


# Models of care for improving health-related quality of life, mental health, or mortality in persons with multimorbidity: A systematic review of randomized controlled trials

Journal of Multimorbidity and Comorbidity  
Volume 12: 1–31  
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DOI: 10.1177/26335565221134017  
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## Abstract

**Objectives:** To categorize and examine the effectiveness regarding health-related quality of life (HRQoL), mental health, and mortality of care models for persons with multimorbidity in primary care, community care, and hospitals through a systematic review.

**Methods:** We searched PubMed, Embase, and Cochrane Central Register of Controlled Trials up to May 2020. One author screened titles and abstracts, and to validate, a second author screened 5% of the studies. Two authors independently extracted data and assessed risk of bias using the tool by the Cochrane Effective Practice and Organisation of Care group. Study inclusion criteria were (1) participants aged  $\geq 18$  years with multimorbidity; (2) referred to multimorbidity or two or more specific chronic conditions in the title or abstract; (3) randomized controlled design; and (4) HRQoL, mental health, or mortality as primary outcome measures. We used the Foundation Framework to categorize the models and the PRISMA-guideline for reporting.

**Results:** In this study, the first to report effectiveness of care models in patients with multimorbidity in hospital settings, we included 30 studies and 9,777 participants with multimorbidity. 12 studies were located in primary care, 9 in community care, and 9 in hospitals. HRQoL was reported as the primary outcome in 12 studies, mental health in 17 studies, and mortality in three studies—with significant improvements in 5, 14, and 2, respectively. The studies are presented according to settings.

**Conclusions:** Although 20 of the care models reported positive effects, the variations in populations, settings, model elements, and outcome measures made it difficult to conclude on which models and model elements were effective.

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## Keywords

Multimorbidity, multiple chronic conditions, systematic review, randomized controlled trials, primary care, community-based care setting, hospitals, integrated care, healthcare organization

## Strengths and limitations of this study

- A major strength is the systematic approach to identify and include the randomized controlled trials.
- The use of the Foundation Framework secured detailed descriptions of the care models.
- It is a strength that the review includes all three settings: primary care, community care, and hospitals.

## Introduction

Multimorbidity is often defined as the coexistence of two or more chronic conditions in the same individual<sup>1,2</sup>; however, the definition varies throughout the literature.<sup>3–5</sup> Multimorbidity is associated with decreased physical functioning, decreased health-related quality of life (HRQoL), increased use of health services, and higher mortality.<sup>6</sup> The prevalence of multimorbidity is rising globally,<sup>7–9</sup> resulting in burdens for individuals and healthcare systems.<sup>10</sup> Social disparities are linked to the prevalence of multimorbidity,<sup>11</sup> and a socioeconomic gradient has been observed in healthcare utilization, with more hospitalizations and bed days among persons with shorter education compared to those with longer education.<sup>12</sup> Furthermore, the lack of integrated care is a common experience among patients with multimorbidity.<sup>13</sup>

Care models, as we defined as a number of model elements aiming to improve the quality of delivered healthcare services, have been developed for providing integrated, patient-centered care for single chronic conditions and multimorbidity. The most notable frameworks for care models are the Chronic Care Model,<sup>14,15</sup> the SELFIE model (Sustainable intEgrated care modeLs for multi-morbidity: delivery, FInancing and performancE),<sup>16</sup> and the World Health Organization (WHO) model of integrated, people-centered care,<sup>17</sup> and more recently, the Multimorbidity Care Model from the European Projects CHRODIS and CHRODIS Plus.<sup>18</sup> These frameworks provide approaches to improve integration of care and increase patient-centeredness, but few have been adequately evaluated for effectiveness among populations with multimorbidity. Consequently, healthcare professionals and decision-makers are left with few options to provide evidence-based care for persons with multimorbidity. At the same time, there is a lack of consensus in describing models of care for multimorbidity as well as the most suitable outcome measures, which complicates concluding on the effectiveness of models of care for patients with multimorbidity.<sup>19</sup> In 2017, the Foundation Framework—a framework for developing and reporting

models of care for multimorbidity—was published, offering an approach to categorizing models of care for multimorbidity.<sup>19</sup> The Foundation Framework is a powerful approach to undertake detailed comparisons of models of care and bring together the heterogeneous field of models targeting multimorbidity through shared descriptions.

To our knowledge, two former reviews have been conducted to test the effectiveness of models of care for multimorbidity. This is a Cochrane review of interventions for improving outcomes in patients with multimorbidity in primary care and community settings.<sup>20</sup> The review was updated in 2016, searched the scientific literature up to 2015, and included 18 randomized controlled trials (RCT).<sup>21</sup> The review was further corrected in 2021 removing one of the studies from the 2016 version.<sup>22</sup> Additionally, a systematic review updated and narrowed the focus of the Cochrane review by excluding comorbidity studies—taken the consequence of the growing discussing toward a distinction between the concept of multimorbidity and comorbidity.<sup>23</sup> The conclusions in the reviews were rather similar, both highlighting that the effectiveness of interventions for people with multimorbidity remained uncertain, with mixed findings overall and a need for further studies on the topic.<sup>21,23</sup> The reviews did, however, only include studies conducted in primary care and community settings and did not include models of care taking place in a hospital setting.

This study aimed to categorize and examine the effectiveness of models of care designed to improve health-related quality of life (HRQoL), mental health, or mortality for persons with multimorbidity in primary care, community-based care settings, or hospitals through a systematic review of RCT studies.

## Methods

We applied the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting and reporting the study.<sup>24</sup> The review protocol was registered with PROSPERO (Ref no: CRD42019119490).

## Search strategy

Our search strategy built upon previous work<sup>21,25</sup> and was modified in collaboration with a research librarian. We searched PubMed, Embase, and the Cochrane Controlled Register of Trials (CENTRAL) databases. Our searches for

**Table 1.** Study characteristics.

	Primary care														Communities										Hospitals									
	Bogner 2016	Camacho 2018	Kamradt 2019	Katon 2010	Kroenke 2019	Kraska 2001	McCusker 2015	Morgan 2013	Sajatovic 2017	Salisbury 2018	Schäfer 2017	Sommers 2000	Alexopoulos 2016	Bove 2016	Druss 2018	Fischer 2015	Gellis 2014	Mantle-Reid 2017	Miklavic 2020	Muralidharan 2019	Sajatovic 2017	Dunbar 2015	Dunbar 2015	Ekdahl 2016	Heislop-Marshall 2018	Johansson 2019	Kanwal 2017	O'Moore 2018	Sharpe 2014	Walker 2014	Ye 2014			
Country																																		
Australia																																		
Canada							*											*		*								*						
Denmark														*																				
Germany			*								*						*																	
Sweden																								*										
U.K.	*	*			*	*				*														*						*	*	*		
U.S.	*			*								*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
<b>Participants</b>																																		
Number	1,226	382	495	214	294	332	120	400	200	1,546	604	543	101	66	400	90	102	159	132	242	30	134	382	279	144	292	69	500	142	157				
<b>Conditions</b>																																		
Anxiety																																		
COPD					*								*	*							*													
Depression	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	
Diabetes	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	
CVD																							*	*	*	*	*	*	*	*	*	*		
Other physical	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	
Other mental															*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
Neuro.																*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
Number of conditions			*			*				*	*	*					*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
<b>Duration and follow-up after baseline (months)</b>																																		
Duration	24	3	9	6	12	3	6	6	12	15	15	15	6.5	1*	6*	-2	3	6	6	6	12*	6	4.5	31	NS	-2	NS	2.5	NS	NS	6			
Follow-up	98	24	9	12	12	6	6	12	15	15	14	36	6.5	3	6	-8	6	6	6	3	6	6	6	36	12	-2	12	5.5	6	8	18			
<b>Primary outcome(s) of interest</b>																																		
Mortality	*												*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
Mental health	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	
HRQoL	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	

Abbreviations: HRQoL: Health-related quality of life; NS: Not specified; \*: number of sessions

models of care in primary care and community-based care settings included the time period from August 2017 through May 2020. For models of care in hospital settings, we searched from January 2013 through May 2020. The time limit of 2013 onwards for hospital settings was applied after observing a spike in publications on the topic of multimorbidity in 2013<sup>26</sup> and deemed a meaningful way to limit the search to recent studies. All search strategies are presented in [Supplemental file 1](#).

**Inclusion criteria for considering studies for this review**

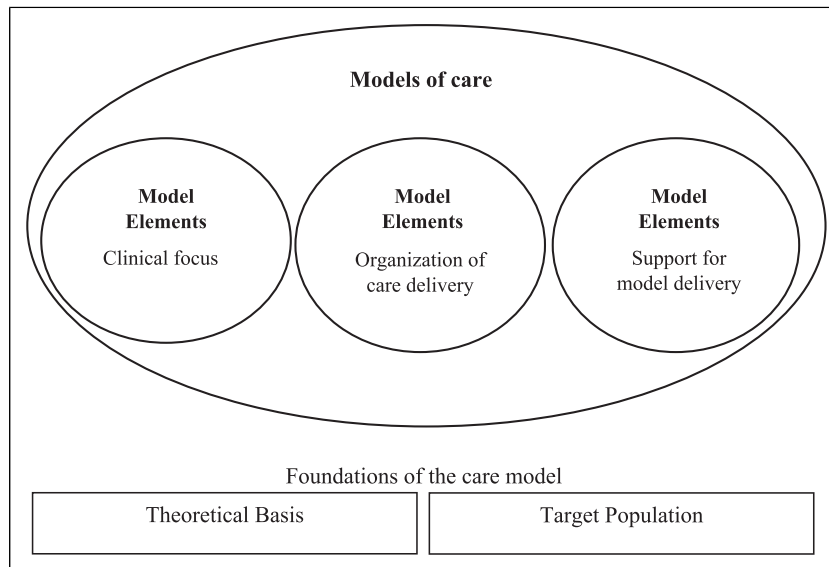
We considered studies with RCT design in which outcome measures were evaluated for models of care. We included studies of participants aged ≥ 18 years with multimorbidity. We defined multimorbidity, in line with the widely used definition as “two or more chronic conditions in the same individual”.<sup>2</sup> Studies had to refer to multimorbidity or two or more specific chronic conditions in the title or abstract to be considered for inclusion. Studies had to report the effectiveness of one of the primary outcome measures: HRQoL, mental health, or mortality. This was based on the core outcome set for multimorbidity research developed using the Delphi method and in which these three outcomes were ranked highest and deemed the most relevant when evaluating models targeting multimorbidity.<sup>27</sup> We included studies taking place in primary care, community-based care settings, and hospitals. Primary care was defined according

to the MeSH term as “care which provides integrated, accessible healthcare services by clinicians who are accountable for addressing a large majority of personal healthcare needs, developing a sustained partnership with patients, and practicing in the context of family and community.”<sup>28</sup> In the search, we included terms as general practice, general practitioners, family physicians, and primary health care. Community-based care was defined as “diagnostic, therapeutic and preventive health services provided for individuals in the community”<sup>29</sup>—and we included terms as community, community health nursing, and homecare services in the search. Hospital was defined as “institutions with an organized medical staff which provide medical care to patients. The branch of medicine concerned with the delivery of comprehensive medical care to hospitalized patients”<sup>30</sup>—and we included terms as hospitals, secondary care, and ambulatory in the search.

