

Bijlage C Systematische literatuuranalyse

Search and select

A systematic review of the literature was performed to answer the following primary question: what kind of methods have been described in literature for a multidisciplinary assessment of patients with multimorbidity in intervention studies?

P: Patients with multimorbidity

I: multidisciplinary assessment involving at least two medical specialists, or two care organizations (such as primary care physician and medical specialist)

The secondary question is: what is the effect of the multidisciplinary assessment compared to usual care?

P: Patients with multimorbidity

I: multidisciplinary assessment involving at least two medical specialists, or two care organizations (such as primary care physician and medical specialist)

C: Usual Care

O: Primary outcome measures as defined by authors, time investment, patient- and care team experiences

Relevant outcome measures

The guideline group considered time investment, patient- and care team experiences as relevant outcome measures for decision making; and will report on primary outcome measures defined by the individual studies. No distinction was made between crucial and important outcome measures.

Search and select (Methods)

The databases Ovid/Medline, Embase.com, and Ebsco/Cinahl were searched with relevant search terms from 2001 until 8-7-2021. The detailed search strategy is depicted under the tab Methods. The systematic search resulted in 2487 hits. Studies were selected based on the following criteria:

- Systematic review, RCT or observational studies;
- Written in English/Dutch language;
- Describing a multidisciplinary assessment for patients with multimorbidity. Multidisciplinary assessment was defined as a collaboration between two or more medical specialists, or across two or more organizations, of which one organization comprises specialist care;
- Multimorbidity was defined as patients with at least two chronic diseases.

Ninety (90) studies were initially selected based on title and abstract screening. After reading the full text, 73 studies were excluded (see the table with reasons for exclusion under the tab Methods). Another 5 relevant articles were identified through reference checking. Fifteen unique studies were included.

Results

Fifteen studies were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables.

Summary of the literature

Defining target population for the intervention

Four studies included patients with concordant multimorbidity: diabetes mellitus and chronic kidney disease. Five studies included patients with an index disease and comorbid depression. Six studies included patients with discordant multimorbidity. Two studies included patients with two or more chronic conditions, one study included patients with three or more chronic condition. One study included “super utilizers” defined as patients with more than two inpatient admissions over the past 12 months and/or more than 6 emergency department (ED) visits over the past year, and answered ‘yes’ to the question: Would you like us to help you stay out of the emergency room and the hospital? Another study included patients with two or more physicians involved and at least two failed treatments, and who required appointments in addition to those scheduled and extra phone calls or e-mail. And finally, one study included community-dwelling frail older adults, using Resident Assessment Instrument-Home Care (RAI-HC) as frailty assessment, and the Contact Assessment tool derived from the InterRAI set of tools as frailty score calculator.

Elements of multidisciplinary assessment and team members according to patient population

Multidisciplinary assessments concerning concordant multimorbidity often included self-management support, patient education, diet and other lifestyle interventions. In one study, a care manager was appointed. Multidisciplinary assessment concerning an index disease and comorbid depression often included a care manager and/or coordinator, pharmacotherapy (adherence) monitoring, self-management support, behavioral therapy and lifestyle intervention. In one study, patient education was part of the intervention.

Multidisciplinary assessments concerning discordant multimorbidity always involved the primary care physician as a member of the team, in addition to a varying number of medical specialists. A nurse was a member of the team in five studies. Other members of the team that were frequent were a dietician, social worker, occupational therapist and a pharmacist. Services provided included frailty assessment (in two studies), patient education (in two studies), care coordination (four studies), self-management (two studies), 24/7 availability of a member of the care team for emergencies (three studies).

Description of studies

Bryk (2018) conducted a pre-post intervention study in the outpatient setting of a primary care facility in the United States. Super utilizers were enrolled in the study, defined by more than two inpatient admissions over the past 12 months and/or more than 6 emergency department (ED) visits over the past year, and answered ‘yes’ to the question: Would you like us to help you stay out of the emergency room and the hospital? Follow-up time was 6 months. The care team consisted of the primary care physician (PCP), nurse care manager, social worker, administrative assistant, psychologist who was collocated with the PCP, psychiatrist and other clinicians based on patient needs. The multidisciplinary assessment was embedded in an Enhanced Care Program (ECP). An initial intake appointment was conducted, which included a full medical and psychosocial assessment. An ECP care plan was created that addresses physical, mental, financial, environmental

and functional health. This was placed in the electronic medical record and could be updated by any member of the team at any time. The ECP provided co-management of mental illness by PCP, psychiatrist and psychologist. ECP provided walk-in clinic visits, home visits, was equipped for care of urgent issues such as emergent blood work, same day scheduling of imaging and procedures, 24/7 phone access to care manager. ED care plans were made to direct patient care to the ECP PCP for non-life-threatening conditions. The ECP also provided education (diabetes, diet, self-monitoring blood pressure) and delivery of medication by local pharmacy. ECP social worker assisted patients with medical costs. All patients were seen for routine checks at least monthly and contacted by their nurse care manager at least monthly. Cancer screenings for cervical, breast and colon cancer were reviewed at each patient encounter.

Chung (2013) conducted a pre-post intervention study in the outpatient, primary care setting in the United States. They included 79 patients with chronic illness (Diabetes Mellitus, coronary artery disease and/or chronic heart failure), at least one abnormal indicator (blood pressure >140/90, Hba1c >8, LDL>100) and comorbid depression (PHQ-9 score \geq 10). Follow up time was after a minimum of 8 weeks. The care team consisted of a primary care physician (PCP), nurse, behavioral health manager (BHM), accountable care manager (ACM) who were experienced registered nurses, and a consulting psychiatrist. The multidisciplinary assessment was embedded in a “synergy program”. In this program, cases were reviewed with a focus on medical indicators (blood pressure, Hba1c, LDL) and depression indicators (PHQ-9 score) as well as overall psychosocial function. The ACM did a psychosocial assessment by phone focused on chronic illness care, medication reconciliation and self-management approaches including motivational interviewing and behavioral activation. The ACM also coordinated with the PCP and other specialists on medical issues and assists with appointments. The BHM evaluated cases onsite and provided psychotherapy, he/she liaised with the psychiatrist and PCP. The PCP educated patients on depression diagnosis and the potential negative impact. The PCP also managed antidepressants with consulting psychiatrist reviews provided through the electronic medical record. If patients did not reach their treatment target or were complex, the psychiatrist provided an individual patient consultation. BHM and ACM documented on the same care management electronic record for coordination and information sharing.

Fogelfeld (2011) conducted a randomized controlled trial of patients between the ages of 18-70 years old, with Diabetes Mellitus type 2 (DMII), chronic kidney disease (CKD) stages 3 and 4 and normal cognitive function. Follow-up time was 2 years. The study was set in the outpatient clinic of a large public hospital in the USA. Fogelfeld compared a multifactorial-multidisciplinary intervention (n=60) to usual care (n=60) The care team consisted of an endocrinologist, nephrologist, diabetes educator and nurse practitioner. The multifactorial-multidisciplinary intervention began with group diet instructions followed by individual visits at an interdisciplinary clinic with the entire care team. Clinic visits took place every month for the first 6 months, followed by every 2 months for 18 months. Additional follow-up visits were planned if needed to reach treatment targets, or case managed with more frequent phone contact if assessed as needing more intensive follow-up. **Khuzively (2018)** conducted a post-legacy effect study of Fogelfeld (2011). Two years after cessation of the intervention, post-trial data was available for 72 patients (n=38 postintervention group vs. n=38 in usual care group).

Frankel (2014) conducted a pre-post intervention study in a psychiatric outpatient clinic of the United States. They included 52 outpatient cases, 12-76 years old, with two or more physicians involved and at least two failed treatments, and who required appointments in addition to those scheduled and extra phone calls or e-mail. Follow-up was at least 18 months. The care team

consisted of a psychiatrist, primary care physician, additional clinicians based on patient needs, pharmacist consultant, social workers, case managers and psychologists. The multidisciplinary assessment was embedded in a Medical-Psychiatric Coordinating Physician-led (MPCP-led) model of care. The MPCP is a psychiatrist who directed or may be embedded in a multidisciplinary office-based team or clinic, taking a clinical leadership role in each situation. The MPCP took the major responsibility for treatment team management and tracking treatment outcomes of both psychiatric and medical diseases. The MPCP communicated with the entire psychosocial-medical system surrounding each case at least weekly, including the referring PCP. The MPCP also organized ongoing consent-based collaboration with the patient's family members, oversaw adherence treatment, managed medication-related complications, resolved differences among team members to maintain treatment cohesion. The MPCP may also provide psychiatric consultation and care.

