

Systematic Review

Specific content for collaborative care: a systematic review of collaborative care interventions for patients with multimorbidity involving depression and/or anxiety in primary care

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Abstract

Background: In primary care (PC) many patients suffer from multimorbidity involving depression and/or anxiety. Collaborative care (CC) has shown promising results for patients with depression, anxiety, and multimorbidity involving depression. However, specific content in CC for patients with multimorbidity involving depression and/or anxiety is unknown.

Objective: (i) To examine the effect of CC interventions in patients with multimorbidity involving depression and/or anxiety compared with usual care; (ii) to identify specific content of CC.

Methods: We conducted a systematic literature review of randomized controlled trial studies evaluating CC models for adults with multimorbidity involving depression and/or anxiety in PC settings. PubMed, CINAHL, Web of Science, and PsycInfo were searched in December 2019. We conducted a qualitative synthesis using an existing framework and developed a new framework to map the content for each studied intervention.

Results: We identified 1,447 studies. Twelve publications were included. Eleven had medium-to-high quality of CC for patients with multimorbidity involving depression. Specific content of CC in these studies is: A stepped care model, involving medication and psychotherapy delivered by a nurse or psychologist Care Manager (CM) focusing on problem-solving techniques; follow-up including monitoring of symptoms and function, and relapse prevention strategies; scheduled CM supervision.

Conclusions: Specific content for CC for patients with multimorbidity involving depression is identified from current research. Research gaps were found regarding CC for patients with multimorbidity and anxiety, depression and anxiety, and depression and/or anxiety and more than 2 diseases.

Lay Summary

Most patients in primary care have multimorbidity, defined as 2 or more chronic diseases. Depression and/or anxiety are common in this population. Collaborative care (CC) can improve symptoms for patients with multimorbidity involving depression. In CC, a Care Manager (CM) establishes a care plan with the patient, cooperates with the patient's physician, and has scheduled

Key Messages

- This literature review and qualitative synthesis adds:
- For patients with multimorbidity involving depression:
 - Specific collaborative care content
- Identified research gaps for collaborative care:
 - For multimorbidity involving anxiety.
 - For depression and/or anxiety, and more than 2 diseases.

patient follow-ups. However, CC can differ in design and content. The focus of this systematic review and qualitative synthesis was to examine effectiveness of CC for patients suffering from multimorbidity involving depression and/or anxiety and identify specific content of CC for patients with multimorbidity involving depression and/or anxiety. We identified specific content of CC for patients with multimorbidity involving depression in medium-to-high-quality studies with positive effect: CM (nurse or psychologist) collaborating with the patient's physician in a stepped care model involving both medication and/or CM-delivered problem-solving psychological treatment; scheduled patient follow-ups with symptom and function monitoring, medication adherence and relapse prevention; regular CM supervision. No conclusions can be drawn regarding the effectiveness of CC in patients with multimorbidity involving anxiety, depression and anxiety, or depression and/or anxiety and more than 2 diseases.

Key words: anxiety disorders, depressive disorder, multimorbidity, patient care management, primary health care, randomized controlled trials as topic

Background

Multimorbidity, defined as 2 or more chronic diseases,¹⁻³ is on the rise.⁴ Patients suffering from multimorbidity often suffer from depression⁵ and/or anxiety.⁶ Multimorbidity involving depression and/or anxiety leads to poor health outcomes^{7,8} and helping these patients is an increasing challenge in primary care (PC).⁹⁻¹¹

Collaborative care (CC) is a promising management strategy for people with multimorbidity involving mental disorders. To date CC has shown to be effective in treating patients with depression,¹² anxiety,¹³ and multimorbidity involving depression.¹⁰ For individuals with multimorbidity involving anxiety, or depression and anxiety, the effect of CC in PC is unknown.

A 4 component framework for CC was developed based on a systematic review of 11 studies of CC for patients with depression, and this framework has been used to define CC thereafter¹⁴: A multiprofessional approach to patient care involving a Care Manager (CM), who can be a nurse, psychologist, social worker, or other health care professional, collaborating with another medical health professional, often a PC physician; the CM follows a structured management plan including medication and/or psychological treatment; the CM has scheduled patient follow-ups with the patient face-to-face, by telephone or digitally; and enhanced interprofessional communication between the CM and the PC physician. However, the specific content of these 4 components varies widely across studies, and it is unclear what specific professional roles, strategies, and concrete content should be included in CC implemented in PC. For patients suffering from depression, a previous systematic review using and meta-regression¹⁵ identified psychological treatment as effective content of the structured management plan for that patient group. For individuals with multimorbidity and depression and/or anxiety, the effective content of CC is unknown.

