

Comparative Effectiveness Research Review Disposition of Comments Report

Research Review Title: *Practice-Based Interventions Addressing Concomitant Depression and Chronic Medical Conditions in the Primary Care Setting*

Draft review available for public comment from October 13, 2011 to November 10, 2011.

Research Review Citation: Watson L, Amick H, Gaynes B, Brownley K, Thaker S, Viswanathan M, Jonas D. Practice-Based Interventions Addressing Concomitant Depression and Chronic Medical Conditions in the Primary Care Setting. Comparative Effectiveness Review No. 75. (Prepared by the RTI International–University of North Carolina Evidence-based Practice Center under Contract No. 290-2007-10056-I.) AHRQ Publication No. xx-EHCxxx. Rockville, MD: Agency for Healthcare Research and Quality. August 2012. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

The Effective Health Care (EHC) Program encourages the public to participate in the development of its research projects. Each comparative effectiveness research review is posted to the EHC Program Web site in draft form for public comment for a 4-week period. Comments can be submitted via the EHC Program Web site, mail or email. At the conclusion of the public comment period, authors use the commentators' submissions and comments to revise the draft comparative effectiveness research review.

Comments on draft reviews and the authors' responses to the comments are posted for public viewing on the EHC Program Web site approximately 3 months after the final research review is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Commentator & Affiliation	Section	Comment	Response
Peer #1	General	The report is very well done and is clinically meaningful. The target population and audience was explicitly defined and the key questions were appropriate with clear definitions	Thank you.
Peer #2	General	This report seeks to compare the effectiveness of primary-care practice-based interventions that seek to improve outcomes among patients with comorbid depression and common chronic illnesses. The goal is to provide information that will help inform decisions of multiple stakeholders including patients, providers, and policy-makers. The key questions were appropriate and explicitly stated.	Thank you.
Peer #3	General	This is a well-written review of interventions to improve outcomes for patients with mental and co-occurring physical health problems in the primary care setting. The systematic review and meta-analyses methods appear sound. A major concern is whether this review adds anything new to the growing meta-analysis literature on practice-based interventions, as the main questions seemed too focused on defining "practice-based" interventions as based on the chronic care model, which not surprisingly, resulted in a limited number of articles that mainly centered around depression.	<p>We intend the term "practice-based" to be inclusive of a range of interventions such as you mention. We reported on the components of these interventions as defined in each trial by study investigators.</p> <p>We have added the following to clarify what this review adds to the body of literature on this topic: <i>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 in these same people.</i></p>

Commentator & Affiliation	Section	Comment	Response
Peer #4	General	<p>The report is well written and clear and should be helpful to the intended audience of clinicians, employers, and policy makers.</p> <p>I was disappointed that practice interventions for the most common substance use disorder, alcohol, were not included in the review and suggest this could be a subject of a future synthesis.</p> <p>The target population was defined. Are the target population and audience defined? Are key questions explicitly stated and appropriate?</p> <p>The authors state that the preliminary evidence reviews revealed that data were insufficient for mental health conditions other than anxiety and depression, two of the most common conditions in primary care. However, the trials that were included in the synthesis all addressed depression.</p> <p>The authors need to further explain the differences and similarities between collaborative care, integrated care, and coordinated care. Not clear how the authors operationalized these approaches and how they differed.</p>	<p>We decided to exclude alcohol misuse and other substance use disorders for several reasons, the main being that we feel that substance use disorders are likely too heterogeneous to include with other conditions in attempts to draw meaningful conclusions. In addition, the question of how to categorize substance abuse (as a mental health condition or a chronic medical condition) is a difficult one to answer in terms of scope of this review.</p> <p>Although we included anxiety-related terms in our literature searches, we did not identify any trials that met our inclusion criteria. To make the review more clear, we have removed mentions of anxiety as a mental health condition of interest.</p> <p>We intend the term “practice-based” to be inclusive of a range of interventions such as you mention. We reported on the components of these interventions as defined in each trial by study investigators.</p>

Commentator & Affiliation	Section	Comment	Response
Peer #5	General	<p>This systematic review examines the impact of collaborative care models in patients with depression and comorbid medical conditions. While the topic is important, there is some lack of clarity about the purpose of the study, which leads to some confusion both about the inclusion criteria and the interpretation of the findings. There are nearly 70 collaborative care studies of depression, and many reviews and meta analyses showing that these improve depression outcomes. Given that we know these interventions work, why wouldn't they also work in patients with medical comorbidity? Is there something about medical comorbidity that makes this a more important subgroup to analyze than, say people from low SES, people with comorbid substance use, racial populations etc.?</p> <p>The question of whether treating depression alone is enough to improve medical outcomes might be of more interest, as a negative finding would point to the need for multidisease management models.</p>	<p>We appreciate the concern about purpose and have worked to clarify our objectives.</p> <p>We did not intend to imply that those with medical comorbidities are “more important” than others. Most of the previous studies using depression as an outcome have drawn from general primary care samples that often did not select for the presence of specific chronic disease.</p> <p>We have added the following to clarify what this review adds to the body of literature on this topic: <i>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.</i></p> <p>As specified in our methods and analytic framework, we examined data for various subgroups (e.g., women, veterans, minorities) whenever they were reported.</p> <p>We agree that this is an important question, and it was one we were hoping to answer. However, a key finding of this review is that there have been few studies designed to look directly at the effects of collaborative care targeting the mental health condition (compared with usual care) on medical outcomes in people with comorbid depression.</p>
Peer #6	General	<p>This review appears to have been conducted according to a now fairly well-established protocol for systematic reviews and to have been performed in an objective way with highly detailed descriptions of the methods used and the findings obtained. Thus, on one level, it is a success. However, if one disagrees with that established protocol and wishes that the authors had instead taken a more inclusive approach that was aimed more at potential users of the information than at the researchers who appear to be the intended audience, then one would come to a very different conclusion. I have the following major disagreements with the approach:</p>	<p>We appreciate these comments about the methods we applied and respond to each below.</p> <p>1) We feel that our use of the two general intervention search terms (“Intervention Studies”[MeSH] and “intervention” or “interventions” in title or abstract) would capture most, if not all, practice-based interventions, regardless of what they are called. The more specific intervention terms we used (e.g., collaborative care, integrated care, chronic disease management) were generated by discussions with stakeholders and in consultation with a research librarian. Those terms were added to the search to supplement the intervention term list.</p>

Commentator & Affiliation	Section	Comment	Response
		<p>1. By choosing only the few MESH terms for the types of interventions included in the lit search, the authors have predetermined that they would end up with only studies of the collaborative care model. However, there is a substantial literature on other interventions (reminder systems, registries, non-physician care providers, clinical decision support, etc.) which seem likely to have been relevant to the Key Questions. Although it is possible that none of those studies addresses both mental and physical condition care, the reader cannot know that because of the boundaries established by the lit search</p> <p>2. By limiting the studies reviewed to those with comparison groups, the authors have eliminated 55 studies which might have contributed value and are left with only 10 studies, so few that it is not surprising that they had to conclude that there is very limited evidence on which to provide answers to the Key Questions. Although not described, I assume the final deleted studies included quasi-experimental, observational, and case studies. Individually, each of these can provide at least suggestive findings, and collectively they can be fairly definitive if they largely point in the same direction. It is regrettable that they were not evaluated and included</p> <p>3. By providing voluminous details and overly cautious language, the authors have guaranteed that this report will not be read, much less used by anyone except researchers. Even the Executive Summary will exclude potential users, both by the style and detailed reporting and by the lack of information relevant to patients, clinicians, health system leaders, and policy makers. It would be difficult to boil the messages down to the 1 page that might reach users, but if one could, the information contained would still mostly be unactionable. In short, the review is not clinically meaningful and is unlikely to be used except to generate additional proposals and studies.</p>	<p>In order to provide assurance that we did not systematically exclude key interventions due to our search terms, we searched MEDLINE for any of the following intervention terms combined with our mental health, chronic medical condition, and study design 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 were reviewed and none met our inclusion criteria.</p> <p>2. We have clarified in the report that excluding studies without a comparison group was a decision that we made in the context of this report, and our rationale for doing so: <i>“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). We recognize that studies without comparison groups can sometimes identify important information, but for the purposes of our questions we would 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 Key Questions (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). As such, we believe that the risk of bias in studies without comparison groups is too high to provide reliable evidence to answer our KQs.”</i></p> <p>3. We hear your message about the complexity of the report and have worked to simplify the main points.</p>
Peer #8	General	The report is thorough, thoughtful, well-organized and the ideas are clearly presented. The right questions are asked and the answers are clearly and explicitly stated, as are the gaps in the evidence. I have made some suggestions in	Thank you. We agree that there are several important questions that remain unanswered, and we hope that this report may inform future studies that address them.