We excluded study protocols, pilot studies, and studies published in other languages than English, Danish, Swedish, or Norwegian. We excluded studies of populations with the combination of mental illness and substance use disorder, as the social and medical complexity arising from these combinations were deemed too different from the remaining populations.

**Review process**

After retrieving identified citations from the three databases, one author screened titles and abstracts for inclusion. To validate the title and abstract screening, a second author



**Figure 1.** Model terminology, inspired by the Foundations Framework (Stokes et al. 2017).

rescreened a randomly selected 5% sample of citations; the value of Cohen’s Kappa was 0.66 indicating substantial inter-rater agreement. Two authors independently read the full text of all included citations and reached a consensus about studies to include in the review. Reference lists of included articles were hand-searched to identify additional relevant studies, and all articles included in the previous reviews<sup>21,23</sup> were assessed for eligibility. Two authors independently applied the risk of bias criteria established by the Cochrane Effective Practice and Organisation of Care (EPOC) group to each study.<sup>31</sup> We assessed the risk of selective reporting for each article by comparing the primary and secondary outcomes listed in the methods section with primary and secondary outcomes reported in the results section. For each study, a low, unclear, or high risk was assigned for each criterion. Disagreements were resolved by consensus.

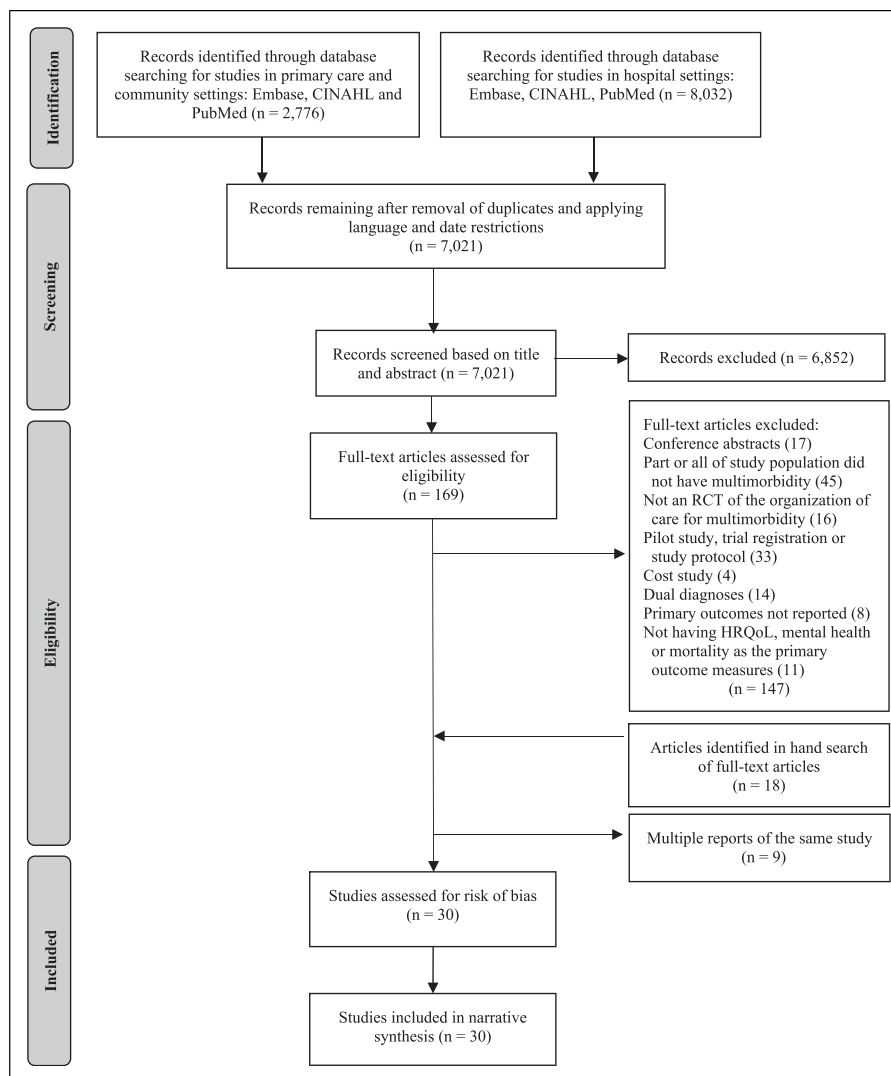
## Analysis

**Data extraction.** Two authors extracted data on the country, number of participants, chronic conditions of the study population, duration and follow-up, primary outcome measures, and setting (Table 1).

**Categorization of models of care—using the Foundation Framework.** To gain a detailed and systematic view of the included care models we used the Foundation Framework for Development and Reporting New Models of Care for Multimorbidity to categorize the care models.<sup>19</sup> The framework is developed for models of care in primary care, and according to the framework, the Theoretical Basis, that

is the underlying assumptions of how a given model may work, and a defined Target Population are the foundations of the care models. The implemented changes are labeled Model Elements and in total the framework lists and describes 28 specific model elements. These model elements are categorized into three groups: Clinical Focus of Care, Organization of Care Delivery, and Support for Model Delivery. Figure 1 illustrates the model terminology and how a model of care consists of different model elements. Supplemental file 2 provides a list of the 28 specific model elements used in the framework, their definitions, and our considerations, adaptations, and interpretations for applying the framework to community-based care and hospital settings—and not only primary care as the framework originally was intended for. One example for adaptation was regarding the model element “Integration with secondary care”—here the original definition was “Primary care working more closely with secondary care”. For care models in community-based care settings and hospital settings this element was changed to “community-based care working more closely with secondary care” and “hospital-based care working more closely with primary care,” respectively. Two authors independently categorized the included care models according to the framework, and disagreements were resolved by consensus. This was done for each of the three settings, separately.

**Effectiveness of the models of care.** We based our effectiveness assessment on the core outcome set for multimorbidity.<sup>27</sup> We therefore only included studies reporting one of the three primary outcome measures: HRQoL,



**Figure 2.** PRISMA flow diagram.

mental health, or mortality. Next, for each setting, we combined the insight from the data extraction, the categorization of the models, and the results of the outcome measures. Due to the heterogeneity of the included studies according to variation of the study populations, care models, and specific model elements, the synthesis of the results is narrative.

## Results

The search strategy yielded 10,808 citations. After removing duplicates and applying language and time restrictions, 7,021 citations remained for the title and abstract screening. Of these, 169 were included in the full-text screening. The full text of an additional 18 articles included in the previous systematic review<sup>22</sup> was also

screened. A total of 30 studies were included in the synthesis.<sup>25,32–60</sup> Figure 2 depicts the selection process.

### Study characteristics

The 30 studies included 9,777 participants with multimorbidity; 22 studies included populations with a specific combination of chronic diseases, and 8 studies focused on the number of conditions in their inclusion of participants. Generally, the examined care models were compared to usual care, which was rarely described in detail. Twelve studies took place in the United States, 13 studies in European countries, and 5 studies in Australia or Canada. Primary care was the most prevalent setting with 12 studies; nine studies were conducted in community settings and nine in hospitals. Studies in primary care

Table 2. Data extraction from studies in primary care settings.

Study	Country	Participants	Duration and follow-up	Care models	Theoretical Basis	Outcomes	Results
Bogner 2016	USA	Age ≥ 60 y, depression and any medical comorbidity (n = 1,226)	Intervention: 2 years Follow-up: 98 months	Depression care manager, educational sessions for the general practitioner, and family education	Integrated care	Primary outcome: • Mortality	Participants with major depression and diabetes who received the care management and education intervention had lower mortality (HR = 0.47, 95% CI = 0.24 to 0.91). For participants with major depression and other comorbidities, point estimates for mortality risk indicated lower risk but did not reach statistical significance. Mean adjusted SCL-D13 score was 0.27 points lower (95% CI = -0.48 to -0.06; p = .014) in the collaborative care intervention group. Unadjusted mean health state index scores improved between baseline and 24 months, while the usual care group worsened. Participants receiving collaborative care accrued significantly more QALYs over 24 months than those receiving usual care (0.136; 95% CI = 0.061 to 0.212).
Camacho 2018	UK	Depression and heart disease and/or diabetes (n = 382)	Intervention: 3 months  Follow-up: 24 months after randomization	Collaborative care: Case manager provided psychological therapy and a collaborative meeting	Collaborative care	Primary outcome: • Self-reported depression severity (SCL-D13) Secondary outcomes: • Health status (EQ-5D-5L) • Cost-effectiveness (QALY)	No statistically significant difference in self-care or health-related quality of life.
Kamradt 2019	Germany	Multimorbid patients with Type 2 diabetes (n = 495)	Intervention: 9 months  Follow-up: 9 months after baseline	Add-on to Type 2 diabetes disease management program. Intervention embedded in regional networks of primary care providers. Included two home visits and 15 structured telephone contacts. The comparator was treatment as usual.	Chronic care model	Outcomes: • Change in patient-reported self-care (Summary of diabetes self-care activities measure, SDSCA-G) • Change in patient-reported health-related quality of life (EuroQoL 5-Dimension, EQ-5D-3L)	

(continued)