Goorden (2017) conducted a randomized controlled trial of patients with moderate to severe Major Depressive Disorder (MDD) and a chronic physical condition (diabetes mellitus, chronic vascular disease or chronic obstructive pulmonary disorder) in the outpatient clinic of a general hospital in the Netherlands. Goorden compared a collaborative care model (N = 42) to usual care (N = 39). Follow-up time was 12 months. The care team of the collaborative care model consisted of a medical specialist, the department nurse, a consultation-liaison psychiatrist and a consultant psychiatric nurse (CPN). The medical specialist provided treatment for the chronic physical condition, the department nurse screened for MDD and referred to the psychiatrist and CPN. The CPN acted as care manager and provided problem solving treatment as well as guided self-help. The psychiatrist prescribed antidepressants. Usual care consisted of the advice to seek treatment for depressive symptoms for a primary care physician if they felt the need.

Kanwal (2016) conducted a randomized controlled trial of patients with hepatitis C virus (HCV) infection and Major Depressive Disorder at an HCV clinic at US department of Veterans Affairs (VA) facilities. Kanwal compared a collaborative care model (N = 114) to usual care (N = 128). Follow-up time was 6 months. The care team of the collaborative care model consisted of nurses, clinicians and physician assistants of the HCV clinic and a depression care team: nurse depression care manager (DCM), a pharmacist and a psychiatrist. The depression care team was located off site and convened once a week and as needed by telephone or in person. The depression care team communicated with treating HCV clinicians and mental health clinicians (if patients were seen by both) via electronic medical record progress notes. The DCM communicated with patients via telephone. The depression care team made treatment suggestions. Treatment decisions were made by the HCV or mental health clinicians in partnership with the patient. The DCM delivered participant education and activation, assessment of treatment barriers and possible resolutions, depression symptom and treatment monitoring, and substance abuse monitoring. The intervention team used a stepped-care model for depression treatment, monitoring treatment was done by the DCM. A clinical pharmacist did a medication review and recommended pharmacotherapy. Usual care consisted of referral to specialty mental health clinics or depression treatment at primary care-mental health clinics.

Lin (2010) conducted a randomized controlled trial of patients with depression and uncontrolled diabetes and/or coronary heart disease at primary care clinics in the U.S.A. Lin compared a TEAM care intervention (N = 106) to usual care (N = 108). Follow-up time was 12 months. The TEAM care team consisted of a nurse care manager (NCM), primary care physician (PCP), medical consultants, psychiatric consultants and psychologists. Prior to the first TEAMcare visit, the NCM reviewed the patients electronic medical record (EMR), discussed the patient with the TEAMcare physician consultants. The intervention began with a comprehensive face-to-face biopsychosocial assessment (first visit NCM) and included goal setting and formulating "my health plan": self-management

support, monitoring of disease indicators, and pharmacotherapy with frequent treatment adjustments to control depression, hyperglycemia, hypertension and hyperlipidemia. Patients, PCPs and patient together created individualized health plan. PCPs prioritized patient's treatment goals, directed treatment titration and specified specialty consultations to help patients achieve treatment targets. The EMR flagged patients who were not making progress on PHQ-9 scores, Hba1c, LDL or blood pressure levels. TEAMcare clinician consultants included two psychiatrists, an internist, a family medicine physician and a psychologist. They conducted a weekly caseload review (treat-to-target review) with the NCMs. Specialty consultations with a diabetologist and or cardiologist were available if needed. Other interventions by the NCM included enhancing medication adherence, pain assessment, behavioral activation to increase confidence and self-efficacy, enhance self-monitoring, promoting smoking cessation, physical activity, pleasurable activities, healthy eating and sleep hygiene. Initial visit frequency was once a week in person, and phone follow-up between weekly visits with more complex patients. Patients could contact NCM on their cell phones. With patients who made progress, visit frequency was decreased to biweekly. This frequency was further reduced once the patients achieved their goals, and eventually they were transitioned back to care with their PCP team. This included a transition to a maintenance care plan and relapse prevention plan for depression and other uncontrolled chronic diseases. The researchers developed a care management tracking system to operationalize systematic chronic illness care: proactive monitoring of outcomes, alerts for patients lost to follow up, and flagging patients who did not achieve their targets.

Weekly caseload review: priorities were new enrolled patients, patients with persistent poor disease control, patients who have not been successfully contacted for a defined number of weeks, patients who were a concern to the NCM or supervisors, patients who presented relationship challenges, patients with PCPs who were more challenging to work with. The supervising physician recommended treatment, which was communicated by the NCM to the PCP who then decided on the actual treatment changes.

Rayner (2011) conducted a pre-post intervention study in the United Kingdom, involving 1002 patients younger than 65 years old, with diabetes mellitus (DM) and estimated glomerular filtration rate (eGFR) $<50\text{ml/min}/1.73\text{m}^2$ with decline over time, not receiving renal replacement therapy or attending pre-dialysis specialty clinics. Follow-up time was 4 years. The care team consisted of the endocrinologist, nephrologist and primary care physician. The multidisciplinary assessment consisted of a weekly database review to identify patients with deteriorating eGFR. The database consisted of all patients who attended diabetes clinics in the area, and included laboratory samples taken in the community and hospital. The surveillance activity took approximately 1 hour per week of the nephrologist's time. Specialist diabetes-kidney clinic visits were offered every 2-4 months until home blood pressure was controlled or eGFR decline slowed. The patients were then referred back to primary care and the nephrologist continued to monitor the eGFR remotely. Education, blood pressure management, diet and self-management support as well as referral for smoking cessation support were offered.

Low (2018) conducted a case-control cohort study in a secondary care diabetes center in Singapore. They compared patients referred to a joint endocrinologist-nephrologist clinic (n = 418 cases) to patients from the same population with the same inclusion criteria but not seen at this joint clinic (n= 419 controls). Median follow-up time was 3 years. Inclusion criteria were diabetes mellitus (DM) and chronic kidney disease (CKD) stages 3-4. The care team consisted of a senior nephrologist and endocrinologist, advance practice nurses (APN), clinical pharmacists, dieticians and social workers. In the clinic, the nephrologist and endocrinologist provided joint consultations with the patient and caregiver. The clinic was supported by the other members of the care team, who helped reinforce

lifestyle management plans, monitoring and titrate medication between physician visits. Monthly staff education sessions were organized to facilitate cohesion of the multidisciplinary team.

McMurray (2002) conducted a randomized controlled trial in two outpatient dialysis units in the United States. Patients with end-stage renal disease (ESRD) requiring renal replacement therapy with either hemodialysis (HD) or peritoneal dialysis (PD) in combination with diabetes mellitus (DM) were included. Follow-up time was 1 year. McMurray compared a multidisciplinary intervention (n= 45) to usual care (n= 38). The care team was composed of a DM care manager, multidisciplinary diabetes advisory committee, renal dietician, and a nephrologist. The DM care manager provided self-management education and motivational coaching during thrice-weekly HD treatments. The DM care manager also routinely monitored blood pressure, lipids, and glycemia and reviewed this together with the physician primarily responsible for the patient (often nephrologist). The DM care manager also performed follow-up foot checks and gave reminders for annual eye examinations. Dietician provided nutrition counseling. Multidisciplinary diabetes advisory committee met quarterly throughout the study period to provide program oversight quality.