Commentator & Affiliation	Section	Comment	Response
		<p>other places in my review that I think will make the report more useful and I hope that the authors will consider them. Readers of this report will come away with the following understandings: 1) collaborative care is, in general, quite effective for treating major depressive disorder in mostly middle aged people with one or more of the common chronic diseases; 2) the key element of collaborative care is the care manager; 3) practices that cannot incorporate a care manager will probably not be able to deliver collaborative care; 4) collaborative care has not been widely disseminated. The main conclusion about the effectiveness of collaborative care was expected but the report adds more detail.</p> <p>The important strength of the report is not so much that it supports evidence already out there but that it takes that evidence and puts it one place. This makes the report really valuable to clinicians, provider organizations, advocacy groups, patients and purchasers of health care. However, by seeing the information in one place, one cannot help but be struck by how little is truly known. For example, for some of the specific chronic diseases, there is little evidence on the effectiveness of collaborative care.</p> <p>There is little evidence of the effectiveness of collaborative outside of HMO type or integrated systems.</p> <p>It was disappointing that one of the most the critical questions that clinicians often ask, "If I treat my patient's depression effectively, will that have any positive effect on their diabetes or heart disease or other chronic diseases" remains unanswered. None of these are the fault of the authors of course.</p> <p>To close on a positive note, the authors have produced a good report and I believe that it will be well received.</p>	<p>In the "Research Gaps" section, we addressed the lack of evidence on effectiveness mentioned in this comment: "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."</p> <p>If you look at the data directly only 3 studies were perceived to be in a "closed" system and several were from safety net and other "non-integrated systems." All showed effectiveness for depression, so while we understand the perspective of the comment based on the majority of previous work, it is not necessarily accurate based on this review.</p> <p>We addressed this question in the "findings in relationship to what is already known" section: "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 followup⁹⁶ 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."</p>

Commentator & Affiliation	Section	Comment	Response
Peer #9	General	<p>The report is important because it covers medical problems that affect a large portion of the population. Also, these problems account for a sizable portion of direct and indirect medical costs.</p> <p>The key questions are appropriate and the analytic framework follows the methods of the USPSTF.</p> <p>The overall focus may be too narrow to be immediately relevant to practice.</p>	<p>Without specific feedback on how the focus may be too narrow, we are unable to address this comment directly. However, we respond to other comments about the scope/focus throughout this document.</p>
AHRQ Multiple Chronic Conditions Research Network	General	<p>This document summarizes comments on AHRQ's Effective Health Care (EHC) Program's draft report draft report: "Practice-Based Interventions Addressing Concomitant Mental Health and Chronic Medical Conditions in the Primary Care Setting," from members of the AHRQ Multiple Chronic Conditions (MCC) Research Network. We find the assessment of the strength of evidence and key findings from the included studies is sound.</p> <p>However, we have concerns about the limited scope of the review in terms of the restricted number of mental health conditions included, and we question if this review adds to what has previously been reported, particularly in terms of what is need to change and advance current clinical practice.</p> <p>Recommendations for additional research needed to fill the existing gaps in knowledge would enhance the usability and impact of this report. Specific comments and additional issues for the EHC to consider are elaborated in more detail below under the relevant sections.</p>	<p>We have added the following to clarify what this review adds to the body of literature on this topic: <i>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.</i></p> <p>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. Importantly, this also excluded substance misuse disorders. The exclusion of other mental health conditions does not reflect a belief that they are not important, but that the literature is not mature enough to answer the questions set forth.</p> <p>As noted in response to comments above, 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.</p>

Commentator & Affiliation	Section	Comment	Response
AHRQ Multiple Chronic Conditions Research Network	Executive Summary	<p>Table 16 (p. 35) contains useful information on costs; it would be helpful to mention this in the executive summary.</p> <p>We also think it would strengthen the tables in the Executive Summary if sample sizes can be added to table ES-2 (p. 9).</p> <p>More discussion of why other mental health conditions were excluded from this review (as can be found in the “Scope of the Review” in the Introduction) should be included in the Executive Study.</p> <p>We also suggest that a sentence or two be included in the executive summary that recognizes that other behavioral health conditions commonly seen in primary care affect chronic disease self-management, outcomes, and quality of life, including substance abuse disorders (e.g. alcohol, abuse of medications in chronic pain syndromes), and cognitive impairments (e.g. traumatic brain injuries, adult learning disabilities, mild or borderline mental retardation and dementias), and that these were not included here because there is not sufficient research, rather than because they are not seen as important.</p>	<p>We have added information about cost of intervention delivery to the ES.</p> <p>Thank you; we have done as suggested.</p> <p>We have expanded the “Scope” section of the Executive Summary with such discussion.</p> <p>We have done so in a general way by adding the following: <i>The exclusion of other mental health conditions does not reflect a belief that they are less important, but that the literature is not mature enough to answer the questions set forth.</i></p>

Commentator & Affiliation	Section	Comment	Response
Rachel Ann Klein	Executive Summary	I was surprised to see that, although the topic is broad and would presumably include practices applicable to those with mental health conditions such as bipolar disorder, schizophrenia, and other psychotic or mood disorders these did not get any attention in the review. This seems a serious omission as there are widely known primary health issues in those with those disorders, and are not confined to depression and anxiety.	<p>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. Importantly, this also excluded substance misuse disorders. The exclusion of other mental health conditions does not reflect a belief that they are not important, but that the literature is not mature enough to answer the questions set forth.</p> <p>We have included psychotic disorders as an underrepresented area, and elaborate further now in the Research Gaps section: “Psychotic disorders such as schizophrenia deserve special attention due the significant early mortality seen in this group [Saha, et al., 2005], although many patients with such disorders do not come to primary care. Reverse “co-location,” [Goff et al., 2005] where 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.”</p>
Denise Dougherty	Executive Summary	Both the title of the report and the executive summary should make clear that the report applies to adults only. This is particularly important because the report points out that children are among the groups with the highest unmet needs in mental health care. I hope that a companion report addressing children can be done.	<p>Thank you. We do not feel that the title needs to be changed, and we feel that inclusion of the word “adults” in our description of the population as well as each of the KQs is sufficient to convey that our results apply to adults only.</p>
Peer #1	Introduction	The introduction and background and significance was well written and complete	Thank you.
Peer #2	Introduction	<p>In introduction (ES-4), Key Question 2b does not cite cost of intervention as a factor in the text (though it is listed in the figure).</p> <p>As costs are of major relevance to stake holders for this review, this should be stated more prominently in the introduction.</p>	<p>We have added the cost of intervention as an outcome to KQ2 in the Executive Summary.</p> <p>The last line of our introduction now reads: <i>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.</i></p>
Peer #3	Introduction	The background is clearly written; though further justification of the clinical impact in focusing on primary care only is warranted (see comments below).	Thank you; we address the clinical impact comment below.