Table 2. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical Basis	Outcomes	Results
Katon 2010	USA	Poorly controlled diabetes and/or coronary heart disease and coexisting depression (n=214)	Intervention: 6 months  Follow-up: 12 months	Collaborative care management and support for self-care provided by a medically supervised nurse. The comparator was enhanced usual care; primary care physicians were informed of the depression diagnosis.	Not stated	<p>Primary outcomes:</p> <ul style="list-style-type: none"> <li>Depression scores (SCL-20)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Glycated hemoglobin (HbA1c)</li> <li>Low-density lipoprotein (LDL-C) cholesterol</li> <li>Systolic blood pressure (SBP)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Composite measure of medical control</li> <li>Patient Global Rating of Improvement for depression</li> <li>Satisfaction with care for depression and for diabetes and/or coronary heart disease</li> <li>Quality of life over the past month</li> </ul>	<p>Adjusted between-group differences favored collaborative care management in the intervention group:</p> <ul style="list-style-type: none"> <li>SCL-20 score -0.41 (95% CI, -0.56 to -0.26)</li> <li>HbA1c -0.56% (95% CI, -0.85 to -0.27)</li> <li>LDL-C -9.1 mg/dl (95% CI, -17.5 to -0.8)</li> <li>SBP -3.4 mm/Hg (95% CI, -6.9 to 0.1).</li> </ul> <p>At 12 months, a significantly higher percentage of patients in the intervention group than in the control group had HbA1c, LDL-C, and SBP either below guidelines or with clinically significant improvement. Compared to controls, patients in the intervention group had significantly greater improvement than controls on the Patient Global Rating of Improvement, greater improvement in quality of life, were more satisfied with care for depression and for diabetes, coronary heart disease, or both and had better quality of life (<math>p &lt; .001</math> for all). There was no significant between-group difference in the proportion of patients adhering to recommended diet and exercise at least 2 days per week. Healthcare costs were not reported.</p>

(continued)

Table 2. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical Basis	Outcomes	Results
Kroenke 2019	US	Patients with chronic musculoskeletal pain of at least moderate intensity and clinically significant depressive and/or anxiety symptoms ( $n = 294$ )	Intervention: 12 months Follow-up: 6 and 12 months after baseline	A nurse-physician team in primary care provided comprehensive symptom management, combining automated self-management with collaborative care management. The comparator was automated self-management consisting of monitoring and self-management web modules.	Collaborative care	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Composite measure of pain-anxiety-depression (PAD consisting of PHQ-9, BPI and GAD))</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Composite PROMIS PAD score (8 items for pain, anxiety and depression, PROMIS-57 Profile)</li> <li>Global improvement</li> <li>Health-related quality of life</li> <li>Treatment satisfaction</li> <li>Disability (Sheehan Disability Index, disability days, % work effective)</li> <li>Analgesics and psychotropic medications</li> <li>Health services use</li> </ul>	Both groups improved, but the intervention group had a $-0.23$ (95% CI $-0.38$ to $-0.08$ ; $p = .003$ ) greater decline in composite PAD.
Krska 2001	UK	Age $\geq 65$ y, $\geq 2$ conditions, $\geq 4$ prescribed regular medications ( $n = 332$ )	Intervention: 3 months Follow-up: 3 months after medication review	Pharmacist review of medication regimens, using information obtained from primary care, medical record, and patient interviews	Not stated	<p>Outcomes:</p> <ul style="list-style-type: none"> <li>Pharmaceutical care issues</li> <li>Health and social services questionnaire</li> <li>Health-related quality of life (SF-36)</li> <li>Medication costs</li> </ul>	<p>The intervention group was more likely to report global improvements, improvements in the composite PROMIS PAD score, and improvements in health-related quality of life. Treatment satisfaction was not significantly better in the intervention group. The intervention group improved significantly on the Sheehan Disability Index compared to controls, but no change was observed for other disability-related outcomes. Intervention group received more analgesics. Psychotropic medication use, mental health visits and healthcare use was similar for the groups.</p> <p>A greater proportion of pharmaceutical care issues were resolved after pharmacist medication review in the intervention group (82.7%) vs. control group (41.2%, <math>p &lt; .001</math>). No significant changes in health and social services use, health-related quality of life, and medication costs.</p>

(continued)



Table 2. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical Basis	Outcomes	Results
McCusker 2015	Canada	Primary care patients aged 40 and over with chronic physical conditions and comorbid depressive symptoms (n = 120)	Intervention: 6 months Follow-up: 6 months after baseline	A depression self-care toolkit with lay telephone coaching. The comparator was the toolkit without telephone coaching.	Not stated	Primary outcome: • Depression (PHQ-9) at 6 months Secondary outcomes: • Depression (PHQ-9) at 3 months • Satisfaction with the intervention at 6 months (shortened version of the CSQ-8) • Depression self-care self-efficacy (items adapted from a validated diabetes scale) • Patient-reported use of healthcare services at 3 and 6 months	No significant difference between groups for PHQ-9 at 6 months.  Significant reduction in PHQ-9 at 3 months for the intervention group. No significant differences between groups for the remaining outcomes.
Morgan 2013	Australia	Depression, type 2 diabetes and/or coronary heart disease (n = 400)	Intervention: 6 months Follow-up: 6 and 12 months	Case management provided by the practice nurse with review of pathology results, lifestyle risk factors, and patient goals and priorities	Collaborative care	Primary outcome: • Depression scores (PHQ-9)  Secondary outcome: • Improvements in physiological measures	In the intervention group receiving case management, significant reductions in mean depression score were maintained at 12 months ( $10.7 \pm 0.7$ to $6.6 \pm 0.7$ , $p < .001$ ). At six months, high-density lipoprotein decreased in the intervention group, but no significant changes in other physiological measures were observed in either group.
Sajatovic 2017	USA	Schizophrenia, schizoaffective disorder, bipolar disorder, or major depressive disorder and type 2 diabetes (n=200)	Intervention: 48 weeks Follow-up: 60 weeks	Group-based psychosocial treatment blending psychoeducation, problem identification, goal-setting, behavioral modeling, and care linkage designed for individuals with serious mental illness and diabetes mellitus; 12 weekly group sessions and brief telephone maintenance sessions	Not stated	Primary outcomes: • Psychiatric symptom severity (Clinical Global Impression [CGI]; Montgomery-Åsberg Depression Rating Scale [MADRS]; and Brief Psychiatric Rating Scale [BPRS]) • Functioning (Global Assessment of Functioning [GAF] and Sheehan Disability Scale [SDS])  • General health (SF-36) Secondary outcomes: • Diabetes knowledge (Brief Diabetes Knowledge Test) Diabetes self-care (Diabetes Self-Care Activities Questionnaire [DSCA])	Significantly greater improvement at follow-up for the intervention group receiving group-based treatment in CGI ( $p \leq .001$ ) and MADRS ( $p = .016$ ). BPRS was unchanged. There was significantly greater GAF improvement in the intervention group ( $p = .003$ ). No between-group differences in SF-36, SDS, or HbA1c.  Diabetes knowledge was significantly improved for intervention vs. usual care. No significant between-group difference in DSCA scores.

(continued)

Table 2. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical Basis	Outcomes	Results
Salisbury 2018	UK	Adults with $\geq 3$ chronic conditions ( $n = 1,546$ )	Follow-up: 9 and 15 months	Model for patient-centered care, replacing disease-focused reviews with a comprehensive multidisciplinary review (including medication review by a pharmacist) every 6 months	<p>Patient-centered care model</p> <p>Primary outcome:  <ul style="list-style-type: none"> <li>Health-related quality of life (EQ-5D-5L)</li> </ul> </p> <p>Secondary outcomes:  <ul style="list-style-type: none"> <li>Illness burden (single self-rated health question, the Bayliss measure; Hospital Anxiety and Depression score)</li> <li>Treatment burden (Mean Multimorbidity Treatment Burden Questionnaire score; mean eight-item Morisky Medication Adherence Score; median number of different drugs prescribed in past 3 months)</li> <li>Patient-centered care (Patient Assessment of Care for Chronic Conditions (PACIC); Consultation and Relational Empathy (CARE); single questions about the proportion of patients reporting care related to their priorities, experiencing their care as coordinated, reporting having a written care plan, and overall satisfaction with care)</li> <li>Care processes (Continuity of Care Index; the Visit Entropy measure; summary of disease-specific measures; high-risk prescribing; cost-effectiveness and carer experience)</li> <li>Number of consultations</li> </ul> </p>	<p>No difference between intervention group receiving multidisciplinary care review and control group on EQ-5D-5L.</p> <p>No between-group differences on illness burden, treatment burden, the number of drugs prescribed, or improved medication adherence. At 15 months, all patient-centered care measures showed benefits from the intervention, as did the Continuity of Care Index. No between-group differences in quality of disease management or high-risk prescribing. Patients in the intervention group had more nurse consultations and primary care physician consultations over 15 months, compared to controls; there were no between-group differences in hospital admissions or outpatient visits. Separate report on cost-effectiveness and carer experience planned.</p>	

(continued)