Objective

The aim of this study is to summarize the evidence of effectiveness for CC interventions in PC for patients with multimorbidity involving depression and/or anxiety compared with usual care, and to identify specific content of the components of CC in this setting.

Methods

The full protocol for this systematic review can be found in the PROSPERO international prospective register of systematic reviews database (registration number CRD42019117533. 2019/05/09).

Following the Cochrane Handbook for Systematic Reviews of Interventions, we conducted a systematic literature review to identify high-quality randomized controlled trials (RCTs) of CC for patients with multimorbidity involving depression and/or anxiety. Findings are reported according to PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines ([Supplementary data](#)).

Search strategy

We included RCTs or cluster-RCTs conducted in PC or community settings including individuals 18 years old or older with at least 1 chronic physical disease and depression and/or anxiety, assessed by rating scales or prescribed antidepressant drugs. The intervention of interest was CC compared with usual care or enhanced usual care. Primary outcome was improvement in depressive and/or anxiety symptoms. We excluded pilot studies, studies testing only a psychological or medication intervention, and studies of mental health diagnoses other than depression and/or anxiety.

We searched the Cochrane Library December 11, 2019 for reviews of complex interventions for patients with multimorbidity,

and found 1 review of 18 studies of multimorbidity, of which 7 included depression symptoms.¹⁰ Three of the 7 studies from that review met our inclusion criteria^{16–18} and all of these were found in our search. Of the excluded studies: 2 were pilot studies,^{19,20} 1 examined cognitive behavioral therapy (CBT),²¹ and 1 was a cohort study.²²

We searched PubMed, CINAHL, PsycInfo, and Web of Science December 11, 2019 using a broad search strategy that was developed using MeSH and free text terms (Supplementary data).

Data extraction and management

CK and CW read all titles ($n = 1,447$). Duplicates ($n = 249$) and ineligible articles ($n = 983$) were excluded. CK and CW read the remaining abstracts ($n = 215$) and in consensus excluded abstracts not meeting inclusion criteria ($n = 170$). Remaining articles ($n = 45$) were read in entirety by CK and CW and consensus reached regarding final inclusion ($n = 12$). We searched references of included studies for further eligible articles. We used backward citation searching of PubMed based on included studies.

Synthesis and analysis of results

We extracted information regarding setting, number of participants, inclusion criteria, recruitment, study design including type of study, length of intervention, comparison group, exclusion criteria, primary outcome, and effect size. We used the Swedish version of GRADE²³ to evaluate risk of bias and summarized the findings in a table. All articles were evaluated by CK and CW independently and the evaluation of risk of bias was discussed for each study. We planned to resolve conflicts in evaluation with AC, but this was not necessary.

We conducted a deductive qualitative content analysis²⁴ of studies with low or medium risk for bias. We coded the methods section of each included article using the preexisting CC framework.¹⁴

Based on clinical questions regarding how to form a CC intervention, we developed a matrix to further analyze the structured management plan and the scheduled patient follow-ups. Specific content in the structured management plan included: type of psychological intervention, problem-solving techniques, CBT, or other; therapy provider, CM, or other; use of a stepped care model; use of a care plan; psychoeducation; education on somatic disease, and education on the link between depression and somatic disease. Specific content in the scheduled patient follow-ups included: symptom monitoring; function monitoring; medical adherence; a maintenance phase of less frequent follow-up after symptom reduction; a relapse prevention plan; follow-up occasions as decreasing or continuous over time; and follow-up format (as face-to-face, by telephone, or over the Internet). We extracted data from the methods sections of each study, complemented by study protocols and supplementary material when needed. We coded and mapped the content of the methods section of each article onto this matrix. Furthermore, we summarized the matrix descriptively.²⁴ We also examined CM supervisor profession for the component enhanced interprofessional communication in the preexisting framework.¹⁴ Results were validated and coded by CW and CK.

Due to heterogeneity of the studies regarding population, study setting, study design, primary outcome and effect size, no meta-analysis could be conducted.