Commentator & Affiliation	Section	Comment	Response
Peer #4	Introduction	<p>Abstract: Given the synthesis's original goal, the authors should explicitly state here indicate that there were not sufficient studies to produce a meaningful synthesis for mental health disorders other than depression.</p> <p>Please do not use the word "diabetics".</p> <p>Future research statement calls for studies on a broader range of medical conditions...not sure a long series of studies with collaborative care for depression plus "xx" medical condition is the most innovative or productive direction. The gaps may be more in the area of multiple medical conditions "Clusters" that include depression and interventions that address multiple targets, such as TEAMcare.</p> <p>Introduction: Well written.</p> <p>However, it is not clear to me why the authors state they are focusing on depression and anxiety when all the included trials addressed depression. They likely need to clarify that they did a literature search for both conditions but only described the literature for depression.</p> <p>A major issue in this synthesis is that authors talk about "practice interventions" such as coordinated care, integrated care and collaborative care—however, they never define how they operationalized these different practice interventions and why all of the interventions they examined fell into the rubric of "collaborative care" other than that is the terms the authors used. This section needs additional work.</p> <p>Key Questions: I think the authors need to indicate that some of their key questions were exploratory in nature. Given the small sample of studies, having sufficient data to illuminate the helpfulness of specific components of the practice interventions would be highly unlikely.</p>	<p>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. Importantly, this also excluded substance misuse disorders. The exclusion of other mental health conditions does not reflect a belief that they are not important, but that the literature is not mature enough to answer the questions set forth.</p> <p>We have changed all instances of "diabetics" to "people with diabetes."</p> <p>As above. We have decided to remove discussion of anxiety from the report early on and have explained our rationale. (The exclusion of other mental health conditions does not reflect a belief that they are not important, but that the literature is not mature enough to answer the questions set forth.</p> <p>Please see the rationale behind our definition of "practice-based" (above); we intended the term to be inclusive of a range of interventions such as you mention. We then report on the components of these interventions as defined by the authors. We did not set out to further operationalize or validate these definitions, but to report what we found. We did not specify a rubric <i>a priori</i>; we examined the components of each intervention and generated a broad list of components.</p> <p>We appreciate your point on KQ 4 and 5 and have now clarified that these are secondary in nature using the universe of studies in the PICOS section of the Introduction: <i>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.</i></p>

Commentator & Affiliation	Section	Comment	Response
Peer #5	Introduction	As described above, the motivation for the study needs to be better described.	Please see our comments above regarding what this review adds to the body of evidence.
Peer #6	Introduction	There is some useful information here about the frequency ranges of depression in various chronic conditions, but I found myself wondering about other mental health problems and about the opposite relationship – what is the frequency of various chronic conditions in those with depression and other mental health problems.	Excellent point, but not one we investigated in the scope of this report given that primary care was the setting of choice. The bidirectional nature of these conditions appears to have limited data in general and would be a good target for future work.
Peer #8	Introduction	<p>The introduction is thorough, well-referenced and well-written. It sets the stage well for the report. The use of the term “practice-based interventions” and the description of the kind of interventions included are excellent. For once there is a really clear distinction made between studies that evaluate specific treatments and therapies that might be used in primary care to treat depression and interventions that aim to change the actual care process for treating depression.</p> <p>There is too much time spent on anxiety. One almost gets the impression that this report will include studies of anxiety or, that if it does not, there is something sorely missing in the report. I suggest that the authors mention anxiety early, explain that there are no studies of collaborative care of anxiety possibly because screening and diagnosis of anxiety is not as mature as screening and diagnosis of depression and let it go at that. Otherwise readers will read the report and get a strong feeling that it is lacking in a big way.</p> <p>Early in the section that describes the population on page 3, the authors need to be clear that they are talking about major depressive disorder and not sub-threshold or minor depression. The authors say that later in the report but it needs to be said in the introduction and early in the introduction. Also, there is a sentence in the population section on page 3 that I think will annoy readers because of its lack of clarity. It is the sentence that talks about the fact that the population included is not just symptomatic but has a condition of such severity that it needs to be treated and that treatment is effective. By what standard did the authors decide that the patients studied met those criteria?</p>	<p>Thank you.</p> <p>As noted above, we have removed anxiety from much of the report. We feel that it is clearer now and more in line with what this comment suggests.</p> <p>We have clarified our definition of depression, and changed the sentence you thought might be annoying to readers: <i>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.</i></p> <p>We have removed the questioned phrase and have added the following to the discussion: 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 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. 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 topic had comprehensive data or was a central focus of this report.</p>

Commentator & Affiliation	Section	Comment	Response
		<p>The authors briefly indicate that “Interestingly enough” collaborative care has not been widely disseminated because there are barriers to its implementation. Then nothing else is said about this in the introduction. I think that this is a mistake. First, the use of the phrase “Interestingly enough” seems to imply that it is not understandable why there is not more implementation of this model of care. And, second, I think that one of the most important things that this report could do (since the conclusion is that collaborative is effective for treating patients with both major depressive disorder and chronic disease) is to explore this issue more and provide some ideas for how the barriers might be overcome. I know that the report has a limited scope, but I think the report would be a lot more clinically useful if it addressed this topic more.</p> <p>The research questions are well defined and they are the right questions even if there are not always enough studies to answer them. Also, the analytic framework is good and well summarized.</p>	
Peer #9	Introduction	<p>Introduction is clear and thorough.</p> <p>There should be some mention of the need to address access to primary care in populations with severe mental health problems. These patients die on average 25 years younger than the general population and their number one cause of death is heart disease (significantly higher mortality rate than the general population.)</p>	<p>Thank you.</p> <p>Traditional SMI as seen in primary care is beyond the scope of this review, and while this can include severe depression, it is generally not focused on it specifically. We do now clarify that other such disorders are important - and why they are not included in this review.</p> <p><i>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. Importantly, this also excluded substance misuse disorders. The exclusion of other mental health conditions does not reflect a belief that they are not important, but that the literature is not mature enough to answer the questions set forth.</i></p>

