD) Overall: NR G1: 12.6 (7.0) G2: 13.4 (7.2)	NR
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	Depression 1 of the 2 cardinal depression symptoms ≥ half of the days to nearly every day AND PHQ-9 score ≥ 10 and/or 2 items from the DSM-IV SCI indicating dysthymia	Cancer ≥90 days after cancer diagnosis and receiving acute or follow-up care in oncology clinics	Mean age: NR; % age ≥50 years: Overall: 49.4 G1: 48.3 G2: 50.4 % Hispanic Overall: 87.9 G1: 90.5 G2: 85.2 Overall: 84.5 G1: 83.5 G2: 85.7	PHQ-9, mean (SD) Overall: 13.09 (3.48) G1: 13.30 (3.51) G2: 12.87 (3.44) PHQ-9 ≥15, N(%) Overall: 139 (29.4) G1: 74 (30.6) G2: 65 (28.3)	Cancer Stage, N (%) Stage 0, I, II or unstaged Overall: 340 (72) G1: 174 (71.9) G2: 166 (72.2) Stage III, IV or recurrent Overall: 132 (28) G1: 68 (28.1) G2: 64 (27.8) Cancer treatment phase, N(%) Prior to treatment Overall: 52 (11) G1: 23 (9.5) G2: 29 (12.6) Acute treatment Overall: 193 (40.9) G1: 98 (40.5) G2: 95 (41.3) Follow-up care Overall: 227 (48.1) G1: 121 (50) G2: 106 (46.1)

Evidence Table 2. Characteristics of study populations[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	Depression PHQ-9 score ≥10	Diabetes Medical chart indicates diabetes	Mean age NR; % ≥50 years: G1: 75.1 G2: 69.1 % Hispanic: Overall: 96.5 G1: 94.8 G2: 97.4 Overall: NR G1: 79.8 G2: 84.5	SCL-20, mean (SD) Overall: NR G1: 1.70 (0.73) G2: 1.41 (0.70)	HbAa1c, mean Overall: NR G1: 9.01% G2: 9.05% % with HbAa1c ≥7% G1: 83.0 G2: 82.3 Whitty-9 Diabetes symptoms, mean (SD) G1: 2.33 (0.76) G2: 2.15 (0.75)
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	Depression PHQ-9 score ≥10 AND SCL-90 or SCL-20 depression mean item score ≥ 1.1 two weeks later	Diabetes Diabetes registry that included patients with any of the following: 2 or more fasting glucose > 126 mg/dL; random plasma glucose level >200 mg/dL; current use of diabetic medication; inpatient or outpatient diagnosis of diabetes	Overall: 58.4 (11.8) G1: 58.6 (11.8) G2: 58.1 (12) % non-white: G1: 24.8 G2: 19.9 Overall: NR G1: 65.2 G2: 64.8	SCL-20, mean (SD) G1: 1.71 (0.51) G2: 1.63 (0.46)	HbA1C, mean (SD) G1: 8.0 (1.6) G2: 8.0 (1.5) Mean (SD) # of diabetic complications G1: 1.5 (1.3) G2: 1.5 (1.4)

Evidence Table 2. Characteristics of study populations[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	Depression PHQ-9 score ≥10	Diabetes and/or heart disease At least 1 of the following: HbA1c ≥ 8.5%; LDL cholesterol >130mg/dl; SBP >140mm Hg	Overall: NR G1: 57.4 (10.5) G2: 56.3 (12.1) % non-white: Overall: NR G1: 25 G2: 22 Overall: NR G1: 48 G2: 56	PHQ-9, mean (SD) Overall: NR G1: 14.7 (3.8) G2: 13.9 (3.1) SCL-20, mean (SD) Overall: NR G1: 1.7 (0.6) G2: 1.7 (0.6)	HbAa1c, mean (SD) Overall: NR G1: 8.1 (2.0) G2: 8.0 (1.9) LDL cholesterol, mean (SD) Overall: NR G1: 106.5 (35.3) mg/dl G2: 109.0 (36.5) mg/dl SBP, mean (SD) Overall: NR G1: 136 (18.4) mm Hg G2: 132 (17.2) mm Hg % with diabetes (with or without heart disease) Overall: NR G1: 89 G2: 82 % with coronary heart disease Overall: NR G1: 23 G2: 30
Pyne, 2011[16] HITIDES US Government	Depression PHQ-9 ≥10	HIV/AIDS Veterans being treated in the VA HIV clinic	Overall: NR G1: 49.8 (8.7) G2: 49.8 (10.5) % non-white: Overall: NR G1: 63.4 G2: 61.6 Overall: NR G1: 2.4 G2: 3.2	PHQ-9, mean (SD) Overall: NR G1: 15.7 (4.2) G2: 16.0 (4.7) SCL-20, mean (SD) Overall: NR G1: 1.8 (0.6) G2: 1.9 (0.7)	Mean (SD) # of bothersome HIV symptoms Overall: NR G1: 7.8 (4.1) G2: 8.0 (4.3) Current anti-HIV prescription, % G1: 80.5 G2: 78.6 Adherent to anti-HIV medication, % G1: 93.5 G2: 91.2

Evidence Table 2. Characteristics of study populations[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Rollman, 2009[17] Bypassing the Blues US Government	Depression PHQ-9 score ≥11	Heart disease Post-CABG patients	Overall: NR G1: 64 (10.8) G2: 64 (11.2) % non-white: Overall: NR G1: 12 G2: 7 Overall: NR G1: 46 G2: 37	PHQ-9, mean (SD) Overall: NR G1: 13.5 (3.2) G2: 13.6 (3.6) HRSD, mean(SD) Overall: NR G1: 16.5 (7.1) G2: 15.9 (6.9)	Duke Activity Status Index, mean (SD) Overall: NR G1: 7.1 (5.8) G2: 7.7 (7.6)

Evidence Table 2. Characteristics of study populations[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	Depression HADS ≥15 AND MDD diagnosed by DSM-IV SCI AND SCL-20 depression scale ≥1.75 AND MDD of ≥ 1 month's duration that was not associated with major changes in patient's cancer or its management	Cancer Cancer with prognosis of ≥6 months	Overall: NR G1: 56.6 (11.4) G2: 56.6 (11.4) NR Overall: NR G1: 69 G2: 72	SCL-20, median (IQR) Overall: NR G1: 2.35 (2.05 to 2.75) G2: 2.25 (1.95 to 2.75)	Mths since most recent cancer diagnosis / recurrence / metastases; median (IQR) Overall: NR G1: 13 (5.5-33.7) G2: 20 (9.1-44.7) % disease-free G1: 64 G2: 68 % local disease G1: 20 G2: 22 % metastatic disease G1: 16 G2: 10 % pre-treatment G1: 0 G2: 2 % under investigation G1: 4 G2: 15 % active treatment G1: 19 G2: 15 % post-treatment assessment G1: 2 G2: 3 % monitoring G1: 75 G2: 65

Evidence Table 2. Characteristics of study populations[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation (continued)					% no active treatment G1: 81 G2: 85 % chemotherapy G1: 9 G2: 10 % radiotherapy G1: 7 G2: 3 % both G1: 3 G2: 2

Evidence Table 2. Characteristics of study populations[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Vera, 2010[19] NA Puerto Rico Government	Depression PHQ-9 score (cutoff NR) AND mean SCL-20 score >1.0 over 2 week screening period	Spanish speakers with ≥1 of the following: diabetes, hypothyroidism, asthma, hypertension, chronic bronchitis, arthritis, heart disease, high cholesterol, stroke	Overall: 55.2 (12.6) G1: 57.0 (12.4) G2: 53.5 (12.7) 100% Puerto Rican Overall: 76 G1: 74 G2: 78	SCL-20, mean (SD) Overall: 2.28 (0.56) G1: 2.22 (5.4) G2: 2.34 (0.58)	Mean (SD) # active medical conditions Overall: 2.54 (1.39) G1: 2.58 (1.40) G2: 2.49 (1.38)
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	Depression DSM-IV current MDD and/or dysthymia	Arthritis Older adults (≥60); self-reported arthritis, confirmed in 91.4% via physician diagnosis, radiographic evidence, specialty consultation	Overall: 72.0 (7.4) G1: 71.9 (7.3) G2: 72.1 (7.5) % Non-White (% Black / % Hispanic / % Other) Overall: 24 (13 / 8 / 3) G1: 23 (13 / 7 / 3) G2: 25 (13 / 10 / 2) Overall: 68.3 G1: 67 G2: 70	SCL-20, mean (SD) Overall: 1.7 (0.6) G1: NR G2: NR	Arthritis pain intensity (range 0-10), mean (SD) Overall: 6.1 (2.7) G1: 6.0 (2.7) G2: 6.3 (2.7) Arthritis interference (range 0-10), mean (SD) Overall: 4.9 (3.2) G1: 4.9 (3.1) G2: 5.0 (3.2) Pain interference (range 1-5), mean (SD) Overall: 3.2 (1.1) G1: 3.2 (1.1) G2: 3.2 (1.1)

Evidence Table 2. Characteristics of study populations[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Condition MH Inclusion Criteria	CM Condition(s) CM Condition(S) Inclusion Criteria	Baseline Age - Mean (SD) Baseline % Non-White Baseline % Female	Baseline Depression Score	Baseline Chronic Condition Measure
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	Depression DSM-IV current MDD and/or dysthymia	Cancer Older adults (≥60); ICD-9 diagnosis of non-skin cancer in claims or encounter data in the year before or the year following randomization	Mean (SE) Overall: 71.8 (0.50) G1: 71.7 (0.70) G2: 71.8 (0.71) % Non-White Overall: 25 G1: 22 G2: 27 Overall: 60 G1: 63 G2: 58	SCL-20, mean (SD) Overall: 1.6 (0.04) G1: 1.7 (0.06) G2: 1.6 (0.06)	Type of cancer (%) Overall: female breast (29) male reproductive (23) occult (13) digestive system (12) urinary system (10) hematologic (10) female reproductive (9) respiratory system (7) other (8) G1: NR G2: NR
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	Depression DSM-IV current MDD and/or dysthymia	Diabetes Older adults (≥60); positive response to "Has a doctor or another health care worker diagnosed you with or treated you for high blood sugar or diabetes in the past 3 years?"	Overall: NR G1: 70.1 (6.9) G2: 70.3 (7.1) % Non-White (% Black / % Hispanic / % Other) Overall: NR G1: 35 (22 / 10 / 3) G2: 37 (18 / 16 / 3) Overall: NR G1: 54 G2: 53	Overall: NR G1: 1.7 (0.62) G2: 1.7 (0.63)	HbA1c (%) Overall: 7.3 (0.1) G1: 7.3 (1.3) G2: 7.3 (1.5)

[a] G1 = intervention arm; G2 = control arm

Abbreviations: CABG = coronary artery bypass graft; CM = chronic medical; dL = deciliter; DSM = Diagnostic and Statistical Manual of Mental Disorders; HADS = Hospital Anxiety and Depression Scale; HbA1c = hemoglobin A1c; HRSD = Hamilton Rating Scale for Depression; ICD = International Classification of Diseases; IQR = interquartile range; LDL = low density lipoprotein; MDD = major depressive disorder; MH = mental health; mg = milligrams; mths = months; NR = not reported; PHQ = Patient Health Questionnaire; RCT = randomized controlled trial; SBP = systolic blood pressure; SCI = structured clinical interview; SCL = Symptom Checklist; SD = standard deviation; SE = standard error; US = United States; VA = Veterans' Affairs

Evidence Table 3. Intervention components

First Author, Year Trial Name Country Funding Source	Components of Collaborative Care Intervention	Type of Control Condition	Components of Control Condition
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	Access to a CDCS who provided manualized psychotherapy (problem solving therapy), supported antidepressant medication adherence, and assisted with systems navigation; Education about and choice of PST or medication as first-line treatment; Treatment plan put in medical chart; feedback given to oncologist; PST included weekly sessions for 8 weeks with additional sessions or addition of medication for non-responders after evaluation by study psychiatrist; Medication for 8 weeks with adjustments available after for non-responders	Usual care	Patients were informed of their depression diagnosis and the usual mental health resources available to them at clinic system. Recruiters suggested that they talk with their PCP or the clinic social worker. Recruiters placed a note in the patient's medical record indicating the presence of depressive symptoms.
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	Access to a CDCS who offered education, structured psychotherapy, and maintenance/ relapse prevention and outcomes monitoring; Depression- and cancer-related community services navigation by the CDCS or a patient navigator under CDCS direction; Psychiatrist supervised the CDCS and prescribed antidepressants; Personalized treatment plan that included medication or PST; Structured algorithm for stepped care management and protocol for PST	Enhanced usual care	Standard oncology care plus: Patient/family depression and cancer education pamphlets and a listing of financial, social services, transportation, and childcare resources; Treating oncologist was informed of patients' depression status.

Evidence Table 3. Intervention components (continued)

First Author, Year Trial Name Country Funding Source	Components of Collaborative Care Intervention	Type of Control Condition	Components of Control Condition
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	Socioculturally-enhanced structured stepped-care algorithm with problem solving and/or medication; Monthly phone consult with diabetes specialist for relapse prevention and symptom monitoring; Care and service system navigation	Enhanced usual care	Standard clinic care plus: Patient- and family-focused depression education pamphlets plus community resource lists (e.g., social services, transportation, childcare)
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	Individualized, stepped-care depression treatment program provided by a depression clinical specialist nurse; Education about depression, behavioral activation (i.e., increasing positive activities such as exercise) Choice of first-line treatment: medication or PST;	Enhanced usual care	PCPs were notified about the patient's depression diagnosis; Patients were advised to consult with their physicians about depression.
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	Personalized care plan and treat-to-target adjustments; Nurses monitored progress and support for medication adherence; Problem solving and goal setting using motivational coaching; Self-care materials related to depression and chronic disease management; Maintenance plan development and follow-up phone calls by nurse every 4 weeks	Enhanced usual care	Patients were advised to consult PCP to treat MH and chronic condition; Depression and lab results shared with PCP with patients' permission

Evidence Table 3. Intervention components (continued)

First Author, Year Trial Name Country Funding Source	Components of Collaborative Care Intervention	Type of Control Condition	Components of Control Condition
Pyne, 2011[16] HITIDES US Government	Depression care team consisted of DCM, clinical pharmacist, and psychiatrist; Education and activation, assessment of treatment barriers and possible resolutions, depression symptom and treatment monitoring, substance abuse monitoring, and instruction in self-management (e.g., encouraging patients to exercise and participate in social activities); Stepped-care model for depression treatment: watchful waiting; depression care team suggestions for treatment; medication suggestions from team pharmacist; combination medication and specialty MH counseling; referral to specialty MH	Usual care	Patients delivered depression screening results to their HIV clinicians.
Rollman, 2009[17] Bypassing the Blues US Government	Nurse care manager provided basic depression psychoeducation including treatment options (e.g., workbook to enhance self-care; start or adjust antidepressant medication via PCP; watchful waiting for mild symptoms; referral to MH specialist); Weekly case review and report of treatment recommendations to patient and to PCP	Usual care	Patients and PCPs were informed of depression status.
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	Usual care plus manual-based, cancer nurse-delivered complex intervention called Depression Care for People with Cancer: Education about depression and its treatment (including antidepressant medication); PST to teach coping strategies designed to overcome feelings of hopelessness; Communication about management of depression with each patient's oncologist and PCP; PCP prescribed all medication.	Usual care	Patients' PCPs and oncologists were informed of diagnosis of depression and were given advice on choice of antidepressant drug, if requested

Evidence Table 3. Intervention components (continued)

First Author, Year Trial Name Country Funding Source	Components of Collaborative Care Intervention	Type of Control Condition	Components of Control Condition
Vera, 2010[19] NA Puerto Rico Government	Program oversight and teamwork among PCPs, MH care specialists and DCMs. Depression education, choice of evidence-based treatment options: medication or 13-session CBT; DCM participated in coordination of treatment initiation and monitoring of adherence, side effects and clinical response. DCM consulted with psychiatrist regarding treatment and forwarded psychiatrist recommendations to PCP.	Usual care	Patients were informed of depression diagnosis and available MH resources; Patients were encouraged to discuss depression with PCP; Note was placed in medical record.
Williams, 2004[23] Fann, 2009[22] Lin, 2006[20] Katon, 2006[24] Lin, 2003[21] IMPACT (secondary analyses) US Multiple sources	DCM (nurse or clinical psychologist) worked with patient and PCP; Education and behavioral activation planning; Identifying treatment preferences: structured 6-8 session PST and/or stepped-care algorithm medication prescribed by PCP	Usual care	Routinely available depression treatment in primary care

Abbreviations: CBT = Cognitive-Behavioral Therapy; CDCS = Cancer Depression Clinical Specialist; DCM = Depression Care Manager; MH = mental health; PCP = primary care provider; PST = Problem-Solving Treatment; US = United States

Evidence Table 4. Intervention logistics

First Author, Year Trial Name Country Funding Source	Research Staff or Clinic Staff; Name Given to Interventionist; Intervention Provider Type	Intervention delivery mechanism	Description of Intervention Contacts Length of Intervention Contacts Length of Time Over Which Intervention was Delivered
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	Research staff Cancer / Depression Clinical Specialist Social worker	In-person & phone	PST sessions weekly for 8 weeks minimum; Phone follow-up every 2 weeks NR ≥8 weeks
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	Research staff NR Social worker	In-person & phone	Initial visit + the following, based on treatment selected: Medication only: NR (mean 5.6 months on medication) PST only: mean (SD) 7.7 (5.5) sessions Medication + PST: mean (SD) 11 (9.8) sessions # phone contacts NR NR ≤12 months
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	Unclear Diabetes / Depression Clinical Specialist Social worker	In-person with phone follow-up	Acute phase: weekly Maintenance: monthly PST participants had a mean (SD) of 8.7 (5.4) sessions 90 minutes per patient visit; 45 minutes per phone follow-up; 10-15 minutes per patient navigation call 12 months

Evidence Table 4. Intervention logistics (continued)

First Author, Year Trial Name Country Funding Source	Research Staff or Clinic Staff; Name Given to Interventionist; Intervention Provider Type	Intervention delivery mechanism	Description of Intervention Contacts Length of Intervention Contacts Length of Time Over Which Intervention Was Delivered
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	Research staff Depression Care Manager Nurse	In-person & phone	Acute phase (enrollment through response or 12 weeks): twice-monthly contact; additional for non-responders; Continuation phase (after response achieved): once-monthly phone contact (up to the 12-month time point) initial 1-hour visit; acute-phase: 30 minutes; continuation phase: NR 12 months
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	Unclear Study nurse Nurse	In-person with phone follow-up	In-person visits "every 2-3 weeks;" phone follow-ups every 4 wks after achievement of relevant target measures. 30 minutes in-person; 10-15 minutes phone (mean = 10.0 minutes in person and 10.8 minutes phone) 12 months
Pyne, 2011[16] HITIDES US Government	Research Staff HIV Depression Care Team Nurse	Phone	DCM monitoring call every 2 weeks during acute treatment and every 4 weeks after (for 2 months after remission or 6 months after response); Mean number of DCM intervention phone contacts per patient during the acute and continuation phases of treatment = 7.2 (SD, 4.5; range, 0-19) NR Varied

Evidence Table 4. Intervention logistics (continued)

First Author, Year Trial Name Country Funding Source	Research Staff or Clinic Staff; Name Given to Interventionist; Intervention Provider Type	Intervention delivery mechanism	Description of Intervention Contacts Length of Intervention Contacts Length of Time Over Which Intervention Was Delivered
Rollman, 2009[17] Bypassing the Blues US Government	Research staff NR Nurse	Phone	Median = 10 (range 0 to 28): 8 to 12 (biweekly for initial 2 to 4 months followed by contact every 1 to 2 months for the next 4 months) 15 to 45 minutes 8 months
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	Unclear NR Nurse	In-person & phone	Maximum of 10 sessions over first 3 months with "booster" sessions available during months 3-6 if PHQ-9 scores worsened; Mean: 7; range 2-10 during first 3 months 45 minutes Majority during first 3 months; booster during 3-6 months if needed
Vera, 2010[19] NA Puerto Rico Government	Research staff Care Manager Counselor or psychologist	In-person & phone	Mean 1.4 (range 0-6) in-person contacts with care manager and 8.2 (0-23) phone contacts. Mean = 11.7 minutes (range 4.3 to 34.5) NR
Williams, 2004[23] Fann, 2009[22] Lin, 2006[20] Katon, 2006[24] Lin, 2003[21] IMPACT (secondary analyses) US Multiple sources	Research staff Depression clinician specialist Nurse or psychologist	In-person & phone	6-8 patient visits + 12-18 follow-up calls or brief visits; PST visits, mean (SD): Overall: 6.34 (4.26) G1/G2: NR In-person visits, mean (SD): Overall: 9.15 (6.17) G1/G2: NR Phone contacts, mean (SD): Overall: 6.10 (5.13) G1/G2: NR NR 12 months

Abbreviations: DCM = Depression Care Manager; mins = minutes; mths = months; NR = not reported; PST = Problem-Solving Treatment; SD = standard deviation; US = United States; wks = weeks

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a]

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	**N (%) with improved PHQ-9** *@ 8 mths* G1: 20 (74) G2: 12 (46) OR (95% CI) = 3.33 (1.05 to 10.59); p=0.04	**N (%) achieving ≥50% reduction in PHQ-9** *@ 8 mths* G1: 10 (37) G2: 3 (12) OR (95% CI): 4.51 (1.07 to 18.93); p=0.03	NR
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	**Adj PHQ-9 score, mean (SE)** *@ 6 mths* G1: 7.34 (0.34) G2: 8.14 (0.34) adj mean between-group difference (95% CI): -0.8 (-1.7 to 0.11); p = 0.08 *@ 12 mths* G1: 6.4 (0.36) G2: 7.14 (0.39) 12-month between-group difference (95% CI): -0.74 (-1.74 to 0.27); p = 0.15 Change in mean PHQ-9 scores across time between groups p=0.06	**N (%) achieving ≥50% reduction in PHQ-9 (as treated)** *@ 6 mths (N=318)* G1: 82 (49.4) G2: 63 (41.4) Adj OR (95% CI): 1.43 (0.88 to 2.32); p = 0.15 *@ 12 mths (N=258)* G1: 91 (63.2) G2: 57 (50.0) Adj OR (95% CI): 2.02 (1.18 to 3.47); p = 0.01 *@ 18 mths (N=272)* G1: 87 (60) G2: 66 (52) Adj OR (95% CI)=1.45 (0.87 to 2.41); p=0.16 *@ 24 months (N=210)* G1: 51 (46) G2: 32 (32) Adj OR (95% CI)=2.09 (1.13 to 3.86); p=0.02	**N (%) achieving remission (PHQ-9 score <5), as treated** *@ 6 months (N=318)* G1: 57 (34) G2: 44 (29) Adj OR (95% CI)=1.41 (0.85 to 2.36); p=0.18 *@ 12 months (N=258)* G1: 54 (38) G2: 41 (36) Adj OR (95% CI)=1.25 (0.72 to 2.19); p=0.43 *@ 18 months (N=272)* G1: 64 (44) G2: 43 (34) Adj OR (95% CI)=1.84 (1.07 to 3.16); p=0.03 *@ 24 months (N=210)* G1: 35 (32) G2: 25 (25) Adj OR (95% CI)=1.58 (0.82 to 3.07); p=0.17

