

# Chronic care management for patients with COPD: a critical review of available evidence

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## Keywords

chronic care management, chronic obstructive pulmonary disease, disease management, heterogeneity, meta-analysis, systematic review

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## Abstract

**Rationale, aims and objectives** Clinical diversity and methodological heterogeneity exists between studies on chronic care management. This study aimed to examine the effectiveness of chronic care management in chronic obstructive pulmonary disease (COPD) while taking heterogeneity into account, enabling the understanding of and the decision making about such programmes. Three investigated sources of heterogeneity were study quality, length of follow-up, and number of intervention components.

**Methods** We performed a review of previously published reviews and meta-analyses on COPD chronic care management. Their primary studies that were analyzed as statistical, clinical and methodological heterogeneity were present. Meta-regression analyses were performed to explain the variances among the primary studies.

**Results** Generally, the included reviews showed positive results on quality of life and hospitalizations. Inconclusive effects were found on emergency department visits and no effects on mortality. Pooled effects on hospitalizations, emergency department visits and quality of life of primary studies did not reach significant improvement. No effects were found on mortality. Meta-regression showed that the number of components of chronic care management programmes explained present heterogeneity for hospitalizations and emergency department visits. Four components showed significant effects on hospitalizations, whereas two components had significant effects on emergency department visits. Methodological study quality and length of follow-up did not significantly explain heterogeneity.

**Conclusions** This study demonstrated that COPD chronic care management has the potential to improve outcomes of care; heterogeneity in outcomes was explained. Further research is needed to elucidate the diversity between COPD chronic care management studies in terms of the effects measured and strengthen the support for chronic care management.

## Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world [1]. It represents an enormous burden on individuals, families and societies, by its impact on quality of life and health resource utilization,

as well as mortality [2]. COPD, like other chronic conditions, therefore pose significant challenges to health care systems of many countries. The World Health Organization (WHO) estimates that COPD was the fifth leading cause of death worldwide in 2001 and will be the third leading cause by 2020 [3]. Moreover, within chronic care gaps exist between what is appropriate care for

chronic conditions and the care actually received [4]. Meanwhile, the need for more patient-centred care is significantly increasing [4–6].

As maintaining the status quo is no option to deal with these challenges [7,8], chronic care programmes, such as the chronic care model (CCM) [9] and disease management programmes [10], are increasingly implemented in daily health care. Although these two concepts are the best known, case management, integrated care and care coordination are also often referred to in the context of chronic care management [11]. The common aim of these programmes is to improve processes and outcomes of care while making a more efficient use of scarce health care resources, or even generate cost savings. Notwithstanding the awareness among policy makers, payers, professionals and patients of the importance of chronic care management, insight into the effectiveness of the various approaches is limited. The complex nature of chronic care programmes makes that current research designs either experimental studies, which reveal little about the underlying mechanisms why programmes are effective, or descriptive studies, which lack methodological rigor. Still, Coleman *et al.* [12] descriptively analyzed interventions aimed at improving the quality of chronic care by looking at the relationship between the presence of elements of the CCM [9] and outcomes of care. Coleman concluded that ‘accumulated evidence appears to support the CCM as an integrated framework to guide practice redesign’ [13]. In addition, knowledge is available on the effectiveness of chronic care management in COPD care [14,15], though heterogeneity exists between studies (clinical diversity) [16], and thus in outcomes. Moreover, heterogeneity on methodological features, such as length of follow-up, outcome measures and study design, is also apparent [14,15].

Significant international challenges in chronic care management in combination with the inadequate description and explanation of the effects of chronic care management programmes that have already been implemented call for thorough exploration of heterogeneity in current literature. A meta-analysis of chronic care management programmes was performed for patients with COPD assuming the following three hypotheses. First, differences in the methodological quality of studies may account for differences in outcomes. Second, differences in the length of follow-up may account for differences in outcomes. Third, differences between chronic care management programmes may account for differences in outcomes. This meta-analysis aims to support the understanding of and decision making about chronic care management strategies for COPD by reporting on the effect and the factors explaining the heterogeneity in outcomes.