Commentator & Affiliation	Section	Comment	Response
Rachel Ann Klein	Introduction	I have a major concern that treatment of mental health conditions in primary care settings will only be by the use of medications, which have many side effects and have not been shown to be any more effective than therapy, which has no side effects or medical co-morbidities. This study is based on a pharmacological approach which has not been shown to be cost effective over the long-term, as expenses climb due to co-morbidities of the actual intervention. This was not studied.	We appreciate your concern but feel that we have made it clear that this review does not focus on pharmacotherapy (and specifically excludes medication-only studies which seem to be the commenter's concern).
Peer #1	Methods	The inclusion and exclusion criteria were clear and justifiable and the search strategies explicitly stated and logical. The only issue I had with definitions was it wasn't clear to me how study quality was rated i.e. fair, good, etc.	We have provided additional information in the methods about our quality rating methods.
Peer #2	Methods	The methods are clearly described and included an appropriate literature search and process to identify eligible articles. The statistical methods for meta-analysis were also appropriate.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer #3	Methods	<p>There is insufficient justification for focusing on practice-based primary care interventions, especially since there are a number of public-health-based interventions (e.g., diabetes, obesity) that have been studied, and their inclusion would have helped practitioners and policy-makers think outside the box in terms of programs beyond the chronic care model.</p> <p>The review mainly focused on CCM-based interventions, which can be complicated to implement and sustain in routine care practice. In contrast, self-management, psychosocial, or health behavior change interventions were not included.</p> <p>Also, the focus on primary care does not seem sufficiently justified and only based on the intent of the particular request. Moreover, the lines between outpatient and primary care are often hard to discern. HITIDES was conducted in infectious disease clinics, and many studies focused on interventions for other chronic mental disorders seen in community-based mental health programs were not included, yet were also conducted in outpatient settings akin to those included in this review.</p>	<p>Without specific references to those interventions, we are unable to assess whether they would have met our inclusion criteria. We identified several trials in populations with either a chronic medical condition or depression, but we excluded them for not having both conditions.</p> <p>We acknowledge the limitations of our scope and refer the reviewer back to the detailed methods for further rationale and PICOTS. Multiple stakeholders provided input on the definition of “practice-based interventions” as well as our choice of settings and other parameters. In CER work, we strive to achieve a balance between applicability and breadth of evidence reviewed. In order to maintain a certain level of homogeneity (thereby increasing our confidence in assessing applicability), some studies inevitably are excluded.</p> <p>We agree that the lines between outpatient and primary care are often hard to discern, and we attempted to account for this by applying a broad definition of primary care. In addition to traditionally-defined primary care settings, we also included studies in which the patient and provider have a primary care-type relationship. HITIDES is an excellent example of this, given that infectious disease clinics are often the primary source of care for people with HIV.</p> <p>Our focus on primary care stemmed from the original topic nomination and was supported by stakeholders. In doing so, we acknowledge the crucial role of primary care (and primary care-type) settings, where most patients receive care and from which care is optimally coordinated. Because of that focus, we excluded studies in any type of mental health-specific setting, outpatient and otherwise.</p>

Commentator & Affiliation	Section	Comment	Response
Peer #4	Methods	<p>The inclusion and exclusion criteria are reasonable. The search strategies are defined and reasonable. However, given the widespread “early publication” of articles on the web, the authors need to explicitly comment on their inclusion. (I do not think they were included.)</p> <p>The authors need to likely separate out and clarify the outcomes that were addressed using meta-analytic techniques and those that only had a qualitative synthesis. Currently both appear in the same tables and in the same topical paragraphs.</p> <p>Appendix D lays out the quality criteria for the included studies—but no studies were perfect and it was not entirely clear to me why a couple of these studies had “good ratings” while the rest had “fair” ratings. The authors also do not comment on why the two excluded studies had “poor ratings”. Maybe this distinction could be made a bit clearer for the reader? Perhaps a summary statement of why “good” versus “fair” designation for each of the studies could also be included in the executive summary?</p>	<p>MEDLINE includes references published both in print and online (including electronic posting ahead of hard copy printing). As long as a reference is in the MEDLINE database, it will appear in our search results, regardless of the medium.</p> <p>The results sections clearly identify which data have been pooled and present summary data with these references.</p> <p>We have clarified how quality was determined earlier in the report, and in more detail throughout. In brief, studies that met all or all but one of the specified quality criteria were rated “good,” and studies that met fewer criteria but did not have fatal flaws as described were rated “fair.” We have updated the methods section to reflect this but feel that the tables in Appendix D adequately detail the ways in which each study met or did not meet the quality criteria. We have added text to this Appendix that explains the rationale for rating two studies “poor.”</p>
Peer #5	Methods	<p>The study appears to include a mixture of large collaborative care trials with subanalyses of particular medical conditions, of interventions for patients with depression and particular medical comorbidities, and for studies that sought to treat both depression and the medical conditions. As such it is not clear how meaningful it is to pool results.</p>	<p>We acknowledge these limitations in the methods but feel there was enough homogeneity in design and measures to provide meaningful data from pooling the preplanned IMPACT sub analyses with larger trials.</p> <p>As we wrote in our methods, the chi-squared and I^2 statistics were calculated to assess heterogeneity in effects between studies. Whenever we included a meta-analysis with considerable heterogeneity (defined by $I^2 \geq 75\%$), we provided an explanation for doing so, considering the magnitude and direction of effects. We also conducted a sensitivity analysis in cases of considerable heterogeneity to determine the likely source of heterogeneity in order to qualitatively account for them.</p> <p>As a result of the above, we feel confident that our pooled estimates are appropriate and, when present, high levels of heterogeneity in our results are adequately explained.</p>
Peer #6	Methods	<p>The Inclusion criteria and search strategies are reasonable except, as noted above, in limiting interventions to collaborative care variations and in excluding studies without concurrent controls.</p>	<p>Please see our earlier response to the concern about study design.</p>
Peer #8	Methods	<p>The inclusion and exclusion strategies are the right ones</p>	<p>While we appreciate the interest in non-adult populations, this</p>

Commentator & Affiliation	Section	Comment	Response
		<p>although it is unfortunate that studies of non-adult populations were excluded.</p> <p>The search strategies were clearly stated and logical. However, the authors might have included “disease management” as a term in their searches. While it is a term that has fallen out of favor of late, the authors might have picked up some more trials if they had used it.</p> <p>In Table 2 it would have been better if the actual measures and cut points the authors used were included in the table since they are such an important part of the inclusion/exclusion strategy. The specific definition of major depressive disorder the authors used, the specific instruments and the cut-points that determined inclusion or exclusion should be in the Methods section even if not in Table 2.</p> <p>The procedures for the two raters and the statistical methods used are consistent with other studies of this type. While the grading of the evidence was appropriately done, it was not clear if there needed to be a minimum number of studies conducted using a particular outcome in order for a conclusion to be drawn that collaborative care was effective or ineffective regarding that outcome. Was more than one study needed for a conclusion to be drawn?</p> <p>The issues raised in the section on Applicability include ethnicity, type of practice setting, and ease or difficulty with which the intervention could be incorporated into routine practice. The last issue was described as related to questions about the resources, staff, time, and also probably cost (which was not mentioned there but should be) required for delivering the intervention. While the framework for looking at applicability partially came from a recognized methods guide, this is the area where I believe the report falls short. The report is an opportunity not only to answer the research questions about treating depression with collaborative care in a population with chronic disease, but to also explore means for overcoming the barriers to disseminating this type of care if it is effective across conditions. In the Methods section, the authors could have</p>	<p>topic was intended to address only adults from the inception. Future work should include a focus on similar efforts in children.</p> <p>We included a search for “chronic disease management” in all fields. In response to this comment, we performed a search using “disease management” rather than “chronic disease management,” and the additional yield was 66 abstracts. Upon review, none of these met all of our inclusion criteria.</p> <p>We have added a more clear definition of depression to the methods section, and refer to specific cut points on respective instruments in the detailed tables of each study in the results section.</p> <p><i>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.</i></p> <p>There is not a specific requirement for the number of studies necessary to inform the strength of evidence. We cited the methods paper on strength of evidence assessment (Owens, et al.), which details the process in depth. In general, the strength of evidence grade reflects “confidence” in the estimate of effect. For instance, a single large, high quality RCT may be as compelling as multiple smaller studies.</p> <p>Applicability as a term has a slightly unique meaning in this report template; “for whom do these data actually apply,” which may be different than this commenter’s question. Issues of dissemination likely fall under future research needs or gaps, and we have addressed them in more detail based in the section of the Discussion called “Implementation, Dissemination, and Role of Decisionmakers.”</p>