Results

Study selection

The initial search resulted in 1,447 studies. After review, we considered 12 studies eligible (Fig. 1). No further studies were found

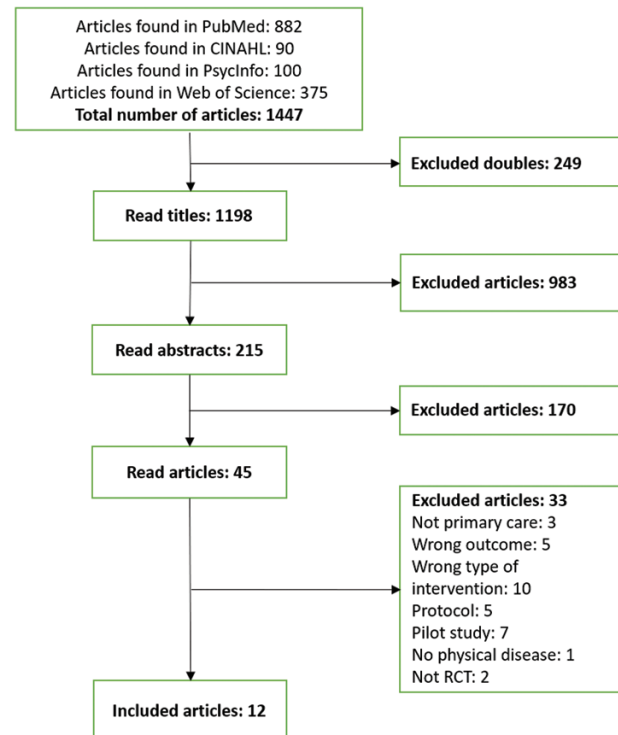


Fig. 1. Flow chart of our search in December 2019 to the final inclusion of the 12 included studies published in 2004–2019.

in reference lists of included studies nor citation search of included studies.

Description of studies

All included studies were peer-reviewed, had ethical approval, and were published between 2004 and 2019 (Table 1). No study required participants to have 2 or more physical diseases. Eleven studies included depressive symptoms,^{16–18,25–32} and 1 included depressive and/or anxiety symptoms.³³ All participants were adults, mean age 55–68 years. One study recruited patients in a hospital setting and conducted the study in a test environment,³² all others recruited participants in PC or community settings.

Study outcomes

Depressive symptoms were measured using different depressive symptom scales: PHQ-9 in 4 studies,^{17,27,28,33} SCL-D13 in 1,¹⁶ SCL-20 in 2,^{18,31} SCL-90 in 1,²⁶ HSCL-20 in 3,^{25,29,30} and BDI in 1.³²

Anxiety was measured by the anxiety symptom scale GAD-7 as one of 2 primary outcomes in 1 study.³³ Primary outcome was measured by decreased depression or anxiety scale points in 7 studies.^{16,25,28,29,31–33} In the remaining 5 studies, primary outcome was measured as remission in 1,²⁷ as 5-point reduction in 1,¹⁷ and 40–50% reduction in 3 studies.^{26,30,31}

Risk of bias

Two studies, conducted in the United States and the United Kingdom, were of high quality with low overall risk of bias.^{16,25} One study from the Netherlands had medium-to-high overall risk of bias³³ and was therefore included in the study (Tables 1 and 2), but not in the analysis (Tables 3 and 4). The remaining studies had low-to-medium risk of bias (Table 2).

Table 1. An overview of the 12 included studies published in 2004–2019 regarding setting, number of participants, recruitment, inclusion criteria, study design, primary outcome, and effect size.