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government (continued)		**N (%) achieving 5-point decrease in PHQ-9 (as-treated)** *@ 6 mths (N=318)* G1: 102 (61.5) G2: 76 (50.0) Adj OR (95% CI): 1.58 (0.97 to 2.57); p = 0.06 *@ 12 mths (N=258)* G1: 104 (72.2) G2: 68 (59.7) Adj OR (95% CI): 2.03 (1.15 to 3.58); p = 0.01 *@ 18 mths (N=272)* G1: 100 (69) G2: (70 (55) Adj OR (95% CI)=1.81 (1.07 to 3.04); p=0.03 *@ 24 months (N=210)* G1: 60 (54) G2: 37 (37) Adj OR (95% CI)=2.07 (1.15 to 3.72); p=0.02	**N (%) who experienced recurrence (PHQ-9 >=10) at 18 or 24 months** G1: 35 (36) G2: 29 (39) **Of those experiencing recurrence, N (%) who received depression treatment after 12 months** G1: 12 (34) G2: 3 (10) p=0.03 **Of G1 patients achieving remission:** **N (%) experiencing relapse** *between 6 and 12 mths* G1: 16 (14) **N (%) continuing to respond** *between 6 and 12 mths* G1: 19 (17)
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	Regression estimated effect intervention for # depression-free days through 18 months, coefficient (p)=32.57(<0.001) SCL-20 score, Adj mean diff at 24 months, -0.22, p=0.001	**N (%) achieving ≥50% reduction in SCL-20** *@ 6 mths* G1: 86 (57.0) G2: 55 (36.4) p < 0.001 *@ 12 mths* G1: 88 (62.0) G2: 59 (42.4) Adj OR (95% CI)=2.59 (1.51 to 4.46); p <0.001 *@ 18 mths* G1: 89 (61.8) G2: 60 (43.8) Adj OR (95% CI)=2.64 (1.52 to 4.60); p<0.001	**N (%) achieving SCL-20 < 0.5** *@ 6 mths* G1: 58 (38.4) G2: 42 (27.8) p = 0.01 *@ 12 mths* G1: 56 (39.4) G2: 49 (35.3) Adj OR (95% CI)=2.07 (1.17 to 3.66); p=0.01 *@ 18 mths* G1: 58 (40.3) G2: 48 (35.0)

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government (continued)		*@ 24 months* G1: 80 (58.0) G2: 62 (49.2) Adj OR (95% CI)=1.69 (0.97 to 2.96); p=0.06 Overall time by group interaction p=0.13 **N (%) achieving ≥50% reduction in PHQ-9 score** *@ 12 mths* G1: 86 (60.6) G2: 66 (47.5) Adj OR (95% CI)=3.35 (1.87 to 6.03); p<0.0001 *@ 18 mths* G1: 82 (56.9) G2: 63 (46.0) Adj OR (95% CI)=2.89 (1.63 to 5.12); p<0.001 *@ 24 mths* G1: 74 (53.6) G2: 65 (51.6) Adj OR (95% CI)=1.87 (1.05 to 3.32); p=0.03 Overall time by group interaction p=0.01	Adj OR (95% CI)=2.66 (1.45 to 4.90); p=0.002 *@ 24 months* G1: 46 (33.3) G2: 41 (32.5) Adj OR (95% CI)=2.06 (1.09 to 3.90); p=0.03 Overall time by group interaction p=0.22 **N (%) achieving PHQ-9 <5** *@ 12 months* G1: 565(38.7) G2: 40 (28.8) Adj OR (95% CI)=3.00 (1.62 to 5.53); p<0.001 *@ 18 months* G1: 51 (35.4) G2: 43 (31.4) Adj OR (95% CI)=2.36 (1.27 to 4.40); p=0.01 *@ 24 months* G1: 41 (29.7) G2: 42 (33.3) Adj OR (95% CI)=1.31 (0.72 to 2.38); p=0.38 Overall time by group interaction p=0.02 **N (%) with PHQ-9 >=10 (clinical depression)** *@12 months* G1: 40 (28.2) G2: 54 (38.8) Adj OR (95% CI)=0.37 (0.20 to 0.66); p=0.001

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government (continued)			*@ 18 months* G1: 49 (34.0) G2: 62 (45.3) Adj OR (95% CI)=0.34 (0.19 to 0.61); p<0.001 *@ 24 months* G1: 55 (39.9) G2: 45 (35.7) Adj OR (95% CI)=0.66 (0.37 to 1.2); p=0.17 Overall 24-month time by group interaction p=0.003
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	**Improvement on SCL-90** *@ 6 mths* G1 scores lower than G2; p=0.04 change (95% CI) from BL to 6 mo: G1: -0.56 (-0.46 to -0.67) G2: -0.39 (-0.28 to -0.49) *@ 12 mths* G1 scores lower than G2, p=0.03 change (95% CI) from BL to 12 mths: G1: -0.65 (-0.54 to -0.76) G2: -0.44 (-0.33 to -0.56) **SCL-90 score** *@ 24 mths* G1: 1.10 G2: 1.22 P=0.048 **N (%) showing improvement on PGI** *@ 6 mths* G1: 100 (69.4) G2: 59 (39.3) OR (95% CI): 3.50 (2.16 to 5.68) *@ 12 mths* G1: 105 (71.9) G2: 60 (42.3) OR (95% CI): 3.50 (2.14 to 5.72)	**N (%) achieving ≥40% reduction in SCL-90** *@ 6 mths* G1: 61 (42.4) G2: 51 (34.2) OR (95% CI): 1.40 (0.87 to 2.25) *@ 12 mths* G1: 79 (54.1) G2: 54 (38.0) OR (95% CI): 1.89 (1.18 to 3.02) **N (%) achieving ≥50% reduction in SCL-90** *@ 6 mths* G1: 53 (36.8) G2: 39 (26.2) OR (95% CI): 1.62 (0.98 to 2.67) *@ 12 mths* G1: 60 (41.1) G2: 45 (31.7) OR (95% CI): 1.47 (0.90 to 2.39)	NR

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Katon, 2004[7]	**Mean (SD) depression-free days**		
Katon, 2008[8]	*BL through 12 mths*		
Simon, 2007[9]	G1: 186 (97)		
Kinder, 2006[10]	G2: 166 (97)		
Ciechanowski, 2006[11]	Difference (95% CI)= +20 (−2 to 42)		
	Mth 12 through mth 24		
Lin, 2006[12]	G1: 226 (118)		
	G2: 193 (117)		
Pathways	Difference (95% CI)=+33 (5 to 61)		
	BL through 24 mo		
US	G1: 412 (202)		
	G2: 359 (207)		
Government (continued)	Difference (95% CI)=+53 (0 to 97)		
	Also reported as:		
	Difference (95% CI) = +61 (11 to 82)		

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	**SCL-20, mean (SD)** *Baseline:* G1: 1.74 (0.59) G2: 1.65 (0.60) *@ 6 months* G1: 0.84 (0.68) G2: 1.26 (0.72) G1 Change from baseline to 6 mths: -0.90 G2 Change from baseline to 6 mths: -0.39 *@ 12 mths* G1: 0.83 (0.68) G2: 1.14 (0.66) G1 Change from baseline to 12 mths: -0.91 G2 Change from baseline to 12 mths: -0.51 12-month between-group difference (95% CI): -0.41 (-0.56 to -0.26) p < 0.001 **N (%) with improvement on PGI** *@6 mths* G1: 64 (67) G2: 15 (16) *@12 mths* G1: 41 (45) G2: 16 (18) Between-group change over time, p < 0.001	**N (%) with ≥ 50% decrease in SCL-20** *@ 6 mths* G1: 57 (59) G2: 22 (23) *@ 12 mths* G1: 56 (60) G2: 28 (30) Between-group change over time, p < 0.001	NR

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Pyne, 2011[16] HITIDES US Government	Unadjusted SCL-20 scores were not significantly different between the intervention and usual care groups at the 6- or 12-month follow-up **Change in depression-free days, from baseline to 12 mths (derived from SCL-20)** G1: +147.3 G2: +120.0 Effect size = 0.3; p=0.04 Adjusted mean group diff, Beta (95% CI) = +19.3 (10.9 to 27.6); p<0.001	**N (%) achieving ≥50% decrease in SCL-20** *@ 6 mths* G1: 41 (33.3) G2: 22 (17.5) Unadjusted OR (95% CI) 2.50 (1.37 to 4.56); p= 0.004 Adjusted OR (95% CI) 2.60 (1.39 to 4.86); p=0.003 *@ 12 mths* G1: 49 (39.8) G2: 41 (32.5) Unadjusted OR (95% CI) 1.37 (0.78 to 2.41); p=NS Adjusted OR (95% CI) 1.29 (0.72 to 2.32); p=0.39	**N (%) achieving SCL-20 < 0.5** *@ 6 mths* G1: 27 (22.0) G2: 15 (11.9) Unadjusted OR (95% CI): 2.25 (1.11 to 4.54) ; p=0.03 Adjusted OR (95% CI): 2.40 (1.10 to 5.22); p = 0.03 *@ 12 mths* G1: 28 (22.8) G2: 21 (16.7) Unadjusted OR (95% CI): 1.52 (0.78 to 2.98) ; p=NS Adjusted OR (95% CI): 1.36 (0.66 to 2.88); p = 0.40

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Rollman, 2009[17] Bypassing the Blues US Government	**$HRSD_{17}$ mean (SE)** FULL SAMPLE *@ 8 mths* G1: 9.0 (0.7) G2: 11.4 (0.7) *Change from baseline @ 8 mths:* G1: - 7.6 (0.6) G2: - 4.5 (0.6) Between-group difference (95% CI): 3.1 (1.3 to 4.9), p = 0.001 Effect Size (95% CI): 0.30 (0.08 to 0.53), p = 0.009 MEN ONLY *@ 8 mths* G1: 7.8 (0.9) G2: 10.9 (0.8) *Change from baseline @ 8 months:* G1: - 7.9 (0.8) G2: - 4.9 (0.8) Between-group difference (95% CI): 3.0 (0.8 to 5.3), p = 0.009 Effect Size (95% CI): 0.39 (0.09 to 0.69), p = 0.01 WOMEN ONLY *@ 8 mths* G1: 10.2 (1.0) G2: 12.0 (1.1) *Change from baseline @ 8 months:* G1: - 7.4 (0.9) G2: - 4.2 (1.0) Between-group difference (95% CI): 3.2 (0.5 to 5.9), p = 0.02 Effect Size (95% CI): 0.23 (-0.13 to 0.59), p = 0.20	**N (%) achieving 50% reduction in $HRSD_{17}$** *@ 8 mths* G1: 75 (50.0) G2: 45 (29.6) Effect size (95% CI): 0.42 (0.19 to 0.65), p < 0.001 MEN ONLY G1: 60.5% G2: 33.3% Effect size (95% CI): 0.55 (0.26 to 0.85), p < 0.001 WOMEN ONLY G1: 37.7% G2: 23.2% Effect size (95% CI): 0.32 (-0.04 to 0.67), p = 0.08	NR

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	**SCL-20, mean (SD)** *@ BL: median (IQR)* G1: 2.35 (2.05 to 2.75) G2: 2.25 (1.95 to 2.75) *@ 6 mths* G1: 1.03 (0.79) G2: 1.51 (0.81) Adj mean diff (95% CI): -0.59 (-0.81 to -0.37) *@ 12 mths* G1: 1.12 (0.89) G2: 1.43 (0.94) Adj mean diff (95% CI): -0.42 (-0.67 to -0.17)	NR	NR
Vera, 2010[19] NA Puerto Rico Government	**SCL-20** Regression coefficient: treatment X time = -0.3; p <0.001	**N (%) achieving ≥50% decrease in SCL-20** *@ 6 mths* G1: 41 (46%) G2: 16 (19%) Ratio: 4.04 (2.01 to 8.31)	NR
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	NR	**% achieving 50% reduction on SCL** *@ 12 mths* G1: 41% G2: 18% OR (95% CI): 3.28 (2.4 to 4.5), p < 0.001	**% no longer meeting DSM criteria for MDD** *@ 6 mths* G1: 24 G2: 38

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	**SCL-20, mean (SD):** *@ BL* G1: 1.65 (0.06) G2: 1.59 (0.06) *p = 0.487* *@ 6 mths* G1: 0.89 (0.07) G2: 1.16 (0.08) p = 0.008 *@ 12 mths* G1: 1.05 (0.07) G2: 1.39 (0.07) p = 0.004 *@ 18 mths* G1: 1.10 (0.08) G2: 1.39 (0.07) p = 0.012 *@ 24 mths* G1: 1.15 (0.08) G2: 1.34 (0.08) p = 0.087 **Depression-free days, mean (SD):** *@ 12 mths* G1: 185.8 (10.9) G2: 135.0 (10.2) Between group diff, p < 0.001 *During second year* G1: 356.5 (21.7) G2: 247.6 (19.6) Between group diff, p < 0.001	**N (%) with ≥50% reduction on SCL-20** *@ 6 mths* G1: 59 (55%) G2: 34 (34%) p = 0.003 *@ 12 mths* G1: 39 (39%) G2: 19 (20%) p = 0.029 *@ 18 mths* G1: 38 (39%) G2: 16 (18%) p = 0.012 *@ 24 mths* G1: 30 (31%) G2: 16 (19%) p = 0.088 **Overall depression treatment response, %** G1: 39 G2: 20 Between group diff, p = 0.029 OR (95% CI): 2.69 (1.54 to 4.71)	**N (%) with SCL-20 < 0.5** *@ 6 mths* G1: 34 (32%) G2: 15 (15%) p = 0.006 *@ 12 mths* G1: 22 (22%) G2: 9 (9%) p = 0.031 *@ 18 mths* G1: 18 (19%) G2: 7 (8%) p = 0.053 *@ 24 mths* G1: 17 (18%) G2: 6 (7%) p = 0.087 OR (95% CI): 2.44 (1.51 to 3.94)

Evidence Table 5. Mental health outcomes: symptom improvement, response rate, remission and/or recurrence[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Symptom Improvement	MH Response Rate	MH Remission and/or Recurrence
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	**SCL-20, mean (SD):** *@ BL* G1: 1.7 (0.6) G2: 1.7 (0.6) *@ 6 mths* G1: 0.93 (0.67) G2: 1.28 (0.72) between-group diff (95% CI): -0.34 (-0.48 to -0.20) *@ 12 mths* G1: 1.00 (0.68) G2: 1.46 (0.68) between-group diff (95% CI): -0.43 (-0.57 to -0.29) **Depression-free days, mean (SD),** G1 vs G2 1st 12 mths, mean (95% CI) 59.4 (37.3 to 81.4) 2nd 12 mths, mean (95% CI) 56.1 (31.8 to 80.4) Over 24 mths, mean (95% CI) 115.4 (71.7 to 159.1)	NR	NR

[a] G1 = intervention arm; G2 = control arm

Abbreviations: Adj = adjusted; BL = baseline; CI = confidence interval; HRSD = Hamilton Rating Scale for Depression; MH = mental health; mths = months; NR = not reported; OR = odds ratio; PGI = Patient Global Improvement; PHQ = Patient Health Questionnaire; SCL = Symptom Checklist; SD = standard deviation; SE = standard error; US = United States

Evidence Table 6. Mental health outcomes: treatment adherence and treatment satisfaction[a]

First Author, Year Trial Name Country Funding Source	MH Treatment Adherence	MH Treatment Satisfaction
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	NR	NR
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	NR	**N (%) "satisfied" or "very satisfied" with emotional care, as treated:** *Over 24 mths* G1: 138 (93) G2: 101 (80); p=0.001 **% satisfied to extremely satisfied with PST** (among G1 patients choosing PST) *@ 6 mths* 84.4% *@ 12 mths* 92.3% **% satisfied to extremely satisfied with medication** (among G1 patients choosing medication) *@ 6 mths* 40.5% *@ 12 mths* 42.3%
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	G1 > G2 in length of time of adherence to antidepressant medications	**% reporting "satisfied" to "very satisfied" with emotional care** *@ 18 mths* G1: 89.5 G2: 77.9 OR 2.43 (95% CI 1.23 to 4.77), p = 0.01 *@ 24 mths* G1: 88.9 G2: 74.2 p=0.002

Evidence Table 6. Mental health outcomes: treatment adherence and treatment satisfaction[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Treatment Adherence	MH Treatment Satisfaction
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	**Adherence to antidepressant refills, N (%)** *@ 6 mths* G1: 99 (60.4) G2: 80 (48.5) Adj OR (95% CI): 2.29 (1.38 to 3.82) *@ 9 mths* G1: 98 (59.8) G2: 76 (46.1) Adj OR (95% CI): 2.78 (1.62 to 4.76) *@ 12 mths* G1: 94 (57.3) G2: 76 (46.1) Adj OR (95% CI): 2.18 (1.32 to 3.62)	**N (%) moderately to very satisfied with depression care:** *@ 6 mths* G1: 104 (72.7) G2: 89 (60.1) Adj OR (95% CI): 2.01 (1.18 to 3.43) *@ 12 mths* G1: 106 (72.6) G2: 76 (53.9) OR (95% CI): 2.88 (1.67 to 4.97)
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	**Adherence as measured by % of days with available antidepressant medication, mean (SD)** *@ BL* G1 (N=43): 0.79 (0.23) G2: 0.80 (0.19) *@ 12 mths* G1: 0.85 G2: 0.80 p=NS	**N (%) satisfied with depression care; change from BL** *@ Baseline* G1: 47 (51%) G2: 43 (47%) *@ 6 mths* G1: 84 (87%); +37 (+36%) G2: 53 (62%); +10 (+15%) *@ 12 mths* G1: 81 (90%); +34 (+39%) G2: 46 (55%); +3 (+8%) Overall P < 0.001

Evidence Table 6. Mental health outcomes: treatment adherence and treatment satisfaction[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Treatment Adherence	MH Treatment Satisfaction
Pyne, 2011[16] HITIDES US Government	**Antidepressant medication regimen adherence, N (%)** (defined as # pills taken over past 4 days / # pills prescribed over past 4 days ≥ 80%) *@ 6 mths* G1: 52 (78.8) G2: 50 (69.4) Unadj OR (95% CI)=1.60 (0.74 to 3.45) Adj OR (95% CI)=1.65 (0.75 to 3.62); p=0.22 *@ 12 mths* G1: 45 (76.3) G2: 51 (85.0) Unadj OR (95% CI): 0.55 (0.21 to 1.44) Adj OR (95% CI)= 0.56 (0.20 to1.57); p=0.27	NR
Rollman, 2009[17] Bypassing the Blues US Government	NR	NR
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	NR	**Care rated as very good or excellent N (%)** G1: 68 (79) G2: NR
Vera, 2010[19] NA Puerto Rico Government	NR	NR

Evidence Table 6. Mental health outcomes: treatment adherence and treatment satisfaction[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Treatment Adherence	MH Treatment Satisfaction
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	NR	NR
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	NR	**% rating "good or excellent"** *@ BL* Overall: 44 G1:42 G2:47 Between-groups difference, p = 0.713 *@ 12 mths* Overall: 85 G1: 93 G2: 74 Between-groups difference, p = 0.015 *@ 18 mths* Overall: 55 G1: 61 G2: 49 Between-groups difference, p = 0.209 *@ 24 mths* Overall: 54 G1: 56 G2: 51 Between-groups difference, p = 0.684

Evidence Table 6. Mental health outcomes: treatment adherence and treatment satisfaction[a] (continued)

First Author, Year Trial Name Country Funding Source	MH Treatment Adherence	MH Treatment Satisfaction
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	NR	NR

[a] G1 = intervention arm; G2 = control arm

Abbreviations: Adj = adjusted; BL = baseline; CI = confidence interval; MH = mental health; mths = months; NR = not reported; OR = odds ratio; US = United States

Evidence Table 7. Mental health outcomes: morbidity, mortality, self-reported health status, and quality of life[a]

First Author, Year Trial Name Country Funding Source	MH-Related Morbidity and / or Mortality	MH-Related Self-Reported Health Status	MH-Related Quality of Life
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	NR	NR	**FACT social/family well-being score** *mean change BL to 8 mths (SD)* G1: +0.39 (5.35) G2: -1.37 (5.07) Between-groups diff (95% CI): +1.76 (-1.12 to 4.63); p = 0.88 **FACT emotional well-being score** *mean change BL to 8 mths (SD)* G1: +2.15 (3.56) G2: -0.50 (5.26) Between-groups diff (95% CI): +2.65 (0.18 to 5.12); p = 0.03
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	Investigators were unaware of any attempted or completed suicides in either the intervention or control group	**SF-12 mental, mean (SE)** *@ BL* G1: 32.15 (0.71) G2: 33.97 (0.71) Adj mean diff (95% CI): -1.82 (-3.64 to 0.01); p = 0.05 *@ 6 mths* G1: 44.49 (0.83) G2: 41.74 (0.84) Adj mean diff (95% CI): +2.75 (0.54 to 4.96); p = 0.01 *@ 12 mths* G1: 45.65 (0.88) G2: 43.46 (0.96) Adj mean diff (95% CI): +2.19 (-0.26 to 4.63); p = 0.08	**FACT social/family well-being, mean (SD), as-treated** *@ BL (N=470 to 472)* G1: 13.42 (6.46) G2: 14.40 (5.73) Adj mean diff (95% CI): 0.53 (-1.75 to 0.70); p= 0.40 *@ 6 mths (N=317 to 318)* G1: 17.10 (6.79) G2: 14.65 (6.53) Adj mean diff (95% CI): 0.47 (-0.95 to 1.90); p = 0.51 *@ 12 mths (N=258)* G1: 15.83 (6.92) G2: 15.89 (5.96) Adj mean diff (95% CI): 2.86 (1.31 to 4.41); p <0.001 *@ 18 mths (N=272)* G1: 16.38 (6.90) G2: 14.79 (6.65) Adj mean diff (95% CI)=0.21 (-1.30 to 1.71); p=0.79