Commentator & Affiliation	Section	Comment	Response
		<p>indicated that while there are few demonstration trials of implementation of collaborative care, they could still discuss some of the current efforts and ideas for overcoming barriers to dissemination. I will talk more about this issue later in my review.</p> <p>With the exception of some shortcomings in the section on Applicability, the methods section is quite good.</p>	
Peer #9	Methods	<p>Considering the evidence that depression and anxiety are underdiagnosed in primary care there may be inadequate consideration given to screening in primary care as an intervention in and of itself.</p> <p>Usually considered as a harm would be the stigma associated with a mental health diagnosis and the possibility of misclassification.</p> <p>Should pregnant women have been excluded from this analysis?</p> <p>Did anyone study group visits as an intervention?</p>	<p>We did not address any stand-alone interventions such as screening as they fall outside the scope of this review, but we agree that this is a good point and one that may be appropriate for future review.</p> <p>We agree and considered a broad range of possible harms, but few (including perceived stigma) were measured and/or reported.</p> <p>We did not exclude studies enrolling pregnant women <i>a priori</i>, but we did not find any studies meeting our criteria that included pregnant women. The same is true for group visits.</p>

Commentator & Affiliation	Section	Comment	Response
AHRQ Multiple Chronic Conditions Research Network	Methods	<p>We agree that “narrowing the scope [...] selects for a population with known burden and associated higher risk for poor outcomes” (p.3). However, we question whether restricting the review to only those studies examining the common conditions of depression and anxiety adequately captures the universe of mental health-related interventions in primary care.</p> <p>We also believe that such a narrow focus limits the report’s additions to the field and reiterates much of what was already stated in the AHRQ 2008 report “Integration of Mental Health/Substance Abuse and Primary Care.”</p> <p>Additionally, the inclusion criteria appear to omit several studies about care management and those that use observational design approaches in complex populations.</p> <p>We recommend broadening the inclusion criteria to capture interventions aimed at mental-health conditions other than depression or anxiety, such as substance abuse or post-traumatic stress disorder.</p> <p>At a minimum, because of the narrow focus in terms of mental health, the report would be more accurately titled “Practice-Based Interventions Addressing Concomitant Depression [emphasis added] and Chronic Medical Conditions in the Primary Care Setting.”</p> <p>We also suggest adding two Key Questions: 1) What is the relationship between improved depression status and improved physical health status irrespective of type of care? And 2) How can these findings be generalizable to more conditions and more setting?</p>	<p>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. Importantly, this also excluded substance misuse disorders. The exclusion of other mental health conditions does not reflect a belief that they are not important, but that the literature is not mature enough to answer the questions set forth.</p> <p>Please see our earlier comment about intervention search terms and our earlier comment regarding the exclusion of observational studies.</p> <p>Please see our comment above regarding the exclusion of other mental health conditions</p> <p>We agree and have changed the title as suggested. The KQs were generated and reviewed during the Topic Refinement process with input from stakeholders. They were posted for review and comment on the AHRQ Effective Health Care Web site. We are unable to add KQs at this time, but we appreciate these perspectives.</p> <p>We are still unsure about what this is asking. We comment on the bidirectional nature of these conditions and the paucity of data in that regard.</p>

Commentator & Affiliation	Section	Comment	Response
Peer #1	Results	<p>The amount of detail in the results section and tables was appropriate and characteristics of studies reviewed were also clear.</p> <p>Two studies that could be potentially added were the recent ones by John Piette on a depression and diabetes telephone based intervention and Hilary Bogner on collaborative care for depression and hypertension.</p>	<p>Thank you.</p> <p>We identified these studies in our literature search and excluded both from this review. The Piette study was excluded because the intervention did not meet our inclusion criteria. Specifically, it used a telephone-delivered CBT program with an exercise component – this reflects an individual-level intervention rather than a practice-based one. The Bogner pilot study met all of our inclusion criteria except for duration; we required a follow-up of at least 6 months, and Bogner et al., reported no data beyond 6 weeks.</p>
Peer #2	Results	<p>While the authors clearly describe methods for assigning quality rating and show the quality ratings in an appendix, it would have been helpful to provide study-specific factors that led to suboptimal quality ratings in the text (as opposed to just the Appendix table). This would/could assist researchers in designing future studies.</p> <p>Some summary of range of costs of intervention in text would be helpful even though no comparator data were reported for any studies. (Had to look for this in a Table)</p> <p>It might have been helpful to attempt to contact authors of the included to studies to get more information regarding practice characteristics (i.e., unpublished information) as this is a key piece of information for stakeholders.</p>	<p>We have clarified how quality was determined earlier in the report, and in more detail throughout. This includes a description of why poor studies were excluded.</p> <p>We have added data on costs of interventions to KQ 2b..</p> <p>Thank you. We agree that contacting individual investigators would have painted a larger picture, but in the interest of time and resources were limited to report only published data.</p>
Peer #3	Results	<p>The results appear thorough; though it might be helpful to present the meta-analysis results as part of the main findings. It might also be helpful to present how each of the interventions might be potentially reimbursable in primary care.</p>	<p>We have presented estimates from meta-analyses in several places for each KQ in the results section. When applicable, results are presented in the Key Findings as well as the detailed synthesis. We also present summary tables of the meta-analyses per KQ.</p> <p>Speculation about reimbursement is beyond the scope of this review.</p>
Peer #4	Results	<p>I believe several of the tables in the executive summary could be further clarified.</p> <p>Table ES-2: I believe the intervention described in the first row is the “Impact” intervention to which the rest of the rows then refer. However, this should be made clearer for readers.</p>	<p>We have clarified this in the table.</p> <p>For summary strength of evidence tables, it is not standard practice to report which studies contributed to meta-analyses. However, we have added citations in a few places in the tables and to the text and other types of table as appropriate and feel that in doing so we have addressed this comment.</p>

Commentator & Affiliation	Section	Comment	Response
		<p>In table ES-3 (and in the following tables), it would be helpful to give citations for the specific studies for each row of evidence in superscripts and specify whether a meta-analysis was done and how many (and which) studies were included in any meta-analysis. These citations are listed in the more detailed sections for each study question and in the appendices but many people will be using the tables in the executive summary. (For example for treatment adherence row in ES-3, it would be helpful to cite the single study that reported greater adherence and the study that found no difference, and so on. When commenting on the meta-analyses that included four studies, please cite studies included in the meta-analysis.)</p> <p>It may be advisable to separate out ES-3 results into two tables here, one of which summarizes data from the various meta-analyses and one that includes the results of the qualitative summary.</p> <p>ES-6 Mortality row: Please clarify 8 studies in a meta-analysis here. Please cite studies for the presented evidence in other rows for general health outcomes. Again, a reader would have to go to detailed sections or appendices to get an idea of which studies were included for quality of life evidence row.</p> <p>Key Question 3: Harms Multiple med adjustments could be prompted by close monitoring in collaborative care so I wouldn't just dismiss this as something not resulting from the collaborative care model. Detection bias clearly results from additional assessments rather than the intervention per se.</p> <p>Appendix F, it would be helpful to give citations for specific studies in the table of Strength of Evidence.</p>	<p>Please see above comment regarding citations in strength of evidence tables.</p> <p>We have edited this section to read: <i>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</i></p> <p>Please see above comment regarding citations in strength of evidence tables.</p>