Nieto-Martin (2019) conducted a pre-post intervention study in the outpatient setting in Spain. They included 420 adults with two or more chronic conditions, excluding cancer patients and patients on hemodialysis or waiting for a transplant. Mean age was 77.3 years, mean Charlson Comorbidity Index was 3.99. Follow up time was 12 months. The care team was composed of an internal medicine physician (IM), team care nurses (TCN), hospital pharmacist (HP) and general practitioner (GP). The multidisciplinary assessment consisted of the IM constructing a personal therapeutic plan (pharmacological and non-pharmacological) and a structured medical visit 15 days after inclusion. There was an availability of programmed admissions to avoid the emergency room, and there was the availability of a medical visit within 24 hours if necessary. The TCN ensured the continuity of the care plan, provided education workshops for patients and caregivers. The HP evaluated treatment compliance and appropriateness of treatment and implemented interventions to improve treatment compliance. The GP performed an evaluation of function and cognition, and provided risk stratification to identify patients who need high level care and contacted the IM.

Pariser (2019) conducted a pre-post intervention study in the outpatient setting in Canada. They included 76 patients with three or more chronic conditions. Follow up time was not reported. The multidisciplinary assessment was embedded in the Telemedicine IMPACT Plus (TIP) care model. The care team consisted of a registered TIP nurse, the TIP team (specialists from psychiatry and internal medicine, a social worker, pharmacist, home care and community coordinator, other professionals based on patient's needs such as occupational therapist or dietitian), and the primary care physician (PCP). The dedicated TIP nurse met with the PCP and patient in advance to prioritize issues most important to the patient. The TIP nurse enhanced self-management and care coordination, aligned care and goals with appropriate reduction in medications and serial specialists consultations, and equipped the PCP with local resources. A clinical consultation using videoconference took place with the PCP in his office, the patient at home, and the TIP team present as well. The team developed recommendations that formed the nucleus of a coordinated care plan. The TIP nurse helped with follow-through of team's recommendations together with the patient's PCP. The TIP nurse invested 6.1 hours per patient on average (2.4 hour preintervention, 2.0 hour for intervention, 1.7 hour postintervention). The multidisciplinary conference lasted 1 hour.

Pollina (2017) conducted a prospective non-randomized controlled trial including community dwelling frail and dependent people of 60 years and older, in Switzerland. Follow-up time was 5-41 months (mean 16.3). Pollina compared a multidisciplinary intervention (n=122) to usual care (n=170). The care team was composed of a primary care physician (PCP), home visiting nursing service centers

(HVNS), Nursing Teams (NT) and Community Geriatric Unit (CGU). Patients in the intervention group received care as usual by their PCP and NT, and in addition were provided with an in-home geriatric assessment by the CGU doctor. This assessment included functional and cognitive status, nutrition and medication review. Results were transmitted in writing to the PCP and NT with recommendations, and in case of complex issues, meeting between the CGU and NT were organized. Participants and NT received writing instructions to first contact the PCP in case of an emergency, if unavailable, the CGU provided 24h/7days a week medical call service. CGU also had a day hospital.

Sampalli (2012) conducted a pre-post intervention study in the outpatient setting in Canada. They included 20 adult patients with two or more chronic conditions, with a mean age of 42 years and a mean number of chronic conditions of 3.75. Follow-up time was 6 months. The care team was composed of clinicians from different disciplines, an occupational therapist, nurse and primary care physician (PCP). The multidisciplinary assessment consisted of an intake phase, intervention phase, transition phase and discharge phase. During the intake phase, a physician drew up a diagnosis and symptom profile, an occupational therapist drew up coordination and rehabilitation needs, and a nurse provided education. During the intervention phase, the patient had a multidisciplinary care appointment with multidisciplinary clinicians, individual and group interventions and education programs that addressed the needs of the whole person. The individual interventions included occupational therapy, dietary management, counseling and return to work support. Group interventions included mindfulness, tools to manage ADL, pain and fatigue management. During the transition phase, readiness for discharge was evaluated by the occupation therapist. During the discharge phase, the patient was discharged to the PCP. Between each phase there was a care coordination appointment.

Van Eck van der Sluijs (2018) conducted a systematic review, including 20 RCTs or cluster RCTs that evaluated the effect on physical outcomes of collaborative care for patients with chronic medical conditions and co-morbid depression or anxiety disorders. The total number of patients in these trials was 4774. The collaborative care model consisted of a care manager (CM) with training in the treatment of depression and anxiety disorders, a medical doctor (GP, medical specialist and/or pharmacist) and a psychiatrist. The CM had regular contact with the patient and organized care in collaboration with the medical doctor and/or pharmacist, supervised by the psychiatrist. Focus was on monitoring symptoms and adherence to medication and other treatments, and the CM may have provided psychotherapy such as Problem Solving Treatment (PST). The authors included articles from 2003-2015 but did not explicitly state the window of their search.

Results

Quality of life

Five studies assessed quality of life as an outcome measure, all studies showed a positive effect of the intervention on quality of life.

The RCT of Goorden (2017) showed that the quality of life significantly improved over time in the collaborative care group (0.07 (95% CI 0.02-0.13) compared to baseline, using the EQ-5D. The difference in effect between groups was not significant over time (0.07 (95% CI -0.003-0.14).

The RCT of McMurray (2002) showed that the quality-of-life assessment category of diabetes symptoms improved significantly after the multidisciplinary care intervention ($p < 0.001$), as well as a significant improvement in patient health perception ($p < 0.002$). There was no significant improvement in social functioning, role limitations and mental health score.

The pre-post intervention study of Frankel (2014) showed that health-related quality of life (HR-QOL), measured by a modified version of the Centers for Disease Control Health-Related Quality of Life measure, improved significantly for general health (2.54 ± 1.03 to 2.12 ± 1.06 ($p < 0.001$)). The HR-QOL sick days per month decreased (11.22 ± 7.76 to 6.60 ± 7.51 ($p < 0.0001$)). No effect was seen on other indices on HR-QOL, including pain and physical activity.

The pre-post intervention study of Chung (2013) showed that the mean score of the answer to the question: "Overall, I feel my health has improved because of the program" was 4.0 (SD 0.95) indicating 'agree' on a 5-point Likert scale.

The pre-post intervention study of Sampalli (2012) showed that the rating of health since onset of illness improved after the multidisciplinary intervention (1: worst, 7: best possible): mean score increased from 2.62 ± 1.2 to 6.2 ± 2 ($p < 0.001$). Fatigue symptoms (1: no symptoms, 12: worst) decreased from 7.3 ± 2.4 to 2.8 ± 1.1 ($p < 0.001$). Pain (1: none, 12: worst) did not improve significantly (6.4 ± 2.5 to 4.5 ± 1.3 $p = 0.06$).

QALY

One study assessed QALY.

The RCT of Goorden (2017) showed that the average QALY gained in the collaborative care group was 0.07 higher than in the usual care group, indicating that CC is more costly but also more effective than CAU. The incremental cost-effectiveness ratio was calculated as 24.690/QALY in euros.

Disease-specific outcomes

Ten studies included disease-specific outcomes in their analysis. All studies showed improvements in some or all of the disease-specific outcomes measured.

The RCT of Kanwal (2016) showed no difference in treatment response along the 20-item Hopkins Symptom Checklist (SCL-20) for depression symptom severity at six months. At twelve months, the collaborative care group had a higher treatment response (31.6% v.s. 14.8% $p = .002$) and higher rates of remission (19.3% v.s. 7.0%). There were no significant differences between groups for depression free days and antiviral treatment.

The RCT of Lin (2010) showed a significant improvement in HbA1c (-1.20 (95% CI -1.76 - -0.63) among patients with less favorable medical controls at baseline who received TEAMcare. No significant difference was found for blood pressure and lipid control. For patients with favorable medical

controls at baseline, no significant improvements were found for Hba1c, BP or lipid control in the intervention group.

The pre-post intervention study of Rayner (2011) showed significantly lower rate of eGFR decline after intervention in an analysis of 66 patients: $-5.2 \text{ ml/min/1.73m}^2/\text{year}$ prior to attending the clinic to $1.1 \text{ ml/min/1.73m}^2 / \text{year}$ afterwards until death, renal replacement therapy or up to 4 years of follow up ($p < 0.001$). Fewer patients with diabetes started renal replacement therapy after the introduction of the model of care.

The RCT of Fogelfeld (2011) showed that a lower proportion of patients developed end stage renal disease after the multifactorial-multidisciplinary intervention compared to usual care (13 vs. 28%, $p < 0.05$). Two years after cessation of the two-year multifactorial-multidisciplinary intervention, no significant differences between groups were found.