Evidence Table 7. Mental health outcomes: morbidity, mortality, self-reported health status, and quality of life[a] (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Morbidity and / or Mortality	MH-Related Self-Reported Health Status	MH-Related Quality of Life
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government (continued)			*@ 24 mths (N=210)* G1: 14.66 (6.96) G2: 14.89 (6.21) Adj mean diff (95% CI)=1.89 (0.22 to 3.56); p=0.03 Overall 24 month time by group interaction p<0.001 **FACT emotional well-being, mean (SD), as-treated** *@ BL (N=470 to 472)* G1: 12.31 (3.94) G2: 13.58 (4.39) Adj mean diff (95% CI): 1.41 (-2.23 to -0.59); p < 0.001 *@ 6 mths (N=317 to 318)* G1: 17.31 (4.52) G2: 16.32 (4.75) Adj mean diff (95% CI): 0.58 (-0.40 to 1.55); p = 0.25 *@ 12 mths (N=258)* G1: 17.73 (4.40) G2: 17.38 (4.79) Adj mean diff (95% CI): 0.98 (-0.10 to 2.06) p = 0.07 *@ 18 mths (N=272)* G1: 16.84 (4.82) G2: 16.55 (4.48) Adj mean diff (95% CI)=0.69 (-0.35 to 1.73); p=0.19 *@ 24 mths (N=210)* G1: 15.77 (5.65) G2: 15.57 (4.46) Adj mean diff (95% CI)=0.28 (-0.89 to 1.45); p=0.64 Overall 24 month time by group interaction p<0.001

Evidence Table 7. Mental health outcomes: morbidity, mortality, self-reported health status, and quality of life[a] (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Morbidity and / or Mortality	MH-Related Self-Reported Health Status	MH-Related Quality of Life
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	NR	**SF-12 mental, mean (SD unless noted otherwise):** *@ BL* G1: 32.27 (8.48) G2: 34.06 (9.63) p = 0.40 *@ 6 mths* G1: 46.21 (10.33) G2: 42.15 (12.27) p < 0.001 *@ 12 months* G1: 48.22 (SE 1.15) G2: 42.00 (SE 1.15) Mean difference (95% CI)=6.22 (3.79 to 8.64); p<0.001 *@ 18 months* G1: 46.26 (SE 1.14) G2: 42.09 (SE 1.14) Mean difference (95% CI)=4.17 (1.75 to 6.60); p=0.001 *@ 24 months* G1: 46.26 (SE 1.14) G2: 42.48 (SE 1.17) Mean difference (95% CI)=2.28 (-0.21 to 4.77); p=0.07 Overall time by group interaction p<0.0001	**Number of social stressors, mean (SD)** *@ BL* G1: 4.31 (2.70) G2: 3.15 (2.38) p < 0.001 *@ 6 mths* G1: 2.53 (2.18) G2: 2.34 (2.07) p = 0.96 *@ 12 mths* G1: 2.29 (2.14) G2: 2.40 (2.13) p = 0.19 *@ 18 mths* G1: 2.58 (2.06) G2: 2.39 (2.02) p = 0.70
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	NR	NR	NR

Evidence Table 7. Mental health outcomes: morbidity, mortality, self-reported health status, and quality of life[a] (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Morbidity and / or Mortality	MH-Related Self-Reported Health Status	MH-Related Quality of Life
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	NR	NR	NR
Pyne, 2011[16] HITIDES US Government	NR	**SF-12 mental** *@ BL* G1: 34.3 (10.5) G2: 35.1 (11.0) *Change from BL* *@ 6 mths* G1: +5.8 G2: +3.7 p=0.26 Adjusted group diff beta (95% CI): +2.0 (−1.0 to 5.0); p=0.19 *@ 12 mths* G1: +7.1 G2: +5.8 p=0.50 Adjusted group diff beta (95% CI): +1.7 (−1.7 to 5.2); p=0.32	NR

Evidence Table 7. Mental health outcomes: morbidity, mortality, self-reported health status, and quality of life[a] (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Morbidity and / or Mortality	MH-Related Self-Reported Health Status	MH-Related Quality of Life
Rollman, 2009[17] Bypassing the Blues US Government	**Hospitalization for suicidal ideation (N):** G1: 1 G2: 0	**SF-36 mental, mean (SE)** *@ BL* G1: 43.1 (1.0) G2: 42.5 (1.0) *@ 8 mths* G1: 50.0 (1.0) G2: 46.2 (1.1) *Change from BL to 8 mths:* G1: + 6.8 (1.0) G2: + 3.6 (1.0) Between-group difference (95% CI): +3.2 (0.5 to 6.0), p = 0.02 Effect Size (95% CI): 0.30 (0.17 to 0.52), p = 0.01 *MEN ONLY* *@ 8 mths* G1: 52.1 (1.4) G2: 45.4 (1.3) *Change from BL to 8 mths:* G1: + 7.8 (1.3) G2: + 2.1 (1.2) Between-group difference (95% CI): 5.7 (2.2 to 9.2), p = 0.001 Effect Size (95% CI): 0.53 (0.23 to 0.84), p < 0.001 *WOMEN ONLY* *@ 8 mths* G1: 47.8 (1.6) G2: 46.9 (1.7) *Change from BL to 8 months:* G1: + 5.9 (1.5) G2: + 5.1 (1.6) Between-group difference (95% CI): 0.7 (-3.3 to 4.9), p = 0.74 Effect Size (95% CI): 0.08 (-0.28 to 0.43), p = 0.68	NR
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	**Suicide** G1: 0 G2: 1	NR	NR

Evidence Table 7. Mental health outcomes: morbidity, mortality, self-reported health status, and quality of life[a] (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Morbidity and / or Mortality	MH-Related Self-Reported Health Status	MH-Related Quality of Life
Vera, 2010[19] NA Puerto Rico Government	NR	NR	NR
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	NR	NR	NR
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	**Suicidality** remained significantly lower in G1 than G2, values and p = NR	NR	NR
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	NR	**SF-12 mental** Between-groups diff (95% CI): +2.44 (0.79 to 4.09), favoring G1	NR

[a] G1 = intervention arm; G2 = control arm

Abbreviations: Adj = adjusted; BL = baseline; CI = confidence interval; diff = difference; FACT = Functional Assessment of Cancer Therapy; MH = mental health; mths = months; NR = not reported; SD = standard deviation; SE = standard error; US = United States

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	Among G1 patients: 5 (18%) received no intervention services 12 (43%) received ≥4 PST sessions 3 (11%) chose medication as first-line treatment Study psychiatrist recommended medication for 4 patients after non-response to PST Of 7 patients on medication, only 3 received antidepressants for ≥5 mths	NR
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	**N (%) receiving any depression treatment, as-treated:** *@ BL (N=472)* G1: 25 (10) G2: 28 (12) OR (95% CI)=0.83 (0.47 to 1.47); p=0.53 *Over 12 months (N=472)* G1: 175 (72) G2: 24(10) OR (95% CI)=22.42 (13.49 to 37.26); p<0.001 *@ 18 months (N=272)* G1: 31 (21) G2: 8 (6) OR (95% CI)=4.04 (1.78 to 9.17); p=0.001 *@ 24 months (N=210)* G1: 20 (18) G2: 13 (13) OR (95% CI)=1.45 (0.68 to 3.10); p=0.33 **N (%) receiving antidepressant medication, as-treated:** *@ BL (N=472)* G1: 14 (6) G2: 19 (8) OR (95% CI)=0.68 (0.33 to 1.39); p=0.29 *Over 12 months (N=472)* G1: 81 (33) G2: 20 (9) OR (95% CI)=5.28 (3.11 to 8.98); p<0.001	$524 per intervention patient over 12 mths

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government (continued)	*@ 18 months (N=272)* G1: 13 (9) G2: 7 (6) OR (95% CI)=1.69 (0.65 to 4.37); p=0.28 *@ 24 months (N=210)* G1: 17 (15) G2: 10 (10) OR (95% CI)=1.61 (0.70 to 3.70); p=0.26 **N (%) receiving PST or mental health counseling, as-treated analysis:** *@ BL (N=472)* G1: 20 (8) G2: 16 (7) OR (95% CI)=1.20 (0.61 to 2.39); p=0.59 *Over 12 months (N=472)* G1: 165 (68) G2: 11 (5) OR (95% CI)=42.66 (21.98 to 82.81); p<0.001 *@ 18 months (N=272)* G1: 24 (17) G2: 4 (3) OR (95% CI)=6.10 (2.06 to 18.10); p=0.001 *@ 24 months (N=210)* G1: 7 (6) G2: 6 (6) OR (95% CI)=1.04 (0.34 to 3.22); p=0.94	

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Ell, 2010[4]	**Antidepressant during the past 6 mths, N (%)**	**Estimated costs of intervention components:**
Ell, 2011[5]	*@ BL:*	$71 per patient visit (90 minutes)
Hay, 2011[6]	G1: 36 (18.9)	$35 per DDCS phone followup (45 minutes)
Multifaceted Diabetes and	G2: 24 (12.7)	$10 per patient navigation call (10-15 minutes)
Depression Program	p = 0.08	$10 per relaxation tape
US	*Over 12 mths:*	$136 per patient for DDCS communication with PCP
Government	G1: 113 (58.5)	$21 per patient for clinical supervision
	G2: 52 (26.8)	
	p < 0.001	Mean=$820 per patient (or $515, per the cost-effectiveness paper)
	@ 18 mths:	
	G1: 52 (36.1)	
	G2: 27 (19.7)	
	p = 0.002	
	@ 24 mths:	
	G1: 53 (38.4)	
	G2: 32 (25.4)	
	p=0.02	
	PST or counseling during the past 6 mths, N (%)	
	@ BL:	
	G1: 29 (15.0)	
	G2: 20 (10.3)	
	p = 0.11	
	Over 12 mths:	
	G1:153(79.3)	
	G2: 26 (13.4)	
	p < 0.001	
	@ 18 mths:	
	G1: 35 (24.3)	
	G2: 17 (12.4)	
	p = 0.01	
	@ 24 mths:	
	G1: 23 (16.7)	
	G2: 19 (15.1)	
	p=0.72	

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government (continued)	**Antidepressant + PST/counseling during the past 6 months, N (%):** *@ 12 mths:* G1: 104 (53.8) G1: 15 (7.7) p=NS *@ 24 mths:* G1: 15 (10.9) G2: 10 (7.9) p=0.42 **Any depression treatment in the past 6 mths, N (%)** *@ BL:* G1: 43 (22.3) G2: 30 (15.5) p = 0.07 *Over 12 mths:* G1: 162 (83.9) G2: 63 (32.5) p < 0.001 *@ 18 mths:* G1: 66 (45.8) G2: 33 (24.1) p < 0.001 *@ 24 mths:* G1: 61 (44.2) G2: 41 (32.5) p=0.05	

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	**4 or more specialty mental health visits at 12 mo, N(%)** G1: 111 (67.7) G2: 11 (6.7) Adj OR (95% CI) =29.31 (14.65 to 58.66) **N (%) receiving adequate dosage of antidepressant** *BL to 6-mth* G1: 94 (57.3) G2: 66 (40.0) Adj OR (95% CI): 4.15 (2.28 to 7.55) *6 mth to 12 mth* G1: 87 (53.0) G2: 63 (38.2) Adj OR (95%): 2.90 (1.69 to 4.98)	**Total intervention service costs, mean (SD):** *BL through 12 mths* $545 ($222) **Intervention visit costs, mean (SD) / median (IQR)** *@ 5 yrs* $543 ($228) / $546 ($331) **Screening costs** $27
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	**Initiation of antidepressants over 12 months:** Rate (95% CI)=3.5 (2.0 to 6.3)	$79 per in-person nurse visit $31 per telephone nurse contact $100 fixed per-patient for costs of supervision and information systems support
Pyne, 2011[16] HITIDES US Government	**Receipt of antidepressant, N (%)** *@ 6 mths* G1: 72 (66.7) G2: 78 (67.8) Unadj OR (95% CI): 0.89 (0.49 to 1.78) Adj OR (95% CI): 0.89 (0.46 to 1.74); p=0.93 *@ 12 mths* G1: 65 (61.9) G2: 69 (62.7) Unadj OR (95% CI): 0.93 (0.49 to 1.78) Adj OR (95% CI): 0.93 (0.49 to 1.78); p=0.98	NR

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Rollman, 2009[17] Bypassing the Blues US Government	**Self-reported antidepressant use, N (%)** *@ BL* G1: 22 (15) G2:13 (9) *@ 8 mths* G1: 55 (44) G2:40 (31) Difference (95% CI): 13 (1 to 24) p = 0.008 **Mental health specialist care use N (%):** G1: 5 (4) G2: 7 (6) p = 0.56	NR
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	**Receipt of therapeutic dose of antidepressant, N (%)** *@ BL* G1: 17 (17) G2: 20 (20) *@ 6 mths* G1: 62 (65) G2: 32 (34) p<0.0001	**Cost of nurse time + psychiatrist time:** $523 per patient **Total average extra cost (95% CI) of the intervention per patient over 6 months** (British pounds) £334.86 (£276 to £393) per patient
Vera, 2010[19] NA Puerto Rico Government	**% receiving depression treatment (N per treatment type):** G1: 97% (47 CBT, 36 medication, 3 combination, 3 none) G2: 57% (25 medication, 19 psychotherapy, 39 none)	NR

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	**Antidepressant use** *@ BL* G1: 43% G2: 47% *@ 12 mths* G1: 66% G2: 52% p <0.001 **MH service use / psychotherapy** *@ BL* G1: 8% G2: 7% *@ 12 mths* G1: 47% G2: 16% p<0.001	NR

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	**Antidepressant use over 12 months** OR (95% CI): 2.07 (1.45 to 2.94), p = NR **Antidepressant use over past 3 months, %** *@ BL* Overall: 43 G1: 49 G2:36 *@ 6 mths* Overall:56 G1:64 G2:48 Between group diff, p = 0.036 *@ 12 mths* Overall:57 G1:67 G2:45 Between group diff, p = 0.010 *@ 18 mths* Overall:48 G1:56 G2:40 Between group diff, p = 0.041 *@ 24 mths* Overall:46 G1:52 G2:39 Between group diff, p = 0.121	NR

Evidence Table 8. Mental health outcomes: health care utilization and intervention costs (continued)

First Author, Year Trial Name Country Funding Source	MH-Related Health Care Utilization	Intervention Costs
Fann, 2009[22] IMPACT: cancer (secondary analyses) (continued)	**MH Utilization** OR (95% CI): 4.48 (2.80 to 7.10), p = NR **Any MH visit past 3 months: %** *@ BL* Overall: 8 G1:14 G2:2 *@ 6 mths* Overall:28 G1:40 G2:15 Between group diff, p < 0.001 *@ 12 mths* Overall:29 G1:42 G2:16 Between group diff, p < 0.001 *@ 18 mths* Overall:14 G1:15 G2:12 Between group diff, p = 0.561 *@ 24 mths* Overall:15 G1:17 G2:12 Between group diff, p = 0.386	
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	**Antidepressant Use @ 12 months, %** G1: 76 G2: 51 Between group diff, p < 0.001	$597 (95% CI: 560 to 635) per patient over 24 mths

Abbreviations: BL = baseline; CI = confidence interval; IQR = interquartile range; mths = months; NR = not reported; SD = standard deviation; US = United States

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a]

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	NR	NR
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	**Brief Pain Inventory score, mean (SE)** *@ BL* G1: 11.66 (0.81) G2: 11.35 (0.81) Adj mean diff (95% CI): + 0.32 (-1.75 to 2.38); p = 0.76 *@ 6 mths* G1: 9.79 (0.94) G2: 11.65 (0.95) Adj mean diff (95% CI): -1.86 (-4.33 to 0.61); p = 0.14 *@ 12 mths* G1: 8.83 (0.99) G2: 11.55 (1.07) Adj mean diff (95% CI): -2.72 (-5.44 to 0.01); p =0.05	NR

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	**HbA1c, mean (SD unless otherwise noted)** *@ BL* G1: 9.01 (2.15) G2: 9.05 (2.22) p = 0.98 *@ 6 months:* G1: 8.45 (2.06) G2: 8.42 (2.00) p = 0.85 *@ 12 months:* G1: 8.88 (SE 0.27) G2: 8.87 (SE 0.27) Mean difference (95% CI)=0.01 (-0.50 to 0.51); p=0.98 *18 months:* G1: 8.86 (SE 0.28) G2: 8.69 (SE 0.28) Mean difference (95% CI)=0.17 (-0.37 to 0.70); p=0.54 *24 months* G1: 9.10 (SE 0.29) G2: 8.87 (SE 0.29) Mean difference (95% CI)=0.23 (-0.34 to 0.81); p=0.42 Overall 24-month time by group interaction p=0.80 **Whitty-9 Diabetes Symptoms, mean (SD)** *@ BL* G1: 2.33 (0.76) G2: 2.15 (0.75) p = 0.07 *@ 6 months:* G1: 1.65 (0.59) G2: 1.79 (0.65) p = 0.003 *@ 12 months:* G1: 1.69 (SE 0.07) G2: 1.87 (SE 0.07) Mean difference (95% CI)=-0.18 (-0.33 to -0.04); p=0.01 *@ 18 months:* G1: 1.79 (SE 0.07) G2: 1.89 (SE 0.07)	**Sheehan Disability Scale of Functional Impairment, mean (SD):** *@ BL* G1: 6.30 (2.67) G2: 5.74 (2.84) p = 0.47 *@ 6 mths* G1: 3.07 (2.93) G2: 3.55 (2.90) p = 0.01 *12 months:* G1: 3.23 (SE 0.31) G2: 4.17 (SE 0.30) Mean difference (95% CI)=-0.94 (-1.58 to -0.30); p=0.004 *18 months:* G1: 3.53 (SE 0.30) G2: 4.14 (SE 0.30) Mean difference (95% CI)=-0.61 (-1.25 to 0.03); p=0.06 *24 months:* G1: 3.89 (SE 0.30) G2: 3.86 (SE 0.31) Mean difference (95% CI)=0.02 (-0.64 to 0.68); p=0.95 Overall 24-month time by group interaction p=0.02 **Diabetes complications, mean (SE)** *@ 12 months* G1: 1.20 (0.12) G2: 1.48 (0.12) Mean difference (95% CI)=-0.28 (-0.53 to -0.04); p=0.02 *@ 18 months* G1: 1.42 (0.12) G2: 1.41 (0.12) Mean difference (95% CI)=0.02 (-0.23 to 0.26); p=0.90

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government (continued)	Mean difference (95% CI)=-0.10 (-0.24 to 0.04); p=0.17 *@ 24 months* G1: 1.76 (SE 0.07) G2: 1.84 (SE 0.07) Mean difference (95% CI)=-0.08 (-0.23 to 0.06); p=0.27 Overall 24-month time by group interaction p<0.0001 **Pain Impact score, mean (SD):** *@ BL* G1: 2.91 (1.24) G2: 2.66 (1.34) p = 0.22 *@ 6 mths* G1: 2.23 (1.23) G2: 2.59 (1.33) p = 0.001 *@ 12 mths* G1: 2.44 (1.32) G2: 2.55 (1.39) p = 0.12 *@ 18 mths* G1: 2.54 (1.32) G2: 2.36 (1.41) p = 0.50	*@ 24 months* G1: 1.40 (0.12) G2: 1.60 (0.12) Mean difference (95% CI)=-0.20 (-0.45 to 0.05); p=0.12 Overall 24-month time by group interaction p=0.13
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	**HbA1c, mean (SD)** NSD between groups at any timepoint; group values presented only in graph. Overall (both groups) mean (SD): *BL* 7.99 (1.55) *@ 6 mths* 7.58 (1.47) *@ 12 mths* 7.64 (1.57) *@ 24 mths* G1: 7.87 G2: 7.82 p = 0.68	NR

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	**HbA1c** *BL* G1: 8.14 (2.03) G2: 8.04 (1.87) *6 months:* G1: 7.42 (1.32) G2: 7.87 (1.93) G1 change from BL to 6 months: -0.72 G2 change from BL to 6 months: -0.17 *12 months:* G1: 7.33 (1.21) G2: 7.81 (1.90) G1 change from BL to 12 months: -0.81, p =NR G2 change from BL to 12 months: -0.23, p = NR 12-month between-group difference (95% CI): -0.56 (-0.85 to -0.27); p < 0.001 **LDL Cholesterol (mg/dL) mean (SD)** Baseline: G1: 106.8 (35.4) G2: 109.4 (36.7) 12 months: G1: 91.9 (36.7) G2: 101.4 (36.6) G1 change: -14.9, p =NR G2 change: -8.0, p = NR 12-month between-group difference (95% CI): -9.1 (-17.5 to -0.8); p = NR **SBP (mmHg), mean (SD)** Baseline: G1: 135.7 (18.4) G2: 131.9 (17.0) 6 months: G1: 131.9 (15.2) G2: 133.5 (20.4) G1 change from BL to 6 months: -3.8 G2 change from BL to 6 months: +1.6 12 months: G1: 131.0 (18.2) G2: 132.3 (17.4)	**Sheehan Disability Scale of Functional Impairment, mean (SD):** *BL* G1: 5.6 (2.4) G2: 5.1 (2.6) p = NR *6 months:* G1: 3.7 (3.2) G2: 4.2 (2.6) p = NR *12 months:* G1: 3.8 (3.0) G2: 4.5 (2.9) p = 0.015 p for combined 6 and 12 mths = 0.006 Estimated mean difference (95% CI):-0.9 (-1.5 to -0.2) Intervention effect size @ 12 mths = 0.30 **WHODAS (World Health Organization Disability Assessment Schedule), mean (SD):** *BL*: G1: 15.8 (9.6) G2: 13.8 (9.6) p = NR *6 mths:* G1: 12.3 (10.7) G2: 12.4 (9.8) p = NR *12 mths:* G1: 12.9 (10.0) G2: 12.9 (11.2) p = 0.2 p for combined 6 and 12 mths = 0.1 Estimated mean difference (95% CI):-1.5 (-3.3 to 0.4) Intervention effect size @ 12 mths = 0.12