Commentator & Affiliation	Section	Comment	Response
Peer #5	Results	I am not sure that reporting that these models improve depression in patients with comorbidity adds much to the literature. A better rationale is needed to provide motivation for the study.	This topic was deemed important and worth of review by stakeholders and representatives of AHRQ. In terms of rationale, as noted above, we have added the following language to the report: <i>We believe this will add to the literature by (1) synthesizing depression outcomes among people with defined chronic medical conditions, and (2) synthesizing data on chronic medical outcomes... 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.</i>
Peer #6	Results	The amount of detail is only appropriate for researchers interested in this topic. It is completely overwhelming to any potential user of the information. See General Comments for problems with excluding potentially valuable studies	We have reduced detail and attempted to simplify key messages through this review process. Please see response to exclusion of studies in general comments.
Peer #8	Results	Please know that most of my comments that relate to the Results section appear in other parts of my review. Please see my General Comments, Comments on Discussion and Comments on Clarity in addition to my comments here. This section included the right studies and described them well. The key points were clearly stated and relevant. My main complaint with this section has to do with the Applicability sections and a bias that seems to indicate a bit of dismissiveness towards collaborative care. Please see my recommendations for additional tables in my comments on Clarity and my comments in the Discussion section. I know that the authors were not charged with looking at barriers to dissemination but I think to make the report more than a summation of what has already been said and relevant to a broad audience including policy-makers, some presentation of the experiences of those disseminating collaborative care would really make the report more useful.	Please see our responses to these comments elsewhere in this document. Thank you. We disagree that we have a bias that seems to indicate dismissiveness toward collaborative care. We were tasked with assessing the applicability of our findings to primary care in general; upon reviewing the components and conduct of interventions, we noted that most of the interventions made use of resources that may not be available in the broad scheme of primary care (e.g., dedicated case managers, physician willingness to participate). Please see our responses in those sections. We agree that the barriers to dissemination are of significant importance and utility, but (as the commenter notes) a thorough assessment of such barriers is beyond the scope of this review.

Commentator & Affiliation	Section	Comment	Response
Peer #9	Results	<p>Information about screening methods should be included in the tables.</p> <p>The results are detailed relative to the methods. The characteristics of the studies are presented well. Tables and figures are clear and appropriate.</p> <p>Is there sufficient consideration given to differences in outcomes by sex and race?</p>	<p>Depression inclusion criteria are reported for each study in Tables 4-9. We do not report on screening <i>per se</i>.</p> <p>Thank you.</p> <p>We feel that these differences are adequately discussed in the overview of results and repeated in the discussion.</p>
Peer #1	Discussion/ Conclusion	<p>The implications of the studies were clearly stated. One additional suggestion was to add studies on cost effectiveness which have now been completed for the depression diabetes interventions i.e. (Simon G et al 2007 Archives General Psychiatry, Katon W 2006 Diabetes Care, and Hay J in press Value in Health). I also believe Bruce Rollman has a cost effectiveness study on his depression heart disease intervention in press.</p>	<p>Thank you for this suggestion. While cost-effectiveness is outside the scope of this review, we have added data about costs from the included studies to the review, including costs reported in the Simon, Katon, and Hay papers. Data from the Rollman study were not published as of our most recent search date.</p>
Peer #2	Discussion/ Conclusion	<p>In the discussion, the authors might more clearly highlight that with respect to improving mental health outcomes, all the interventions were successful, and while head-to-head comparisons might be helpful, multiple combinations of teams members were successful. This point would be helpful to communicating to stakeholders that there are a lot of evidence-based options for developing a collaborative care approach based on the staff available in their respective organizations.</p> <p>The authors mention that their review did not show conclusive evidence that successful treatment of depression improves chronic medical conditions (ES15 and page 48). In the discussion, the authors could cite the larger field of literature (e.g., Davidson et al. Archives of Internal Medicine 2010; Berkman et al. JAMA 2003) testing the effectiveness of enhanced depression care on cardiac outcomes which includes interventions that are not necessarily primary care practice-based but potentially adaptable to the primary care setting and of relevance to this key question.</p> <p>The lack of cost comparisons should be stated as an important research gap (page 50-51).</p>	<p>We have significantly edited the entire discussion, including comments addressing this issue: <i>Although we did not attempt, as others have, to identify “key ingredients” of collaborative care such as training background of team members, {Bower, 2006} our report suggests that the complexion of teams and their types of training may afford some flexibility.</i></p> <p>We appreciate the reference to this important literature, and the potential relevance of the interventions. These studies of depression and the post-MI state are outside of the scope of primary care, and also reflect an acute vs. chronic medical condition. We have, however, added these citations and made note as below: <i>We excluded some relevant studies because of short duration of followup {Bogner, 2012} or because the treatment occurred outside the purview of a primary care–like setting {Piette, 2011;Davidson, 2010;Berkman, 2003}. 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.</i></p> <p>We have added costs to the discussion of research gaps: <i>Should a model of accountable care{Centers for Medicare &</i></p>

Commentator & Affiliation	Section	Comment	Response
		<p>The authors could more strongly highlight the need for more research examining different models of practice-based care, such as co-located care. Amazingly, there were no eligible studies of either integrated or co-located care.</p>	<p><i>Medicaid Services, 2011} 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. {Brazeau, 2005} 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.</i></p> <p>We were similarly surprised by this, and now highlight this in the Discussion: <i>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, we should test variations of existing efficacious models.</i></p>
Peer #3	Discussion/Conclusion	<p>At the end it was difficult to discern how the review could potentially make an impact on the field. The focus on practice-based interventions rather than practice-based and public health/community-based programs seemed somewhat limiting. Moreover, the call for more cross-diagnosis research has been heard, with studies already underway that have moved beyond depression diagnoses in primary care (e.g., CALM, PCARE studies).</p> <p>The report might also benefit from a discussion on potential sustainability issues, especially in light of health homes and ACOs, which may offer bundled payments for collaborative care management.</p>	<p>Please see our previous responses on what this review adds.</p> <p>Points on the implications of bundled care have been highlighted: <i>Should a model of accountable care {Centers for Medicare & Medicaid Services, 2011} 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. {Brazeau, 2005} 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.</i></p>

Commentator & Affiliation	Section	Comment	Response
Peer #4	Discussion/ Conclusion	<p>The limitations of the included studies are well summarized in the appendices but no summary of study limitations were given in the discussion.</p> <p>Future research directions are clear, although I can't say I agree with the recommendation to continue with a stream of studies of depression plus "x" single medical condition going forward.</p>	<p>In the Discussion, we have revised a summary of the limitations of the CER process and the limitations of the evidence base. A detailed review of the limitations of each study (well elaborated elsewhere) is beyond the intent of this section.</p> <p>Thank you for this comment; we have added the following to the Research Gaps section: <i>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 to understand most is what models of care work best for patients with common clusters of disease in primary care.</i></p>

Commentator & Affiliation	Section	Comment	Response
Peer #5	Discussion/ Conclusion	<p>1. Given the overlap between depression and anxiety, is there really a need to replicate these studies in anxiety disorders? Why wouldn't they also work in patients with anxiety?</p> <p>2. It appears from the evidence presented that treating depression isn't enough to improve chronic medical outcomes. Does the field really need more studies demonstrating this negative finding? Can the authors provide some sort of power calculation to estimate the number of new studies or patients that would be needed to confirm this negative finding?</p> <p>3. Given the dearth of trials treating multiple diseases at once, it would appear that this is what the field needs to better understand. Under what circumstances are such models feasible, and whether there is a tradeoff between breadth and depth? Could studies go beyond the 3 related conditions treated in TEAMCare and treat even more multimorbid conditions? What would be the research, clinical, and administrative challenges in doing so? At least one model, Guided Care (see Boulton, et al) tried to do this but had very limited effect on patient outcomes.</p>	<p>Thank you for your challenging questions.</p> <p>We have rewritten part of the Research Gaps section to consider this point: <i>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 need to be studied in isolation with related medical conditions, or perhaps a more broad-based approach might make sense.</i></p> <p>2. Although we did not find that treating depression improved the chronic condition outcomes, we identified very few studies that measured the latter. As a result, we do not feel comfortable stating that the finding is unequivocally negative. We feel that more studies in that area will yield a more robust estimation of the association between such interventions and chronic condition outcomes.</p> <p>3. We agree that many of those questions are important and hope that future research is undertaken to answer them. We have rewritten part of the Research Gaps section to consider this point: <i>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 need to be studied in isolation with related medical conditions, or perhaps a more broad-based approach might make sense.</i></p>