## Methods

### Literature search

Electronic database searches for English language systematic reviews and meta-analyses published between 1995 and 2009 were conducted on Medline, using the following Medical Subject Headings: patient care team, patient care planning, primary nursing care, case management, critical pathways, primary healthcare, continuity of patient care, guidelines, practice guideline, disease management, comprehensive healthcare and ambulatory care. Further, ‘disease state management’, ‘disease management’, ‘integrated care’, ‘coordinated care’ and ‘shared care’ in combination

with ‘COPD’ were alphanumerically searched as title and/or abstract words.

### Study inclusion

Reviews were included when these (1) reported a systematic review or meta-analysis; (2) focused on interventions consisting of  $\geq 2$  components of the CCM [9] and (3) focused on COPD as the main condition of interest; and (4) focused on adult patients as the main receivers of the interventions. Furthermore, two recently published (2009) reviews were included in which the researchers were involved. Given the expected heterogeneity between the primary studies within the reviews, the primary papers underlying the reviews were obtained for further analysis if these satisfied criteria 2–4 mentioned above. Moreover, studies published before 1995 were excluded, as it was not until 1995 before disease management appeared frequently in the medical literature [17]. Case reports and expert opinions were excluded. Two members of the research team (KL and JB) reviewed citations, removed duplicates and obtained the full text of all potentially relevant papers.

### Sources of heterogeneity: a priori hypotheses

Differences in study outcomes may prove to be greater than would be expected based on chance alone. In anticipation of potentially statistical significant heterogeneity, three hypotheses were established in advance to performing the analyses with the primary papers, which may help explain differences in outcomes.

Hypothesis 1: Differences in the quality of the study may account for (part of the) differences in outcomes.

The methodological quality of primary studies was assessed with the Health Technology Assessment–Disease Management instrument (HTA-DM instrument) [18]. Scores can range from 0 to 100 points. A score of <50 points is considered as poor quality; 50 to 69 points as moderate quality; and  $\geq 70$  points as good quality.

Hypothesis 2: Differences in the length of follow-up (number of months) may account for differences in outcomes.

Hypothesis 3: Differences between the chronic care programmes (i.e. the number of intervention components constituting the chronic care programme) may account for (part of the) differences in outcomes.

The interventions, as described in the primary papers, were mapped to the four components within the health care system of the CCM as stated by Zwar *et al.* [19]: self-management support (SMS; e.g. supporting patients to manage their condition by education, goal setting); delivery system design (DSD; e.g. another system design to structure chronic care management by regular follow-up, other team roles); decision support (DS; e.g. integration of evidence-based clinical guidelines into practice by reminder system, feedback system); or clinical information systems (CIS; e.g. information systems supporting reminders, feedback on performance).

### Data extraction

Two reviewers (KL and JB) independently extracted data, using separate forms for systematic reviews and primary papers. Disagreements were resolved by consensus or referred to a third reviewer (LL). Data extracted from systematic reviews include

(1) methods of data synthesis (i.e. descriptive or meta-analysis); (2) inclusion and exclusion criteria; (3) number of studies included (total and specified by research design); (4) theoretical framework underpinning the chronic care programme of interest; (5) programme components (i.e. SMS, DSD, DS, CIS); (6) primary and secondary end points; (7) effect sizes; (8) methods of the meta-analysis, if applicable (i.e. random or fixed effect model and assessment of heterogeneity); and (9) author's conclusion.

Data extracted from primary papers include (1) study design; (2) length of follow-up; (3) sample size; (4) inclusion and exclusion criteria; (5) mean or median age of included sample; (6) percentage males; (7) disease severity; (8) study setting (i.e. community; primary, secondary or tertiary care; or combination hereof); (9) intervention, including programme components (i.e. SMS; DSD; DS; CIS); (10) control intervention; and (11) process and outcome measures.