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources (continued)	G1 change from baseline to 12 months: -4.7, p =NR G2 change from baseline to 12 months: -0.4, p = NR 12-month between-group difference (95% CI): -3.4 (-6.9 to -0.1); p = NR **≥1.0% decrease from baseline in HbA1c at 12 months, N (%)** G1: 37 (36) G2: 18 (19) p = 0.006 **≥10 mm Hg decrease from baseline in SBP at 12 months, N (%)** G1: 41 (41) G2: 25 (25) p = 0.016 **N (%) achieving clinically significant change / falling below guidelines for all conditions @ 12 months:** G1: 36 (37) G2: 19 (22) p=0.024 **% below ADA guidelines for hemoglobin, SBP, and LDL at 12 months** G1: 16.3 G2: 12.5 p=NS	**Restricted days of household maintenance activities, mean (SD):** *BL* G1: 8.9 (10.2) G2: 8.4 (10.0) *6 mths:* G1: 6.4 (8.7) G2: 5.6 (8.7) *12 mths:* G1: 6.4 (9.2) G2: 6.7 (9.3) Estimated mean difference (95% CI): 0.0 (-0.3 to 0.4); p=0.8
Pyne, 2011[16] HITIDES US Government	**HIV symptom severity: 20-items Symptoms Distress Module, intervention effect** *@ 6 months* G1: −7.6 G2: −4.5 Effect size = -0.2; p=0.06 Adj group diff, beta (95% CI): −2.6 (−3.5 to −1.8); p .001 *@ 12 months* G1: −7.9 G2: −7.3 Effect size = -0.04; p=0.75 Adj grp diff, beta (95% CI): −0.82 (−1.6 to −0.07); p=.03 **HIV symptom severity: 20-items Symptoms Distress Module, intervention effect – minus 7 depression items** *@ 6 months* Adj group diff, beta (95% CI): −0.62 (−1.2 to −0.08); p=0.03 *@ 12 months* Adj grp diff, beta (95% CI): −0.09 (−1.6 to 1.4); p=0.88	NR

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Rollman, 2009[17] Bypassing the Blues US Government	NR	**DASI mean (SE)** *FULL SAMPLE* *@ BL* G1: 7.1 (0.9) G2: 7.9 (0.9) *@ 8 months* G1: 25.2 (1.0) G2: 21.4 (1.0) *Change @ 8 months*: G1: +18.1 (1.0) G2: +13.5 (1.0) Between-group difference (95% CI): 4.6 (1.9 to 7.3), p = 0.001 Effect Size (95% CI): 0.32 (0.09 to 0.54), p = 0.006 *MEN ONLY* *@ BL* G1: 7.5 (1.2) G2: 7.3 (1.1) *@ 8 months* G1: 29.3 (1.3) G2: 22.9 (1.2) *Change @ 8 months:* G1: +21.8 (1.3) G2: +15.6 (1.2) Between-group difference (95% CI): 6.1 (2.7 to 9.6), p = 0.001 Effect Size (95% CI): 0.55 (0.24 to 0.85), p < 0.001 WOMEN ONLY *@ BL* G1: 6.6 (1.3) G2: 8.5 (1.5) *@ 8 months* G1: 21.1 (1.4) G2: 19.9 (1.6)

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Rollman, 2009[17] Bypassing the Blues US Government (continued)		*Change @ 8 months:* G1: +14.5 (1.4) G2: +11.4 (1.6) Between-group difference (95% CI): 3.1 (-1.1 to 7.3), p = 0.14 Effect Size (95% CI): 0.10 (-0.25 to 0.46), p = 0.58
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	NR	NR
Vera, 2010[19] NA Puerto Rico Government	NR	NR

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Lin, 2006 Lin, 2006 #549} Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	**Pain intensity, mean (SE)** *@ baseline* G1: 6.04 (0.29) G2: 6.32 (0.29) Betw-grp diff: -0.28 (-0.6 to +0.04); p = 0.08 *@ 6 mo* G1: 5.48 (0.16) G2: 5.69 (0.15) Betw-grp diff: -0.21 (-0.55 to + 0.13); p = 0.22 *@ 12 mo* G1: 5.62 (0.16) G2: 6.15 (0.16) Betw-grp diff: -0.53 (-0.92 to -0.14); p = 0.009	**GCPS: Arthritis interferes w/daily activities (range 0-10), mean (SE)** *@ BL* G1: 5.17 (0.36) G2: 5.38 (0.37) Betw-grp diff: -0.21 (-0.6 to +0.19); p = 0.30 *@ 6 mths* G1: 4.08 (0.20) G2: 4.65 (0.17) Betw-grp diff: -0.56 (-0.96 to -0.16); p = 0.006 *@ 12 mths* G1: 4.40 (0.18) G2: 4.99 (0.17) Betw-grp diff: -0.59 (-1.00 to -0.19); p = 0.004 **GCPS: Arthritis pain interferes w/daily activities (1-5), mean (SE)** *@ BL* G1: 3.17 (0.12) G2: 3.24 (0.12) Betw-grp diff: -0.07 (-0.21 to +0.06); p = 0.29 *@ 6 mths* G1: 2.88 (0.07) G2: 3.11 (0.07) Betw-grp diff: -0.22 (-0.36 to -0.09); p = 0.005 *@ 12 mths* G1: 2.92 (0.07) G2: 3.17 (0.07) Betw-grp diff: -0.26 (-0.41 to -0.10); p = 0.002 **Sheehan Disability Scale, mean (SE)** *@ 12 mths* G1: 3.9 (0.15) G2: 4.7 (0.15) Betw-grp diff: -0.82 (-1.17 to -0.47); p < 0.001

Evidence Table 9. Chronic medical condition outcomes: symptom improvement and response[a] (continued)

First Author, Year Trial Name Country Funding Source	CM Condition-Related Symptom Improvement	CM Condition-Related Functional Impairment/Disability
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	NR	**Sheehan Disability Scale, mean (SE?):** *@ 6 mths* Overall: 4.13 (0.22) G1: 3.92 (0.29) G2: 4.36 (0.30); p = 0.266 *@12 mths* Overall: 4.34 (0.21) G1: 3.81 (0.28) G2: 4.91 (0.31); p = 0.011 *@ 18 mths* Overall: 3.97 (0.20) G1: 3.69 (0.30) G2: 4.28 (0.29); p = 0.185 *@ 24 mths* Overall: 4.10 (0.25) G1: 4.16 (0.37) G2: 4.03 (0.28); p = 0.774
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	**HbA1c %, mean (SD):** *@ Baseline:* Overall: 7.28 (1.43) G1: 7.26 (1.32) G2: 7.30 (1.54) *@ 6 months:* Overall: 7.07 (1.27) G1: 7.07 (1.23) G2: 7.08 (1.32) *@ 12 months:* Overall: 7.11 (1.37) G1: 7.11 (1.13) G2: 7.11 (1.42) p > 0.20 at all timepoints	**Functional Impairment (range 0-10), mean (SD):** *@ BL* G1: 5.20 (2.46) G2: 5.14 (2.42) Between-group difference (95% CI): +0.12 (-0.35 to 0.59) *@ 6 mths* G1: 4.37 (2.67) G2: 4.63 (2.70) Between-group difference (95% CI): -0.20 (-0.78 to 0.39) *@ 12 mths* G1: 3.91 (2.76) G2: 4.90 (2.63) Between-group difference (95% CI): -0.89 (-1.46 to -0.32)

Abbreviations: ADA = American Diabetes Association; adj = adjusted; betw = between; BL = baseline; CI = confidence interval; CM = chronic medical; DASI = Duke Activity Status Index; diff = difference; dL = deciliter; GCPS = Graded Chronic Pain Scale; grp = group; HbA1c = hemoglobin A1c; HIV = human immunodeficiency virus; LDL = low density lipoprotein; mg = milligrams; mmHg = millimeters of mercury; mths = months; NR = not reported; NS = not significant; NSD = no significant difference; SBP = systolic blood pressure; SD = standard deviation; SE = standard error; US = United States; VA = Veterans' Affairs

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a]

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	"Treatment adherent" if patient had completed or was in the process of completing all doctor-recommended treatment or follow-up visits; nonadherent if treatment was recommended but not received **Adherence to cancer treatment at 8 months N (%)** G1: 25 (89) G2: 19 (70) OR (95% CI) = 3.51 (0.82 to 15.03); p=0.08	NR
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	NR	**N (%) "satisfied" or "very satisfied" with overall care, as treated:** G1: 138 (94.5) G2: 116 (95.9); p=NR
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	**Diabetes self-care management score, mean (SE)** *@12 months:* G1: 3.31 (0.15) G2: 3.34 (0.15) Mean difference (95% CI)=-0.03 (-0.35 to 0.29); p=0.86 *@ 18 months:* G1: 3.67 (0.15) G2: 3.50 (0.15) Mean difference (95% CI)=0.17 (-0.16 to 0.49); p=0.31 *@ 24 months:* G1: 3.60 (0.15) G2: 3.41 (0.16) Mean difference (95% CI)=0.19 (-0.14 to 0.52); p=0.26 Overall 24-month time by group interaction p=0.84	NR

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	**Generally healthy diet (# days in past 7), mean (SD)** @ baseline: G1:3.7 (2.1) G2: 3.7 (2.1) @ 6 months: G1: 4.2 (2.0) G2: 4.4 (1.9) Adj mean diff (95% CI): +0.07 (-0.21 to 0.35) @ 12 months: G1: 4.5 (1.9) G2: 4.5 (2.1) Adj mean diff (95% CI): -0.01 (-0.56 to 0.54) **Recommended Diet, # days (in past 7), mean (SD)** @ baseline: G1:3.5 (1.7) G2: 3.2 (1.6) @ 6 months: G1: 3.9 (1.8) G2: 3.8 (1.7) Adj mean diff (95% CI): -0.01 (-0.22 to 0.20) @ 12 months: G1: 4.1 (1.9) G2: 3.8 (1.8) Adj mean diff (95% CI): -0.05 (-0.42 to 0.32) **# days (in past 7) ≥30 mins physical activity, mean (SD)** @ baseline: G1: 2.6 (2.4) G2: 2.3 (2.2) @ 6 months: G1: 2.3 (2.3) G2: 2.4 (2.3)	NR

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government (continued)	Adj mean diff (95% CI): +0.19 (-0.21 to 0.60) @ 12 months: G1: 2.7 (2.4) G2: 2.6 (2.5) Adj mean diff (95% CI): -0.12 (-0.50 to 0.26)**Exercise session (# days in past 7), mean (SD)** @ baseline: G1: 1.9 (2.2) G2: 1.2 (1.8) @ 6 months: G1: 1.6 (2.2) G2: 1.7 (2.2) Mean adj diff (95% CI): +0.19 (-0.37 to 0.76) @ 12 months: G1:1.9 (2.3) G2: 1.6 (2.1) Mean adj diff (95% CI): -0.19 (-0.57 to 0.19) **% (SD) smoking** Baseline G1: 18 (11.1) G2: 28 (17.3) @12 mo G1: 18 (12.3) G2: 24 (16.9) OR (95% CI): NR (0.4 to 4.9) **Nonadherence, % days, mean (SD):** **Oral hypoglycemics:** Baseline: G1: 19.8 (21.3) G2: 22.9 (24.0) @ 12 months G1: 28.2 (28.9) G2: 24.0 (24.7) Adj mean diff (95% CI): -6.3 (-11.91 to -0.71), p < 0.03	NR

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government (continued)	**ACE Inhibitors:** Baseline G1: 27.4 (27.1) G2: 29.7 (29.3) @ 12 months G1: 24.2 (22.7) G2: 18.9 (17.47) Adj mean diff (95% CI): -2.5 (-8.69 to 3.70) **NONadherence, % days, mean (SD):** **Lipid-lowering Agents:** Baseline G1: 29.3 (26.7) G2: 24.5 (23.0) @ 12 months G1: 28.8 (27.1) G2: 27.7 (24.0) Adj mean diff (95% CI): -0.2 (-7.23 to 6.76)	NR
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	**N (%) adhering to general diet plan for ≥ 2 days/week** @ 12 months: G1: 68 (86) G2: 63 (81) p=0.37 **N (%) adhering to specific diet plan for ≥ 2 days/week** @ 12 months: G1: 66 (84) G2: 60 (77) p=0.30 **N (%) adhering to general exercise plan for ≥ 2 days/week** @ 12 months: G1: 43 (54) G2: 34 (44) p=0.17	**Satisfaction with care of diabetes, HD, or both, N(%):** Baseline: G1: 73 (70) G2: 65 (68) 6 months: G1: 87 (90) G2: 65 (68) G1 change from baseline to 6 mths: +14 (+20%) G2 change from baseline to 6 mths: 0 (0%) 12 months: G1: 79 (86) G2: 62 (70) G1 change from baseline to 12 months: +6 (+16%) G2 change from baseline to 12 months: -3 (+2%) Between-group change over time, p < 0.001

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources (continued)	**N (%) adhering to specific exercise plan for ≥ 2 days/week** @ 12 months: G1: 23 (29) G2: 16 (21) p=0.21 **Blood pressure self-monitoring, mean days per week** *@ 12 months:* G1: 3.6 G2: 1.1 RR=3.20; p<0.001**Blood glucose self-monitoring, mean days per week** *@ 12 months:* G1: 4.9 G2: 3.8 RR=1.28; p=0.006 **Medication adherence, mean (SD) % of days with available medicines:** **Oral hypoglycemic** *@ BL:* G1 (N=66): 0.83 (0.19) G2 (N=58): m.82 (0.20) *@ 12 months:* G1: 0.85 (0.17) G2: 0.83 (0.18) p=NS **Antihypertensive** *@ BL:* G1 (N=73): 0.85 (0.18) G2 (n=68): 0.86 (0.18) *@ 12 months:* G1: 0.88 (0.14) G2: 0.88 (0.16) p=NS	

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources (continued)	**Lipid-lowering** *@ BL:* G1 (N=59): 0.82 (0.21) G2 (n=57): 0.85 (0.18) *@ 12 months:* G1: 0.85 (0.17) G2: 0.88 (0.13) p=NS	
Pyne, 2011[16] HITIDES US Government	**HIV medication regimen adherence, N (%) (defined as # pills taken over past 4 days / # pills prescribed over past 4 days ≥ 95%)** @ 6 mo G1: 74 (77.1) G2: 72 (73.5) Unadj OR (95% CI): 1.23 (0.63 to 2.40) Adj OR (95% CI):1.20 (0.60 to 2.31); p=0 .65 @ 12 mo G1: 68 (73.9) G2: 64 (74.4) Unadj OR (95% CI): 0.93 (0.46 to 1.90) Adj OR (95% CI):1.60 (0.50 to 2.33); p=0 .89	NR
Rollman, 2009[17] Bypassing the Blues US Government	NR	NR
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	NR	NR
Vera, 2010[19] NA Puerto Rico Government	NR	NR
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	NR	NR

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	NR	NR
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	**Followed Recommended Diet (1=always, 5=never), mean (SD)** @ baseline: G1: 2.93 (1.40) G2: 2.63 (1.23) Mean adj diff (95% CI): 0.26 (-0.05 to 0.57), p = 0.10 @ 6 months: G1: 2.69 (1.26) G2: 2.61 (1.14) Mean adj diff (95% CI): -0.19 (-0.51 to 0.12), p > 0.20 @ 12 months: G1: 2.57 (1.08) G2: 2.54 (1.04) Mean adj diff (95% CI): -0.26 (-0.65 to 0.12), p = 0.18 **Took Prescribed Meds (1=always, 5=never), mean (SD)** @ baseline: G1: 1.16 (0.55) G2: 1.07 (0.34) Mean adj diff (95% CI): 0.05 (-0.05 to 0.15), p > 0.20 @ 6 months: G1: 1.15 (0.48) G2:1.23 (0.61) Mean adj diff (95% CI): -0.11 (-0.28 to 0.06), p = 0.20 @ 12 months: G1: 1.16 (0.53) G2: 1.19 (0.50) Mean adj diff (95% CI): -0.01 (-0.18 to 0.15), p > 0.20	NR

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources (continued)	**Weekly Exercise Days, mean (SD)** @ baseline: G1: 1.13 (1.20) G2: 1.33 (1.30) Mean adj diff (95% CI):-0.12 (-0.41 to 0.16), p > 0.20 @ 6 months: G1: 1.23 (1.15) G2: 1.19 (1.14) Mean adj diff (95% CI): +0.08 (-0.27 to 0.43), p > 0.20 @ 12 months: G1: 1.41 (1.23) G2: 1.10 (1.09) Mean adj diff (95% CI): +0.50 (0.12 to 0.89), p = 0.01 **Weekly glucose testing days, mean (SD)** @ baseline: G1: 3.78 (3.18) G2: 4.43 (2.95) Mean adj diff (95% CI): - 0.54 (-1.17 to 0.09), p = 0.10 @ 6 months: G1: 4.27 (2.81) G2: 4.78 (2.78) Mean adj diff (95% CI): +0.25 (-0.39 to 0.89), p > 0.20 @ 12 months: G1: 4.16 (2.88) G2: 4.82 (2.71) Mean adj diff (95% CI): -0.21 (-1.08 to 0.66), p > 0.20 **Weekly foot inspection days, mean (SD)** @ baseline: G1: 5.13 (2.70) G2: 5.04 (2.73)	NR

Evidence Table 10. Chronic medical condition outcomes: treatment adherence and treatment satisfaction[a] (continued)

First author, year Trial name Country Funding source	CM condition-related treatment adherence	CM condition-related treatment satisfaction
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources (continued)	Mean adj diff (95% CI): -0.04 (-0.66 to 0.58), p > 0.20 @6 months: G1: 5.53 (2.29) G2: 5.33 (2.36) Mean adj diff (95% CI): +0.14 (-0.51 to 0.80), p > 0.20 @ 12 months: G1: 5.84 (2.12) G2: 5.46 (2.26) Mean adj diff (95% CI): +0.28 (-0.48 to 1.05), p > 0.20	

Abbreviations: ACE = angiotensin converting enzyme; adj = adjusted; BL = baseline; CM = chronic medical; HD = heart disease; HIV = human immunodeficiency virus; mins = minutes; NR = not reported; OR = odds ratio; SD = standard deviation; SE = standard error; US = United States

Evidence Table 11. Chronic medical condition outcomes: self-reported health status, quality of life, and mortality[a]

First Author, Year Trial Name Country Funding Source	Self-Reported Physical Health Status	Physical Health-Related Quality of Life	Mortality, N (%) Deaths (All-Cause Unless Otherwise Specified)
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	NR	**Mean Change (SD) in Total FACT Score** G1: +4.83 (14.94) G2: -1.70 (16.52) Between-group difference (95% CI): +6.53 (-2.23 to 15.29); p= 0.13 **Mean Change (SD) in FACT Physical Well-being** G1: +0.48 (4.94) G2: +0.49 (6.03) Between-group difference (95% CI): -0.01 (-3.07 to 3.06); p=0.43 **Mean Change (SD) in FACT Functional Well-being** G1: +1.81 (4.85) G2: -0.23 (5.34) Between-group difference (95% CI): +2.05 (-0.77 to 4.86); p=0.14	*@ 8 mths* G1: 0 (0) G2: 8 (30) OR (95% CI) = 0.04 (0.002 to 0.74); p=0.002
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	**Adj SF-12 Physical, mean (SE)** *@ BL* G1: 37.59 (0.69) G2: 36.28 (0.69) Adj mean diff (95% CI): +1.3 (-0.46 to 3.07); p = 0.15 *@ 6 mths* G1: 40.18 (0.8) G2: 38.87 (0.81) Adj mean diff (95% CI): +1.31 (-0.79 to 3.41); p = 0.22 *@ 12 mths* G1: 41.48 (0.84) G2: 38.68 (0.91) Adj mean diff (95% CI): +2.79 (0.49 to 5.1); p = 0.02	**FACT-G Physical Well-being, mean (SD) as treated** *@ BL (N=470 to 472)* G1: 16.88 (5.99) G2: 16.51 (5.87) Adj mean diff (95% CI): 0.45 (-0.60 to 1.50); p = 0.40 *@ 6 mths (N=317 to 318)* G1: 21.51 (5.56) G2: 20.58 (6.02) Adj mean diff (95% CI): 1.76 (0.53 to 2.98); p = 0.01 *@ 12 mths (N=258)* G1: 22.12 (5.61) G2: 20.78 (6.00) Adj mean diff (95% CI): 0.93 (-0.40 to 2.26); p = 0.17 *@ 18 mths (N=272)* G1: 21.86 (6.28) G2: 21.00 (5.95)	*@ 6 mths* G1: 20 (8.26) G2: 24 (10.43) *@ 12 mths* G1: 31 (12.81) G2: 37 (16.09) *@ 24 months* G1: 47 (19.4% of original 242) G2: 55 (23.9% of original 230)

Evidence Table 11. Chronic medical condition outcomes: self-reported health status, quality of life, and mortality[a] (continued)

First Author, Year Trial Name Country Funding Source	Self-Reported Physical Health Status	Physical Health-Related Quality of Life	Mortality, N (%) Deaths (All-Cause Unless Otherwise Specified)
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government (continued)		Adj mean diff (95% CI)=1.49 (0.19 to 2.78); p=0.02 *@24 mths (N=210)* G1: 20.75 (6.09) G2: 19.53 (6.19) Adj mean diff (95% CI)=1.39 (-0.05 to 2.83); p=0.06 Overall 24 month time by group interaction p=0.33 **FACT-G Functional Well-being, mean (SD) as treated** *@ BL (N=470 to 472)* G1: 11.25 (5.28) G2: 11.32 (4.85) Adj mean diff (95% CI): 0.05 (-0.98 to 1.08); p = 0.92 *@ 6 mths (N=317-318)* G1: 14.63 (6.26) G2: 13.53 (4.85) Adj mean diff (95% CI): 1.41 (0.20 to 2.62); p = 0.02 *@ 12 mths (N=258)* G1: 14.67 (6.16) G2: 13.54 (5.70) Adj mean diff (95 CI): 1.54 (0.22 to 2.86); p = 0.02 *@ 18 mths (N=272)* G1: 16.59 (6.20) G2: 15.61 (6.14) Adj mean diff (95% CI)=1.61 (0.33 to 2.89); p=0.01 *@24 mths (N=210)* G1: 13.80 (6.56) G2: 12.82 (5.87) Adj mean diff (95% CI)=1.79 (0.37 to 3.22); p=0.01 Overall 24 month time by group interaction p=0.08	