Table 2. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical Basis	Outcomes	Results
Schäfer 2018	Germany	Age 65 to 84 y, $\geq 3$ chronic conditions ( $n = 604$ )	Intervention: 12 months  Follow-up: 14 months after baseline	In addition to routine consultations, GPs had three 30-minute discussions with participants addressing treatment targets and priorities, brown bag review of all medications, and goal attainment and treatment targets.	Chronic care model and narrative medicine	<p>Primary outcomes:</p> <ul style="list-style-type: none"> <li>Number of medications</li> <li>Health-related quality of life (EQ-5D)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>General practitioner (GP) knowledge about medication taken by the patient</li> <li>Patient satisfaction with general practice services</li> <li>Patient empowerment</li> <li>Healthcare use</li> </ul>	<p>No difference between participants receiving additional discussions in the intervention group and controls in the number of medications taken and health-related quality of life. The intervention had no effect on patient satisfaction, patient empowerment and GP knowledge about medication taken by the patient. Compared with the control group, the intervention group had more contact with GPs, less use of physical, occupational or speech therapy (<math>-1.38</math> units in the last 3 months), and fewer days spent in hospital (<math>-3.07</math> days in the last 6 months).</p> <p>Compared to the control group, participants receiving the multidisciplinary care team intervention were less likely to have hospital admissions (OR = 0.63, 95% CI = 0.41 to 0.96, <math>p = 0.3</math> and <math>\geq 1</math> 60-day readmissions: (OR = 0.26, 95% CI = 0.08 to 0.84, <math>p = .03</math>). Changes in all other types of utilization were nonsignificant, except for other physician visits and mean office visits, which were lower in the intervention group.</p> <p>The intervention group had more social activities (<math>p = 0.4</math>), fewer symptoms (<math>p = 0.08</math>), and better self-rated health (<math>p = 0.08</math>). Confidence interval not reported for the remaining four outcomes, but these were not significant.</p>
Sommers 2000	USA	Age $\geq 65$ y, under treatment for $\geq 2$ chronic conditions ( $n = 543$ )	Intervention: 2 years  Follow-up: 12 months after intervention	Multidisciplinary office-based teams with nurse, physician and social worker; education of professionals in coaching participants in self-management, home visits, care plans, phone calls	Not stated	<p>Outcomes:</p> <ul style="list-style-type: none"> <li>Healthcare utilization, including admissions, office visits, emergency department visits, home visits, and nursing home placements</li> <li>Patient-reported health status, including physical, emotional, and social functioning</li> </ul>	<p>Compared to the control group, participants receiving the multidisciplinary care team intervention were less likely to have hospital admissions (OR = 0.63, 95% CI = 0.41 to 0.96, <math>p = 0.3</math> and <math>\geq 1</math> 60-day readmissions: (OR = 0.26, 95% CI = 0.08 to 0.84, <math>p = .03</math>). Changes in all other types of utilization were nonsignificant, except for other physician visits and mean office visits, which were lower in the intervention group.</p> <p>The intervention group had more social activities (<math>p = 0.4</math>), fewer symptoms (<math>p = 0.08</math>), and better self-rated health (<math>p = 0.08</math>). Confidence interval not reported for the remaining four outcomes, but these were not significant.</p>

Table 3. Data extraction from studies in community-based care settings.

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Alexopoulos 2016	USA	COPD and major depression (n = 101)	Intervention: 26 weeks Follow-up: at 10, 14, and 26 weeks	Two experimental conditions: 1) Personalized Intervention for Depressed Patients with COPD (PID-C), including care managers, telephone contact with physicians and focus on barriers to adherence; 2) Problem-Solving Adherence (PSA) intervention integrating problem-solving into adherence enhancement procedures, including care managers	Not stated	Primary outcome: 24-item Hamilton Depression Rating Scale (HAM-D)	Both intervention arms were equally effective based on between-group HAM-D differences at weeks 14 and 26.
Bove 2016	Denmark	Adults with advanced COPD and anxiety (n = 66)	Intervention: mean duration of 1 hour with booster after two weeks Follow-up: 1 and 3 months	Usual care combined with cognitive behavioral therapy and psychoeducation performed in participant's home. Two weeks later, participants were contacted by telephone and offered a 20 min booster session.	Not stated	Primary outcome:  • Anxiety (HADS-A)  Secondary outcomes: Mastery (CRQ-M)	Compared to the control group, the intervention group had a lower mean postintervention HADS-A score (p = .005). The average between-group difference was 2.16 points (95% CI = 0.62 to 3.71) at one month and 2.32 points (95% CI = 0.74 to 3.89) at three months. The intervention group had a higher mean postintervention CRQ-M score than controls (p = .016)
Druss 2018	USA	Participants with a serious mental illness and ≥ 1 chronic medical condition (n = 400)	Intervention: 6 sessions  Follow-up: 3 and 6 months after baseline	Peer-led program for self-management of medical diseases among individuals with mental disorders developed to address common needs across patients with chronic illnesses	Chronic disease self-management program	Primary outcome: • Health-related quality of life (SF-36) Secondary outcomes: • General medical self-management (Patient Activation Measure) • Diet (Block Fat-Sugar-Fruit-Vegetable Screener) • Medication adherence (Morisky scale) • Mental health recovery (Recovery Assessment Scale)	At six months, compared to controls, participants in the intervention group had greater improvement in the SF-36 physical component summary (2.7 vs. 1.4 points, p = .046). The intervention group had a greater improvement in the mental component summary (4.6 vs. 2.5 points, p = 0.039) and mental health recovery (p = .02). No other between-group differences in outcome measures were significant

(continued)

Table 3. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Fischer 2015	Germany	Age 18–65 y, multiple sclerosis and self-reported depressive symptoms ( $n = 90$ )	Intervention: 9 weeks Follow-up: 6 months after intervention	Online program based on cognitive behavioral therapy; 10 sequential modules covering psychoeducation, behavioral activation, cognitive modification, mindfulness and acceptance, interpersonal skills, relaxation, physical exercise and lifestyle modification, problem-solving, expressive writing and forgiveness, positive psychology, and emotion-focus interventions	Not stated	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Beck Depression Inventory (BDI)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Quality of life (WHO-QoL BREF)</li> <li>Disease-related quality of life (HAQUAMS)</li> <li>Fatigue (Fatigue Scale for Motor and Cognitive Function [FSMC])</li> </ul>	<p>BDI scores decreased in the online cognitive behavioral therapy intervention group and increased in the control group, mean between-group difference <math>-4.02</math> points (95% CI = <math>-7.26</math> to <math>-0.79</math>, <math>p = .015</math>, effect size <math>d = 0.53</math>).</p> <p>Between-group differences were found in only the WHO-QoL BREF psychological wellbeing subscale and the motor fatigue subscale of the FSMC. No between-group differences in cognitive fatigue or HAQUAMS subscales. No evidence of new suicidal ideation during the trial in either group.</p>
Gellis 2014	USA	Medically frail older homebound individuals ( $n = 102$ )	Intervention: 3 months Follow-up: 6 months after baseline (clinical measures), and 12 months (healthcare utilization)	Integrated telehealth chronic illness and depression care with a telehealth nurse conducting telemonitoring, providing problem-solving treatment for depression, and providing communication with participants' primary care physicians; comparator was usual care plus psychoeducation	Chronic care model	<p>Outcomes:</p> <ul style="list-style-type: none"> <li>Clinical outcomes: depression status (HAM-D and PHQ-9), health and functional status (SF-12), problem-solving (SPSL-R)</li> <li>Satisfaction with care</li> <li>Healthcare utilization (episodes of care, emergency department visits, and hospital days)</li> </ul>	<p>Depression scores at 3 and 6 months were significantly lower in the telehealth intervention group. Significant between-group difference for the SF-12 mental component subscale but not the physical component subscale. Intervention recipients significantly improved problem-solving skills and self-efficacy in managing their medical condition. No between-group differences in satisfaction with care. The intervention group had significantly fewer emergency department visits (<math>p = .01</math>) but no between-group differences in hospital days or episodes of care at 12 months after baseline.</p>

(continued)

Table 3. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Markle-Reid 2017	Canada	Aged $\geq 65$ y, type 2 diabetes and $\geq 2$ comorbid conditions ( $n = 159$ )	Intervention: 6 months	Client-driven, customized self-management program with up to 3 in-home visits from a registered nurse or dietitian, a monthly group wellness program, monthly provider team case conferences, and care coordination and system navigation	Not stated	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Quality of life (SF-12): Physical Component Summary (PCS)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Quality of life (SF-12): Mental Component Summary (MCS)</li> <li>Summary of Diabetes Self-Care Activities (SDSCA)</li> <li>Depression (Center for Epidemiologic Studies Depression Scale [CES-D-10])</li> <li>Generalized Anxiety Disorder Scale [GAD-7]</li> <li>Self-efficacy for managing chronic disease</li> <li>Healthcare costs</li> </ul>	No significant between-group differences were observed for PCS at follow-up.
Miklavcic 2020	Canada	Community-living older adults with Type 2 diabetes and two or more chronic conditions ( $n = 132$ )	Intervention: 6 months  Follow-up: 6 months after baseline	Community-based self-management intervention, including three home visits, monthly group wellness program, monthly case conferencing and care coordination. The comparator was treatment as usual.	Social cognitive theory	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Physical functioning (SF-12, physical component summary)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Mental functioning (SF-12, mental component summary)</li> <li>Anxiety (GAD-7)</li> <li>Depressive symptoms (CES-D-10)</li> <li>Self-efficacy (Self-Efficacy for Managing Chronic Disease Scale)</li> <li>Self-management (Summary of Diabetes Self-Care Activities Scale)</li> <li>Cost of healthcare service use (Health and Services Utilization Inventory)</li> </ul>	<p>Between-group differences favored the intervention for MCS (mean difference = 2.68, 95% CI = 0.28–5.09, <math>p = 0.03</math>), SDSCA (mean difference = 3.79, 95% CI = 1.02 to 6.56, <math>p = 0.01</math>), and CES-D-10 (mean difference = -1.45, 95% CI = -0.13 to -2.76, <math>P = .03</math>).</p> <p>No between-group differences were found for self-efficacy, anxiety, or total healthcare costs.</p> <p>No significant group differences in physical functioning (mean difference: -0.74; 95% CI: -3.22, 1.74; <math>p</math>-value: 0.56), mental functioning (mean difference: 1.24; 95% CI: -1.12, 3.60; <math>p</math>-value: 0.30), or other secondary outcomes.</p>

(continued)