Commentator & Affiliation	Section	Comment	Response
Peer #6	Discussion/ Conclusion	<p>The implications of the findings are not very usefully described. Even for other researcher readers, the evidence gaps are very limited, and do not even include Key Question items on which the authors could find little evidence in the literature (1b, 2a, 2b, 3, 4, and 5. If those questions were important enough to create the evidence review, wouldn't they be worth identifying specifically as evidence gaps needing further study? Those are also questions that would have been potentially useful to clinicians, care delivery systems, and policy makers. Payers and policy makers would also have been particularly interested in impact on healthcare costs, but that didn't even make it into the key questions.</p> <p>Finally, if this is meant to address user interests, it would have been helpful to include a section on recommendations for use of the information.</p>	<p>Thank you for these comments. We have attempted to simplify and clarify the scope, purpose and findings of this report, as noted in the preceding responses and in the significant revisions to the introduction and discussion.</p>

Commentator & Affiliation	Section	Comment	Response
Peer #8	Discussion/ Conclusion	<p>This is a well-written and thoughtful section. But I have some disagreements with it and some suggestions for improving it.</p> <p>First, I think that there needs to be more detail on the limitations.</p> <p>Second, the section on Applicability needs to be expanded and changed. I do not agree with the conclusion that only settings that can accommodate and afford a care manager can provide collaborative care.</p> <p>I also do not agree with the final sentence in this section that the trials may reflect a selection bias. What would be a lot more helpful in this section is to acknowledge these issues but then to present information from Dr. Jürgen Unutzer, Dr. Leif Solberg, Drs. Wayne Katon and Elizabeth Lin and others about their efforts to disseminate collaborative care in a broad range of settings.</p> <p>Also, a description of the functions performed in the settings where collaborative care was found to be effective would be more helpful to clinicians than the information presented in this Applicability section. Unfortunately, a somewhat dismissive attitude towards the applicability of collaborative care comes through in the way this section is currently written and it is unwarranted.</p> <p>In addition, I think that the conclusion should be somewhat different. Instead of emphasizing the need for future studies (future studies are always needed), I think that the conclusion should be that while there are needs for future studies, collaborative care has clearly been shown to be an effective way of delivering depression treatment in the primary care setting and that there should be studies to find effective ways to disseminate the model in different ways in a variety of settings.</p>	<p>We took all these comments into consideration as we reworked the discussion section to make it more relevant.</p> <p>The limitations sections have been expanded.</p> <p>We feel that the commenter is misinterpreting our statements. We do not conclude that “only settings that can accommodate and afford a care manager can provide collaborative care.” Rather, we provide the objective evidence that the included studies all made use of a care manager. We agree that collaborative care can occur without a care manager, but without any included studies having done so, we cannot comment on effectiveness of collaborative care in the absence of a care manager.</p> <p>We have removed this sentence. As noted elsewhere, issues of dissemination beyond those described in the Discussion fall outside the scope of this comparative effectiveness review.</p> <p>We feel that such a description is adequately presented in the KQ 4 and 5 sections, and have revised the discussion in a manner that will hopefully come across as reflective of the evidence. We regret that it may have been interpreted as having a dismissive tone.</p> <p>We have made changes to the overall discussion as noted above. Issues of dissemination beyond those described in the Discussion fall outside the scope of this comparative effectiveness review, and are thus not the primary focus of our conclusions.</p>

Commentator & Affiliation	Section	Comment	Response
Peer #9	Discussion/ Conclusion	<p>Given the fact that under our current system of care primary care physicians are disincentivized to screen and treat mental health conditions, should this review have considered a broader range of interventions. For example, under a population based payment system where physicians are "paid" or given salaries to keep patients well then interventions to expand primary care competence and motivation to treat mental health conditions are more feasible. Plus, under this system there may be less time pressure to "churn" patients out. The literature on the effectiveness of primary care physician education for screening and management is not that positive, but that occurred under the culture of the fee for service system. Furthermore, the current system has fostered an erosion of the behavioral health skills of some primary care physicians, and has decreased the emphasis of this education in residency programs.</p> <p>There is evidence that primary care physicians are interested in collaborative care if the barriers can be overcome. Brazeau CM, Rovi S, Yick C, Johnson MS. "Collaboration between Mental Health Professionals and Family Physicians: A Survey of New Jersey Family Physicians," The Primary Care Companion to the Journal of Clinical Psychiatry, 2005, Vol. 7, No. 1, pp. 12-14. However, this begs the question as to should we increase the feasibility of collaborative practice interventions or increase primary care competence, though the two are not mutually exclusive.</p>	<p>Thank you for these helpful comments. We have incorporated them as below, and incorporated the suggested citation.</p> <p><i>Should a model of accountable care{Centers for Medicare & Medicaid Services, 2011} 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.{Brazeau, 2005} 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.</i></p>
AHRQ Multiple Chronic Conditions Research Network	Discussion/ Conclusion	<p>The discussion reflects the specific findings well, however, it could be broadened to more fully reflect how the results expand on current knowledge and where additional knowledge is needed. Below are our specific suggestions for improving this section:</p> <p>"Findings in Relationship to What is Already Known" (p. 48) does not adequately explain how this report's findings differ from those in other reports, such as the AHRQ 2008 report "Integration of Mental Health/Substance Abuse and Primary Care."</p> <p>The "Applicability" subsection (p.49) should explain that the</p>	<p>Your thoughtful and specific comments are appreciated. We have reworked the discussion with them in mind and reflect your feedback in multiple places. We highlight several here, but refer you to the revised discussion at large.</p> <p>As added in the intro: <i>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</i></p>

Commentator & Affiliation	Section	Comment	Response
		<p>literature review supports existing knowledge on the effectiveness of care management interventions for depression but does not surface new clinically relevant information or approaches. Researchers are actively exploring different kinds of interventions, for example the patient-centered medical home. While this emerging discussion is not yet reflected in the published literature as of May 23, 2011, the report would more accurately capture the state of the field if it expressed that additional models are currently being tested.</p> <p>In the Limitations section, reiterate that the scope of the review was fairly limited in terms of mental health conditions thus potentially limiting the amount of new information available.</p> <p>In the Limitations section, please discuss the issue of screening for behavioral health co-morbidity. It is not clear that the studies included in this review screened for other behavioral health co-morbidities, so inconclusive results with regard to medical outcomes might reflect confounding by other behavioral health co-morbidities. For example, depression is often co-morbid with substance use disorders, or cognitive impairments. For these people, the depression may improve while other undiagnosed behavioral health disorders continue to negatively influence medical outcomes and intermediate self-care goals.</p> <p>We are aware of new articles that may be relevant, to include in the discussion, including: “Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial” (Bogner et al, 2012) and “Treatment Adjustment and Medication Adherence for Complex Patients With Diabetes, Heart Disease, and Depression: A Randomized Controlled Trial” (Lin et al, 2012).</p> <p>We agree with the observation that there is not enough research about the bi-directional effect of mental health and primary care integration and the lack of head-to-head comparisons. We also identified additional research gaps: The need for new evidence on treatment models, in</p>	<p><i>outcomes.</i></p> <p>We performed a second literature search on December 19, 2011; it yielded new data from trials we already included but did not yield any additional trials.</p> <p>Added to the discussion (and applies to several of your comments): <i>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{Gaynes, 2010 #4170} 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.</i></p> <p>Thank you for bringing these to our attention. The Bogner et al. paper only reports results through 12 weeks, and therefore it fails to meet our 6-month minimum duration criteria.</p> <p>We have incorporated the data from the Lin et al. paper in our results section as applicable.</p> <p>Re: #6, we have noted that “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.”</p> <p>Re: #7, we have added additional discussion of the PCMH and its relevance to practice-based interventions in primary care, as above. Though interesting, speculation about the future use of large data sets to help look at these issues is beyond the scope of this report.</p>