Evidence Table 11. Chronic medical condition outcomes: self-reported health status, quality of life, and mortality[a] (continued)

First Author, Year Trial Name Country Funding Source	Self-Reported Physical Health Status	Physical Health-Related Quality of Life	Mortality, N (%) Deaths (All-Cause Unless Otherwise Specified)
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	**SF-12 physical, mean (SD):** *@ BL* G1: 34.77 (8.88) G2: 36.57 (9.31) p = 0.26 *@ 6 mths* G1: 40.76 (11.28) G2: 39.32 (10.81) p = 0.04 *@ 12 mths:* G1: 38.07 (SE 1.20) G2: 37.93 (SE 1.19) Mean difference (95% CI)=0.13 (-2.26 to 2.52); p=0.91 *@ 18 mths:* G1: 39.10 (SE 1.19) G2: 38.56 (SE 1.19) Mean difference (95% CI)=0.55 (-1.85 to 2.94); p=0.65 *@ 24 mths:* G1: 38.43 (SE 1.20) G2: 38.35 (SE 1.21) Mean difference (95% CI)=0.08 (-2.36 to 2.53); p=0.95 Overall 24-month time by group interaction p=0.06	NR	Unspecified cause @ 24 mths: G1: 0 G2: 3
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	NR	NR	*@ 5 yrs* G1: 17 (10.3%) G2: 21 (12.8%)

Evidence Table 11. Chronic medical condition outcomes: self-reported health status, quality of life, and mortality[a] (continued)

First Author, Year Trial Name Country Funding Source	Self-Reported Physical Health Status	Physical Health-Related Quality of Life	Mortality, N (%) Deaths (All-Cause Unless Otherwise Specified)
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	NR	**Global QoL, mean (SD):** *@ Baseline*: G1: 4.2 (1.9) G2: 4.7 (1.8) p=NR *@ 6 mths:* G1: 5.8 (2.4) G2: 5.2 (1.8) p = NR *@ 12 mths:* G1: 6.0 (2.2) G2: 5.2 (1.9) p = 0.010 p for combined 6 and 12 mths = 0.005 Estimated mean difference (95% CI): 0.7 (0.2 to 1.2) Intervention effect size @ 12 mths = 0.39	*@ 12 months* G1: 1 (0.9) G2: 2 (1.8)
Pyne, 2011[16] HITIDES US Government	**SF-12 physical, mean (SD)** *@ BL* G1: 41.5 (12.5) G2: 39.5 (11.6) *@ 6 mths* G1: +0.3 G2: −0.1 p=0.79 Adj group diff, beta (95% CI): +1.9 (−1.0 to 4.9); p=0.20 *@ 12 mths* G1: +1.7 G2: +0.9 p=0.62 Adj group diff, beta (95% CI): +0.5 (−2.3 to 3.4); p=0.71	**QWB-SA, mean (SD)** *@ BL* G1: 0.49 (0.12) G2: 0.44 (0.13) *@ 6 mths* G1: +0.02 G2: +0.005 p=0.51 Adj group diff, beta (95% CI): +0.03 (−0.01 to 0.06); p=0.16 *@ 12 mths* G1: +0.01 G2: +0.04 p=0.12 Adj group diff, beta (95% CI): −0.01 (−0.05 to 0.03); p=0.49	*@ 6 mths:* G1: 2 (1.4) G2: 0 (0) *@ 12 mths (cumulative)* G1: 4 (2.9) G2: 5 (3.6)

Evidence Table 11. Chronic medical condition outcomes: self-reported health status, quality of life, and mortality[a] (continued)

First Author, Year Trial Name Country Funding Source	Self-Reported Physical Health Status	Physical Health-Related Quality of Life	Mortality, N (%) Deaths (All-Cause Unless Otherwise Specified)
Rollman, 2009[17] Bypassing the Blues US Government	**SF-36 PCS mean (SE)** *@ BL* G1: 31.2 (0.8) G2: 30.3 (0.8) *@ 8 mths* G1: 44.0 (0.8) G2: 41.4 (0.8) *Change @ 8 mths:* G1: +12.8 (0.8) G2: +11.1 (0.8) Between-group difference (95% CI): 1.6 (-0.5 to 3.8), p = 0.14 Effect Size (95% CI): 0.26 (0.03 to 0.48), p = 0.03 <u>MEN ONLY:</u> *@ BL* G1: 31.9 (1.0) G2: 30.0 (1.0) *@ 8 mths* G1: 46.6 (1.1) G2: 41.0 (1.0) *Change @ 8 mths:* G1: +14.6 (1.0) G2: +11.1 (1.0) Between-group difference (95% CI): 3.6 (0.8 to 6.3), p = 0.01 Effect Size (95% CI): 0.57 (0.26 to 0.87), p < 0.001 <u>WOMEN ONLY</u> *@ baseline* G1: 30.5 (1.1) G2: 30.6 (1.2) *@ 8 mths* G1: 41.4 (1.2) G2: 41.8 (1.3) *Change @ 8 mths:* G1: +10.9 (1.2) G2: +11.2 (1.3)	NR	*@ 8 mths* G1: 1 (0.67) G2: 0 (0)

Evidence Table 11. Chronic medical condition outcomes: self-reported health status, quality of life, and mortality[a] (continued)

First Author, Year Trial Name Country Funding Source	Self-Reported Physical Health Status	Physical Health-Related Quality of Life	Mortality, N (%) Deaths (All-Cause Unless Otherwise Specified)
Rollman, 2009[17] Bypassing the Blues US Government (continued)	Between-group difference (95% CI): -0.3 (-3.6 to 3.0), p = 0.86 Effect Size (95% CI): -0.04 (-0.40 to 0.31), p = 0.82		
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	NR	NR	**All-cause** *@ 12 mths* G1: 9 (8.9) G2:12 (12.1) **Cancer-related** *@12 mths* G1: 9 (8.9) G2: 11 (11.1)
Vera, 2010[19] NA Puerto Rico Government	**SF-36 social functioning score** *(estimated from graph)* G1: 55 G2: 35 p < 0.001 **SF-36 social functioning** @ 6 mo; treatment X time regression β = 0.70; p <0.001	NR	NR
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	**General health status, mean (SE)** *@ 12 mths* G1: 3.3 (0.05) G2: 3.6 (0.05) Betw-grp diff: -0.3 (-0.42 to -0.17); p <0.001	**Quality of life score (range 0-10), mean (SE)** *@ 12 mths* G1: 6.4 (0.13) G2: 6.0 (0.13) Betw-grp diff: +0.42 (0.13 to 0.71); p = 0.005	*@ 6 mths* G1: 8 (1.6) G2: 6 (1.2) *@ 12 mths* G1: 22 (4.3) G2: 15 (3.0)

Evidence Table 11. Chronic medical condition outcomes: self-reported health status, quality of life, and mortality[a] (continued)

First Author, Year Trial Name Country Funding Source	Self-Reported Physical Health Status	Physical Health-Related Quality of Life	Mortality, N (%) Deaths (All-Cause Unless Otherwise Specified)
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	NR	**Quality of life score (range 0-10), mean (SE?):** *@ baseline:* Overall: 5.42 (0.15) G1: 5.39 (0.21) G2: 5.45 (0.20) p = 0.855 *@ 6 mths* Overall: 6.03 (0.19) G1: 6.30 (0.25) G2: 5.74 (0.25) p = 0.097 *@ 12 mths* Overall: 6.32 (0.16) G1: 6.67 (0.23) G2: 5.95 (0.24) p = 0.039 *@ 18 mths* Overall: 5.86 (0.18) G1: 6.33 (0.25) G2: 5.35 (0.24) p = 0.009 *@ 24 mths* Overall: 6.20 (0.19) G1: 6.51 (0.25) G2: 5.84 (0.29) p = 0.117	*@ 6 mths* G1: 5 (4.5) G2: 3 (2.9) *@ 12 mths* G1: 11 (9.8) G2: 9 (8.7) *@ 18 mths* G1: 13 (11.6) G2: 13 (12.6) *@ 24 mths* G1: 15 (13.4) G2: 17 (16.5)
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	**SF-12, Physical** Between group diff: +3.21 (1.78 to 4.63) favoring G1	NR	*@ 6 mths* G1: 4 (2.0) G2: 10 (4.7) *@ 12 mths* G1: 12 (5.9) G2: 12 (5.7)

[a] G1 = intervention arm; G2 = control arm

Abbreviations: Adj, adjusted; BL, baseline; CI, confidence interval; CM, chronic medical; diff, difference; FACT, Functional Assessment of Cancer Therapy; GCPS, Graded Chronic Pain Scale; mths, months; NR, not reported; QWB-SA, Quality of Well-being Self-administered; SD, standard deviation; SE, standard error; US, United States

Evidence Table 12. Chronic medical condition outcomes: health care utilization and other outcomes, including harms

First author, year Trial name Country Funding source	Health care utilization	Other outcomes
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	NR	NR
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	NR	NR
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	NR	**Financial Situation Getting Worse, mean (SD):** *@ BL* G1: 0.43 (0.50) G2: 0.30 (0.46) p = 0.06 *@ 6 mths* G1: 0.15 (0.35) G2: 0.28 (0.45) p = <0.001 *@ 12 mths* G1: 0.17 (0.38) G2: 0.24 (0.43) p = 0.02 *@ 18 mths* G1: 0.36 (0.48) G2: 0.28 (0.45) p = 0.41 **# of socioeconomic stressors, mean (SE)** *@ 12 months* G1: 2.11 (0.20) G2: 2.97 (0.20) Mean difference (95% CI)=-0.87 (-1.31 to -0.42); p=0.0001 *@ 18 months* G1: 2.31 (0.20) G2: 2.93 (0.20)

Evidence Table 12. Chronic medical condition outcomes: health care utilization and other outcomes, including harms (continued)

First author, year Trial name Country Funding source	Health care utilization	Other outcomes
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government (continued)		Mean difference (95% CI)=-0.62 (-1.07 to -0.18); p=0.01 *@ 24 months* G1: 2.24 (0.20) G2: 2.87 (0.20) Mean difference (95% CI)=-0.64 (-1.09 to -0.18); p=0.01
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	NR	**≥1 disenrollment period from the health plan @ 5 yrs** G1: 56(33.9%) G2: 59 (36.0%)
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	**# outpatient visits over 12 study months:** G1: 11.1 G2: 12.3 **# telephone encounters over 12 study months:** G1: 10.1 G2: 10.3 **N (%) with ≥1 hospitalization** G1: 27 (25.5%) G2: 23 (21.3%) **Initiation of lipid-lowering rx over 12 mths** Rate (95% CI)=2.7 (1.1 to 6.2) **Initiation of antihypertensive rx over 12 mths** Rate (95% CI)=1.8 (0.7 to 4.9) **Initiation of insulin therapy over 12 mths** Rate (95% CI)=2.2 (0.7 to 6.8)	**N(%) with ≥1 moderate AE** G1: 18 (17) G2: 3 (2.8) **N(%) with ≥1 mild AE** G1: 2 (1.9) G2: 0 (0) Mild and moderate AE included falls, medication side effects, extremely high lab values, ER visit for chest pain or neurologic symptoms

Evidence Table 12. Chronic medical condition outcomes: health care utilization and other outcomes, including harms (continued)

First author, year Trial name Country Funding source	Health care utilization	Other outcomes
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources (continued)	**Insulin therapy treatment adjustment (# of adjustments over 12 months), rate (95% CI)** G1=3.26 (2.43 to 4.36) G2=1.02 (0.67 to 1.55) Relative rate (95% CI)=2.97 (1.83 to 4.83); p<0.001 **Oral hypoglycemic treatment adjustment (# of adjustments over 12 months), rate (95% CI)** G1=0.62 (0.44 to 0.88) G2=0.34 (0.23 to 0.50) Relative rate (95% CI)=1.80 (1.07 to 3.01); p<0.05 **Antihypertensive treatment adjustment (# of adjustments over 12 months), rate (95% CI)** G1=2.33 (1.86 to 2.92) G2=1.11 (0.81 to 1.51) Relative rate (95% CI)=1.86 (1.28 to 2.71); p<0.001 **Lipid lowering treatment adjustment (# of adjustments over 12 months), rate (95% CI)** G1=0.81 (0.64 to 1.03) G2=0.55 (0.42 to 0.72) Relative rate (95% CI)=1.56 (1.10 to 2.20); p<0.05	
Pyne, 2011[16] HITIDES US Government	NR	NR
Rollman, 2009[17] Bypassing the Blues US Government	**Total rehospitalizations:** G1: 85 (men = 34; women = 51) G2: 68 (men = 46; women = 22) Between-group difference, p = 0.86 **Cardiac/cardiovascular rehospitalizations** G1: 31 (men = 12; women = 19) G2: 35 (men = 25; women = 10) **Non-cardiac/cardiovascular rehospitalizations** G1: 53 (men = 21; women = 32) G2: 33 (men = 21; women = 12)	NR

Evidence Table 12. Chronic medical condition outcomes: health care utilization and other outcomes, including harms (continued)

First author, year Trial name Country Funding source	Health care utilization	Other outcomes
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	NR	NR
Vera, 2010[19] NA Puerto Rico Government	NR	NR
Lin, 2006[20] Lin, 2003[21] IMPACT: arthritis (secondary analyses) US Multiple sources	NR	NR
Fann, 2009[22] IMPACT: cancer (secondary analyses) US Multiple sources	NR	NR
Williams, 2004[23] Katon, 2006[24] IMPACT: diabetes (secondary analyses) US Multiple sources	NR	NR

[a] G1 = intervention arm; G2 = control arm

Abbreviations: AE = adverse event; BL = baseline; CI = confidence interval; CM = chronic medical; ER = emergency room; mths = months; NR = not reported; OR = odds ratio; SD = standard deviation; SE = standard error; US = United States; yrs = years

Evidence Table 13. System factors

First Author, Year Trial Name Country Funding Source	Size Type[a] Urban/Rural/Mixed	IT/EMR Features	Payer Mix Other Payment Details	Other
Dwight-Johnson, 2005[1] Multifaceted Oncology Depression Program US Government	Public sector breast and GYN oncology clinics Open system NR	NR	NR Medication and problem-solving therapy costs were covered by the study.	Patients were low income.
Ell, 2008[2] Ell, 2011[3] ADAPt-C US Government	Public sector oncology clinics - Medical Oncology, Radiation, GYN Oncology Open system NR	NR	NR Participants were reimbursed for time spent completing outcome interviews and for transportation and copays for antidepressant medication if applicable.	Spanish-speaking research staff and study materials in English and Spanish; phone intervention and data collection option; evening and weekend availability for visits; study participants were low income
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] Multifaceted Diabetes and Depression Program US Government	2 public safety-net community clinics: 1 PCP-like and 1 catering to diabetic patients who are referred by PCP Open system NR	NR	Insurance (%): G1: Medi-cal/Medicare: 17.6 County-funded program: 61.1 None: 21.2 G2: Medi-Cal/Medicare: 18.6 County-funded program: 58.2 None: 21.1 NR	Safety net clinics; participants were described as low-income.
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways US Government	9 primary care clinics of Group Health Cooperative (non-profit HMO) serving 500,000 members in Washington and Idaho Closed system NR	IT system for clinical, cost, and utilization measures	Patients were members of Group Health Cooperative, a mixed-model prepaid health plan serving 500,000 members in Washington and Idaho. NR	

Evidence Table 13. System factors (continued)

First Author, Year Trial Name Country Funding Source	Size Type[a] Urban/Rural/Mixed	IT/EMR Features	Payer Mix Other Payment Details	Other
Katon, 2010[13] Von Korff, 2011[14] Lin, 2012[15] TEAMcare US Multiple sources	14 PC clinics in Washington state Closed system NR	EMR system in place	Patients were members of Group Health Cooperative, a mixed-model prepaid health plan NR	
Pyne, 2011[16] HITIDES US Government	3 VA HIV clinics Closed system NR	The depression care team communicated with treating clinicians via EMR progress notes; Prewritten scripts and standardized instruments were supported by the Web-based decision support system during the telephone encounters with patients. Scripted computer-based assessments used at baseline, 6 and 12 months.	NR Free to patients through VA system	
Rollman, 2009[17] Bypassing the Blues US Government	NR; intervention was telephone-based Open system NA	Data and safety monitoring done electronically; searched for HRSD increase of 25% or more; this triggered a written letter to the treating PCP and offer to identify local MH specialists and provide additional treatment advice.	NR NR	

Evidence Table 13. System factors (continued)

First Author, Year Trial Name Country Funding Source	Size Type[a] Urban/Rural/Mixed	IT/EMR Features	Payer Mix Other Payment Details	Other
Strong, 2008[18] SMaRT Oncology 1 United Kingdom Foundation	Regional NHS cancer center that served 1.5 million people in southeast Scotland Open system NR	NR	National Health Service Free to patients through NHS.	
Vera, 2010[19] NA Puerto Rico Government	14 internal med or PC clinics from 4 health care orgs, including independent provider associations, HMOs, a regional health insurance plan, and academically affiliated practices Open system NR	NR	NR Costs for medication and CBT were covered by the study.	
Fann, 2009[22] Lin, 2006[20] Lin, 2003[21] Williams, 2004[23] Katon, 2006[24] IMPACT(secondary analyses) US Multiple sources	18 PC clinics from 8 health care organizations in 5 states Mixed systems (PGP, VA, AGP, HMO, IPA) Mixed	Web-based clinical information system in place	Mixed (<10% to 100% capitated plus one VA clinic) Mixed rates of capitation and types of mental health care financing	Some clinics had mental health practitioner on-site; others did not.

[a] A ―closed" system is one in which elements are accessible to patients who are members of the organization operating the system. An ―open" system is one in which patients are free to choose any provider, regardless of organizational system or network.

Abbreviations: AGP = academic group practice; CBT = Cognitive-behavioral Therapy; EMR = electronic medical record; HMO = health maintenance organization; HRSD = Hamilton Rating Scale for Depression; IPA = independent provider association; IT = information technology; MH = mental health; NHS = National Health Service; NR = not reported; PC = primary care; PCP = primary care provider; PGP = private group practice; US = United States, VA = Veterans' Affairs

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Appendix D. Quality Assessment

This appendix describes the criteria relating to internal validity and the procedures that topic teams follow for all updates and new assessments in making these judgments.

All topic teams use initial ―ifters" to select studies for review that deal most directly with the question at issue and that are applicable to the population at issue. Thus, studies of any design that use outdated technology or that use technology that is not feasible for primary care practice may be filtered out before the abstraction stage, depending on the topic and the decisions of the topic team. The teams justify such exclusion decisions if there could be reasonable disagreement about this step. The criteria below are meant for those studies that pass this initial filter.

Presented below are a set of minimal criteria for each study design and then a general definition of three categories: ―good," ―fair," and ―poor," based on those criteria. These specifications are not meant to be rigid rules but rather are intended to be general guidelines, and individual exceptions, when explicitly explained and justified, can be made. In general terms, a ―good" study has the least risk of bias and its results are considered to be valid. A ―fair" study is susceptible to some bias but probably not sufficient to invalidate its results. A ―poor" study has significant risk of bias (e.g., stemming from serious errors in design or analysis) that may invalidate its results.

Two independent reviewers assigned quality ratings for each study. For each article, one of the two reviewers was always an experienced/senior investigator (LW). Disagreements between the two reviewers were resolved by discussion and consensus or by consulting a third member of the team. We gave good quality ratings to studies that met all, or all but one, criteria. We gave poor quality ratings to studies that had a fatal flaw (defined as a methodological shortcoming that leads to a very high risk of bias) in one or more categories, and we excluded them from our analyses.

Randomized Controlled Trials

Criteria:

- Initial assembly of comparable groups: adequate randomization, including first concealment and whether potential confounders were distributed equally among groups Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- All important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intention to treat analysis.

Definition of Ratings Based on Above Criteria:

Good: Meets all or all but one of the following criteria: Comparable groups are assembled initially and maintained throughout the study (follow-up at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled

out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, for RCTs, intention to treat analysis is used.

Fair: Studies will be graded ―fair" if any or all of the following problems occur, without the fatal flaws noted in the ―poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention to treat analysis is done for RCTs.

Poor: Studies will be graded ―poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. For RCTs, intention to treat analysis is lacking.