Author, year	Setting	Number of participant (N)	Recruitment	Inclusion criteria	Study design	Primary outcome	Effect size
Aragònès, 2019	<ul style="list-style-type: none"> 8 PC clinics Spain 	328	Medical records	<ul style="list-style-type: none"> 18–80 years Musculoskeletal pain (BPI^a ≥ 5) ≥ 3 months Major depressive disorder (MDD) (SCID^b) 	<ul style="list-style-type: none"> Cluster-RCT 12 months Usual care 	<ul style="list-style-type: none"> HSCL-20^c — 12 months 	Cohen's <i>d</i> : -0.31
Bogner, 2012	<ul style="list-style-type: none"> 3 PC clinics Philadelphia, USA 	182	Medical records	<ul style="list-style-type: none"> ≥ 30 years Diabetes mellitus type 2 (DMt2) Prescribed antidepressant medication during the past year 	<ul style="list-style-type: none"> RCT 3 months Usual care 	<ul style="list-style-type: none"> Number of patients with PHQ-9^d < 5 — 3 months 	OR = 6.15 (95% CI = 2.93–12.92), $P < 0.001$
Coventry, 2015	<ul style="list-style-type: none"> 36 PC clinics North west of England 	387	Medical records	<ul style="list-style-type: none"> ≥ 18 years Diabetes mellitus (DM) and/or cardiac heart disease (CHD) MDD (PHQ-9 ≥ 10) 	<ul style="list-style-type: none"> Cluster-RCT 3 months Usual care Ongoing psychotherapy 	<ul style="list-style-type: none"> SCL-D13^e — 4 months 	-0.3 (-0.5 to -0.07), ICC = 0.03 (0–0.10)
Davidson, 2013	<ul style="list-style-type: none"> 2 private centers and 5 academic ambulatory centers New York, Atlanta, Missouri, New Haven, Philadelphia, USA 	150	Medical records	<ul style="list-style-type: none"> ≥ 35 years 2–6 months after acute coronary heart syndrome (ACS) Depressive symptoms (BDI^f ≥ 10) 	<ul style="list-style-type: none"> RCT 6 months Usual care 	<ul style="list-style-type: none"> BDI — 6 months 	Hedges' <i>g</i> : 0.59
Ell, 2010	<ul style="list-style-type: none"> 2 public safety-net clinics California, USA 	387	Medical records	<ul style="list-style-type: none"> ≥ 18 years DM MDD (PHQ-9 ≥ 10) Hispanic background 	<ul style="list-style-type: none"> RCT 12 months Enhanced usual care (patients received information about depression and a community resource list) 	<ul style="list-style-type: none"> $\geq 50\%$ reduction in SCL-20^g — 6, 12, and 18 months 	Adjusted OR: 2.46–2.57, $P < 0.001$
Johnson, 2014	<ul style="list-style-type: none"> 4 PC clinics Alberta, Canada 	157	Medical records	<ul style="list-style-type: none"> ≥ 18 years DMt2 MDD (PHQ-9 ≥ 10) 	<ul style="list-style-type: none"> RCT 12 months Usual care 	<ul style="list-style-type: none"> PHQ-8^h — 12 months 	Cohen's <i>d</i> : -0.41
Katon, 2004	<ul style="list-style-type: none"> 9 PC clinics Washington state, USA 	329	Medical records	<ul style="list-style-type: none"> — DMt2 MDD (PHQ-9 ≥ 10) 	<ul style="list-style-type: none"> RCT 12 months Usual care 	<ul style="list-style-type: none"> $\geq 40\%$ improvement in SCL-90ⁱ — 6 and 12 months 	OR = 1.89 (95% CI = 1.18–3.02), $P = 0.03$
Katon, 2010	<ul style="list-style-type: none"> 14 PC clinics Washington state, USA 	214	Medical records	<ul style="list-style-type: none"> — DM and/or CHD MDD (PHQ-9 ≥ 10) 	<ul style="list-style-type: none"> RCT 12 months Usual care 	<ul style="list-style-type: none"> SCL-20 — 12 months 	Cohen's <i>d</i> : 0.67