The case-control cohort study of Low (2018) showed that a multidisciplinary clinic group had a lower risk of progressing to stage 5 CKD (hazard ratio 0.55; 95% CI 0.36-0.84; $p = 0.004$) compared to the non-interdisciplinary group.

The RCT of McMurray (2002) showed an improvement in Hba1c in the intervention group (6.9% to 6.3%, compared to 7.0 to 7.2 in the control group ($p = 0.006$)), as well as no severe hypoglycemic events, no progression of neuropathic disease (progression in control), no amputations (5 lower extremity and 2 finger amputation in control) and foot risk assessment scores remained unchanged in intervention (2.0 to 2.2) and worsened in controls (2.7 to 3.3).

The pre-post intervention study of Bryk (2018) showed an improvement in Hba1c after implementation of an enhanced care program, as well as improvement in blood pressure. Retinal eye examination completion improved by 33%. Treatment for patients with previously untreated mental illness improved. 19% of 71 patients on opioids were weaned off. Colorectal cancer screening improved. No improvements were found for foot exam completion, cervical- and breast-cancer screening.

The pre-post intervention study of Frankel (2014) showed that symptom severity of anxiety (25.27 ± 7.5 to 18.13 ± 5.74 ($p < 0.001$)) and depression (22.02 ± 7.10 to 14.58 ± 6.46 ($p < 0.001$)) significantly decreased, measured by the Hamilton Depression (HAM-D) and Anxiety (HAM-A) Rating Scales. 44 out of 52 patients met two of three following criteria: reduction in health care utilization, improvement of treatment adherence, and/or reduction of symptom severity.

The systematic review of van Eck van der Sluijs (2018) calculated and pooled effect sizes for both physical and depressive outcomes using a weighted mean that should indicate a combined assessment of illness burden. The overall OR was 1.64 (95% CI 1.47-1.83) with an overall effect size of $d = 0.27$, 95%CI 0.21-0.33, favoring collaborative care (CC). Depressive outcomes also favor CC: OR 1.90 (95%CI 1.70-2.12), effect size of CC was $d = 0.35$ (95% CI 0.29-0.42). Results were significant for all chronic medical conditions (HIV, COPD, multimorbidity, arthritis, cancer and ACS), except for DMII and epilepsy. The highest OR was found for hypertension (4.18, 95% CI 2.18-8.05; $d = 0.79$, 95%CI 0.43-1.15).

The pre-post intervention study of Chung (2013) showed an improvement in PHQ-9 in 44% of patients after the multidisciplinary intervention, and remission in 15% of patients. Reduction of Hba1c of more than 0.5% was seen in 33% of patients. The mean Framingham score reduced by 34% (28.3 to 18.8).

Self-care management activities

Two studies assessed self-care management activities, and both studies showed an improvement after intervention.

The RCT of Lin (2010) showed that at twelve months, average rate of blood pressure self-monitoring was higher in the intervention group (3.6 vs. 1.1 days per week, RR = 3.20 (p<0.001)). The average blood glucose monitoring rate was 4.9 days per week for the intervention group vs. 3.9 days in the usual care group (RR = 1.28, p=0.006).

The RCT of McMurray (2002) showed significant improvements in self-management behaviors, including monitoring blood glucose levels (90 vs. 66%, p=0.023), and undergoing a yearly dilated eye-examination (93 vs. 55%, p=0.001).

Self-efficacy

Three studies assessed self-efficacy as an outcome measure. All showed an improvement of some or all of the questions measuring self-efficacy after intervention.

The RCT of Lin (2010) showed a significant difference between answer value means of one out of four questions relating to self-efficacy, favoring the intervention group: "I am confident that I can maintain lifestyle changes like diet and exercise even during times of stress" (measured on a 4-point Likert scale). There were no differences between groups in answers to the following questions: "I know what each of my prescribed medicines do", "I am confident that I can follow through on medical regimes that are important in managing my health conditions", "I am confident that I can figure out solutions when new situations or problems arise with my health condition".

The RCT of McMurray (2002) showed an improvement in self-knowledge. Both intervention and control group scored 74% on the knowledge assessment test at baseline. After 12 months of education and care management, the study group answered 90% of questions correctly, and the control group was unchanged (p<0.001).

The pre-post intervention study of Chung (2013) showed that the mean score of the answer to the question: "I know more about how I can be more responsible for my health because of the program" was 4.1 (SD 0.92) indicating 'agree'. The mean score of the answer to the question: "I know more about how my mental health affects my physical health because of the program" was 4.3 (0.71), indicating 'agree'.

Mortality

One study assessed mortality as an outcome measure.

The RCT of McMurray (2002) showed no change in mortality between the intervention and the control group.

Health Care Utilization

Four studies assessed health care utilization as an outcome measure. Three studies showed a decrease of health care utilization after intervention. One study showed an increase of health care utilization after intervention.

The RCT of McMurray (2002) showed fewer diabetes/vascular related hospitalizations in the intervention group (n=10) compared to the control group (n=1) (P<0.05).

The systematic review of van Eck van der Sluijs (2018) showed that more procedures were performed in the collaborative care model compared to care as usual, with an OR of 2.25 (95%CI 1.67-3.05), $d = 0.45$ (95%CI 0.28;0.61).

The pre-post intervention study of Nieto-Martin (2019) showed that the number of hospital admissions decreased significantly compared to the previous year (mean decrease of 0.67, SE 0.09). Number of days of hospitalizations decreased significantly as well compared to the previous year (mean decrease of 7.39, SE 0.95).

The non-randomized controlled trial of Pollina (2017) showed no difference in the number of hospitalizations between the group who had received the multidisciplinary assessment by the Community Geriatrics Unit and the usual care group. Unnecessary hospitalizations for social reasons were significantly less frequent in the IG (4.1% v.s. 11.7%, $p=0.03$). Length of hospital stay was lower, but not significantly, in the intervention than in the control group (37.5 vs. 51.0 days $p = 0.18$).

Patient experiences

Three studies assessed patient experiences as an outcome measure. All studies showed that the interventions were positively experienced.

The pre-post intervention study of Chung (2013) showed that the mean score of the answer to the question: "My care team gave me choices when we talked about how to treat my depression" was 4.0 (SD 0.93); 4 corresponding to 'agree' on the five-point Likert Scale. The mean score of the answer to the question: "My care team valued my opinion when we talked about how to treat my depression" was 4.0 (0.97), indicating 'agree'. Patients thought the behavioral health manager, nurse care manager and psychiatrist worked 'very well' with the primary care doctor (BHM 4.1 (0.92), NCM 4.4 (0.67), 4.0 (1.18). 4 indicating 'very well' 5 indicating 'extremely well').

The pre-post intervention study of Pariser (2019) showed that 100% of patients agreed with the statement "TIP has effectively improved my access to new interdisciplinary resources", 97% agreed that "I am hopeful that my chronic condition will improve as a result of the TIP case conference".

The pre-post intervention study of Sampalli (2012) evaluated patient experiences of the novel chronic care model by conducting a PACIC chronic illness care questionnaire (1: none of the time, 5: all of the time). The sub scores of this questionnaire were as follows (mean, SD): Patient activation 3.8 ± 1.1 , delivery system 4.2 ± 1.2 , goal setting 4.3 ± 0.9 , problem solving 4.4 ± 1.3 , follow-up/coordination 3.1 ± 1.1 .

Caregiver experiences

One study assessed caregiver experience as an outcome measure.

The pre-post intervention study of Pariser (2019) showed that 100% of primary care physicians would "use telemedicine technology again to facilitate a case conference", 90% agreed that "TIP case conference increased my confidence in managing this patient's chronic care". 97% of medical specialists and other TIP TEAM members agreed that "the TIP case conference was an effective model to develop a care plan for his complex patient".

Time investment

No studies reported time investment as an outcome measure.

One study explicitly described the time invested in their methods. Pariser (2019) described an investment of 6.1 hours per patient on average for the nurse (2.4 hours preintervention, 2.0 hours for intervention, 1.7 hours postintervention). The multidisciplinary conference lasted one hour.