Table D-1. Quality ratings for efficacy / effectiveness trials

First author, year Trial name	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	Was overall attrition ≥20%?	Was differential attrition ≥15%?	Did the study use ITT analyses?	Were outcome measures equal, valid, and reliable?	Efficacy / Effectiveness quality rating
Dwight-Johnson, 2005[1] MODP	Yes	Yes	Yes	Yes	No	No	Yes[a]	Yes	Modified ITT	Yes	Fair
Ell, 2008[2] Ell, 2011[3] ADAPt-C	Yes	Yes	Yes	Yes	No	No	Yes[a]	No	Modified ITT	Yes	Fair
Ell, 2010[4] Ell, 2011[5] Hay, 2011[6] MDDP	Yes	Yes	No	Unclear/NR	No	No	Yes	No	No	Yes	Fair
Katon, 2004[7] Katon, 2008[8] Simon, 2007[9] Kinder, 2006[10] Ciechanowski, 2006[11] Lin, 2006[12] Pathways	Yes	Yes	Yes	Yes	No	No	No	No	Varied by outcome	Yes	Fair
Katon, 2010[13] Von Korff, 2011[14] TEAMcare	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Fair
Pyne, 2011[15] HITIDES	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Good
Rollman, 2009[16] Bypassing the Blues	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Good

First author, year Trial name	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	Was overall attrition ≥20%?	Was differential attrition ≥15%?	Did the study use ITT analyses?	Were outcome measures equal, valid, and reliable?	Efficacy / Effectiveness quality rating
Strong, 2008[17] SMaRT Oncology 1	Yes	Yes	Yes	Yes	No	No	No	No	Modified ITT	Yes	Fair
Vera, 2010[18] NA	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Good
Williams, 2004[19] Fann, 2009[20] Lin, 2006[21] Katon, 2006[22] Lin, 2003[23] IMPACT (secondary analyses)	No[b]	Yes	Yes	Yes	No	No	No	No	Modified ITT	Yes	Fair

[a] Although attrition rate was high, the study population was patients with cancer – a population known to experience higher dropout rates for multiple reasons;
[b] Although randomization effect was lost by conducting post-randomization subgroup analyses, baseline characteristics were well-match between intervention and control arms. Quality rating was performed for each chronic condition subset, and the results did not vary.
Abbreviations: ADAPt-C = Alleviating Depression Among Patients with Cancer; HITIDES = HIV Implementation of Translating Initiatives for Depression into Effective Solutions; IMPACT = Improving Mood – Promoting Access to Collaborative Treatment; ITT = intent to treat; MDDP = Multifaceted Diabetes and Depression program; MODP = Multifaceted Oncology Depression Program; NA = not applicable; NR = not reported; SMaRT = Symptom Management Research Trials

Comments on efficacy/effectiveness trials rated "poor" (high risk of bias):

Bogner HR, Morales KH, Post EP, et al. Diabetes, depression, and death: a randomized controlled trial of a depression treatment program for older adults based in primary care (PROSPECT). Diabetes Care. 2007 Dec;30(12):3005-10. PMID: 17717284.

- Although the analysis describes adequate strategy for survival analysis, the initial variables chosen for possible confounding are not described and there are baseline differences in medical conditions – thus introducing a high risk for bias in this now observational add-on study

Sriwattanakomen R, Mazumdar S, Belnap B, et al. The effect of comorbid anxiety on post-CABG depressed patients' mental health related quality of life. Journal of General Internal Medicine. 2010 June;25 SUPPL. 3:S401.

- This was an abstract of a submission accepted for presentation at a Society of General Internal Medicine meeting. Although it is a subgroup analysis from a trial we have included (Bypassing the Blues), we feel that the risk of bias in this analysis is high due to unbalanced subgroup sizes and several significant differences at baseline.

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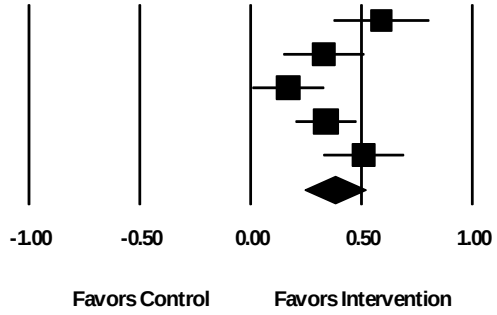
Appendix E. Meta-Analyses

Depression Symptom Improvement at 6 Months

Studyname	Chronic Medical Condition	Statistics for each study		
		Difference in means	Lower limit	Upper limit
SMaRT Oncology 1 (Strong, 2008)	Cancer	0.59	0.37	0.81
IMPACT (Fann, 2009)	Cancer	0.33	0.14	0.52
Pathways (Katon, 2004)	Diabetes	0.17	0.01	0.33
IMPACT (Williams, 2004)	Diabetes	0.34	0.20	0.48
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.51	0.33	0.69
		0.38	0.24	0.51



Note: All trials measured depressive symptoms with the Hopkins Symptom Checklist (HSCL).

Measures of Heterogeneity

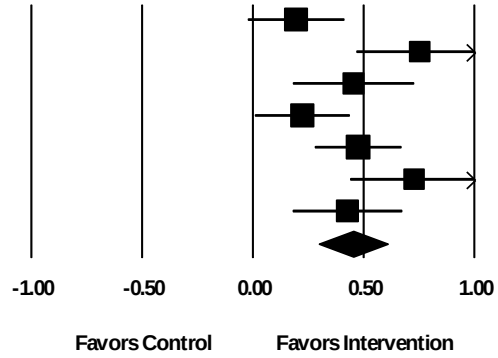
Q-Value	df (Q)	p-Value	I-Squared
12.101	4	0.017	66.944

Depression Symptom Improvement at 6 Months - WMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	SMaRT Oncology 1 (Strong, 2008)	Cancer	0.334	0.203	0.464	0.000
	IMPACT (Fann, 2009)	Cancer	0.392	0.219	0.566	0.000
	Pathways (Katon, 2004)	Diabetes	0.428	0.308	0.548	0.000
	IMPACT (Williams, 2004)	Diabetes	0.393	0.206	0.579	0.000
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.346	0.194	0.498	0.000
Random			0.378	0.241	0.515	0.000

Depression Symptom Improvement at 6 Months

Studyname	Chronic Medical Condition	Std diff in means	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.20	-0.03	0.42
SMaRT Oncology 1 (Strong, 2008)	Cancer	0.75	0.46	1.04
IMPACT (Fann, 2009)	Cancer	0.45	0.18	0.73
Pathways (Katon, 2004)	Diabetes	0.22	0.01	0.44
IMPACT (Williams, 2004)	Diabetes	0.48	0.28	0.67
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.73	0.44	1.02
Bypassing the Blues (Rollman, 2009)	Heart Disease	0.43	0.18	0.68
		0.45	0.29	0.61



Notes: The ADAPt-C trial measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); the Bypassing the Blues trial used the Hamilton Rating Scale for depression (HAM-D); all other trials used the Hopkins Symptom Checklist (HSCL). The Bypassing the Blues data are from the 8-month endpoint.

Measures of Heterogeneity

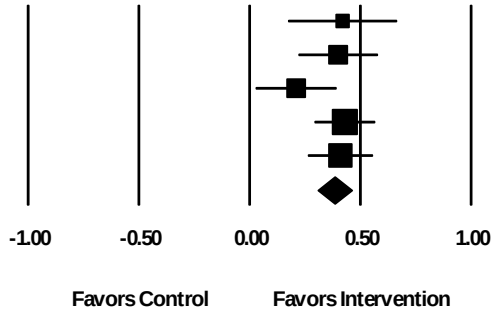
Q-Value	df (Q)	p-Value	I-Squared
16.912	6	0.010	64.522

Depression Symptom Improvement at 6 Months - SMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**SMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.494	0.338	0.651	0.000
	SMaRT Oncology 1 (Strong, 2008)	Cancer	0.404	0.256	0.551	0.000
	IMPACT (Fann, 2009)	Cancer	0.452	0.272	0.632	0.000
	Pathways (Katon, 2004)	Diabetes	0.491	0.328	0.655	0.000
	IMPACT (Williams, 2004)	Diabetes	0.449	0.259	0.638	0.000
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.408	0.256	0.561	0.000
	Bypassing the Blues (Rollman, 2009)	Heart Disease	0.457	0.273	0.640	0.000
Random			0.450	0.295	0.605	0.000

Depression Symptom Improvement at 12 Months

Studyname	Chronic Medical Condition	Statistics for each study		
		Difference in means	Lower limit	Upper limit
SMaRT Oncology 1 (Strong, 2008)	Cancer	0.42	0.17	0.67
IMPACT (Fann, 2009)	Cancer	0.40	0.22	0.58
Pathways (Katon, 2004)	Diabetes	0.21	0.03	0.39
IMPACT (Williams, 2004)	Diabetes	0.43	0.29	0.57
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.41	0.26	0.56
		0.38	0.30	0.46



Note: All trials measured depressive symptoms with the Hopkins Symptom Checklist (HSCL).

Measures of Heterogeneity

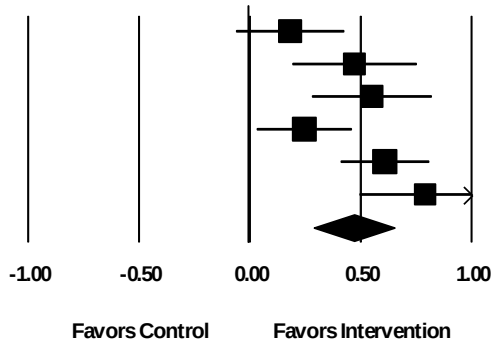
Q-Value	df (Q)	p-Value	I-Squared
4.044	4	0.400	1.094

Depression Symptom Improvement at 12 Months - WMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	SMaRT Oncology 1 (Strong, 2008)	Cancer	0.374	0.281	0.466	0.000
	IMPACT (Fann, 2009)	Cancer	0.373	0.274	0.472	0.000
	Pathways (Katon, 2004)	Diabetes	0.416	0.333	0.500	0.000
	IMPACT (Williams, 2004)	Diabetes	0.360	0.262	0.457	0.000
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.368	0.265	0.471	0.000
Random			0.381	0.304	0.458	0.000

Depression Symptom Improvement at 12 Months

Studyname	Chronic Medical Condition	Std diff in means	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.18	-0.06	0.43
SMaRT Oncology 1 (Strong, 2008)	Cancer	0.47	0.19	0.76
IMPACT (Fann, 2009)	Cancer	0.55	0.28	0.82
Pathways (Katon, 2004)	Diabetes	0.25	0.03	0.46
IMPACT (Williams, 2004)	Diabetes	0.61	0.41	0.81
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.79	0.49	1.09
		0.47	0.29	0.65



Note: The ADAPt-C trial measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); all other trials used the Hopkins Symptom Checklist (HSCL).

Measures of Heterogeneity

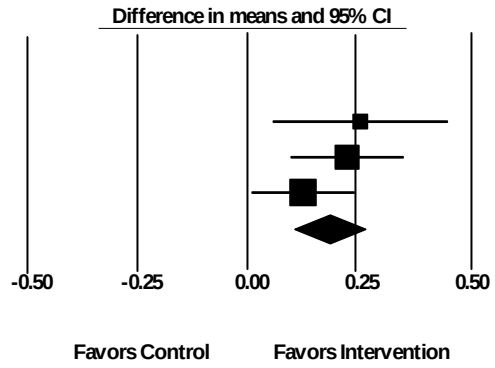
Q-Value	df (Q)	p-Value	I-Squared
15.898	5	0.007	68.549

Depression Symptom Improvement at 12 Months - SMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**SMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.523	0.345	0.702	0.000
	SMaRT Oncology 1 (Strong, 2008)	Cancer	0.468	0.251	0.685	0.000
	IMPACT (Fann, 2009)	Cancer	0.453	0.238	0.667	0.000
	Pathways (Katon, 2004)	Diabetes	0.516	0.323	0.710	0.000
	IMPACT (Williams, 2004)	Diabetes	0.435	0.225	0.645	0.000
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.411	0.236	0.585	0.000
Random			0.467	0.286	0.649	0.000

Depression Symptom Improvement at 24 Months

Studyname	Chronic Medical Condition	Statistics for each study		
		Difference in means	Lower limit	Upper limit
IMPACT (Fann, 2009)	Cancer	0.25	0.05	0.45
MDDP (Ell, 2010)	Diabetes	0.22	0.09	0.35
Pathways (Katon, 2004)	Diabetes	0.12	0.00	0.24
		0.18	0.10	0.26



Measures of Heterogeneity

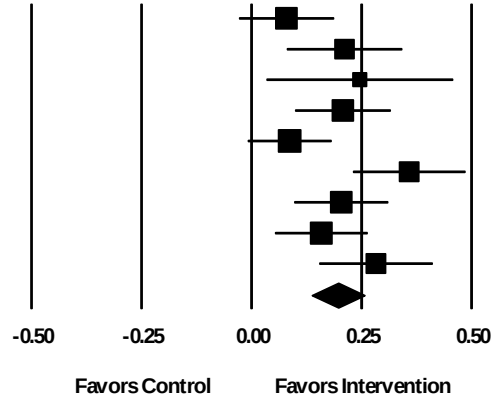
Q-Value	df (Q)	p-Value	I-Squared
1.820	2	0.403	0.000

Depression Symptom Improvement at 24 Months - WMD

			Statistics With Study Removed			
Model	Study Name	Chronic Medical Condition	WMD	Lower Limit	Upper Limit	p-value
	IMPACT (Fann, 2009)	Cancer	0.166	0.069	0.264	0.001
	MDDP (Ell, 2010)	Diabetes	0.159	0.042	0.276	0.008
	Pathways (Katon, 2004)	Diabetes	0.229	0.120	0.338	0.000
Random			0.179	0.099	0.259	0.000

Reduction (at least 50%) in Mental Health Score at 6 Months

Studyname	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.08	-0.03	0.19
IMPACT (Fann, 2009)	Cancer	0.21	0.08	0.34
MDDP (Dwight-Johnson, 2005)	Diabetes	0.25	0.03	0.46
MDDP (Ell, 2010)	Diabetes	0.21	0.10	0.32
Pathways (Katon, 2004)	Diabetes	0.09	-0.01	0.18
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.36	0.23	0.49
Bypassing the Blues (Rollman, 2009)	Heart Disease	0.20	0.10	0.31
HITIDES (Pyne, 2011)	HIV	0.16	0.05	0.27
Vera, 2010	Multiple Conditions	0.28	0.15	0.41
		0.20	0.14	0.26



Notes: The ADAPt-C and MDDP (Dwight-Johnson, 2005) trials measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); the Bypassing the Blues trial used the Hamilton Rating Scale for depression (HAM-D); all other trials used the Hopkins Symptom Checklist (HSCL). The Bypassing the Blues and MDDP (Dwight-Johnson, 2005) data are from 8-month endpoints.

Measures of Heterogeneity

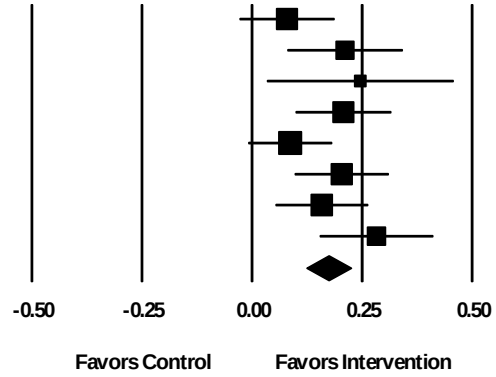
Q-Value	df (Q)	p-Value	I-Squared
17.644	8	0.024	54.659

Reduction (at least 50%) in Mental Health Score at 6 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.211	0.151	0.270	0.000
	IMPACT (Fann, 2009)	Cancer	0.194	0.128	0.261	0.000
	MDDP (Dwight-Johnson, 2005)	Diabetes	0.193	0.129	0.256	0.000
	MDDP (Ell, 2010)	Diabetes	0.195	0.127	0.263	0.000
	Pathways (Katon, 2004)	Diabetes	0.211	0.152	0.271	0.000
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.173	0.122	0.223	0.000
	Bypassing the Blues (Rollman, 2009)	Heart Disease	0.195	0.127	0.264	0.000
	HITIDES (Pyne, 2011)	HIV	0.202	0.133	0.270	0.000
	Vera, 2010	Multiple Conditions	0.185	0.123	0.247	0.000
Random			0.195	0.136	0.255	0.000

Reduction (at least 50%) in Mental Health Score at 6 Months

Study name	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.08	-0.03	0.19
IMPACT (Fann, 2009)	Cancer	0.21	0.08	0.34
MDDP (Dwight-Johnson, 2005)	Diabetes	0.25	0.03	0.46
MDDP (Ell, 2010)	Diabetes	0.21	0.10	0.32
Pathways (Katon, 2004)	Diabetes	0.09	-0.01	0.18
Bypassing the Blues (Rollman, 2009)	Heart Disease	0.20	0.10	0.31
HITIDES (Pyne, 2011)	HIV	0.16	0.05	0.27
Vera, 2010	Multiple Conditions	0.28	0.15	0.41
		0.17	0.12	0.22



Sensitivity Analysis: Removing TEAMcare (Katon, 2010)

Measures of Heterogeneity

Q-value	df (Q)	p-Value	I-squared
10.111	7	0.182	30.771

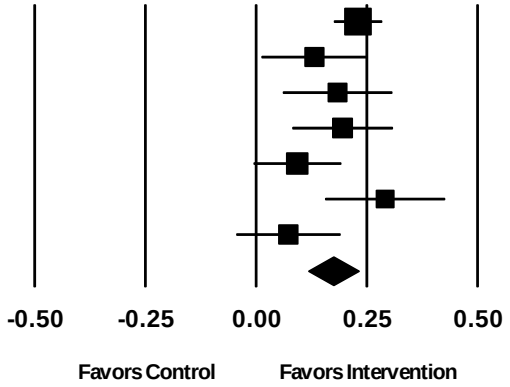
Notes: The ADAPt-C and MDDP (Dwight-Johnson, 2005) trials measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); the Bypassing the Blues trial used the Hamilton Rating Scale for depression (HAM-D); all other trials used the Hopkins Symptom Checklist (HSCL). The Bypassing the Blues and MDDP (Dwight-Johnson, 2005) data are from 8-month endpoints.

Reduction (at least 50%) in Mental Health Score at 6 Months - Sensitivity Analysis Removing TEAMcare (Katon, 2010)

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.186	0.137	0.235	0.000
	IMPACT (Fann, 2009)	Cancer	0.169	0.113	0.225	0.000
	MDDP (Dwight-Johnson, 2005)	Diabetes	0.169	0.116	0.223	0.000
	MDDP (Ell, 2010)	Diabetes	0.168	0.111	0.226	0.000
	Pathways (Katon, 2004)	Diabetes	0.188	0.139	0.237	0.000
	Bypassing the Blues (Rollman, 2009)	Heart Disease	0.169	0.111	0.227	0.000
	HITIDES (Pyne, 2011)	HIV	0.177	0.117	0.236	0.000
	Vera, 2010	Multiple Conditions	0.157	0.110	0.204	0.000
Random			0.173	0.122	0.223	0.000

Reduction (at least 50%) in Mental Health Score at 12 Months

Study name	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
IMPACT (Lin, 2003)	Arthritis	0.23	0.17	0.29
ADAPt-C (Ell, 2008)	Cancer	0.13	0.01	0.25
IMPACT (Fann, 2009)	Cancer	0.18	0.06	0.31
MDDP (Ell, 2010)	Diabetes	0.20	0.08	0.31
Pathways (Katon, 2004)	Diabetes	0.09	-0.01	0.19
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.29	0.15	0.43
HITIDES (Pyne, 2011)	HIV	0.07	-0.05	0.19
		0.17	0.12	0.23



Note: The ADAPt-C trial measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); all other trials used the Hopkins Symptom Checklist (HSCL).

Measures of Heterogeneity

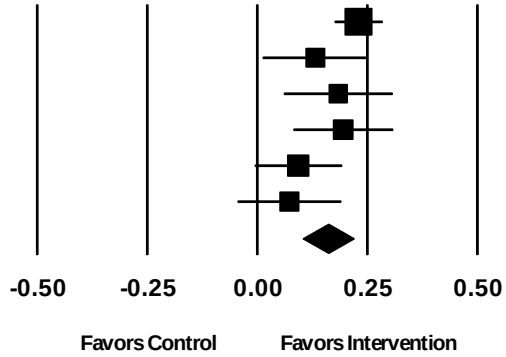
Q-Value	Df (Q)	p-Value	I-Squared
12.232	6	0.057	50.947

Reduction (at least 50%) in Mental Health Score at 12 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower limit**	**Upper limit**	**p-Value**
	IMPACT (Lin, 2003)	Arthritis	0.155	0.095	0.216	0.000
	ADAPt-C (Ell, 2008)	Cancer	0.179	0.115	0.242	0.000
	IMPACT (Fann, 2009)	Cancer	0.171	0.105	0.236	0.000
	MDDP (Ell, 2010)	Diabetes	0.169	0.102	0.235	0.000
	Pathways (Katon, 2004)	Diabetes	0.189	0.132	0.245	0.000
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.159	0.102	0.217	0.000
	HITIDES (Pyne, 2011)	HIV	0.189	0.134	0.243	0.000
Random			0.173	0.116	0.230	0.000

Reduction (at least 50%) in Mental Health Score at 12 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Risk difference	Lower limit	Upper limit
IMPACT (Lin, 2003)	Arthritis	0.23	0.17	0.29
ADAPt-C (Ell, 2008)	Cancer	0.13	0.01	0.25
IMPACT (Fann, 2009)	Cancer	0.18	0.06	0.31
MDDP (Ell, 2010)	Diabetes	0.20	0.08	0.31
Pathways (Katon, 2004)	Diabetes	0.09	-0.01	0.19
HITIDES (Pyne, 2011)	HIV	0.07	-0.05	0.19
		0.16	0.10	0.22



Sensitivity Analysis: Removing TEAMcare (Katon, 2010)

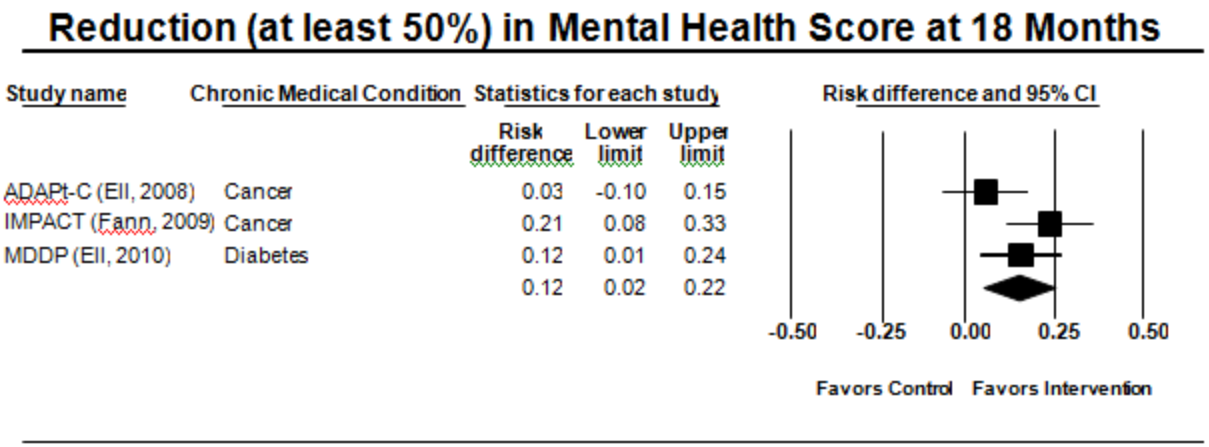
Note: The ADAPt-C trial measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); all other trials used the Hopkins Symptom Checklist (HSCL).