Commentator & Affiliation	Section	Comment	Response
		<p>primary care settings, for other common mental health conditions in addition to anxiety, for example substance abuse disorders, post-traumatic stress disorder, and cognitive impairments including ADHD, learning disabilities, mental retardation, and dementias.</p> <p>Need for studies on impact of improved behavioral health status on a broad range of interventions and outcomes for diabetes and other chronic medical conditions.</p> <p>Need for trials evaluating the impact of improved prevention and treatment of chronic medical conditions on behavioral health outcomes, particularly among persons with serious and persistent mental illness.</p> <p>Intervention trials that use a generalist approach similar to what is done in practice: starting with assessment of overall mental health and then move into specific screenings, rather than the reductionist approach of screening for specific diseases first.</p> <p>Interventions that can be generalizable to broader populations with a range of chronic medical conditions (as compared to the current approach which directs interventions toward specific target conditions), including attention to methodological issues such as the differential measures available depending on the data source (e.g., if depression diagnosis is available in an EHR or not). The need for longitudinal studies to look at outcomes over a longer length of time, especially for chronic medical conditions.</p> <p>As more states move to health homes, patient centered medical homes, and apply to CMS for state plan amendments to provide health homes to persons with multiple chronic disease and behavioral health conditions, researchers might take better advantage of services data, e.g. from CMS, to study variability among states or practices that are/and are not medical homes and what policies and programs might account for that variability. It would be worthwhile for future research to explore other quality of life and patient reported quality of life measures</p>	<p>Re: #8, while this is an interesting and important issue about optimal measures for QoL, it was not the focus of this review. Several studies used measures other than the SF-12, and they are reported as well.</p> <p>Please see responses above that address the remainder of these comments</p>

Commentator & Affiliation	Section	Comment	Response
		beyond the SF 12. Additional discussion is needed around next steps for researchers, including the need to develop interventions that will be generalizable to a broader population of patients with concomitant mental health and chronic medical conditions.	
Peer #1	Clarity and Usability	Overall the report is well structured and organized and the main points are clear. The conclusions should help inform policy and practice. One important fact here is that most NIH funded depression chronic illness interventions studies are quite small i.e. 200 to 400 patients. To evaluate important outcomes such as medical complications and mortality much larger samples and budgets will be need for these studies. Also NIH has a poor record of divisions working together to fund these grants such as NIDDK and NIMH. Structural changes in NIH will be needed to stimulate and reinforce joint funding of comorbid populations.	See changes below, now reflected in the Discussion. <i>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.</i>
Peer #2	Clarity and Usability	The report was well-structured, comprehensive, and very organized. It might have been helpful to include a table that summarized selected key outcomes for each intervention in one place. It was confusing to go back and forth between tables to get a full perspective on each study. I was looking for a summary of cost comparisons earlier on in report. Unfortunately, the studies did not provide data that are key for informing policy such as cost effectiveness of interventions and components of practice settings in which successful interventions were completed. Nevertheless, the information provided still could be helpful to inform policy and future research.	Thank you. Although cost-effectiveness is beyond the scope of this review, we have added data on costs to the report.
Peer #3	Clarity and Usability	Well-written report	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer #4	Clarity and Usability	<p>The report is well structured and the main points are clearly presented. As indicted in the comments above, I believe that summary tables could be further clarified. Descriptions of the various collaborative interventions and their commonalities/ should be included somewhere in the executive summary rather than only the detailed summary.</p> <p>Further distinction of collaborative care versus other practice interventions needs to occur.</p>	<p>Thank you. We acknowledge the limited space in the ES, but feel that the existing tables convey the main elements if the interventions.</p> <p>We have added this to the Discussion: <i>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.</i></p>
Peer #5	Clarity and Usability	The review is well organized; the main concern is whether the questions being addressed add much to the literature.	This issue has been addressed throughout the responses. Please refer to the revised introduction and discussion for further clarification.
Peer #6	Clarity and Usability	Any chance for clarity has been overwhelmed by the length and depth of this report, which also make it difficult to provide usability, even in a later document intended for users. I don't see how the conclusions can be used to inform either policy or practice.	We have edited the report with the goal of improving clarity and usability.
Peer #8	Clarity and Usability	<p>The report is well-structured and well organized. The main points are clearly presented. In its present form it is somewhat useful to inform policy decisions but it could be more useful. The way the report is written now it would be too easy to agree that collaborative care is effective but to also think that it is not something to implement in settings that do not deliver integrated care. In other words, one could agree with the findings, find them useful and dismiss them. I think that there should be more discussion of the barriers to disseminating collaborative care and suggestions for overcoming them. Information on this topic could be obtained from Dr. Leif Solberg from his experience with the DART project, Dr. Jürgen Unutzer from his experience with the AIMS center and Drs. Wayne Katon and Elizabeth Lin from their experience with their TEAMcare project.</p> <p>I also have some suggestions for some additional tables that will make the report more useful. They would appear in the section on Components of the Intervention on pages 37-39. While there are tables on the components of the intervention, there are some additional ones that could be added. The tables would have the studies down the left hand side and the functionalities of collaborative care across the top. I suggest putting the studies that found</p>	<p>Please see our previous comments regarding conclusions and dissemination.</p> <p><i>We appreciate the suggestion for an additional table, but have included all of the reported data relevant to components in the existing table. While we agree it would be interesting to look at these data in some sort of hierarchical way, we cannot reliably "rank" studies per each outcome based on intervention components (there are many outcomes, and depression symptom improvement only one) especially considering the large amount of heterogeneity, so have grouped studies in alphabetical order. Table 17 in its current format shows areas of consistency and variability (such as in care provider training) across studies that should be useful to the reader considering all possible outcomes.</i></p> <p>We have made reference to the Gilbody (Bower) work, and added the following: <i>Although we did not attempt, as others have, to identify "key ingredients" of collaborative care such as training background of team members, {Bower, 2006} our report suggests that the complexion of teams and their types of training may afford some flexibility.</i></p>

Commentator & Affiliation	Section	Comment	Response
		<p>collaborative care most effective first and the studies where it was found less effective or not effective lower down. The studies could be grouped by specific chronic diseases if that is thought to be useful. Then “X’s” could be put under the functions that the intervention in each study included. Separate tables would be presented for the variables related to symptom reduction.</p> <p>Then there could be a written summary in the body of the report that talks about the collaborative care functions that the most effective studies included. While it would not be a formal look at the effectiveness of the different components of collaborative care it could be very helpful to clinicians not practicing in HMO-like or integrated care systems. It might give clinicians who do not envision having a care manager some ideas of how they might add collaborative care functions to their current practices and improve the care they delivered for depression.</p> <p>Articles by Dr. Simon Gilbody and Dr. Greg Simon on the components of collaborative care might be useful to use here.</p>	
Peer #9	Clarity and Usability	<p>The organization of the report is standard and thus is easy to follow for someone who is use to reading this kind of report. The main points are well presented.</p> <p>The conclusions may be difficult to translate into policy because of the funding considerations. Yet, in this age of health care reform if new models are going to be truly considered then this report can be helpful.</p>	Thank you.