Table 3. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Muralidharan 2019	US	Adults (veterans) with serious mental illness and chronic respiratory or cardiovascular condition, diabetes or arthritis ( $n = 242$ )	Intervention: 12 sessions of 75 minutes	12 session self-management intervention. Intervention included peer facilitator, skills training in goal-setting, action planning, and problem-solving, setting of weekly health goals, and positive reinforcement of steps towards goals. The comparator was a similar intervention without the components described above.	Chronic disease self-management program, and chronic care model	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Health-related quality of life (SF-12)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Self-efficacy (Self-Management Self-Efficacy scale)</li> <li>Patient activation (Patient Activation Measure)</li> <li>Internal Health Locus of Control (subscale of Multidimensional Health Locus of Control Scale)</li> <li>Illness self-management behaviors (Instrument to Measure Self-Management and Morisky Medication Adherence Scale)</li> <li>Psychiatric symptoms and recovery (Behavior and Symptom Identification Scale 24, self-report, and Maryland Assessment of Recovery Scale)</li> <li>Emergency room use</li> </ul>	<p>The intervention group had greater improvements in mental health-related quality of life (<math>p = .032</math>). The control group exhibited greater increases in physical health-related quality of life (<math>p = .026</math>).</p> <p>Intervention group experienced greater improvements in self-management self-efficacy (<math>p &lt; .0001</math>), patient activation (<math>p = .038</math>), internal health locus of control (<math>p = .045</math>), behavioral/cognitive symptom management (<math>p = .006</math>), and overall psychiatric symptoms (<math>p = .044</math>), and at follow-up in physical activity related self-management (<math>p = .011</math>) and relationship quality (<math>p = .015</math>). There was no difference in emergency room use.</p>
Sajatovic 2017	USA	Parkinson's disease and comorbid unipolar major depression ( $n = 30$ )	Intervention: 6 months  Follow-up: 12 and 24 weeks	<p>Two interventions combined group exercise and chronic disease self-management (CDSM). Enhanced EXerCise thErapy for Parkinson's Disease: sessions with peer support and guided group exercise, focusing on problem identification and goal-setting.</p> <p>Self-guided CDSM plus exercise: single initial in-person group orientation to the same fitness facility followed by flexible free access. Weekly phone calls during the first 12 weeks to self-report on their exercise. Participants received the same CDSM information.</p>	<p>Disease self-management program</p>	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Change in depression (Montgomery-Asberg Depression Rating Scale [MADRS])</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>General cognition (Montreal Cognitive Assessment [MoCA])</li> <li>Anxiety (Covi Anxiety Scale)</li> <li>Apathy (Apathy Scale)</li> <li>Self-efficacy (General Self-Efficacy Scale)</li> <li>Sleep (Scales for Outcomes in PD – Sleep [SCOPA-Sleep])</li> </ul> <p>Motor symptoms (Movement Disorders Society-Unified Parkinson's Disease Rating Scale-III [MDS-UPDRS-III])</p>	<p>Intervention and control groups showed improvement in MADRS (<math>p &lt; .001</math>) with no between-group differences. At 24-week follow-up, both groups maintained MADRS improvements in (<math>p = .001</math>).</p> <p>No between-group differences for secondary outcomes.</p>

**Table 4.** Data extraction from studies in hospital settings.

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Dunbar 2015	USA	Age 21–80 y, heart failure and diabetes re-hospitalized for a heart failure exacerbation (n = 134)	Intervention: 4.5 months Follow-up: 3 and 6 months	Education/counseling on self-care (diet, medications, self-monitoring, symptoms, and physical activity); follow-up home visit; and phone counseling. The comparator was usual care combined with standard patient education brochures and phone contact.	Not stated	<p>Outcomes:</p> <ul style="list-style-type: none"> <li>Quality of life (heart failure-specific quality of life [MLHFQ], diabetes-specific quality of life [ADDQOL], and general quality of life [EQ-5D])</li> <li>Physical function, including six-minute walk test (6MWT)</li> </ul> <p>Physical activity, including self-reported daily physical activity (CHAMPS)</p>	<p>At 3 months, the intervention group had improved total MLHFQ (<math>p &lt; .001</math>) and physical scale (<math>p &lt; .001</math>) scores. ADDQOL scores remained stable for intervention and control groups. The control group had significant decreases in EQ-5D (<math>p = .01</math>) with no significant change in the intervention group. The intervention group had a significant increase in mean EQ-5D VAS from baseline to 6 months (<math>p = .04</math>). At 6 months, compared to controls, a significantly higher percentage of intervention participants walked more than 984 feet (<math>p = .002</math>). Significant increases in self-reported physical activity occurred for the intervention group from baseline to 3 months and from baseline to 6 months.</p>

(continued)



Table 4. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Ekdahl 2016	Sweden	Age $\geq$ 75 y, inpatient hospital care $\geq$ 3 times in past 12 months, $\geq$ 3 medical diagnoses (n = 382)	Intervention: 24 to 31 months Follow-up: 36 months after study inclusion	Comprehensive geriatric assessment-based care at the geriatric ambulatory unit in addition to usual care; individually tailored care, follow-up visits at the unit, home visits, telephone calls.	Not stated	Outcomes: • Mortality • Transfer to nursing home • Days in hospital • Hospitalizations • Total costs of health and social care	Participants in the geriatric care intervention group lived 69 days longer than did those in the control group. 27.9% of participants in the intervention group and 38.5% in the control group died (HR = 1.49, 95% CI = 1.05 to 2.12; $p = .026$ ). Mean number of inpatient days was lower in the intervention group ( $p = .01$ ). No between-group differences were found for transfers to nursing homes, hospitalizations, and total costs.
Heslop-Marshall 2018	UK	Patients with COPD and anxiety (n = 279)	Follow-up: 3, 6 and 12 months	Between 2 and 6 CBT sessions were delivered by respiratory nurses. Leaflets were also provided. The comparator was leaflets and usual care.	Not stated	Primary outcome: • Change in group mean HADS-Anxiety subscale after 3 months Secondary outcome • Change in group mean HADS-Anxiety subscale after 6 and 12 months • Change in HADS-Depression subscale, COPD Assessment Test, and quality of life (EQ-5D-3L) at 3, 6 and 12 months	The CBT group was superior to leaflets at 3 months (mean difference in the HADS-Anxiety subscale was 1.52 (95% CI 0.49 to 2.54, $p = 0.003$ ). At 6 months, the difference in the HADS-Anxiety subscale was borderline significant ( $p = .05$ ), favoring the intervention group. No difference between groups was observed at 12 months ( $p = 0.016$ ). The change in HADS-Depression subscale was significant, but it did not reach the minimal clinically important difference. The intervention was more cost-effective based on the EQ-5D-3L. Results of the COPD Assessment Test are not reported

(continued)

Table 4. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Johansson 2019	Sweden	Patients with cardiovascular disease (CVD) and at least mild depression (n = 144)	Intervention: 9 weeks Follow-up: 9 weeks	The intervention was internet CBT adapted to fit patients with CVD. The comparator was a web-based discussion forum.	Not stated	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>• Depression (PHQ-9)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>• Depression (MADRS-S)</li> <li>• Health-related quality of life (SF-12)</li> <li>• EuroQol Visual Analogue Scale (EQ-VAS)</li> <li>• Level of adherence</li> </ul>	<p>Significant effect on PHQ-9 (mean group difference = -2.34, 95% CI -3.58 to -1.10, <math>p &lt; .001</math>).</p> <p>Significant effects on MADRS-S; (<math>p &lt; .001</math>), the mental component scale of the SF-12 (<math>p &lt; .001</math>)—not the physical component scale—and the EQ-VAS (<math>p &lt; .001</math>).</p> <p>Adherence was higher in the intervention group.</p>
Kanwal 2018	USA	Hepatitis C virus clinic patients screened positive for depression (n = 292)	Intervention: Not specified	Off-site depression collaborative care, delivered by depression care manager, pharmacist and psychiatrist; communication via electronic medical record progress notes; participant education and activation, assessment of treatment barriers and possible resolutions.	Collaborative care model	<p>Primary outcomes:</p> <ul style="list-style-type: none"> <li>• Depression improvement (treatment response, remission, and depression-free days)</li> <li>• Antiviral treatment for HCV</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>• Health-related quality of life</li> <li>• Street drug or alcohol use</li> <li>• Treatment satisfaction</li> <li>• Antidepressant medication regimen adherence</li> </ul>	<p>Participants receiving the depression care intervention were more likely to meet criteria for treatment response (adjusted OR = 3.35, 95% CI = 1.71 to 6.53) and remission (adjusted OR = 3.69, 95% CI = 1.56 to 8.74) and had more depression-free days (adjusted beta = 30.70 days, 95% CI = 10.5 to 50.8) than the control group. No significant change in antiviral treatment for HCV.</p> <p>The intervention resulted in significantly better 12-month SF-12 mental health component summary score compared with usual care (adjusted mean difference = 3.73, 95% CI = 0.47 to 6.99).</p> <p>No unadjusted or adjusted between-group differences were found for SF-12 physical component summary score, satisfaction with care, antidepressant regimen adherence, and at-risk alcohol or drug use.</p>

(continued)

Table 4. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
O'Moore 2018	Australia	Age $\geq$ 50 y, major depressive disorder and osteoarthritis of the knee ( $n = 69$ )	Intervention: 10 weeks	10-week internet cognitive behavioral therapy program for depression added to usual care	Not stated	<p>Primary outcomes:</p> <ul style="list-style-type: none"> <li>• Self-reported depression severity (PHQ-9)</li> <li>• General psychological distress (Kessler-10)</li> </ul> <p>Secondary outcomes:</p>	<p>Significant between-group superiority of the cognitive behavioral intervention (iCBT) were found on primary outcomes at week 11 (PHQ-9: Hedges <math>g = 1.01</math>, 95% CI = 0.47 to 1.54; Kessler-10: Hedges <math>g = 0.75</math>, 95% CI = 0.23 to 1.28) and 3 months (PHQ-9: Hedges <math>g = 0.90</math>, 95% CI = 0.36 to 1.44; Kessler-10: Hedges <math>g = 0.94</math>, 95% CI = 0.41 to 1.48).</p> <p>With the exception of PCS scores, there were significant group by time interactions for all secondary outcome measures (ASES: <math>F [2,125.18] = 4.54</math>, <math>p &lt; .05</math>; WOMAC pain: <math>F [2,125.78] = 5.99</math>, <math>p &lt; .01</math>; WOMAC stiffness: <math>F [2,123.66] = 6.64</math>, <math>p &lt; .01</math>; WOMAC physical function: <math>F [2,124.50] = 5.95</math>, <math>p &lt; .01</math>; and SF-12 MCS: <math>F [2,112.93] = 11.41</math>, <math>p &lt; .001</math>). The proportion of recovered patients in the iCBT group was significantly higher than usual care, as measured by MINI (<math>p &lt; 0.01</math>)</p>
			Follow-up: 1 week and 3 months after intervention			<ul style="list-style-type: none"> <li>• Physical (PCS) and mental (MCS) health component summary scores of the SF-12</li> <li>• Self-efficacy (Arthritis Self-Efficacy Scale [ASES])</li> <li>• Osteoarthritis-specific pain, stiffness, and physical function (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC])</li> </ul> <p>Major depressive disorder diagnostic status (MINI)</p>	