Table 1. Continued

Author, year	Setting	Number and type of clinic(s)	Number of participant (N)	Recruitment	Inclusion criteria	Study design	Primary outcome	Effect size
	<ul style="list-style-type: none"> Number Country 				<ul style="list-style-type: none"> Age Somatic disease Mental health problem Other 	<ul style="list-style-type: none"> RCT/cluster-RCT Length of intervention Comparison group (CG): usual care or enhanced usual care Exclusion criteria 	<ul style="list-style-type: none"> Reduction in depressive symptoms by scale Reduction in anxiety symptoms by scale Time for outcome evaluation 	
Kroenke, 2009	<ul style="list-style-type: none"> 6 PC clinics, 1 center for veterans' affairs and 5 general medical clinics Indianapolis, Indiana, USA 	250	Medical records	<ul style="list-style-type: none"> ≥3 months of hip, knee or lower back pain (BPI ≥5) MDD (PHQ-9 ≥10) 	<ul style="list-style-type: none"> RCT 12 months Usual care 	<ul style="list-style-type: none"> HSL-20 and ≥50% decrease HSL-20 — 12 months 	0.67	
Morgan, 2013	<ul style="list-style-type: none"> 11 PC clinics Australia 	400	Medical records	<ul style="list-style-type: none"> ≥18 years DM and/or CHD Depressive symptoms (PHQ-9 >5) 	<ul style="list-style-type: none"> Cluster-RCT 6 months Usual care 	<ul style="list-style-type: none"> Number of patients with a 5-point reduction in PHQ-9 — 6 months 	No effect size presented, but a between group difference of improvement in depressive symptoms ($P = 0.012$)	
Stoop, 2015	<ul style="list-style-type: none"> 24 PC clinics The Netherlands 	46	Medical records	<ul style="list-style-type: none"> — DM2, chronic obstructive pulmonary disease (COPD) and/or asthma Depressive symptoms (PHQ-9 ≥7) or anxiety symptoms (GAD-7 ≥8) 	<ul style="list-style-type: none"> RCT 12 months Usual care Ongoing psychotherapy 	<ul style="list-style-type: none"> PHQ-9 GAD-7 Cohen's <i>d</i>: 12 and 18 months 	<ul style="list-style-type: none"> After 12 months: 0.61 After 18 months: 0.74 	
Vera, 2010	<ul style="list-style-type: none"> 14 PC clinics or internal medicine clinics Puerto Rico 	179	Waiting room	<ul style="list-style-type: none"> ≥18 years One chronic medical disease MDD (PHQ-9 ≥10) 	<ul style="list-style-type: none"> RCT 6 months Usual care Ongoing mental health treatment 	<ul style="list-style-type: none"> HSL-20, ≥50% decrease in HSL-20 — 6 months 	<ul style="list-style-type: none"> OR: 4.04 (95% CI: 2.01–8.31). 	

^aBPI: Brief Pain Inventory.
^bSCID: Structural Clinical Interview for DSM.
^cHSL-20: 20-item Hopkin's Symptom Checklist.
^dPHQ-9: Patient Health Questionnaire-9.
^eSCL-D13: Symptoms Checklist—Depression 13.
^fBDI: Beck's Depression Inventory.
^gSCL-20: Symptoms Checklist-20.
^hPHQ-8: Patient Health Questionnaire-8.
ⁱSCL-90: Symptoms Checklist-90.
^jGAD-7: Generalized Anxiety Disorder 7 item scale.

Table 2. Risk of bias evaluation of the 12 included studies published in 2004–2019.

Author, year	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	Interest conflict bias	Overall risk of bias
Aragonès, 2019	Low	Medium	Low	Medium/high	Low	Low/medium	Medium
Boger, 2012	Low/medium	Medium	Medium	Low	Medium	Low/medium	Medium
Coventry, 2015	Low	Low/medium	Low	Low	Low	Low/medium	Low
Davidson, 2013	Low	Medium	Low/medium	Low	Low	Low/medium	Low/medium
Ell, 2010	Medium	Medium	Medium/high	Medium	Low/medium	Medium	Medium
Johnson, 2014	Low	Medium	Medium	Low/medium	Low	Low/medium	Low/medium
Katon, 2004	Low	Medium	Medium	Medium	Medium	Low/medium	Medium
Katon, 2010	Low	Medium	Medium	Medium/high	Medium	Medium	Medium
Kroenke, 2009	Low	Medium	Low	Low	Low	Low/medium	Low
Morgan, 2013	Low	Medium	Medium	Medium	Low	Low/medium	Low/medium
Stoop, 2015	Medium/high	Medium	Medium/high	Low	Medium	Low/medium	Medium/high
Vera, 2010	Medium	Medium	Medium	Low/medium	Medium	Medium	Medium

Impact of interventions on outcomes

All studies but one³³ showed a significant decrease in depressive symptoms between intervention group and control group. The exception was the study with medium-to-high risk of bias, with the least number of participants, that had 2 primary outcomes, showing significant decrease in anxiety symptoms with effect size of 0.61–0.74.³³ The other 6 studies investigating decreased depressive symptoms as primary outcome^{16,25,28,29,31,32} included the 2 high-quality studies.^{16,25} Four had medium effect sizes,^{16,28,29,32} and 2 studies had large effect sizes.^{18,25} Results of 5 studies using proportional reduction^{17,26,30,31} or remission²⁷ as primary outcome, are presented as odds ratios except in one¹⁷ where calculation was not possible (see [Table 1](#)).