Measures of Heterogeneity

Q-value	df (Q)	p-Value	I-squared
9.742	5	0.083	48.677

Reduction (at least 50%) in Mental Health Score at 12 Months - Sensitivity Analysis Removing TEAMcare (Katon, 2010)

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Lin, 2003)	Arthritis	0.132	0.081	0.184	0.000
	ADAPt-C (Ell, 2008)	Cancer	0.162	0.096	0.229	0.000
	IMPACT (Fann, 2009)	Cancer	0.153	0.085	0.222	0.000
	MDDP (Ell, 2010)	Diabetes	0.151	0.082	0.220	0.000
	Pathways (Katon, 2004)	Diabetes	0.176	0.117	0.234	0.000
	HITIDES (Pyne, 2011)	HIV	0.176	0.121	0.232	0.000
Random			0.159	0.102	0.217	0.000



Notes: The ADAPt-C and MDDP (Dwight-Johnson, 2005) trials measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); the IMPACT (Fann, 2009) trial used the Hopkins Symptom Checklist (HSCL).

Measures of Heterogeneity

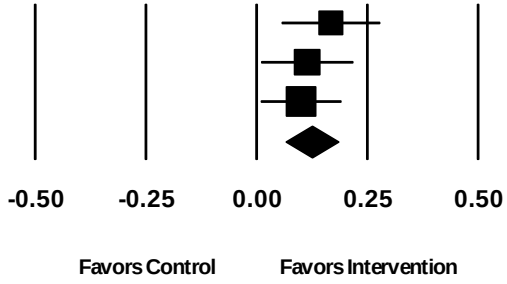
Q-value	df (Q)	p-Value	I-squared
4.302	2	0.116	53.509

Reduction (at least 50%) in Mental Health Score at 18 Months - RD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Fann, 2009)	Cancer	0.163	0.080	0.247	0.000
	MDDP (Ell, 2010)	Diabetes	0.076	-0.021	0.173	0.123
	Pathways (Katon, 2004)	Diabetes	0.116	-0.062	0.293	0.201
Random			0.118	0.017	0.219	0.022

Remission of Depression at 6 Months

Study name	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
IMPACT (Fann, 2009)	Cancer	0.168	0.055	0.280
MDDP (Ell, 2010)	Diabetes	0.114	0.009	0.220
HITIDES (Pyne, 2011)	HIV	0.100	0.008	0.193
		0.123	0.064	0.183



Note: All included studies defined remission as SCL-20 < 0.5.

Measures of Heterogeneity

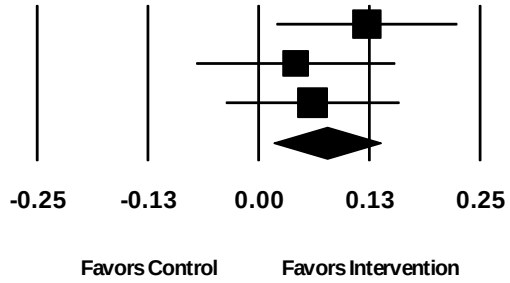
Q-Value	df (Q)	p-Value	I-Squared
0.860	2	0.650	0.000

Remission of Depression at 6 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Fann, 2009)	Cancer	0.107	0.037	0.176	0.003
	MDDP (Ell, 2010)	Diabetes	0.128	0.056	0.199	0.000
	HITIDES (Pyne, 2011)	HIV	0.139	0.062	0.216	0.000
Random			0.123	0.064	0.183	0.000

Remission of Depression at 12 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Risk difference	Lower limit	Upper limit
IMPACT (Fann, 2009)	Cancer	0.122	0.020	0.225
MDDP (Ell, 2010)	Diabetes	0.042	-0.071	0.155
HITIDES (Pyne, 2011)	HIV	0.061	-0.038	0.160
		0.077	0.016	0.137



Note: All included studies defined remission as SCL-20 < 0.5.

Measures of Heterogeneity

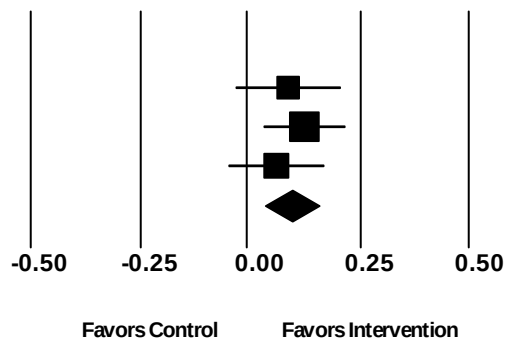
Q-Value	df (Q)	p-Value	I-Squared
1.218	2	0.544	0.000

Remission of Depression at 12 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Fann, 2009)	Cancer	0.053	-0.022	0.127	0.164
	MDDP (Ell, 2010)	Diabetes	0.090	0.019	0.161	0.013
	HITIDES (Pyne, 2011)	HIV	0.086	0.007	0.164	0.032
Random			0.077	0.016	0.137	0.013

Remission of Depression at 18 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Risk difference	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.067	-0.053	0.188
IMPACT (Fann, 2009)	Cancer	0.104	0.010	0.198
MDDP (Ell, 2010)	Diabetes	0.040	-0.070	0.150
		0.075	0.013	0.136



Measures of Heterogeneity

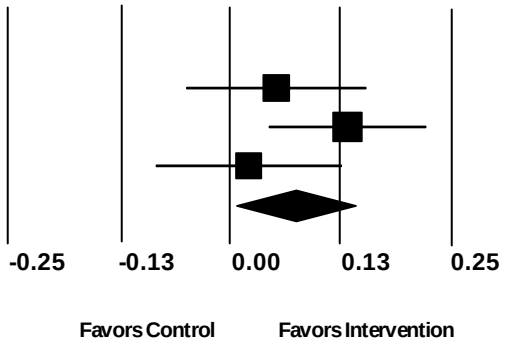
Q-Value	df (Q)	p-Value	I-Squared
0.761	2	0.683	0.000

Remission of Depression at 18 Months - RD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.077	0.006	0.149	0.034
	IMPACT (Fann, 2009)	Cancer	0.053	-0.029	0.134	0.205
	MDDP (Ell, 2010)	Diabetes	0.090	0.016	0.164	0.017
Random			0.075	0.013	0.136	0.017

Remission of Depression at 24 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Risk difference	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.024	-0.080	0.127
IMPACT (Fann, 2009)	Cancer	0.105	0.015	0.195
MDDP (Ell, 2010)	Diabetes	-0.008	-0.114	0.099
		0.045	-0.023	0.113



Notes: The ADAPt-C and MDDP (Dwight-Johnson, 2005) trials measured depressive symptoms with the Patient Health Questionnaire (PHQ-9); the IMPACT (Fann, 2009) trial used the Hopkins Symptom Checklist (HSCL).

Measures of Heterogeneity

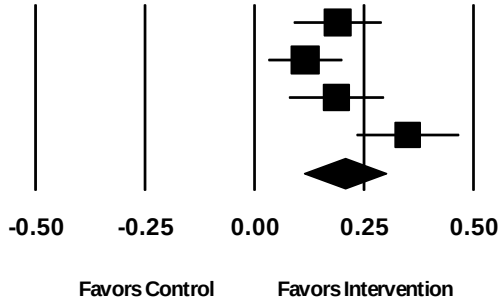
Q-Value	df (Q)	p-Value	I-Squared
2.783	2	0.249	28.139

Remission of Depression at 24 Months – RD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.052	-0.058	0.163	0.351
	IMPACT (Fann, 2009)	Cancer	0.009	-0.066	0.083	0.821
	MDDP (Ell, 2010)	Diabetes	0.068	-0.011	0.148	0.091
Random			0.045	-0.023	0.113	0.191

Mental Health Treatment Satisfaction at 12 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Risk difference	Lower limit	Upper limit
IMPACT (Fann, 2009)	Cancer	0.190	0.088	0.292
MDDP (Ell, 2010)	Diabetes	0.116	0.030	0.202
Pathways (Katon, 2004)	Diabetes	0.187	0.077	0.297
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.350	0.232	0.468
		0.205	0.112	0.299



Note: Treatment satisfaction was measured as follows:

MDDP: care was rated "satisfied" to "very satisfied"

Pathways: care was rated "moderately satisfied" to "very satisfied"

TEAMcare: care was rated "very satisfied" to "extremely satisfied"

IMPACT: care was rated "good" or "excellent"

Measures of Heterogeneity

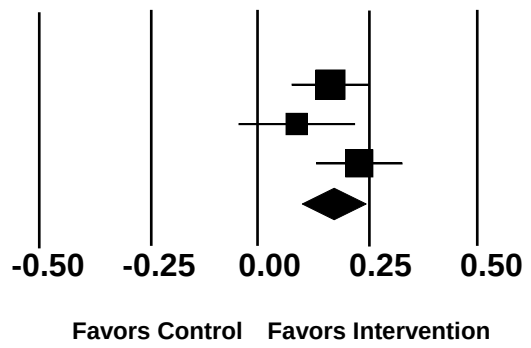
Q-Value	df (Q)	p-Value	I-Squared
9.878	3	0.020	69.629

Mental Health Treatment Satisfaction at 12 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Fann, 2009)	Cancer	0.213	0.080	0.346	0.002
	MDDP (Ell, 2010)	Diabetes	0.239	0.138	0.340	0.000
	Pathways (Katon, 2004)	Diabetes	0.214	0.084	0.343	0.001
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.157	0.101	0.214	0.000
Random			0.205	0.112	0.299	0.000

Mental Health Treatment Satisfaction at 24 Months

Study name	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.13	0.04	0.22
IMPACT (Fann, 2009)	Cancer	0.05	-0.08	0.19
MDDP (Ell, 2010)	Diabetes	0.20	0.10	0.30
		0.14	0.06	0.21



Note: Treatment satisfaction was measured as follows: ADAPt-C and MDDP: emotional care was rated "satisfied" to "very satisfied;" IMPACT: depression care was rated "good" or "excellent."

Measures of Heterogeneity

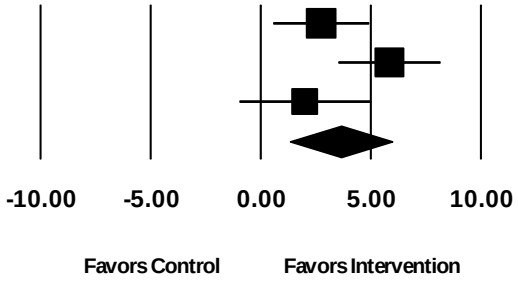
Q-Value	df (Q)	p-Value	I-Squared
2.843	2	0.241	29.648

Mental Health Treatment Satisfaction at 24 Months – RD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.133	-0.005	0.270	0.059
	IMPACT (Fann, 2009)	Cancer	0.160	0.094	0.227	0.000
	MDDP (Ell, 2010)	Diabetes	0.107	0.033	0.182	0.005
Random			0.137	0.065	0.209	0.000

Mental Health Status at 6 Months

Study name	Chronic Medical Condition	Difference in means	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	2.75	0.55	4.95
MDDP (Ell, 2010)	Diabetes	5.85	3.51	8.19
HITIDES (Pyne, 2011)	HIV	2.00	-0.99	4.99
		3.62	1.30	5.94



Notes: Mental health status was measured with the 12-Item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials.

Measures of Heterogeneity

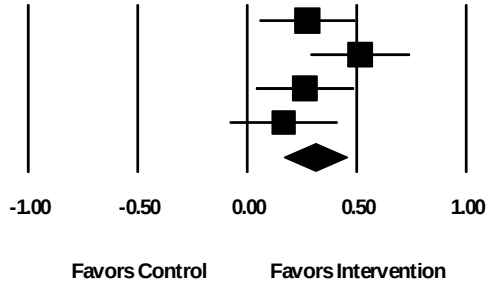
Q-Value	df (Q)	p-Value	I-Squared
5.199	2	0.074	61.531

Mental Health Status at 6 Months - WMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	4.041	0.275	7.807	0.035
	MDDP (Ell, 2010)	Diabetes	2.486	0.714	4.258	0.006
	HITIDES (Pyne, 2011)	HIV	4.273	1.236	7.311	0.006
Random			3.619	1.303	5.935	0.002

Mental Health Status at 6 Months

Studyname	Chronic Medical Condition	Std diff in means	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.27	0.05	0.50
MDDP (Ell, 2010)	Diabetes	0.52	0.29	0.74
Bypassing the Blues (Rollman, 2009)	Heart Disease	0.26	0.04	0.49
HITIDES (Pyne, 2011)	HIV	0.17	-0.08	0.42
		0.31	0.16	0.45



Notes: Mental health status was measured with the 12-Item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials except Bypassing the Blues, which used the SF-36. The Bypassing the Blues data are from the 8-month endpoint.

Measures of Heterogeneity

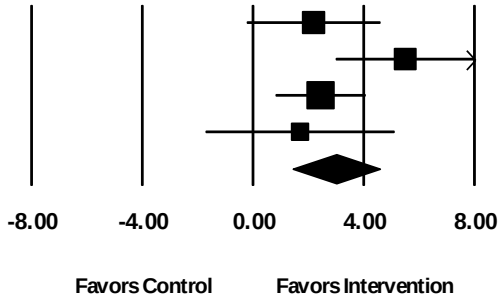
Q-Value	df (Q)	p-Value	I-Squared
4.638	3	0.200	35.313

Mental Health Status at 6 Months - SMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**SMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.319	0.115	0.522	0.002
	MDDP (Ell, 2010)	Diabetes	0.240	0.106	0.373	0.000
	Bypassing the Blues (Rollman, 2009)	Heart Disease	0.322	0.123	0.522	0.002
	HITIDES (Pyne, 2011)	HIV	0.350	0.190	0.510	0.000
Random			0.308	0.165	0.452	0.000

Mental Health Status at 12 Months

Study name	Chronic Medical Condition	Difference in means	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	2.19	-0.24	4.62
MDDP (Ell, 2010)	Diabetes	5.50	2.97	8.03
IMPACT (Williams, 2004)	Diabetes	2.44	0.80	4.08
HITIDES (Pyne, 2011)	HIV	1.70	-1.73	5.13
		2.98	1.41	4.55



Note: Mental health status was measured with the 12-Item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials.

Measures of Heterogeneity

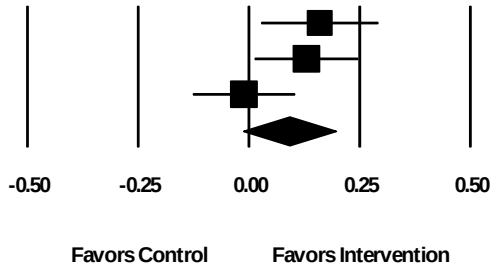
Q-Value	df (Q)	p-Value	I-Squared
5.152	3	0.161	41.772

Mental Health Status at 12 Months

Model	Study Name	Chronic Medical Condition	Statistics With Study Removed			p-Value
			WMD	Lower Limit	Upper Limit	
	ADAPt-C (Ell, 2008)	Cancer	3.261	1.088	5.433	0.003
	MDDP (Ell, 2010)	Diabetes	2.272	1.005	3.538	0.000
	IMPACT (Williams, 2004)	Diabetes	3.249	0.848	5.650	0.008
	HITIDES (Pyne, 2011)	HIV	3.250	1.342	5.159	0.001
Random			2.983	1.413	4.553	0.000

Prescription Antidepressant Use at 6 Months

Studyname	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
IMPACT (Fann, 2009)	Cancer	0.160	0.026	0.294
Bypassing the Blues (Rollman, 2009)	Heart Disease	0.130	0.012	0.248
HITIDES (Pyne, 2011)	HIV	-0.011	-0.128	0.106
		0.090	-0.015	0.195



Note: The Bypassing the Blues data are from the 8-month endpoint.

Measures of Heterogeneity

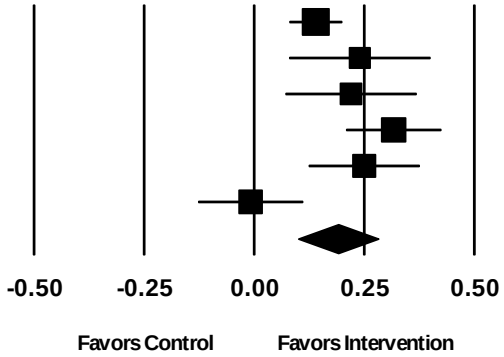
Q-Value	df (Q)	p-Value	I-Squared
4.368	2	0.113	54.216

Prescription Antidepressant Use at 6 Months

Model	Study Name	Chronic Medical Condition	Statistics With Study Removed			
			RD	Lower Limit	Upper Limit	p-Value
	IMPACT (Fann, 2009)	Cancer	0.059	-0.079	0.197	0.402
	Bypassing the Blues (Rollman, 2009)	Heart Disease	0.071	-0.096	0.239	0.404
	HITIDES (Pyne, 2011)	HIV	0.143	0.055	0.232	0.002
Random			0.090	-0.015	0.195	0.092

Prescription Antidepressant Use at 12 Months

Study name	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
IMPACT (Lin, 2003)	Arthritis	0.140	0.079	0.201
ADAPt-C (Ell, 2008)	Cancer	0.240	0.078	0.402
IMPACT (Fann, 2009)	Cancer	0.220	0.070	0.370
MDDP (Ell, 2010)	Diabetes	0.317	0.208	0.426
IMPACT (Williams, 2004)	Diabetes	0.250	0.122	0.378
HITIDES (Pyne, 2011)	HIV	-0.008	-0.128	0.112
		0.189	0.099	0.280



Measures of Heterogeneity

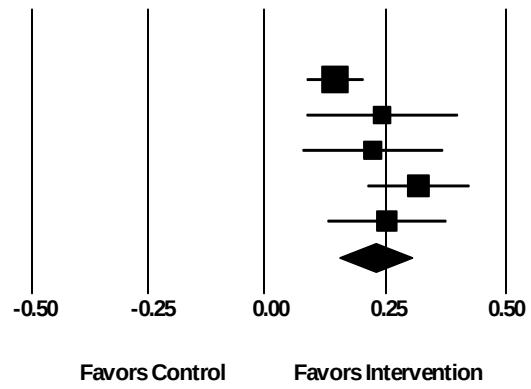
Q-Value	df (Q)	p-Value	I-Squared
18.867	5	0.002	73.498

Prescription Antidepressant Use at 12 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Lin, 2003)	Arthritis	0.203	0.082	0.324	0.001
	ADAPt-C (Ell, 2008)	Cancer	0.182	0.079	0.285	0.001
	IMPACT (Fann, 2009)	Cancer	0.185	0.080	0.290	0.001
	MDDP (Ell, 2010)	Diabetes	0.160	0.073	0.247	0.000
	IMPACT (Williams, 2004)	Diabetes	0.178	0.073	0.283	0.001
	HITIDES (Pyne, 2011)	HIV	0.225	0.148	0.301	0.000
Random			0.189	0.099	0.280	0.000

Prescription Antidepressant Use at 12 Months

Studyname	Chronic Medical Condition	Statistics for each study		
		Risk difference	Lower limit	Upper limit
IMPACT (Lin, 2003)	Arthritis	0.140	0.079	0.201
ADAPt-C (Ell, 2008)	Cancer	0.240	0.078	0.402
IMPACT (Fann, 2009)	Cancer	0.220	0.070	0.370
MDDP (Ell, 2010)	Diabetes	0.317	0.208	0.426
IMPACT (Williams, 2004)	Diabetes	0.250	0.122	0.378
		0.225	0.148	0.301



Sensitivity Analysis: Removing HITIDES (Pyne, 2011)

Measures of Heterogeneity

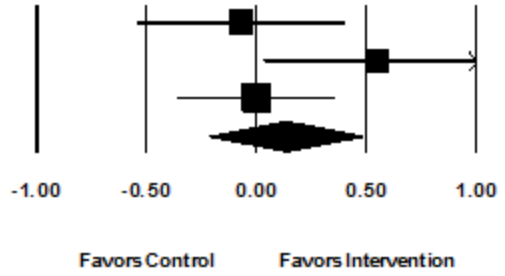
Q-Value	df (Q)	p-Value	I-Squared
8.936	4	0.063	55.236

Prescription Antidepressant Use at 12 Months – Sensitivity Analysis

			Statistics with study removed			
Model	**Study name**	**Chronic Medical Condition**	**RD**	**Lower limit**	**Upper limit**	**p-Value**
	IMPACT (Lin, 2003)	Arthritis	0.267	0.201	0.333	0.000
	ADAPt-C (Ell, 2008)	Cancer	0.224	0.133	0.315	0.000
	IMPACT (Fann, 2009)	Cancer	0.228	0.135	0.322	0.000
	MDDP (Ell, 2010)	Diabetes	0.183	0.125	0.242	0.000
	IMPACT (Williams, 2004)	Diabetes	0.221	0.127	0.315	0.000
Random			0.225	0.148	0.301	0.000

Change in HbA1C Levels at 6 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Difference in means	Lower limit	Upper limit
MDDP (Ell, 2010)	Diabetes	-0.07	-0.55	0.41
TEAMcare (Katon, 2010)	Diabetes	0.55	0.03	1.07
IMPACT (Williams, 2004)	Diabetes	0.00	-0.36	0.36
		0.13	-0.22	0.48



Measures of Heterogeneity

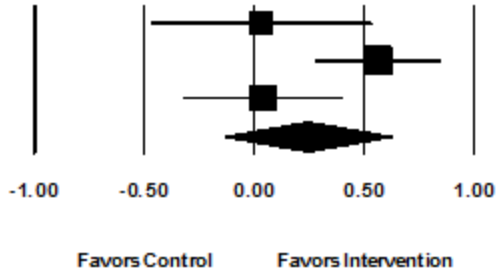
Q-Value	df (Q)	p-Value	I-Squared
3.671	2	0.160	45.524

Change in HbA1C Levels at 6 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	MDDP (Ell, 2010)	Diabetes	0.242	-0.293	0.777	0.375
	TEAMcare (Katon, 2010)	Diabetes	-0.026	-0.313	0.262	0.862
	IMPACT (Williams, 2004)	Diabetes	0.231	-0.376	0.838	0.456
Random			0.132	-0.217	0.482	0.458

Change in HbA1C Levels at 12 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Difference in means	Lower limit	Upper limit
MDDP (Ell, 2010)	Diabetes	0.03	-0.48	0.54
TEAMcare (Katon, 2010)	Diabetes	0.56	0.27	0.85
IMPACT (Williams, 2004)	Diabetes	0.04	-0.32	0.40
		0.24	-0.14	0.62



Measures of Heterogeneity

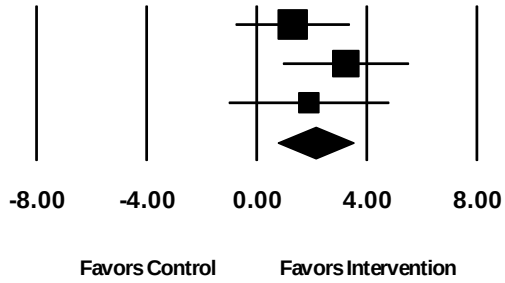
Q-Value	df (Q)	p-Value	I-Squared
6.208	2	0.045	67.785

Change in HbA1C Levels at 12 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	MDDP (Ell, 2010)	Diabetes	0.312	-0.197	0.821	0.230
	TEAMcare (Katon, 2010)	Diabetes	0.037	-0.257	0.331	0.807
	IMPACT (Williams, 2004)	Diabetes	0.337	-0.175	0.850	0.197
Random			0.239	-0.143	0.622	0.220

Change in Physical Health Status at 6 Months

Study name	Chronic Medical Condition	Difference in means	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	1.31	-0.78	3.40
MDDP (Ell, 2010)	Diabetes	3.24	0.94	5.54
HITIDES (Pyne, 2011)	HIV	1.90	-1.04	4.84
		2.12	0.75	3.49



Notes: Physical health status was measured with the 12-Item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials.

