



# Effective Health Care Program

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

### 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 “urgent importance.”<sup>1</sup> In the United States, half of the care for common mental health disorders is delivered in general medical settings,<sup>2</sup> 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,<sup>3</sup> 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.<sup>4-6</sup> 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.<sup>2,7</sup> However, to date, no synthesis has been done of the evidence on practice-based interventions

#### Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).

that accounts for the primary care patient with “multiple chronic conditions”<sup>8,9</sup> and examines both mental health and chronic medical outcomes simultaneously.



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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.<sup>10</sup> By 2030, depression itself is projected to be the single leading cause of overall disease burden in high-income countries.<sup>11</sup> 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.<sup>12</sup> In 2000, the U.S. economic burden of depressive disorders was estimated to be \$83.1 billion.<sup>13</sup> More than 30 percent of these costs were attributable to direct medical expenses.<sup>13</sup>

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

Chronic medical conditions commonly associated with depression include arthritis, heart disease, diabetes, asthma, lung disease, and cancer.<sup>17,18</sup> (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.<sup>19,20</sup>

### 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.<sup>4,32-34</sup> An emerging literature addresses whether better treatment of depression in primary care can also improve chronic medical outcomes, such as for diabetes.<sup>35-37</sup> 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

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

MDD = major depressive disorder

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<sup>32</sup> and a 2009 National Institute for Health and Clinical Excellence (NICE) guideline for depression in adults with a chronic physical health problem.<sup>33</sup> 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,<sup>38</sup> 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,<sup>39</sup> and the patient-centered medical home (PCMH),<sup>40</sup> 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.”<sup>41</sup> Numerous barriers, many financial, have hindered implementation of collaborative depression treatment in primary care, despite its considerable evidence base.<sup>4,42,43</sup> 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.<sup>44</sup>

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<sup>45</sup> and the Institute of Medicine (IOM):<sup>46</sup> 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.

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.

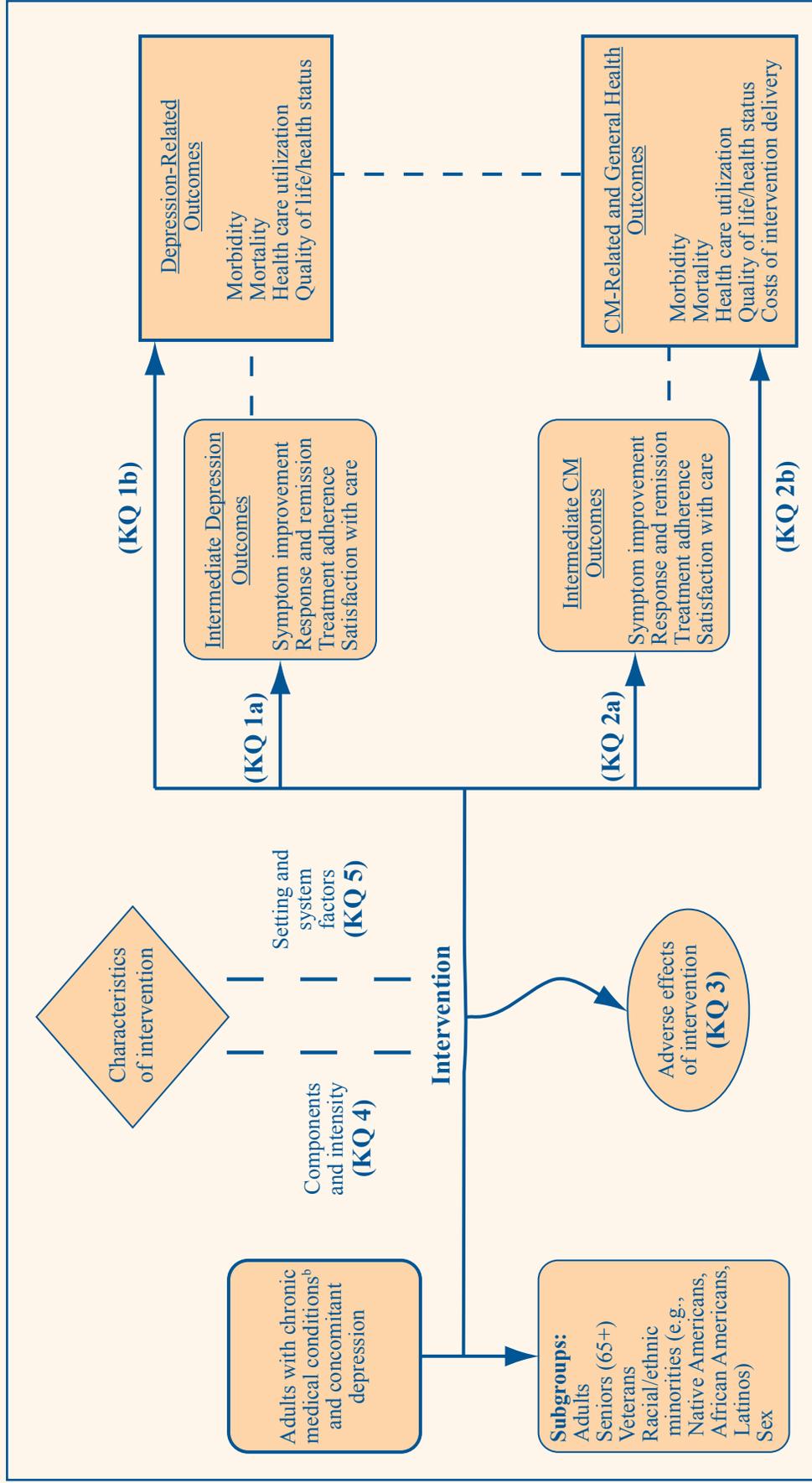
We developed eligibility (inclusion and exclusion) criteria with respect to patient PICOTS, and study designs and durations for each part of KQs 1 and 2. We included controlled studies of at least 6 months’ duration in adults (age 18 or older) with depression and/or anxiety (the only conditions represented 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).