Content of CC framework

For patients with multimorbidity involving depression and either cardiovascular disease, diabetes, or pain, specific content of CC involved a nurse or psychologist CM collaborating with a PC Physician to deliver a structured management plan including both medication and psychotherapy in most studies ([Table 3](#)).^{17,18,25,26,28,30,32} Number of follow-up visits varied, but in studies with large effect size and good quality follow-up ranged from 8 to 12 occasions.^{16,25} Liaison methods between the CM and the physician varied. In most studies, the CM had scheduled supervision by a psychiatrist or psychologist.^{16,18,25,26,28,30–32}

Specific content of the structured management plan and scheduled patient follow-ups

Using our extended matrix for descriptive analysis we found that the structured management plan included a stepped care model in which CM-delivered psychological treatment and psychoeducation, education on depression and/or somatic disease including the link between depression and the somatic disease was included in most studies ([Table 4](#)).^{16,18,25,28,30,31} Nurse CMs provided support for self-care, problem-solving techniques, and behavioral activation based on CBT principles. Psychologist CMs provided brief psychotherapy or CBT. However, there was no indication that CM profession had any impact on study results. Only 3 studies used a written care plan.^{16,17,28}

Specific content of the scheduled patient follow-ups included symptom and function monitoring and medical adherence, a maintenance phase beyond treatment response, and/or a relapse prevention plan.^{16,18,25,27–32} Follow-up appointments decreased over time

or in response to treatment in most studies.^{18,25,26,28–30,32} Follow-ups were conducted face-to-face and/or by telephone in all studies but one in which participants were followed-up over the Internet or by telephone.³²

Discussion

This systematic review synthesizes the evidence from 12 studies identified in a thorough search of 4 databases of CC for patients with multimorbidity involving depression and/or anxiety, compared with usual care. The results from 11 studies show that CC effectively decreases depressive symptoms in patients with multimorbidity involving depression and 1 somatic disease in studies with medium-to-high quality. No conclusions can be drawn regarding the effectiveness of CC in patients with multimorbidity involving anxiety, or for patients with multimorbidity involving depression and 2 or more somatic diseases. No statistical conclusions can be made regarding specific content of the CC models in the included studies. However, we found common content in medium-to-high-quality studies with positive effect in reducing depressive symptoms: a physician working together with a nurse or psychologist CM in a stepped care model combining medication and CM-delivered CBT-based psychological treatment; scheduled follow-ups with symptom and function monitoring and relapse prevention strategies such as medical adherence, a maintenance phase, and/or a relapse prevention plan. In addition, the CM had scheduled supervision by a psychiatrist and/or a psychologist.

This study compared with other research

Our findings align with the Cochrane review published 2016 in which CC was shown effective for patients with multimorbidity involving depression.¹⁰ A systematic review and meta-regression¹⁵ found inclusion of psychological interventions in CC for patients with only depression predicted improvement in depressive symptoms. In the current study, all but 1 study²⁷ included a psychological component, indicating that this also may be useful for patients suffering from multimorbidity involving depression. We expanded a preexisting CC framework¹⁴ in order to broaden our understanding of the content of the structured management plan and the scheduled patient follow-ups. In our matrix, we included 3 of 4 strategies of relapse prevention recently discussed in a review of CC for patients with depression by Moriarty et al.³⁴ regarding medical adherence, a maintenance phase and a relapse prevention plan. In our study, all studies but 1¹⁷ included at least one of these 3 strategies, suggesting

Table 3. Content of the 4 components of CC models of the 11 included studies with good to medium quality and positive results published in 2004–2019.