### Data analyses

Extracted data were entered into a spreadsheet (Excel®; Microsoft, Seattle, WA, USA). Data collected from reviews were analyzed descriptively (i.e. theoretical scope, inclusion/exclusion criteria and outcome measures). Additionally, data collected from primary studies were analyzed descriptively (number and type of intervention components, methodological quality, length of follow-up) as well as meta-analyzed to predict the differences in changes in process and outcome measures between intervention and control groups over time. A priori stated that the most frequently measured outcomes in the primary studies, i.e. COPD hospitalizations, health-related quality of life, mortality and emergency department visits, were meta-analyzed. RevMan (5.0.2) (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used for the meta-analysis using a random model to test the heterogeneity by the Cochran  $Q$   $\chi^2$  test. Pooled risk ratios and 95% confidence intervals (CIs) were computed by means of a random effects model Mantel–Haenszel test for dichotomous outcomes [20]. Pooled mean differences were calculated with the random effect model of DerSimonian and Laird [21].

Meta-regression analysis was performed to identify to which degree the heterogeneity can be explained by respectively the quality of the study, the length of follow-up and the number of components. In contrast to the subgroup analyses, all three factors were taken into account as continuous variables in this meta-regression analysis. The effect sizes of primary studies were weighted by the inverse variance weight formulas [20] and imported together with the covariates in the SAS statistical package (version 9.2) (SAS Institute Inc., Cary, NC, USA) [22]. For these calculations, relative risk ratios were logarithm transformed. The extent to which study-level variables explained the variance between studies was examined by fitting of univariable meta-regression model [23]. The relative decrease of the between-study variance in the univariable model compared to an intercept-only model is interpreted as the percentage of heterogeneity explained.

## Results

### Results of the search strategy

Eight systematic reviews [14,15,24–29] and 29 primary papers [30–58] were identified that met the inclusion criteria (see flow-

chart, Fig. 1). Four of the included systematic reviews also performed meta-analyses [14,15,24,28]; four were descriptive reviews [25–27,29]. The set of primary papers included 20 randomized controlled trials (RCT) [30,32–41,43,47–51,55–57], two controlled clinical trials [42,44], two controlled before-after studies [45,46] and five pre-post studies [31,52–54,58].

### Findings from systematic reviews

The definitions of chronic care programmes included in the reviews vary from disease management or integrated care programmes to nurse-led interventions. Common aspect of the programmes, however, is their strong focus on improving quality of life and reducing hospital admissions, and therefore improving the management of COPD including self-management. Variation in the inclusion of interventions was found; for example, Peytremann-Bridevaux *et al.* [15] and Lemmens *et al.* [14] set a criterion to avoid studies focusing on pulmonary rehabilitation only because they had already been shown to be effective, whereas Niesink *et al.* [25] included various pulmonary rehabilitation studies.

In a majority of reviews, positive results are found on hospitalizations and quality of life (see Table 1). Four reviews found a significant decrease of hospitalizations [14,15,24,27]; an earlier study by Sin *et al.* [26] observed no effect on hospitalizations. Three reviews found modest improvements in quality of life [14,15,26] compared to inconclusive results by Niesink *et al.* [25]. Significant effects in emergency department visits were found in one review [24], but not in another [14]. So far, no effects were found on mortality. All reviews conclude that more research is needed. Moreover, it remains unclear which specific (combination of) interventions or components are most effective.

### Findings from primary studies

The most frequently included CCM components are SMS ( $n = 28$ ) and DSD ( $n = 28$ ), followed by DS ( $n = 17$ ) and CIS ( $n = 7$ ; see Table 2). Thirteen studies evaluated a programme with two components, 10 with three components and six with four components. Eleven of the 13 programmes with two components included the combination of SMS and DSD. The most common combination of three components was SMS, DSD and DS (90%). Interpretation of the chronic care management components differed between studies, but some general trends could be identified. SMS often consisted of patient education and self-management tools and support; DSD was often performed by the introduction of a specialized nurse and/or case manager; CIS mainly consisted of telephone follow-up and DS often consisted of specific protocols.