**Figure A. Analytic framework for interventions addressing concomitant depression<sup>a</sup> and chronic medical conditions<sup>b</sup> in primary care**



CM = chronic medical; MH = mental health interventions

<sup>a</sup>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.

<sup>b</sup>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.

## 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)<sup>47</sup> and the University of York Centre for Reviews and Dissemination.<sup>48</sup> 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.<sup>49</sup> 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.<sup>50</sup> 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.<sup>51</sup> 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;<sup>52-56</sup> 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,<sup>57-59</sup> Spanish speakers,<sup>57-60</sup> and predominantly African-American male veterans with HIV;<sup>61</sup> 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<sup>52-56</sup> are secondary analyses from the Improving Mood—Promoting Access

to Collaborative Treatment (IMPACT) trial;<sup>5</sup> 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,<sup>53,56</sup> cancer,<sup>52,57,59,62</sup> diabetes,<sup>35,37,58,63-66</sup> heart disease,<sup>67</sup> and HIV.<sup>61</sup> Two studies involved patients with one or more active medical conditions.<sup>60,68</sup>

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

For IMPACT,<sup>52-56</sup> Bypassing the Blues,<sup>67</sup> Symptom Management Research Trials (SMaRT) Oncology 1,<sup>62</sup> HITIDES (HIV Implementation of Translating Initiatives for Depression into Effective Solutions),<sup>61</sup> the Multifaceted Oncology Depression Program,<sup>57</sup> and Vera et al.,<sup>60</sup> 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,<sup>59</sup> Pathways,<sup>35,37,63,64,66</sup> TEAMcare,<sup>68</sup> and the Multifaceted Diabetes and Depression Program<sup>58</sup> 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 B. Summary of collaborative care intervention trials**

Author/Trial Name	Quality Rating <sup>a</sup>	Intervention Summary	Delivery Method Delivered by Psychiatrist Supervision?
Lin et al., 2003; <sup>56</sup> Lin et al., 2006; <sup>53</sup> Fann et al., 2009; <sup>52</sup> Williams et al., 2004; <sup>55</sup> Katon et al., 2006 <sup>54</sup> IMPACT Arthritis, cancer, diabetes <sup>b</sup> 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 <sup>57</sup> 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