Author, year	Multiprofessional approach to patient care		Structured management plan (psychotherapy/medication)	Number of scheduled follow-ups	Enhanced inter professional communication	
	Medical professional	CM			CM and physician liaison	CM supervision/CM supervisor
Aragonès, 2019	Physician	Psychologist	Psychotherapy	6	Written communication	Scheduled/research team
Bogner, 2012	Physician	Research coordinator	Medication	5	Oral communication	Scheduled/research team
Coventry, 2015	Physician and practice nurse	Psychologist	Psychotherapy	8 (2 with PN)	Not fully described	Scheduled/psychologist
Davidson, 2013	Physician or advanced practice nurse	PST-therapist/nurse	Psychotherapy/medication	8	Oral communication	Scheduled/psychiatrist, psychologist
Ell, 2010	Physician	Social work specialist	Psychotherapy/medication	6	Not fully described	Scheduled/psychiatrist
Johnson, 2014	Physician	Nurse	Psychotherapy/medication	9	Not fully described	Scheduled/psychiatrist, endocrinologist
Katon, 2004	Physician	Nurse	Psychotherapy/medication	7	Written or oral communication	Scheduled/psychiatrist, psychologist
Katon, 2010	Physician	Nurse with diabetic background	Psychotherapy/medication	10	Not fully described	Scheduled/psychiatrist, psychologist, physician
Kroenke, 2009	Physician	Nurse	Psychotherapy/medication	12	Oral communication	Scheduled/psychiatrist
Morgan, 2013	Physician	Nurse	Psychotherapy/medication	3	Written communication	Ad hoc/research team
Vera, 2010	Physician	Psychologist	Psychotherapy/medication	10	Not fully described	Scheduled/psychiatrist

PST, problem-solving technique.

relapse prevention strategies for patients with multimorbidity involving depression to be of interest in intervention development. In that review, one third of the included studies lacked information on relapse prevention strategies.³⁴ We also identified insufficient content details in our included studies, making it hard to further extend our evaluation matrix.

Previous studies have shown promising results of CC for patients with anxiety alone.^{12,13} However, in our review we identified only 1 study of CC for multimorbidity involving anxiety and/or depression.³³

Strengths and limitations of this study

We investigated specific content of CC for patients with multimorbidity involving depression and/or anxiety, using both a well-tested existing framework¹⁴ and a new matrix that allowed us to explore the content of the structured management plan and scheduled patient follow-ups in more detail. However, as single disease management has seen to be insufficient for patients suffering from multimorbidity, this systematic review does not aim to decompose the concept of CC by examine each component alone nor being able to show effectiveness of an active ingredient, but to identify what content is most commonly occurring aiming to help to form a functioning CC intervention by looking into specific content. A limitation of this review might be the lack of identification of how CC components work in the best way together. In addition, this systematic review does not look into effectiveness of other care models. Hence, no conclusions can be drawn regarding the need of further content, than the content of CC of today, nor if CC is the best intervention design compared with other intervention designs to help patients with multimorbidity involving depression in the best way.

Because of low number of identified studies and heterogeneity between studies regarding length, content, settings, participants, and inclusion criteria, meta-regression was deemed inappropriate and we can therefore not draw statistical conclusions. This is a limitation of the study.

The search strategy was broad, to find as many eligible articles as possible. However, we focused on multimorbidity involving depression and/or anxiety and specifically restricted for this in our search strategy. The search strategy might therefore be narrowed, missing relevant studies. However, no further studies were identified using backward and forward snowballing, nor in the included studies of the Cochrane systematic review from 2016,¹⁰ indicating completeness of our initial search. In addition, a high number of studies did not meet our inclusion criteria and were excluded in our search strategy already on title and abstract level not meeting our inclusion criteria, which on the other hand suggests our search strategy possibly being too broad. Nevertheless, we consider the completeness of our search in this systematic review more important than a narrower search strategy with the risk of missing out on important studies. Two independent reviewers assessed the inclusion and exclusion of articles, as well as data extraction, to avoid selection bias.

One study included patients 2–6 months after ACS identified in a hospital setting. Since patients with cardiac heart disease are common in PC settings and since the study was conducted in a test environment, this study was considered eligible.

All studies but 1 showed positive effect of CC for patients with multimorbidity involving depression. This may reflect publication bias as negative studies of CC may remain unpublished.

In our study, inclusion criteria were depression and/or anxiety and 1 or more chronic physical disease. Multimorbidity is defined as 2 or more chronic diseases and in the current study we identified

Table 4. Key content of the intervention design in the CC models of the 11 included studies with medium-to-high-quality and positive results published in 2004–2019.