(continued)

Table 4. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Sharpe 2014	UK	Outpatients with major depression from three cancer centers ( $n = 500$ )	Follow-up: Primary outcome collected at 24 weeks	Intensive, manualized, collaborative care-based, multicomponent treatment program specifically designed to be integrated with cancer treatment	Collaborative care model	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Treatment response, defined as <math>\geq 50\%</math> reduction in depression severity on the self-rated Symptom Checklist Depression Scale (SCL-20)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Average depression severity (SCL-20)</li> <li>Depression remission (SCL-20)</li> <li>Self-rated improvement in depression</li> </ul>	62% of participants in the collaborative care group and 17% of participants in the usual care group responded to treatment: absolute difference 45% (95% CI = 37 to 53), adjusted odds ratio 8.5 (95% CI = 5.5 to 13.4; $p < .001$ ). Significant between-group differences were found for average depression severity, self-rated improvement in depression, and remission of depression ( $p < .001$ for all)
Walker 2014	UK	Diagnosis of lung cancer and major depression ( $n = 142$ )	Follow-up: every 4 weeks until 32 weeks after randomization	Manualized, multicomponent collaborative care treatment systematically delivered by a team of cancer nurses and psychiatrists in collaboration with primary care physicians and integrated with lung cancer care	Collaborative care model	<p>Primary outcome:</p> <ul style="list-style-type: none"> <li>Summary measure of depression severity (SCL-20)</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>Self-rated depression improvement</li> </ul> <ul style="list-style-type: none"> <li>Anxiety (Symptom Checklist Anxiety Scale)</li> <li>Pain, fatigue, physical, social and role functioning, overall health, and quality of life (EORTC-QLQ-C30)</li> <li>Perceived quality of depression care</li> </ul>	Participants in the multicomponent collaborative intervention had lower average depression severity than did those allocated to usual care (difference $-0.38$ , 95% CI = $-0.58$ to $-0.18$ ; standardized mean difference $-0.62$ , 95% CI = $-0.94$ to $-0.29$ ). Self-rated depression improvement, anxiety, quality of life, role functioning, and perceived quality of care were significantly better in the intervention group. No between-group differences were found for overall health, social functioning, physical functioning, pain, and fatigue.

(continued)

Table 4. (continued)

Study	Country	Participants	Duration and follow-up	Care models	Theoretical basis	Outcomes	Results
Ye 2014	USA	Depression after hospitalization for acute coronary syndrome ( $n = 157$ )	Intervention: 6 months Follow-up: 6 and 12 months after end of treatment	Enhanced depression treatment involving stepped, patient preference-driven care with problem-solving therapy, pharmacotherapy, or both	Not stated	Primary outcome Composite outcome of death or hospitalization for myocardial infarction/unstable angina	At 6 months, death or hospitalization occurred in 3 (4%) participants in the intervention group, compared with 11 (14%) control group participants (HR = 0.25, 95% CI = 0.07–0.90, $p = 0.03$ ). At 12 months of additional follow-up, 11 (14%) participants in the treatment group experienced the composite outcome, compared to 3 (4%) in the usual care group (HR = 2.91, 95% CI = 0.80–10.56, $p = 0.10$ ).

**Table 5.** Categorization of models of care located in primary care—using the model elements defined in the Foundation Framework.

Author, year	Clinical focus										Organization of care delivery										Support for model delivery										Results		
	Self-management support	Biopsychosocial approach	Prevention focus	Polyparmacy/attention	Shared decision making	Mental health focus	Guidelines/protocols focus	Number of elements	Case care management	Integration social/community care	Integration secondary care	MDT/collaborative care	Home care	Co-location of services	Scheduled chronic appointments	Extended appointments	Nurse led	Group visits	Single professional responsible	24/7 support available	Trained by navigator/coach	Number of elements	Unpacking of primary care workforce	Education of professionals	Telephone management	Funding/payment change	Clinical IT linkage	Risk stratification tool	Telehealth	Primary care provider network	Number of elements	Total number of elements	Primary outcomes
Sommers 2000							3														6									3	12	Quality of life	✓
Schäfer 2018							4														3									1	8	Quality of life	✓
Salisbury 2018							6														5									3	14	Quality of life	-
Krka 2001							1														2									2	5	Pharmaceutical care issues	✓
Kamradt 2019							4														5									5	14	Healthcare use	-
Camacho 2018							4														3									2	9	Quality of life	-
Katon 2010							6														4									4	14	Mental health	✓
Kroenke 2019							3														3									2	8	Blood sugar, cholesterol and pressure	✓
Morgan 2013							4														5									2	11	Mental health	✓
Sajatovic 2017							5														2									2	9	Quality of life	✓
McCusker 2015							3														1									1	5	Functioning	✓
Bogner 2016							2														1									2	5	Disability	✓
Studies including the element (%)	11	5	4	5	9	8	3	8	2	2	7	3	1	8	2	2	2	1	1	2	-	8	7	7	1	3	0	1	2	-	-	-	-

included the highest number of participants, that is, 6,356, while studies in community and hospitals only included 1,322 and 2,099 participants, respectively. The duration of the studies in primary care ranged from 3 to 24 months, with community-care settings and hospitals ranging from a single visit to 6,5 months and 2–31 months, respectively (Table 1). Furthermore, the specific care models and the results regarding effectiveness are described in Tables 2–4.

**Categorization of models included in the review—using the Foundation Framework**

The theoretical basis of the models was reported in 15 of the 30 studies with Collaborative Care (6/30) and the Chronic Care Model (4/30) being the two most frequently used theoretical basis (Tables 2–4). The most common target population was patients with depression in combination with one other condition (17/30). In

Tables 5–7, the included care models are categorized according to the Foundation Framework. Regarding specific model elements in the care models, self-management support (25/30) and mental health focus (23/30) were the most used clinical focus across settings. Organization of care delivery mostly included scheduled chronic appointments (17/30), case management (17/30), and collaborative care (17/30). Support for model delivery most often consisted of telephone management (19/30) and education of professionals (16/30). The total number of model elements used in the models ranged from five to 14 (Table 5–7).

**Risk of bias**

Based on the EPOC criteria,<sup>31</sup> we judged the overall risk of bias in the included studies as low (Figure 3). Studies in primary care were primarily cluster-randomized, with the unit of randomization being the practice; thus, there is an

**Table 6.** Categorization of models of care located in community-based care settings—using the model elements defined in the Foundation Framework.

Author, year	Clinical focus								Organization of care delivery													Support for model delivery										Results	
	Self-management support	Biopsychosocial approach	Prevention focus	Shared decision making	Mental health focus	Guidelines/protocols focus	Number of elements	Case care management	Integration primary care	Integration secondary care	MDT/collaborative care	Home care	Co-location of services	Scheduled chronic appointments	Extended appointments	Nurse led	Group visits	Single professional responsible	24/7 support available	Trained lay navigator/coach	Number of elements	Upskilling of workforce	Education of professionals	Telephone management	Funding/payment change	Clinical IT linkage	Risk stratification tool	Telehealth	Care provider network	Number of elements	Total number of elements	Primary outcomes	Significant improvements
Druss 2018							5													3									0	8	Quality of life	✓	
Muralidharan 2019							3													2									2	7	Quality of life (mental)	✓	
Markle-Reid 2017							3													6									1	10	Quality of life (physical)	-	
Miklavic 2020							7													5								2	14	Quality of life (physical)	-		
Gellis 2014							4													3								3	10	Mental health	✓		
Fischer 2015							3													1								1	5	Mental health	✓		
Bove 2016							2													2								2	6	Mental health	✓		
Alexopoulos 2016							4													4								3	11	Mental health	-		
Sajatovic 2017							4													2								1	7	Mental health	-		
Studies including the element (%)	9	3	6	1	5	8	3	-	4	3	1	2	4	0	3	0	2	4	0	0	5	-	3	4	5	0	0	0	2	1	-		

**Table 7.** Categorization of models of care located in hospitals—using the model elements defined in the Foundation Framework.

Author, year	Clinical focus								Organization of care delivery													Support for model delivery										Results	
	Self-management support	Biopsychosocial approach	Prevention focus	Shared decision making	Mental health focus	Guidelines/protocols focus	Number of elements	Case care management	Integration primary care	Integration secondary care	MDT/collaborative care	Home care	Co-location of services	Scheduled chronic appointments	Extended appointments	Nurse led	Group visits	Single professional responsible	24/7 support available	Trained lay navigator/coach	Number of elements	Upskilling of workforce	Education of professionals	Telephone management	Funding/payment change	Clinical IT linkage	Risk stratification tool	Telehealth	Care provider network	Number of elements	Total number of elements	Primary outcomes	Significant improvements
Dunbar 2015							4													5									1	10	Quality of life	✓	
Heslop-Marshall 2018							3													3									2	8	Physical activity	✓	
Johansson 2019							3													2								3	8	Mental health	✓		
Kanwal 2018							6													3								2	11	Mental health	✓		
O'Moore 2018							2													1								2	5	Antiviral treatment	-		
Sharpe 2014							2													4								3	9	Mental health	✓		
Walker 2014							2													4								4	10	Mental health	✓		
Ekdahl 2016							2													4								1	7	Mortality	✓		
Ye 2014							4													5								1	10	Transfer to nurs. home	-		
Studies including the element (%)	6	0	3	2	7	7	3	-	5	2	4	7	4	0	6	0	3	0	0	0	-	2	4	7	0	1	2	3	0	-			

overall low risk of the control group being contaminated in those studies. However, the category “incomplete outcome data” were a risk of bias in some of the studies in primary care. Studies in community-based care settings had a high

risk of bias for more criteria than studies in other settings because many did not have similar baseline characteristics and had incomplete outcome data or a high risk of control group contamination. We judged the risk of selective