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

<b>Author/Trial Name</b>			<b>Delivery Method</b>
<b>Disease</b>	<b>Quality Rating<sup>a</sup></b>	<b>Intervention Summary</b>	<b>Delivered by</b>
<b>Sample Size</b>			<b>Psychiatrist Supervision?</b>
Ell et al., 2008; <sup>59</sup> Ell et al., 2011 <sup>69</sup> 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; <sup>58</sup> Ell et al., 2011; <sup>70</sup> Hay et al., 2012 <sup>71</sup> 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; <sup>37</sup> Katon et al., 2008; <sup>63</sup> Katon et al., 2004; <sup>35</sup> Kinder et al., 2006; <sup>64</sup> Lin et al., 2006; <sup>65</sup> Simon et al., 2007 <sup>66</sup> 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; <sup>68</sup> Von Korff, 2011; <sup>72</sup> Lin, 2012 <sup>73</sup> 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
Pyne et al., 2011 <sup>61</sup> 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 <sup>67</sup> 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

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

<b>Author/Trial Name</b>			<b>Delivery Method</b>
<b>Disease</b>	<b>Quality Rating<sup>a</sup></b>	<b>Intervention Summary</b>	<b>Delivered by</b>
<b>Sample Size</b>			<b>Psychiatrist Supervision?</b>
Strong et al., 2008 <sup>62,c</sup> 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 <sup>60</sup> 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

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

<sup>a</sup>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.

<sup>b</sup>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.

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

## 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<sup>35,52,56-60,67,68</sup> (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.

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<sup>65</sup> and one did not.<sup>61</sup> We found insufficient data to draw conclusions about recurrence of depression (only one study<sup>59,69</sup>).

### 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,

**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 <sup>59,69</sup> (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 <sup>65</sup> reported significantly greater adherence to antidepressants in the intervention arm at 6 and 12 months; the other <sup>61</sup> 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), <sup>a</sup> and this extended to 24 months (RD, 0.14, 95% CI, 0.06 to 0.21) (3 studies).	Moderate

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

<sup>a</sup>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.

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.<sup>62</sup> Meta-analysis from three studies<sup>52,61,67</sup> 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<sup>52,55,56,58,59,61</sup> 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<sup>35,52,53,58,59,69,70</sup> 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<sup>52</sup> 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 <sup>a</sup> ), 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

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

<sup>a</sup>Results of the meta-analysis excluding the HITIDES data, which was an outlier and accounted for significant heterogeneity (Appendix E in the full report).

### 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.

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,<sup>68</sup> 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<sup>70</sup> 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.<sup>55,65,68</sup> 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<sup>55,65,68</sup> (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.<sup>58,70</sup> 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 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 <sup>70</sup> showed no difference between groups at 18 and 24 months.	Low
	Heart disease: $\geq 10$ 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

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

### 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).

All but one study<sup>60</sup> 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<sup>52,55-57,59,61,67,69</sup>) or 12 months (RD, 0.00; 95% CI, -0.02 to 0.02; seven studies<sup>52,55,56,59,61,62,68,69</sup>) (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<sup>52,56,57,59,61,69,72</sup> (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,<sup>68</sup> 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.

**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

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

The TEAMcare study<sup>68</sup> 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<sup>60</sup>), and 1<sup>62</sup> 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<sup>57-60,62,67</sup> and closed in three trials.<sup>35,37,61,63-66,68</sup> 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.<sup>34</sup> 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,<sup>27,74,75</sup> 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<sup>76</sup> or because the treatment occurred outside the purview of a primary care–like setting.<sup>77-79</sup> 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,<sup>68</sup> 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,<sup>80</sup> uptake of such interventions has been poor. Although financial and system barriers have been identified,<sup>81</sup> 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<sup>39</sup> 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.<sup>82</sup> 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.<sup>40</sup>

**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)<sup>58,59</sup> and male veterans<sup>61</sup> 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,<sup>38</sup> 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;<sup>83</sup> 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<sup>84</sup> 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<sup>68</sup> 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"<sup>38</sup>). 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.<sup>85</sup>

## 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.<sup>86,87</sup> 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<sup>88</sup> 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-to-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,<sup>38</sup> 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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