Measures of Heterogeneity

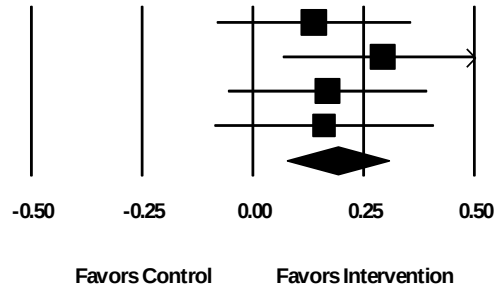
Q-Value	df (Q)	p-Value	I-Squared
1.505	2	0.471	0.000

Change in Physical Health Status at 6 Months - WMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	2.729	0.916	4.542	0.003
	MDDP (Ell, 2010)	Diabetes	1.509	-0.195	3.212	0.083
	HITIDES (Pyne, 2011)	HIV	2.212	0.325	4.099	0.022
Random			2.120	0.750	3.490	0.002

Change in Physical Health Status at 6 Months

Studyname	Chronic Medical Condition	Std diff in means	Lower limit	Upper limit
ADAPt-C (Ell, 2008)	Cancer	0.14	-0.08	0.36
MDDP (Ell, 2010)	Diabetes	0.29	0.07	0.52
Bypassing the Blues (Rollman, 2009)	Heart Disease	0.17	-0.06	0.39
HITIDES (Pyne, 2011)	HIV	0.16	-0.09	0.41
		0.19	0.08	0.31



Notes: Physical health status was measured with the 12-Item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials except Bypassing the Blues, which used the SF-36. The Bypassing the Blues data are from the 8-month endpoint.

Measures of Heterogeneity

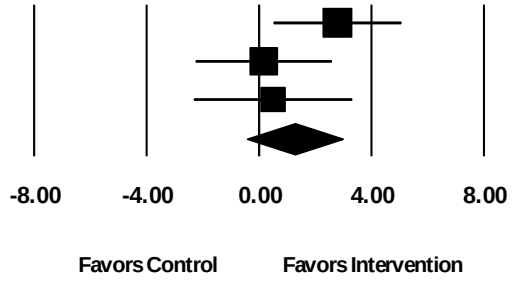
Q-Value	df (Q)	p-Value	I-Squared
1.101	3	0.777	0.000

Change in Physical Health Status at 6 Months - SMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**SMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.210	0.076	0.345	0.002
	MDDP (Ell, 2010)	Diabetes	0.155	0.022	0.288	0.023
	Bypassing the Blues (Rollman, 2009)	Heart Disease	0.198	0.065	0.332	0.004
	HITIDES (Pyne, 2011)	HIV	0.199	0.069	0.328	0.003
Random			0.191	0.076	0.305	0.001

Change in Physical Health Status at 12 Months

Study name	Chronic Medical Condition	Statistics for each study		
		Difference in means	Lower limit	Upper limit
ADAPt-C (El, 2008)	Cancer	2.79	0.50	5.08
MDDP (El, 2010)	Diabetes	0.17	-2.27	2.61
HITIDES (Pyne, 2011)	HIV	0.50	-2.34	3.34
		1.25	-0.45	2.95



Note: Physical health status was measured with the 12-Item Short Form Survey from the RAND Medical Outcomes Study (SF-12) for all trials.

Measures of Heterogeneity

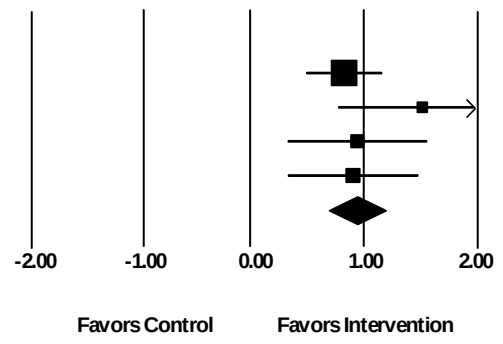
Q-Value	df (Q)	p-Value	I-Squared
2.748	2	0.253	27.212

Change in Physical Health Status at 12 Months - WMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	ADAPt-C (Ell, 2008)	Cancer	0.311	-1.540	2.162	0.742
	MDDP (Ell, 2010)	Diabetes	1.803	-0.420	4.026	0.112
	HITIDES (Pyne, 2011)	HIV	1.515	-1.052	4.082	0.247
Random			1.251	-0.446	2.948	0.149

Change in Functional Impairment at 12 Months

Studyname	Chronic Medical Condition	Statistics for each study		
		Difference in means	Lower limit	Upper limit
IMPACT (Lin, 2003)	Arthritis	0.82	0.47	1.17
IMPACT (Fann, 2009)	Cancer	1.53	0.76	2.30
MDDP (Ell, 2010)	Diabetes	0.94	0.30	1.58
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.90	0.30	1.50
		0.93	0.68	1.19



Measures of Heterogeneity

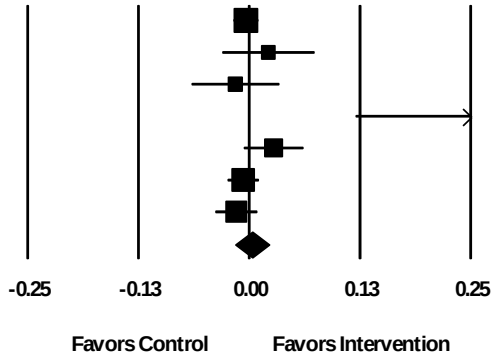
Q-Value	df (Q)	p-Value	I-Squared
2.726	3	0.436	0.000

Change in Functional Impairment at 12 Months - WMD

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**WMD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Linn, 2003)	Arthritis	1.067	0.688	1.446	0.000
	IMPACT (Fann, 2009)	Cancer	0.859	0.586	1.131	0.000
	MDDP (Ell, 2010)	Diabetes	0.970	0.614	1.327	0.000
	TEAMcare (Katon, 2010)	Diabetes	0.983	0.620	1.347	0.000
Random			0.934	0.677	1.190	0.000

Risk of All-Cause Mortality at 6 Months

Studyname	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
IMPACT (Lin, 2003)	Arthritis	-0.00	-0.02	0.01
ADAPt-C (Ell, 2008)	Cancer	0.02	-0.03	0.07
IMPACT (Fann, 2009)	Cancer	-0.02	-0.07	0.03
MDDP (Dwight-Johnson, 2005)	Diabetes	0.30	0.12	0.47
IMPACT (Williams, 2004)	Diabetes	0.03	-0.01	0.06
Bypassing the Blues (Rollman, 2009)	Heart Disease	-0.01	-0.02	0.01
HITIDES (Pyne, 2011)	HIV	-0.01	-0.04	0.01
		0.00	-0.02	0.02



Note: The Bypassing the Blues and MDDP data are from 8-month endpoints.

Measures of Heterogeneity

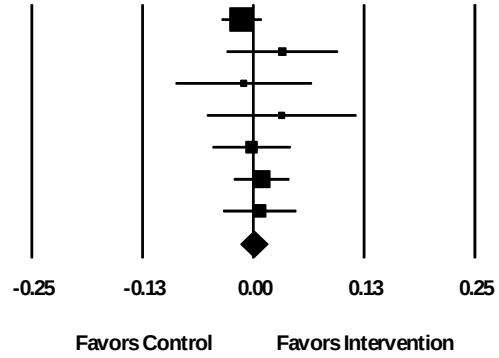
Q-Value	df (Q)	p-Value	I-Squared
16.194	6	0.013	62.949

Risk of All-Cause Mortality at 6 Months

Model	Study Name	Chronic Medical Condition	Statistics With Study Removed			
			RD	Lower Limit	Upper Limit	p-Value
	IMPACT (Lin, 2003)	Arthritis	0.008	-0.020	0.035	0.582
	ADAPt-C (Ell, 2008)	Cancer	0.001	-0.019	0.021	0.923
	IMPACT (Fann, 2009)	Cancer	0.005	-0.016	0.026	0.630
	MDDP (Dwight-Johnson, 2005)	Diabetes	-0.003	-0.013	0.007	0.519
	IMPACT (Williams, 2004)	Diabetes	-0.002	-0.022	0.018	0.846
	Bypassing the Blues (Rollman, 2009)	Heart Disease	0.008	-0.018	0.034	0.562
	HITIDES (Pyne, 2011)	HIV	0.008	-0.015	0.031	0.507
Random			0.003	-0.016	0.022	0.785

Risk of All-Cause Mortality at 12 Months

Study name	Chronic Medical Condition	Risk difference	Lower limit	Upper limit
IMPACT (Lin, 2003)	Arthritis	-0.01	-0.04	0.01
ADAPt-C (Ell, 2008)	Cancer	0.03	-0.03	0.10
IMPACT (Fann, 2009)	Cancer	-0.01	-0.09	0.07
SMaRT Oncology 1 (Strong, 2008)	Cancer	0.03	-0.05	0.12
IMPACT (Williams, 2004)	Diabetes	0.00	-0.05	0.04
TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	0.01	-0.02	0.04
HITIDES (Pyne, 2011)	HIV	0.01	-0.03	0.05
		-0.00	-0.02	0.01



Measures of Heterogeneity

Q-Value	df (Q)	p-Value	I-Squared
3.325	6	0.767	0.000

Risk of All-Cause Mortality at 12 Months

			Statistics With Study Removed			
Model	**Study Name**	**Chronic Medical Condition**	**RD**	**Lower Limit**	**Upper Limit**	**p-Value**
	IMPACT (Lin, 2003)	Arthritis	0.009	-0.011	0.028	0.374
	ADAPt-C (Ell, 2008)	Cancer	-0.002	-0.018	0.013	0.780
	IMPACT (Fann, 2009)	Cancer	0.000	-0.015	0.015	0.983
	SMaRT Oncology 1 (Strong, 2008)	Cancer	-0.001	-0.017	0.014	0.869
	IMPACT (Williams, 2004)	Diabetes	0.000	-0.016	0.016	0.997
	TEAMcare (Katon, 2010)	Diabetes +/- Heart Disease	-0.003	-0.020	0.014	0.732
	HITIDES (Pyne, 2011)	HIV	-0.001	-0.017	0.015	0.870
Random			0.000	-0.015	0.015	0.974

Appendix F. Strength of Evidence

Table F-1. Strength of Evidence for collaborative care interventions for people with depression and one or more chronic medical conditions: KQ1a

Outcome	Number of Studies; Subjects	Risk of bias; Design; Quality	Consistency	Directness	Precision	Summary Effect Size (95% CI)[a]	Strength of Evidence
Symptom improvement	11; 3,868	Low; 9 RCTs, 2 subgroup analyses from an RCT; 3 good, 8 fair	Consistent	Indirect	Precise	6 mths: SMD = 0.45 (0.29 to 0.61; 7 studies) 12 mths: SMD = 0.47 (0.29 to 0.65; 6 studies) 24 mths: WMD=0.18 (0.10 to 0.16; 4 studies)	Moderate
Depression-free days	5; 1,624	Low; 3 RCTs, 2 subgroup analyses from an RCT; 1 good, 4 fair	Consistent	Indirect	Imprecise	Not calculated; intervention always favored	Moderate
Response (at least 50% reduction)	10; 3,430	Low; 8 RCTs, 2 subgroup analyses from an RCT; 3 good, 7 fair	Consistent	Indirect	Precise	6 mths: RD = 0.20 (0.14 to 0.26; 9 studies) 12 mths: RD = 0.17 (0.12 to 0.23; 7 studies) 18 mths: RD=0.12 (0.02 to 0.22; 3 studies)	Moderate
Remission	5; 2,351	Low 3 RCTs, 2 subgroup analyses from an RCT; 1 good, 4 fair	Consistent	Indirect	Precise	6 mths: RD = 0.12 (0.06 to 0.18; 3 studies) 12 mths: RD = 0.08 (0.02 to 0.14) 18 mths: RD=0.08 (0.01 to 0.14; 3 studies) 24 mths: RD=0.05 (-0.02 to 0.11; 3 studies)	Moderate
Recurrence	1; 472	Low 1 RCT; 1 Fair	Unknown (single study)	Indirect	Unknown (single study)	No significant difference between groups	Insufficient
Treatment adherence	2; 605	Low; 2 RCTs; 1 good, 1 fair	Inconsistent	Indirect	Imprecise	Mixed results[b]	Insufficient
Treatment	4; 1,145[c]	Low;	Consistent	Indirect	Precise	6 mths:	Moderate

Outcome	Number of Studies; Subjects	Risk of bias; Design; Quality	Consistency	Directness	Precision	Summary Effect Size (95% CI)[a]	Strength of Evidence
satisfaction		3 RCTs, 1 subgroup analysis from an RCT; 4 fair				RD = 0.21 (0.11 to 0.30; 4 studies) 12 mths: RD=0.14 (0.06 to 0.21; 3 studies)	

[a] All of the effect sizes reported in this Table favor collaborative care over controls. Effect sizes and confidence intervals are rounded to the nearest hundredth.
[b] One trial reported significantly greater adherence to antidepressants in the intervention arm at six and 12 months; the other reported no difference between groups at six and 12 months.
[c] Two additional trials reported treatment satisfaction for the intervention arm but not the usual care arm.
Abbreviations: CI = confidence interval; mths = months; NA = not applicable; RCT = randomized controlled trial; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference

Table F-2. Strength of Evidence for collaborative care interventions for people with depression and one or more chronic medical conditions: KQ 1b

Outcome	Number of Studies; Subjects	Risk of bias; Design; Quality	Consistency	Directness	Precision	Summary effect Size (95% CI)	Strength of Evidence
Suicide	2; 255	Low; 1 RCT; 1 fair	Inconsistent	Direct	Imprecise	Not calculated[a]	Insufficient
Use of anti-depressants	10; 3,813	Low; 7 RCTs, 3 subgroup analyses from an RCT; 2 good, 8 fair	Inconsistent	Direct	Imprecise	6 mths: RD = 0.09 (-0.02 to 0.20; 3 studies) 12 mths: RD = 0.23 (0.15 to 0.30; 5 studies)[b]	Low
MH-related quality of life	5; 1,854	Low; 4 RCTs, 1 subgroup analysis from an RCT; 2 good; 3 fair	Consistent	Direct	Imprecise	6 mths: SMD = 0.31 (0.16 to 0.45; 4 studies) 12 mths: WMD = 2.98 (1.41 to 4.56; 4 studies)	Moderate
MH care utilization	8; 2940	Low; 6 RCTs, 2 subgroup analyses from an RCT; 2 good; 6 fair	Consistent	Direct	Imprecise	Not calculated	Low
MH-related sick days	0;0	N/A	N/A	N/A	N/A	N/A	Insufficient
MH-related employment stability	0;0	N/A	N/A	N/A	N/A	N/A	Insufficient

Note: IMPACT trial is divided by condition (arthritis, cancer, diabetes) and each condition is considered a ~~–s~~study" in this table.
[a] One study reported one suicide in the usual care group; another reported that they were unaware of any attempted or completed suicides in either group.
[b] Results of the meta-analysis excluding the HITIDES data
Abbreviations: CI = confidence interval; MH = mental health; mths = months; N/A = not applicable; RCT = randomized controlled trial; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference

Table F-3. Strength of Evidence for collaborative care interventions for people with depression and one or more chronic medical conditions: KQ 2a

Outcome	Number of Studies; Subjects	Risk of bias; Design; Quality	Consistency	Directness	Precision	Summary effect size (95% CI)	Strength of Evidence
Symptom improvement							
Arthritis: pain	1; 1,001	Medium; 1 subgroup analysis of an RCT; 1 Fair	N/A	Indirect	Imprecise	Change in pain score (0-10 scale, higher = worse) 6 mths: -0.21(-0.55 to 0.13) 12 mths: -0.53 (-0.92 to -0.14)	Insufficient
HIV: symptom severity	1; 276	Low; 1 RCT; 1 Good	N/A	Indirect	Imprecise	6 mths: Beta = -0.62 (-1.2 to -0.08) 12 mths: Beta = -0.09 (-1.58 to 1.40)	Insufficient
Response							
Diabetes: HbA1c	4; 1,347[a]	Medium, 3 RCTs, 1 subgroup analysis of an RCT; 4 Fair	Inconsistent	Indirect	Imprecise	6 mths: WMD = 0.13 (-0.55 to 0.41; 3 studies) 12 mths: WMD = 0.24 (-0.14 to 0.62; 3 studies)	Low
Heart disease: ≥ 10 mg Hg decrease in SBP	1; 214[a]	Medium; 1 RCT; 1 Fair	N/A	Indirect	Precise	At 12 mths, 41 intervention subjects vs. 25 controls achieved response (p=0.016)	Insufficient
Adherence							
Cancer: followed treatment	1; 55	Medium; 1 RCT; 1 Fair	N/A	Indirect	Precise	12 mths: OR = 3.51 (0.82 to 15.03)	Insufficient
Diabetes: diet	3; 960[a]	Medium; 2 RCTs, 1 subgroup analysis from an RCT; 3 Fair	Consistent	Indirect	Precise	Not calculated; no between group difference at any time points in all studies examined	Moderate
Diabetes: exercise	3; 960[a]	Medium; 2 RCTs, 1 subgroup analysis from an RCT; 3 Fair	Inconsistent	Indirect	Imprecise	Not calculated; 2 studies favored intervention, 1 study found no difference	Low

Outcome	Number of Studies; Subjects	Risk of bias; Design; Quality	Consistency	Directness	Precision	Summary effect size (95% CI)	Strength of Evidence
Diabetes: medications	2; 746	Medium; 1 RCT, 1 subgroup analysis from an RCT; 2 Fair	Inconsistent	Indirect	Imprecise	Not calculated; 1 study found no difference in adherence to lipid-lowering agents or ACE inhibitors but a higher rate of non-adherence to oral hypoglycemics in the intervention group at 12 mths; the other found no difference in general medication adherence at any time point.	Insufficient
HIV: medications	1; 276	Low; 1 RCT; 1 Good	N/A	Indirect	Imprecise	Not calculated; no between-group differences at 6 and 12 months	Insufficient
Satisfaction with care							
Diabetes, heart disease or both	1; 214	Medium; 1 RCT; 1 Fair	N/A	Indirect	Imprecise	Mean improvement from baseline was 16% in the intervention vs. 2% in control (p<0.001)	Insufficient

Note: IMPACT trial is divided by condition (arthritis, cancer, diabetes) and each condition is considered a ~~–s~~tudy" in this table.
[a] Total number includes patients from the TEAMcare study who had diabetes, heart disease, or both.
Abbreviations: CI = confidence interval; N/A = not applicable; OR = odds ratio; RCT = randomized controlled trial; RD = risk difference; SMD = standardized mean difference; WMD = weighted mean difference

Table F-4. Strength of Evidence for collaborative care interventions for people with depression and one or more chronic medical conditions: KQ 2b, general health outcomes and costs

Outcome	Number of Studies; Subjects	Risk of bias; Design; Quality	Consistency	Directness	Precision	Summary effect Size (95% CI)	Strength of Evidence
Condition-specific morbidity	2; 1,303	Medium; 1 RCT, 1 subgroup analysis from an RCT; 1 Good, 1 Fair	Inconsistent	Direct	Imprecise	Not calculated	Insufficient
Mortality	11; 3,868	Low; 8 RCTs, 3 subgroup analyses from an RCT; 2 Good; 9 Fair	Consistent	Direct	Precise	6 mths: RD = 0.00 (-0.02 to 0.02; 7 studies) 12 mths: RD = 0.00 (0.02 to 0.01; 7 studies)	Moderate
Health care utilization	2; 516	Low; 2 RCTs; 1 Good; 1 Fair	Inconsistent	Direct	Imprecise	Not calculated	Insufficient
Quality of life	6; 2,768	Medium; 3 RCTs, 3 subgroup analyses from an RCT; 1 Good, 5 Fair	Consistent	Direct	Imprecise	Not calculated;[a] Intervention favored across measures.	Moderate
Cost of intervention	6; 2,019	High; 5 RCT, 1 subgroup analysis from an RCT; 6 Fair	N/A	Direct	N/A	$705 per patient[b]	Insufficient

Note: IMPACT trial is divided by condition (arthritis, cancer, diabetes) and each condition is considered a ~~"~~study" in this table.
[a] Not calculated because of highly variable measures used by the studies to measure quality of life.
[b] Crude estimate of average cost of intervention.
Abbreviations: CI = confidence interval; mths = months; RD = risk difference; WMD = weighted mean difference