Level of evidence of the literature

The level of evidence regarding all outcome measures was ungraded due to the multi-faceted aspects of the interventions in the study.

Search strategy

Embase

No	Query	Results
#18	#5 AND #17 Artikel Barely niet gevonden, Pariser wel	1
#17	#15 OR #16	2
#16	the AND upbeat AND 'nurse delivered' AND personalized AND care AND intervention AND for AND people AND with AND coronary AND barley	1
#15	connecting AND people AND with AND multimorbidity AND to AND interprofessional AND teams AND using AND telemedicine AND pariser	1
#14	#5 NOT #11 NOT #10 NOT #9 Overige	1079
#13	#11 NOT #10 NOT #9 OBS	326
#12	#10 NOT #9 RCT	281
#11	#5 AND #8	509
#10	#5 AND #7	322
#9	#5 AND #6 SR	143
#8	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	65741 50
#7	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	33023 94
#6	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR (((critical* OR rapid*) NEAR/3	73340 9

	(review* OR overview* OR synthes*):ab AND (search*:ab OR database*:ab OR 'data base*':ab) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	
#5	#4 NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab OR child*:ti,ab OR schoolchild*:ti,ab OR infant*:ti,ab OR girl*:ti,ab OR boy*:ti,ab OR teen:ti,ab OR teens:ti,ab OR teenager*:ti,ab OR youth*:ti,ab OR pediatr*:ti,ab OR paediatr*:ti,ab OR puber*:ti,ab) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab OR man:ti,ab OR men:ti,ab OR woman:ti,ab OR women:ti,ab)) hoolchild*:ti,ab OR infant*:ti,ab OR girl*:ti,ab OR boy*:ti,ab OR teen:ti,ab OR teens:ti,ab OR teenager*:ti,ab OR youth*:ti,ab OR pediatr*:ti,ab OR paediatr*:ti,ab OR puber*:ti,ab) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab OR man:ti,ab OR men:ti,ab OR woman:ti,ab OR women:ti,ab))	1796
#4	#3 AND [1-1-2001]/sd	1391
#3	#1 AND #2	6623
#2	'multidisciplinary team'/exp OR 'integrative medicine'/exp OR 'collaborative care team'/exp OR 'personalized medicine'/exp OR (('multi disciplinar*' OR collaborative OR multidisciplinar* OR interprofessional OR multiprofessional OR integrative) NEAR/3 (medicine OR care OR team* OR healthcare OR collaborati*)):ti,ab,kw) OR mdt:ti,ab,kw OR (((individuali?ed OR personali?ed OR precision) NEAR/2 (medicine OR therap* OR care)):ti,ab,kw)	24248 7
#1	('chronic disease'/de OR 'chronic':ti,kw) AND ('comorbidity'/exp OR 'comorbidit*':ti,ab,kw OR 'comorbidit*':ti,ab,kw) OR 'multiple chronic conditions'/exp OR (((concurrent OR multiple OR simultaneous) NEAR/2 chronic):ti,ab,kw) OR multimorbid*:ti,ab,kw OR multidisease*:ti,ab,kw OR ((multiple NEAR/2 (disease* OR condition*)):ti,ab,kw)	74562

Ovid/Medline

#	Searches	Results
14	5 not 11 not 10 not 9 Overige	703
13	11 not 10 not 9 OBS	166
12	10 not 9 RCT	191
11	5 and 8	237
10	5 and 7 SR	214
9	5 and 6	74
8	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies]	3880893
7	(exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic*	2138980

	adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	
6	(meta-analysis/ or meta-analysis as topic/ or metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	506178
5	4 not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediater*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	1134
4	limit 3 to yr="2001 -Current"	1172
3	1 and 2	1234
2	exp Patient Care Team/ or Integrative Medicine/ or exp Precision Medicine/ or (('multi disciplinar*' or collaborative or multidisciplinar* or interprofessional or multiprofessional or integrative) adj3 (medicine or care or team* or healthcare or collaborati*)).ti,ab,kf. or mdt.ti,ab,kf. or ((inividuali?ed or personali?ed or precision) adj2 (medicine or therap* or care)).ti,ab,kf.	214923
1	((exp chronic disease/ or chronic.ti,kf.) and (exp Comorbidity/ or comorbid*.ti,kf. or co morbid*.ti,kf.)) or exp Multiple Chronic Conditions/ or ((concurrent or multiple or simultaneous) adj2 chronic).ti,ab,kf. or multimorbid*.ti,ab,kf. or multidisease*.ti,ab,kf. or (multiple adj2 (disease* or condition*)).ti,ab,kf.	42064

Cinahl

#	Query	Results
S14	S5 NOT S11 NOT S10 NOT S9 Overige	275
S13	S11 NOT S10 NOT S9 OBS	112
S12	S10 NOT S9 RCT	158
S11	S4 AND S8	172
S10	S4 AND S7	176
S9	S4 AND S6 SR	42
S8	(MH "Case Control Studies+") OR (MH "Case Studies") OR (MH "Cross Sectional Studies") OR (MH "Prospective Studies+") OR (MH "Retrospective Panel Studies") OR (MH "Correlational Studies") OR TI "case control" OR TI "case referent" OR AB "case referent*" OR TI "case stud*" OR AB "case stud*" OR TI "case series" OR AB "case series" OR TI cohort* OR AB cohort* OR TI "cross sectional" OR AB "cross sectional" OR TI "follow up" OR AB "follow up" OR TI longitudinal OR AB longitudinal OR TI retrospective* OR AB retrospective* OR TI prospective* OR AB prospective* OR TI observational OR AB observational OR TI "Controlled before and after" OR AB "Controlled	1,253,776

	before and after" OR TI "Interrupted time series" OR AB "Interrupted time series" OR TI Correlational OR AB Correlational	
S7	(MH "Clinical Trials+") OR (PT (Clinical trial)) OR (MH "Random Assignment") OR (MH "Quantitative Studies") OR (TX ((clini* N1 trial*) OR (singl* N1 blind*) OR (singl* N1 mask*) OR (doubl* N1 blind*) OR (doubl* N1 mask*) OR (tripl* N1 blind*) OR (tripl* N1 mask*) OR (random* N1 allocat*) OR placebo* OR ((waitlist* OR (wait* and list*)) and (control* OR group)) OR "treatment as usual" OR tau OR (control* N3 (trial* OR study OR studies OR group*)) OR randomized OR randomised))	1,559,203
S6	(MH "Meta Analysis") or TX (meta-analy* or metanaly* or metaanaly* or meta analy*) or TX (systematic* N5 review*) or (evidence* N5 review*) or (methodol* N5 review*) or (quantitativ* N5 review*) or TX (systematic* N5 overview*) or (evidence* N5 overview*) or (methodol* N5 overview*) or (quantitativ* N5 overview*) or TX (systematic* N5 survey*) or (evidence* N5 survey*) or (methodol* N5 survey*) or (quantitativ* N5 survey*) or TX (systematic* N5 overview*) or (evidence* N5 overview*) or (methodol* N5 overview*) or (quantitativ* N5 overview*) or TX (pool* N2 data) or (combined N2 data) or (combining N2 data) or (pool* N2 trials) or (combined N2 trials) or (combining N2 trials) or (pool* N2 studies) or (combined N2 studies) or (combining N2 studies) or (pool* N2 results) or (combined N2 results) or (combining N2 results)	245,200
S5	S4 NOT ((MH ("Adolescence" OR "Child+") OR TI (adolescenc* OR child* OR schoolchild* OR infant* OR girl* OR boy* OR teen OR teens OR teenager* OR youth* OR pediater* OR paediatr* OR puber*) OR AB (adolescenc* OR child* OR schoolchild* OR infant* OR girl* OR boy* OR teen OR teens OR teenager* OR youth* OR pediater* OR paediatr* OR puber*)) NOT (MH ("Adult+") OR TI (adult* OR man OR men OR woman OR women) OR AB (adult* OR man OR men OR woman OR women)))	532
S4	S1 AND S2	587
S3	S1 AND S2	602
S2	(MH "Integrative Medicine") OR (MH "Multidisciplinary Care Team+") OR(TI ("multi disciplinar*" or collaborative or multidisciplinar* or interprofessional or multiprofessional or integrative) N1 (medicine or care or team* or healthcare or collaborati*)) or (TI mdt) or (TI ((individuali?ed or personali?ed or precision) N2 (medicine or therap* or care))) or (AB ("multi disciplinar*" or collaborative or multidisciplinar* or interprofessional or multiprofessional or integrative) N1 (medicine or care or team* or healthcare or collaborati*)) or (AB mdt) or (AB ((individuali?ed or personali?ed or precision) N2 (medicine or therap* or care)))	78,779
S1	((MH "Chronic Disease+") OR (TI chronic)) AND ((MH "Comorbidity") OR (TI comorbid* OR "comorbid*")) OR (TI ((concurrent or multiple or simultaneous) N2 chronic)) or (TI (multimorbid* or multidisease*)) or (TI (multiple N2 (disease* or condition*))) or (AB ((concurrent or multiple or simultaneous) N2 chronic)) or (AB (multimorbid* or multidisease*)) or (AB (multiple N2 (disease* or condition*)))	15,857