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Baseline outcome measurements similar	Baseline characteristics similar	Incomplete outcome data (attrition bias)	Knowledge of the allocated interventions adequately prevented during the study	Protection against contamination	Selective reporting (reporting bias)	Other bias
<b>Primary care</b>									
Bogner 2016	Low	Low	Low	Unclear	Unclear	Unclear	Low	Low	Low
Camacho 2018	Low	Low	Low	Unclear	Unclear	Unclear	Low	Low	Low
Kamradt 2019	Low	Low	Low	Low	Low	High	High	Low	Low
Katon 2010	Low	Low	Low	Low	Unclear	Low	Low	High	Unclear
Kroenke 2019	Low	Low	Low	Low	Low	Low	Low	Low	Low
Krska 2001	Unclear	Unclear	Low	Low	Low	Unclear	Low	Low	Low
McCusker 2015	Low	Low	Low	Low	Low	Low	Low	Low	Low
Morgan 2013	Low	Low	Low	Low	Unclear	Unclear	Low	Low	Unclear
Sajatovic 2017	Low	Low	Low	Low	Unclear	Unclear	Low	Low	Unclear
Salisbury 2018	Low	Low	Low	Low	Low	Low	Low	Low	Low
Schäfer 2018	Low	Low	Low	Low	Low	High	Low	Low	Low
Sommers 2000	Low	Low	Low	High	Unclear	Low	Low	Low	Unclear
<b>Community-based care settings</b>									
Alexopoulos 2016	Low	Low	Low	Low	Low	Low	High	Low	High
Bove 2016	Low	Low	Low	Low	High	Low	Low	Low	Low
Druss 2018	Unclear	Unclear	Low	Low	Unclear	Unclear	Low	Low	Low
Fischer 2015	Low	Low	Low	Low	Low	Low	Low	Low	Unclear
Gellis 2014	Low	Low	Low	Low	Low	Low	Low	Low	Low
Markle-Reid 2017	Low	Low	Low	Low	Low	Low	Low	Low	Low
Miklavcic 2020	Low	Low	Unclear	High	Unclear	Low	Unclear	Low	Low
Muralidharan 2019	Low	Low	Low	Low	Low	Low	Low	Low	Low
Sajatovic 2017	Unclear	Unclear	High	High	Unclear	Low	Low	Low	Unclear
<b>Hospitals</b>									
Dunbar 2015	Low	Low	Low	Low	Low	Low	Low	Low	Low
Ekdahl 2016	Low	Low	Low	Low	Low	Low	Low	Low	Low
Heslop-Marshall 2018	Low	Low	Low	Low	Low	Low	Unclear	High	Low
Johansson 2019	Low	Low	Low	Low	Low	Low	Low	Low	Low
Kanwal 2017	Low	Low	Low	Low	Unclear	Low	Low	Low	Unclear
O'Moore 2018	Low	Low	Low	High	Low	Low	Unclear	Low	Low
Sharpe 2014	Low	Low	Low	Low	Low	Low	High	Low	Low
Walker 2014	Low	Low	Low	Low	Low	Low	High	Low	Low
Ye 2014	Low	Low	Low	Low	High	Low	Unclear	Low	Low

Figure 3. Risk of bias.

reporting to be low; all but three studies reported all results for primary and secondary outcomes described in the methods sections. We also judged studies in hospitals as generally having a low risk of bias except for control group contamination, as most models took place in single hospital departments. Figure 3 provides detailed results of the risk of bias assessment.

**Outcome measures and effectiveness**

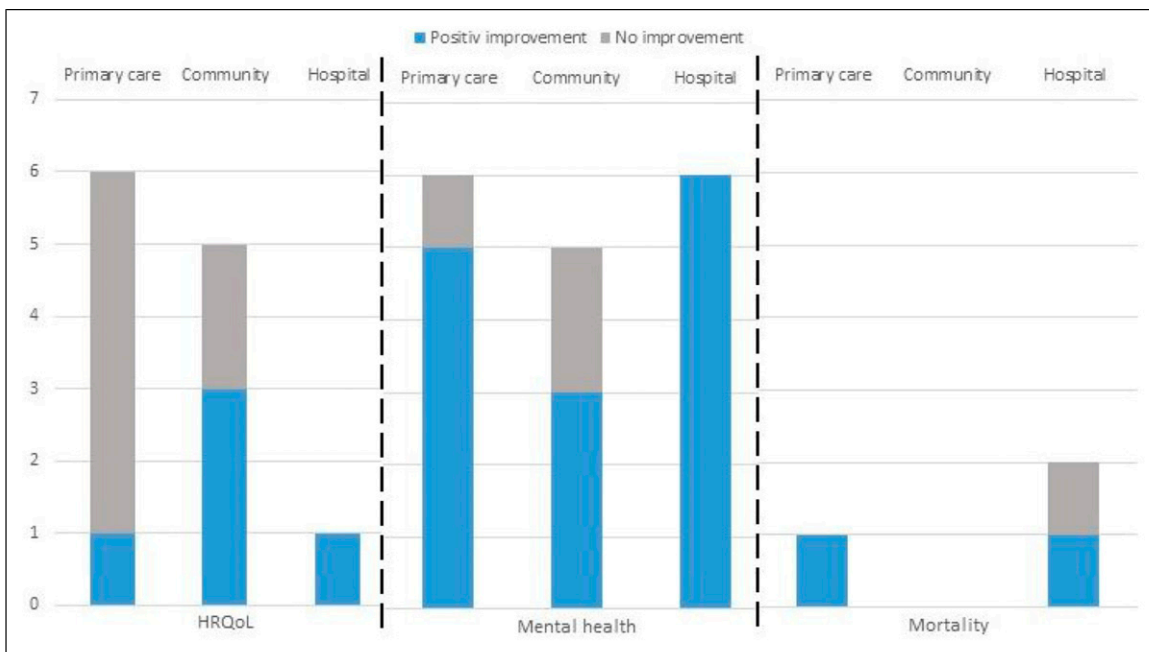
HRQoL was reported in 10 studies as the primary outcome measure, mental health in 15 studies, and mortality in three studies—two studies reported both HRQoL and mental health as the primary outcomes. HRQoL included specific outcomes such as disease-specific quality of life, health and functional status, physical functioning, and self-rated health. For mental health, specific outcomes included self-reported depression severity, depression and anxiety scores, a composite measure of pain, anxiety, and depression, psychiatric symptom severity, depression

improvement (including depression-free days, remission, and treatment response), and psychological distress. Mortality outcomes included standard outcomes for mortality such as survival time. Overall, 20 of the studies showed significant improvement in the primary outcome of interest—seven in primary care, five in communities, and eight in hospitals. Figure 4 shows the effectiveness of the care models for each of the three primary outcome measures HRQoL, mental health, and mortality—and divided for each of the settings primary care, community, and hospital.

In the following sections, the results from the 30 studies are reported separately for primary care, community-based care, and hospital settings (Tables 5–7).

**Primary care settings.** Overall, seven of the 12 studies taking place in primary care reported significant improvement in the primary outcome. Six studies reported outcomes for HRQoL,<sup>25,44–47,60</sup> and significant improvements were reported in only one of these studies.<sup>44</sup> The study, which found significant improvements in HRQoL, included three model





**Figure 4.** Effectiveness of the care models for each of the three primary outcome measures health-related quality of life (HRQoL), mental health, and mortality (x-axis)—and divided for each of the settings primary care, community, and hospital. The y-axis indicates numbers of care models. The blue color indicates positive improvements and the gray color indicates no improvements.

elements categorized as Clinical Focuses, six model elements characterized as Organization of Care Delivery, and three model elements characterized as Support for Delivery. Outcomes for mental health were reported in six studies,<sup>48–52,60</sup> of which five reported significant improvements.<sup>48–51,60</sup> These five studies had between three and six Clinical Focuses and between two and five model elements characterized as Organization of Care Delivery. One of the models included four model elements characterized as Support for Model Delivery,<sup>49</sup> while the four remaining models included two model elements characterized as Support for Model Delivery. The one study reporting mortality found a significant reduction in mortality and had two model elements in Clinical Focus, one model element characterized as Organization of Care Delivery, and two model elements characterized as Support for Model Delivery.<sup>53</sup>

**Community-based care settings.** Overall, five of the nine studies taking place in community-based settings reported significant improvement in the primary outcome. HRQoL measures were reported in five studies<sup>32,43,54–56</sup> and the outcome measures improved significantly in three of the studies.<sup>32,43,56</sup> The studies that reported significant improvements had between three and five model elements with a Clinical Focus, two or three model elements were characterized as Organization of Care Delivery, and between zero and three model elements were characterized as Support for Model Delivery. However, for two of these

studies, improvements were only observed for the mental health aspect of HRQoL.<sup>43,56</sup> Mental health was reported in five studies,<sup>33,56–59</sup> and in three studies, significant improvements were observed.<sup>33,56,58</sup> These care models included between two and four different model elements with a Clinical Focus, between one and three model elements characterized as Organization of Care Delivery, and between one and three model elements characterized as Support for Model Delivery.

**Hospital settings.** Overall, eight of the nine studies taking place in hospital settings reported significant improvement in the primary outcome. HRQoL was reported in one study and a significant improvement was found.<sup>34</sup> In this study, the care model included four Clinical Focus model elements, five model elements were characterized as Organization of Care Delivery, and one model element as Support for Model Delivery. Six studies reported results for mental health outcomes,<sup>35–40</sup> with significant improvements observed for all studies. These care models mostly included two or three Clinical Focus model elements, and one model included six Clinical Focus model elements, between one and four model elements characterized as Organization of Care Delivery, and between two and four model elements characterized as Support for Model Delivery. Two studies reported mortality,<sup>41,42</sup> and one of the studies found significant improvements.<sup>41</sup> The study reporting significant improvement in mortality included two model elements

with Clinical Focus, four model elements characterized as Organization of Care Delivery, and one model element characterized as Support for Model Delivery.

Across the three settings, no given number or combination of model elements was linked to improvements in the three outcomes.

## Discussion

In this review, we included 30 studies assessing the effectiveness of care models for persons with multimorbidity; 12 studies took place in primary care, nine in community settings, and nine in hospitals. Totally, 9,777 participants with multimorbidity were included in the studies. The studies included between five and 14 different model elements—with self-management support, mental health focus, case management, scheduled chronic appointments, and telephone management being the most frequent. The content of the care models showed a very high heterogeneity according to the defined multimorbidity populations and to the complexity of the care models. Twenty of the studies showed significant improvement in the primary outcome of interest; these were fairly evenly distributed across settings. However, the variations in target populations regarding type of conditions, number of conditions, the model elements, settings, and outcome measures are some of the topics that complicate drawing conclusions of the effectiveness of the care models for people with multimorbidity.