Author, year	Key content of the structured management plan					Key content of the scheduled patient follow-ups					Follow-up format		
	Psychological treatment	Therapy provider	Stepped care model	Care plan	Psychoeducation	Education on somatic disease	Symptom monitoring	Function monitoring	Medical adherence	Maintenance phase		Relapse prevention plan	Follow-up occasions
Aragonès, 2019	Group cognitive behavioral therapy: 9 sessions for 3 months	CM	—	—	✓	✓	✓	✓	✓	✓	✓	Decreased over time	Telephone
Bogner, 2012	—	—	—	—	✓	✓	✓	✓	—	—	—	Fixed	Face-to-face/telephone
Coventry, 2015	Brief psychotherapy up to 8 sessions.	CM	✓	Workbook	✓	The link with depression	✓	✓	✓	—	✓	Fixed	Face-to-face and/or telephone
Davidson, 2013	Internet-based problem-solving therapy	CM	✓	—	—	—	✓	—	✓	—	—	Decreased over time	Telephone/Internet
Ell, 2010	Problem-solving therapy	CM	✓	—	✓	The link with depression	✓	✓	✓	✓	✓	Fixed	Telephone
Johnson, 2014	Problem-solving therapy	CM	✓	Shared care plan	—	✓	✓	✓	✓	✓	✓	Decreased when treatment response	Face-to-face/telephone
Katon, 2004	Problem-solving therapy	CM	✓	—	—	—	✓	—	✓	—	—	Decreased when treatment response	Face-to-face/telephone
Katon, 2010	Problem-solving therapy	CM	✓	—	✓	✓	✓	✓	✓	✓	✓	Decreased when treatment response	Face-to-face
Kroenke, 2009	Pain self-management programme 6 sessions over 3 months	CM	✓	—	✓	✓	✓	✓	✓	✓	✓	Decreased over time, extra contacts if needed	Face-to-face/telephone
Morgan, 2013	Problem-solving therapy	CM	✓	Care plan	—	—	✓	✓	—	—	—	Fixed	Face-to-face
Vera, 2010	CBT 13 sessions	Psychologist	✓	—	✓	—	✓	✓	—	—	—	Decreased over time, extra contacts if needed	Face-to-face/telephone

depression and/or anxiety as 1 chronic disease, following the definition used in the 2016 Cochrane Review of complex interventions for patients with multimorbidity.¹⁰ Nevertheless, focusing on depression and/or anxiety and 1 more disease might be considered as focusing on comorbidity.^{2,3} However, RCTs that include patients with multimorbidity with more diseases than 2 are lacking³⁵ why we decided to choose these inclusion criteria. Moreover, none of the studies we found actively included individuals with 2 or more somatic diseases supporting a previously defined research gap that future intervention design should include individuals with multimorbidity involving more than 2 somatic diseases and depressive and/or anxiety symptoms to address this common patient group.³⁵ Nevertheless, patients with 1 chronic somatic disease in PC settings often have other chronic diseases,³⁶ why many of the patients in the included studies likely have more than 1 somatic disease.

In the excluded full-text studies (Supplementary data) 2 of 33^{37,38} included multimorbid patients with at least 2 chronic diseases. These were excluded as depression and/or anxiety were not inclusion criterion, and primary outcome was health improvement. Furthermore, single disease outcomes may not be relevant for people with multimorbidity, but there is currently no consensus on other meaningful outcomes for individuals with more than 2 chronic diseases and mental health problems.

Implications for practice/research

This systematic review and qualitative synthesis add a map of the content of CC components for patients with multimorbidity involving depression used in well-designed studies with positive outcomes. This content can be used when developing a CC model in PC for this patient group. However, further research should investigate the potential active components using statistical methodology.

The current study has identified a research gap regarding the effect of CC in patients with multimorbidity involving anxiety, depression and anxiety, and depression and/or anxiety and more than 2 chronic diseases.

Conclusions

The content of CC for patients with multimorbidity involving depression is identified from current research. Further research is necessary on CC for patients with multimorbidity and: anxiety, depression and anxiety, and depression and/or anxiety and more than 2 chronic diseases.

Supplementary material

Supplementary material is available at *Family Practice* online. Appendix 1. Search strategy PubMed: December 11, 2019. Appendix 2. Excluded full-text studies after review in December 2019.

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Ethical approval

No ethical approval was required.

Conflict of interest

None declared.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary material.

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