Exclusion table

Arnold 2020	Not the original study
Berry 2013	Not the original study
Davis 2020	Not the original study
Ekdahl 2015	Does not comply with PICO: monodisciplinair
Hawker 2020	Interprofessional collaboration not described
Hemmelgarn 2007	Does not comply with PICO: monodisciplinair
Hermann-Lingen 2020	Not the original study
Horn 2007	Not the original study
Lamiquiz-Linares 2017	Not the original study
Nuez 2016	Not the original study
Pangioti 2016	Interprofessional collaboration not described
Paulus 2013	Interprofessional collaboration not described
Ranheim 2010	Interprofessional collaboration not described
Rijken 2014	Not the original study
Sempe 2019	Does not comply with PICO: monodisciplinair
Tyack 2013	Not the original study
Adams, 2012	Not the original study
Bell, 2011	Not the original study
Bhattacharyya 2016	Interprofessional collaboration not described
Blaum 2018	Not the original study
Caffrey, 2016	Not the original study
Camacho, 2018	Does not comply with PICO: primary care
Case management, 2014	Does not comply with PICO: primary care
Chiolero, 2020	Interprofessional collaboration not described
Chwastiak, 2014	Not the original study
Cimpean, 2011	Does not comply with PICO: primary care
Coleman, 2017	Not the original study
Deschodt, 2020	Does not comply with PICO: primary care
Drost, 2020	Not the original study
Eldonna, 2015	Not the original study
Haggerty 2012	Not the original study
Hardin 2009	Interprofessional collaboration not described
Heslop 2014	Does not comply with PICO: primary care
Ho 2008	Does not comply with PICO: wrong P
Ho 2014	Does not comply with PICO: wrong P
Ho 2015	Does not comply with PICO: wrong P
Hsu 2021	Does not comply with PICO: wrong P
Jeffery 2014	Not the original study
Johnston 2013	Not the original study
Jonese 2015	Not the original study
Keel 2020	Does not comply with PICO: wrong O
Kilpatrick 2014	Interprofessional collaboration not described
Krause 2006	Does not comply with PICO: primary care

Lo 2018	Not the original study
Looman 2021	Interprofessional collaboration not described
Lyne 2021	Not the original study
Martinez-Garcia 2013	Not the original study
Mathew-Maich 2016	Does not comply with PICO: wrong I
Mazya 2018	Does not comply with PICO: primary care
Radini 2017	Not the original study
McGregor 2011	Not the original study
Merino 2017	Not the original study
Morgan 2015	Does not comply with PICO: primary care
Morilla-Herrera 2016	Does not comply with PICO: wrong I
Onder 2017	Interprofessional collaboration not described
O'Neill 2017	Does not comply with PICO: monodisciplinair
Ribeiro 2016	Not the original study
Ritchi 2016	Does not comply with PICO: monodisciplinair
Rosenbaum 2021	Interprofessional collaboration not described
Rosenberg 2012	Does not comply with PICO: primary care
Salerno 2014	Not the original study
Samal 2015	Does not comply with PICO: wrong P
Toh 2017	Not the original study
Valatis 2020	Not the original study
Vandevelde2021	Not the original study
Wang 2021	Interprofessional collaboration not described
Welsh 2015	Not the original study
Yu 2015	Does not comply with PICO: monodisciplinair
Davis 2016	Not the original study
Lin 2012	Not the original study
Witter 2012	Not the original study
Unsworth 2016	Not the original study
McDermott 2014	Not the original study

Evidence table

Review reference (author, year)	Study reference (author, year)	Study characteristics (design, setting, country)	Patient characteristics (P) (number included, population characteristics)	Care team composition	Multidisciplinary assessment (I)	Other elements of intervention (i.e., casemanager, selfmanagement)	Comparison (C)	Follow-up	Outcome measures and effect size * (O)	Comments
	Chung, 2013	pre-post intervention study, outpatient care, USA	Inclusion criteria: chronic illness (diabetes mellitus, coronary artery disease and/or chronic heart failure), at least one abnormal indicator (BP >140/90, Hba1C > 8, LDL > 100) and comorbid depression (PHQ9 score \geq 10). 79 patients included, mean age 59, 37% male.	primary care physician, nurse, behavioural health manager, accountable care manager (experienced RNs), consulting psychiatrist	"Synergy program" Team reviews cases with a focus on medical (BP, Hba1C, LDL) and depression (PHQ9 score) indicators as well as overall psychosocial function. BHM provides onsite evaluation and short-term psychotherapy. Liaises with psychiatrist and PCP. PCP educates patients on depression diagnosis and potential negative impact. PCP manages antidepressants with consulting psychiatrist reviews provided through EMR. If	case management and self-management: ACM provides biopsychosocial assessment by phone focused on chronic illness care, medication reconciliation, and self-management approaches including motivational interviewing and behavioural activation. Coordinates with PCP and other specialists on medical issues and assists with appointments.	None	Minimum treatment 8 weeks	PHQ9 reduced to <10 (response) = 44%, PHQ9 reduced to <5 (remission) = 15%, Reduction Hba1C by >0,5% = 33%, Mean Framingham score reduced 28.3 to 18.8 (34% reduction). Patients experience of collaboration between primary care doctor, BHM, ACM and psychiatrist was judged as 'very well'. Patients agreed they know more about their mental health affecting their physical health, how to be responsible for their health, feel their health has improved, agreed that they were given treatment options and choices, and	

					patients do not respond or complex, psychiatrist provides an individual patient consultation. BHM and ACM document on the same care management electronic record for coordination and information sharing.				that their opinion was valued	
Clemens , 2019	Rayner, 2011	pre-post intervention study, outpatient care, UK	Inclusion criteria: <65, DM and eGFR <50ml/min/1.73m2 with decline over time, not receiving RRT or attending pre-dialysis specialty clinics. 1002 patients included, mean age 62 years, 62% male	endocrinologist, nephrologist, primary care physician	Weekly database review to identify patients with deteriorating eGFR. Specialist diabetes-kidney clinic visits, with both the endocrinologist and nephrologist present, were offered every 2-4 months until home BP was controlled or eGFR decline showed. The patients were then referred back to primary care and the nephrologist continued to monitor the eGFR remotely.	self-management support, education, diet support, referral for smoking cessation	None	4 years	Significantly lower rate of eGFR decline after intervention (-5.2v.s. 1.1ml/min/1.73m2), fewer started RRT	