This is the first study to report effectiveness of care models in patients with multimorbidity in hospital settings—and the results indicate a strong tendency for studies taking place in hospital settings to show positive results. As previous reviews<sup>21,23</sup> only included studies performed in primary care and community settings, the studies from the hospital settings add important evidence to the field regarding effectiveness of care models in hospital settings. Further, there was a tendency for studies with mental health as the primary outcome to show positive results. This was in contrast to the previous review by Smith and colleagues in which they found “little or no difference to the main outcomes of mental health.”<sup>23</sup> However, most of included hospital setting studies in this review were not included in the Smith review because they were characterized as comorbidity studies—with patients having an index disease and any additional disease.<sup>61</sup> As all the included studies from the hospital setting reported positive improvements, the dissimilar results regarding mental health might be explained by reporting results from these studies, which are not included in previous reviews. Our findings concerning the outcome measure HRQoL were mixed, although we found a potential beneficial effect on HRQoL for some community-based care models. Overall, our results indicate that in many cases, the health outcomes, HRQoL, mental health, or mortality, among people with

multimorbidity can be improved if something beyond the usual care is provided. Despite the fact that 20 of the 30 studies reported improvement in the primary outcome, there is still no clear evidence to guide healthcare professionals in which care models or model elements to implement to improve effectiveness of care. The mixed results are in line with the results from the previous reviews of Smith et al., in which it was concluded that the effectiveness of models of care for multimorbidity is uncertain.<sup>21,23</sup> Only, three of the 30 included studies reported on mortality as primary outcome measure. This is not that surprising since it is challenging to improve mortality rates and often it requires a longer follow-up time for assessment.

The use of the Foundation Framework clarified the variety of the included model elements—regarding types, number, and combinations—which complicated conclusions regarding which elements were effective. We found that self-management support was the model element (Clinical Focus) most used in the care models—included in 25 of the 30 studies in this review. This agrees well with the fact that self-management has been assessed as one of the most effective elements in models of chronic care.<sup>62</sup> Further, case management and scheduled chronic appointments were most often used in the category Organization of Care Delivery. It is well-documented that patients with multimorbidity often describe care as fragmented, meeting many health professionals in different organizations, and challenges with information transfer between organizations.<sup>13,63,64</sup> Case management is expected to improve integrated care and supposedly, the patients’ perception of the care as more integrated, with one healthcare profession having the overall responsibility for the care plan, which might be the reason why case management is so often included in the care models. Interestingly, the newest review highlighted that self-management support and care coordination interventions may improve patients’ experience of care.<sup>23</sup> We found no obvious association between the number and types of model elements used in the models of care and the results of the outcome measures. None of the studies reported the implementation level of the model elements, which also complicates comparison of the model elements and their effectiveness. Process evaluation could be a valuable method to improve the understanding of which model elements are effective for whom under which circumstances.<sup>65</sup> Some studies mentioned parallel qualitative process assessment but also included key care processes as secondary outcomes, to open the “black box”.<sup>25</sup> This is, however, beyond the scope of this review but could be relevant to review in future work.

Even though the Foundation Framework originally was developed to characterize care models in primary care settings,<sup>19</sup> we applied the framework for care models implemented in community and hospital settings. We adapted

few of the model elements in the framework, before using them for the community-care and hospital settings. We found it reasonable to use the model elements defined in the framework for studies taking place in all three settings. The framework is based on the best available evidence, and it provides specific definitions of model elements constituting the care models. Using the framework ensured a systematic description of the care models and a nuanced categorization of the models based on their model elements.

Less than half of the included studies reported a theoretical basis of the care models of which Collaborative Care and the Chronic Care Model were the two most frequently used theoretical models.<sup>14,15</sup> None of the studies applied care models developed for multimorbidity, such as the WHO model, the SELFIE model, or the Multimorbidity Care Model.<sup>16–18</sup> This is problematic, as these frameworks for care models are developed to support the complex care provision needed in patient populations with multimorbidity. The models are expected to support integrated patient-centered care and so provide higher quality of care. The reason for not using the WHO, the SELFIE model, or the Multimorbidity Care Model can supposedly be explained by the fact that these models did not exist when many of the included studies were designed. Future research should benefit from these models when designing new studies to improve outcomes in patients with multimorbidity.

In the current review, we used the widely used definition of multimorbidity, namely, the coexistence of two or more chronic conditions in the same individual.<sup>1,2</sup> Despite all included studies met the inclusion criteria about referring to multimorbidity or two or more specific chronic conditions in the title or abstract, the included multimorbidity populations were very heterogeneous across the studies. Some of the studies in the present review included populations with specific chronic conditions; other studies had no condition-specific inclusion criteria and others again included populations with both somatic and psychiatric conditions. This variety in the definition of multimorbidity is a well-known problem in the research area of multimorbidity<sup>3–5</sup> and is a general challenge when comparing outcomes from studies in multimorbidity populations.<sup>4</sup> Furthermore, an ongoing discussion about a necessary distinction between the two closely related concepts multimorbidity and comorbidity is evolving.<sup>61</sup> In this distinction, comorbidity is seen as the co-occurrence of any additional disease entity in a patient who has the index disease, and multimorbidity is seen as the coexistence of two or more chronic conditions, where one is not necessarily more central than the others.<sup>61</sup> Multimorbidity is the more general term and individuals with comorbidity also have multimorbidity, but the reverse does not necessarily apply. Therefore, we choose not to consider comorbidity separately in our study. However, the varying definitions—

and the distinction between the two concepts—make the overall evaluation of outcomes of models of care for multimorbidity difficult because observed effects are likely specific to the conditions and the combinations of conditions being studied. Moving forward, there is a need to establish consensus about clinically meaningful definitions of multimorbidity—both for consensus in the research area and for the daily clinical work with patients.<sup>4</sup> We found that patients with depression in combination with other conditions were the most used targeted population in the included studies. This is not that surprising since this population includes patients known to have poor health—among other aspects, reflected in the significantly poorer HRQoL and higher mortality compared to the general population.<sup>66,67</sup> However, it is a difficult population to target because people with mental illness often have difficulties in receiving somatic care as needed for several reasons—and integrated care will be even more important for this patient group. Furthermore, for most included studies, particularly those in primary care and hospitals, participants were over the age of 50 years. The prevalence of multimorbidity is also high among younger individuals,<sup>68</sup> and the feasibility and effectiveness of models of care among younger populations merit investigation.

The difficulty of drawing conclusions on the effectiveness of complexity that characterize the care models of this study is a well-known problem.<sup>65</sup> Understanding the effect of models of care in patients with multimorbidity is, however, further complicated due to the different combinations of conditions with varying duration, levels of severity, and activity of the conditions, and with varying impact on patients' perception of their health status. In addition, it is becoming increasingly acknowledged that the single-disease approaches to measuring the quality of care for patients with multimorbidity do not capture the complexity of the processes involved in meeting the more multifaceted needs for this population.<sup>64</sup> The study from Smith et al.<sup>27</sup> is one of the first attempts to characterize a core outcome set for multimorbidity research and HRQoL, mental health, and mortality were the highest-ranked outcomes between 17 outcome measures; wherefore we focused on those three outcomes in this review.

### *Strengths and limitations*

A major strength of the current review is the systematic approach to identifying and including studies. Furthermore, the selection process is in accordance with PRISMA-guidelines and the use of the Foundation Framework secured detailed descriptions and comparisons of the models of care. Additionally, it is a strength that the review includes studies conducted in primary care, community care, and hospital—and not, as previous reviews, only primary care and community care. However, some limitations deserve attention as well. By

using the three highest-ranked outcomes from the core outcome set for multimorbidity, we excluded 11 studies (Figure 2). We are aware of the importance of this selection and for such, we could have included other outcomes and showed other results. However, we chose these three outcomes because it was the highest-ranked outcomes in the Delphi panel study by Smith et al. In the assessment of bias, we used the risk of bias criteria established by the Cochrane Effective Practice and Organisation of Care (EPOC) group, which is a recognized tool for assessment of bias. Assessment of Certainty through a specific GRADE assessment could have been considered. Due to the heterogeneity of the included studies, we used a narrative nature of our synthesis; this makes it difficult to draw conclusions about the potential effects of models of care. We addressed this by discussing the findings of the studies for each of the three settings when forming conclusions.

## Conclusion and implications

This review highlights the heterogeneity in the research area of multimorbidity. Due to different populations with different conditions, different settings, and use of different models and model elements, it is difficult to conclude and attain valuable evidence regarding effective care models and model elements. Despite the growing number of randomized controlled trials, the evidence regarding effectiveness of care models for people with multimorbidity remains unclear. In this review, 20 of the 30 included studies reported significant improvements in the primary outcome measure; however, it is still not clear which model elements are effective. The results indicate that “doing something” is better than doing nothing. This review has highlighted the need for further research in the area of effective care models for persons with multimorbidity and in multimorbidity in general. It is necessary to design investigations to clinically relevant manifestations of multiple chronic conditions. Further, more research is needed to clarify which model elements are effective and which elements are effective in combination.

## Acknowledgments

We thank Anne Jung, specialist, Charlotte Weiling Appel, registered nurse, and Finn Thomsen Nielsen, specialist, who provided clinical insight and expertise that greatly assisted the research.

## Contributor and guarantor information

CUE is the guarantor of the submitted work. AF is the senior author. CUE planned the searches in collaboration with AF; conducted the searches; carried out study selection in collaboration with NKL, NG, and AF; assessed methodological quality in collaboration with SALH and HB; and extracted and synthesized findings in collaboration with AF, NKL, and JSA. CUE and NKL wrote the manuscript. All authors critically revised the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

## Declaration of conflicting interests

All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: CUE and SALH received financial support from the Danish Health Authority; no authors had financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

## Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by The Danish Health Authority. No funding body has influenced the study design; data collection, analysis, and interpretation of data; the writing of the report; and in the decision to submit the article for publication.

## Data availability statement

All data relevant to the study are included in the article or uploaded as supplementary information.

## Transparency declaration

The guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned have been explained.

## Prospero registration number

CRD42019119490.

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## Supplementary material

Supplementary material for this article is available online.

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