Clemens , 2019	Fogelfeld, 2011 *Khuzively, 2018	Randomized Controlled Trial, outpatient care, USA	Inclusion criteria: DMII, CKD stages 3 and 4 and normal cognitive function. 120 patients included (60 IG, 60 UC), mean age in IG 56 years, 60% male. Post-legacy effect study (Khuzively): 74 patients of the 120 patients enrolled in the trial completed the study ESRD-free. Post-trial data was available for 72 patients (38 IG, 38 UC).	endocrinologist, nephrologist, diabetes educator, nurse practitioner	Multidisciplinary clinic visit, both endocrinologist and nephrologist present, every 1 month for 6 months, followed by every 2 months for 18 months. Additional follow-up visits if needed. Treat to target BP, Hba1c and lipids.	Group diet instructions, education	Usual care	2 years	Lower proportion developed ESRD in intervention group (13 vs 28%) p<0.05. Two years after cessation of the intervention: No significant differences in progression to ESRD or in the yearly eGFR decline rates between study groups
Clemens , 2019	Low, 2018	case-control study, outpatient care, Singapore	Inclusion criteria: DM, CKD stages 3 and 4. 837 patients included (418 IG, 419 UC), mean age 49 years, 53.4% male	nephrologists, endocrinologists, advance practice nurses, clinical pharmacists, dieticians and social workers.	In the clinic, the nephrologist and endocrinologist provided joint consultations with the patient and caregiver. The clinic was supported by the other members of the care team, and helped reinforce lifestyle management plans, monitoring and titrate medication between physician visits. Monthly staff education sessions were organized to	Lifestyle management	Usual care	3 years	interdisciplinary clinic group had a lower risk of progressing to stage 5 CKD (hazard ratio 0.55; 95% CI 0.36-0.84; p=0.004 compared to the non-interdisciplinary group.

					facilitate cohesion of the multidisciplinary team.					
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Clemens , 2019	McMurray, 2002	Randomized Controlled Trial, outpatient care, USA	Inclusion criteria: DM on Peritoneal Dialysis or haemodialysis. 83 patients included (45 IG, 38 UC), mean age in IG 63 years, 53% male.	DM care manager, multidisciplinary diabetes advisory committee, nephrologist, dietician	DM care manager provided self-management education, motivational coaching, nutrition counselling, BP-, lipid- and glycaemic monitoring, foot checks, eye screening reminders. Informed physician of need for medication changes. Multidisciplinary diabetes advisory committee provided program oversight quality.	self-management, motivational coaching, nutrition	Usual care	1 year	Hba1c declined from 6.9% to 6.3% in intervention (no change in controls), no severe hypoglycaemic events, no progression of neuropathic disease in intervention (progression in control), no amputations (5 lower extremity and 2 finger amputation in control), fewer diabetes/vascular related hospitalizations (10 v.s. 1 in control) and foot risk assessment scores remained unchanged in intervention (2.0 to 2.2) and worsened in controls (2.7 vs 3.3). No change in mortality. Self-knowledge improved: Both intervention and control group scored 74% on the knowledge assessment test at baseline. After 12 months of education and care
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									<p>management, the study group answered 90% of questions correctly, and the control group was unchanged ($p < 0.001$). Significant improvements in self-management behaviours, including monitoring blood glucose levels (90 vs. 66%, $p = 0.023$), and undergoing a yearly dilated eye-examination (93 vs. 55%, $p = 0.001$).</p>	
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Delaney , 2020	Frankel, 2014	pre-post intervention study, outpatient care, USA	Inclusion criteria: 2 or more physicians involved in addition to a psychiatrist, 2 or more failed treatments, appointments in addition to those scheduled and extra e-mails or phone calls for support required. 52 patients included, mean age NR (ages range from 12-76), 50% male.	psychiatrist, primary care physician, pharmacist consultant, additional clinicians based on patient needs i.e., physician specialists, social workers, case managers, psychologists	Coordinated care model: 'Medical-Psychiatric Coordinating Physician-led' (MPCP) with clinicians in both psychiatry and internal medicine/family medicine. MPCP is responsible for: tailored care plan, weekly care team meetings, comprehensive clinical review and tracking of treatment progress	Consent-based collaboration with patient and family members. Oversee treatment adherence.	None	18 months	Significant outcomes: Symptom severity of anxiety (25.27 ± 7.5 to 18.13 ± 5.74 ($p < 0.0001$)) and depression (22.02 ± 7.10 to 14.58 ± 6.46 ($p < 0.0001$)) decreased, HR-QOL general health improved (2.54 ± 1.03 to 2.12 ± 1.06 ($p < 0.0001$)), HR-QOL sick days per month decreased (11.22 ± 776 to 6.60 ± 7.51 ($p < 0.0001$)). No effect on pain or physical activity. Significance NR: 44 out of 52 patients met two of the following criteria 1. reduction in health care utilization, 2. improvement treatment adherence, 3. symptom severity reduced.
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Delaney , 2020	Bryk, 2018	pre-post study, outpatient care, USA	Inclusion criteria: University health insurance plan, more than 2 inpatient admissions over the past 12 months and/or more than 6 ED visits over the past year and answer yes to the question: would you like us to help you stay out of the emergency room and the hospital? 144 patients included, mean age NR (58% 40-64 years), 25% male.	primary care physician (PCP), nurse care managers, social worker, administrative assistant, psychologist collocated with PCP, psychiatrist and other clinicians based on patient needs	Intake appointment, tailored care plans, walk-in clinic visits and home visits, equipped for care of urgent issues (i.e., nonopioid pain management, emergent blood work), same day scheduling of imaging and procedures, routine (monthly) check-ups, 24/7 phone access to care manager, ED care plans to direct patient care for non-life- threatening conditions	education (diabetes, diet, self-monitoring blood pressure), delivery of medication with local pharmacy	None	More than 6 months	Significant results: Hba1c and BP improved for patients with diabetes, BP improved for patients with hypertension. Retinal exam completion improved by 33%, colorectal screening and successful referrals to mental health services for patients with untreated illnesses all improved. 19% of 81 patients on opioids were weaned off. Nonsignificant results: Foot exam completion, cervical cancer screening, breast cancer screening.	
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	Goorde n, 2017	Randomized Controlled Trial, outpatient care, the Netherlands	Inclusion criteria: moderate to severe MDD (Major Depressive Disorder) and a chronic physical condition (DM, CVD or COPD). 81 patients included (42 IG, 39 UC), mean age IG 75, 52% male.	consultant psychiatric nurse as care manager, a consultation-liaison psychiatrists for diagnosis, supervision and prescription, and a medical specialists who provided treatment for the chronic physical condition, department nurse.	collaborative care model: screening by department nurse, contracting by psychiatrist/CPN, care manager by CPN, prescription of antidepressants by psychiatrist. Consultations by the psychiatrist if necessary.	guided self-help and problem-solving treatment (PST) provided by the CPN care manager in one-to one sessions	Usual Care = advising patients to seek treatment for depressive symptoms from a PCP if they felt the need	12 months	Quality of life was measured by utility scores. The CC group improved significantly over time: 0.07 (95% CI 0.02 to 0.13). The CAU gained 0.01 (95% CI -0.04-0.05). The difference in effect was not significant over time (0.07 95%CI -0.003 to 0.14)	The effect study is van steenbergen, en die zit in de SR van Eck
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	Kanwal, 2016 *Kanwal, 2018	Randomized Controlled Trial, outpatient care, USA	Inclusion criteria: Hepatitis C (HCV) infection + positive outcome for major depression on the PHQ-9 depression screening instrument. 242 patients included (114 IG, 128 UC), mean age 59 years, 96% male.	HCV clinic staff: nurses, physician assistants, clinicians. Depression care team: nurse depression care manager (DCM), a pharmacist, and a psychiatrist.	Collaborative Care model: Depression care team was located off site and convened once a week and as needed by telephone or in person. The team communicated with treating clinicians via electronic medical record progress notes. The DCM communicated with patients via telephone. The DCM monitored depression symptoms and treatment, Review by clinical pharmacist. Stepped-care model.	DCM delivered participant education and activation, assessment of treatment barriers and possible resolution, substance abuse monitoring	Usual Care	6 months	6 months IG: 19% met criteria for treatment response v.s. 13% in UC (p=0.12). 12 months: 31.6% v.s. 14.8% (p=.002). Remission at 12 months: 19.3% v.s. 7.0% (p=.004) IG also had more depression free days, but this did not reach statistical significance. IG more likely to receive antiviral treatment but not significant. Treatment response was defined as a 50% or greater decrease in the mean SCL-20 score compared to baseline. Remission was defined as a mean SCL-20 score of <.5.	
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	Pariser, 2019	pre-post intervention study, outpatient care, Canada	Inclusion criteria: three or more chronic conditions. 76 patients included, mean age 66 years, 35% male.	Registered TIP nurse. TIP team: specialists from psychiatry and internal medicine, a social worker, pharmacist, home care and community coordinator, other professionals based on patient's needs such as occupational therapist or dietitian, primary care physician.	Telemedicine IMPACT Plus (TIP) model. dedicated TIP nurse meets with PCP and patient in advance to prioritize issues most important to the patient. Enhances self-management and care coordination. Aligns care and goals with appropriate reduction in medications and serial specialist consultations, and equips the PCP with local resources. PCP in his office, the patient at home, and the TIP team to simultaneously conduct a clinical consultation using videoconferences. Team develops recommendations that form the nucleus of a coordinated care plan. TIP nurse helps with follow-through of team's recommendations together with the patients PCP.	Self management, care coordination	None	NR	% agree or strongly agree: PATIENTS Tip has effectively improved my access to new interdisciplinary resources 100%; I am hopeful that my chronic condition will improve as a result of the TIP case conference 97%; PCP I would use telemedicine technology again to facilitate a case conference 100%; TIP case conference increased my confidence in managing this patient's chronic care 90%; TEAM The tip case conference was an effective model to develop a care plan for this complex patient 97%	
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van Eck, 2018	Systematic Review, including 20 RCTs or cluster RCTs, outpatient care. Search ran until august 2017, beginning NR.	Inclusion criteria: patients 18 years and older with comorbid depressive disorder and chronic medical conditions. The meta-analysis included a total of 4774 patients.	Collaborative care model: care manager (CM) with training in the treatment of depression and anxiety disorders, medical doctor (primary care physician, medical specialist or pharmacist) and a psychiatrist.	Collaborative care model: CM with training in the treatment of depression and anxiety disorders, has regular contact with the patient and organises care in collaboration with the medical doctor and pharmacist, supervised by the psychiatrist. The focus is on monitoring of symptoms and adherence to treatment. CM may also provide psychotherapy such as problem-solving treatment.		Usual Care	3-12months	burden of disease based on physical and depressive outcomes favours CC: OR 1.64 (95%CI 1.47-1.83) with an effect size $d=0.27$ (95%CI 0.21-0.33). Depressive outcomes favor CC: OR 1.90 (95% 1.70-2.12). $d=0,35$ 95%CI 0.29-0.42). Results were significant for all chronic medical conditions (HIV, COPD, multimorbidity, arthritis, cancer and ACS), except for DMII and epilepsy. The highest OR was found for hypertension (4.18, 95% CI 2.18-8.05; $d=0.79$, 95%CI 0.43-1.15). More procedures were performed in the collaborative care model compared to care as usual: OR 2.25 (95%CI 1.67-3.05), $d = 0.45$ (95%CI 0.28;0.61).	
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	<p>Lin, 2010 *Lin, 2014 * Ludman, 2013</p>	<p>Randomized Controlled Trial, outpatient care, USA</p>	<p>Inclusion criteria: depression, uncontrolled diabetes and/or CHD. 214 patients included (106 IG, 108 UC). Mean age 57 years, 48% male.</p>	<p>TEAM care: nurse care manager (NCM), PCP, medical and psychiatric consultants, psychologists.</p>	<p>comprehensive face-to-face biopsychosocial assessment, including goal setting, formulating 'my health plan', self-management support, monitoring of disease indicators, pharmacotherapy adjustments. Nurses followed patients proactively to monitor clinical progress, support adherence, healthy eating and physical activity. Electronic registry tracked disease indicators and flagged patients who were not making progress. Weekly case reviews interdisciplinary meetings focused on patients who were not making progress. Nurse communicated the recommendations to the patients PCP who was responsible for</p>	<p>Lifestyle management</p>	<p>Usual Care</p>	<p>12 months</p>	<p>At 12 months, average rate of blood pressure self-monitoring was more than 3 times higher in the TEAMcare group (3.6vs1.1days per week, RR=3.20 (P<0.001). The average blood glucose monitoring rate was 4.9 days per week vs 3.9 days UC (RR=1.28, p=0.006) . At 12 months there was a significant improvement in Hba1c (-1.20 (95% CI -1.76 - -0.63) among patients with less favorable medical controls at baseline. No significant difference was found for blood pressure and lipid control. For patients with favorable medical controls at baseline, no significant improvements were found for Hba1c, BP or lipid control in the intervention group. There was a significant difference between answer value means of one</p>	
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					medication management.				out of four questions relating to self-efficacy, favouring the intervention group: "I am confident that I can maintain lifestyle changes like diet and exercise even during times of stress".	
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	Nieto-Martin, 2019	pre-post intervention study, outpatient care, Spain	Inclusion criteria: adults, two or more chronic conditions, excluding cancer patients and HD or transplant waiting list. 420 patients included, mean age 77,3, 47% male.	Internal Medicine physician (IM), team care nurses (TCN), hospital pharmacist (HP), general practitioner (GP)	IM: Personal therapeutic plan, structured medical visit 15 days after inclusion, availability of programmed admissions avoiding the emergency room, availability of medical visits <24u if necessary. TCN: Continuity of care plan, education workshops for patients and caregivers. HP: treatment compliance evaluation, appropriateness of treatment evaluation, intervention to improve treatment compliance. GP: Risk stratification, integral evaluation of function and cognition	Education	None	12 months	Number of hospital admissions and days of hospitalizations decreased significantly compared with the previous year: 0.67 (SE: 0.09) and 7.39 (SE: 0.95) respectively (p<0.001).	
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	Sampalli , 2012	pre-post intervention study, outpatient care, Canada	Inclusion criteria: adults, two or more chronic conditions. 20 patients included, mean age 42 years, 25% male.	occupational therapist, nurse, multidisciplin ary clinicians, primary care physician	Intake phase - physician: diagnosis and symptom profile, Occupational therapist: care coordination and rehabilitation needs, nurse: education and orientation to care delivery process. Intervention phase - multidisciplinary care appointment with multidisciplinary clinicians, individual and group interventions and educational programs to address the needs of the whole person. Transition phase where readiness for discharge is evaluated by occupational therapist. Discharge phase - discharge to family physician. Between each phase is a care coordination appointment.	Group interventions: mindfulness, tools to manage ADL, pain and fatigue management. Individual: occupational therapy, dietary management, counselling and coaching, return to work support	None	6 months	Rating of health since onset of illness (1, worst; 7, best possible) Pre/post mean 2.62± 1.2 v.s. 6.2±2 P<0.0001. Fatigue (1, no symptoms; 12 worst) 7.3±2.4 v.s. 2.8 ±1.1 p<0.0001). Pain (1, none;12,worst) 6.4 ±2.5 v.s.4.5±1.3 p=0.06). Patient Assessment of chronic illness care questionnaire: I = none of the time 5 = all of the time. Patient activation 3.8 ±1.1, delivery system 4.2± 1.2, goal setting 4.3±0.9, problem solving 4.4±1.3, Follow- up/coordination: 3.1±1.1	
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	Pollina, 2017	Prospective Controlled Trial, outpatient care, Switzerland	Inclusion criteria: community dwelling frail and dependent people older than 60 years. 301 patients included (122 IG, 179 UC). Mean age IG 82 years, 36% male.	Primary care physician (PCP), home visiting nursing service centers (HVNS), Nursing Teams (NT), Community Geriatric Unit (CGU). The CGU home intervention team included doctors, physical and occupational therapists, psychologists, dieticians and social workers.	IG received usual care by their PCP, the intervention NT, and additionally were provided with an in-home geriatric assessment by the community geriatrics unit (CGU) doctor. This includes functional and cognitive status, nutrition and medication review. Results were transmitted in writing to the PCP and NT with recommendations, and in case of complex issues, meeting between the CGU and NT were organized.	Participants and NT received writing instructions to first contact the PCP in case of an emergency, if unavailable, the CGU provided 24h/7days a week medical call service. CGU also has a day hospital.	Usual Care = care with PCP and prescribed services of HVNS	5-41 months (mean 16.3)	Unnecessary hospitalizations for social reasons were significantly less frequent in the IG (4.1% v.s. 11.7%, p=0.03). Length of hospital stay was lower, but not significantly, in the intervention than in the control group (37.5 v.s. 51.0 days p = 0.18).	
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