Of the 29 primary papers, 45% scored high on methodological quality [32–34,37,41,47–49,51,53–56], 41% scored moderate [30,35,36,38–40,42–44,46,50,57] and 14% scored poor on quality [31,45,52,58]. The length of follow-up varied from 2 to 24 months. Twelve studies reported a follow-up of 12 months [32,34,37,42,46,47,49,50,52–54,56] and four of 24 months [31,41,44,51]. Most of the studies were performed in the United States ( $n = 10$ ). Outcome measures mostly assessed in primary studies are quality of life ( $n = 21$ ), hospitalizations ( $n = 20$ ), mortality ( $n = 16$ ) and emergency department visits ( $n = 15$ ). Data on processes of care were collected in 15 studies; changes in patient

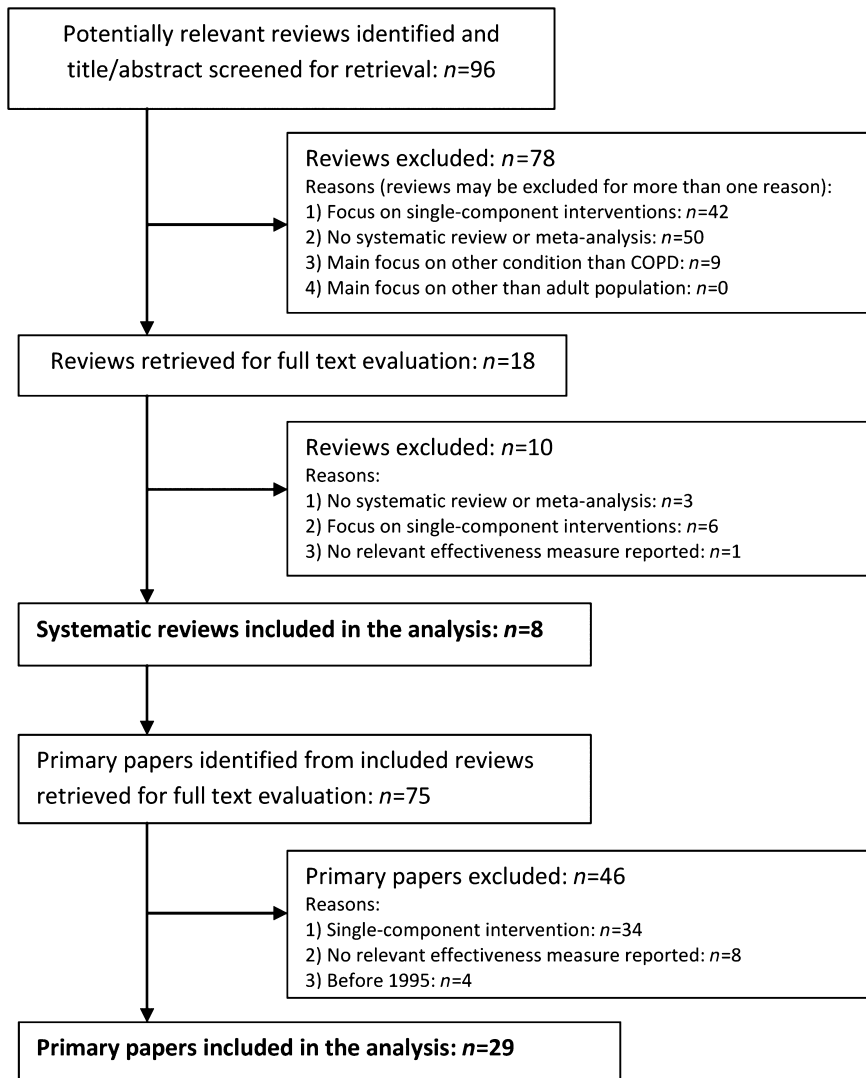


Figure 1 Study inclusion/exclusion flowchart.

behaviour were most often measured, for example, education, knowledge and medication adherence. Doctor behaviour, for example, guideline adherence, was rarely reported.

### Quality of life

Quality of life measures were reported in most studies ( $n = 21$ ). A variety of instruments is used to assess (disease-specific) quality of life; the St. George's Respiratory Questionnaire (SGRQ) was most often used ( $n = 10$ ). The SGRQ total scores range from zero (no impairment) to 100 (maximum impairment) [59]. Three studies were excluded due to missing data [36,40,47]. Meta-analysis of the remaining seven studies demonstrated statistically significant improvements ( $P < 0.01$ ) on the SGRQ in favour of chronic care management [32,35,37,39,50,54,55]. However, moderate statistical heterogeneity was apparent ( $I^2 = 37\%$ ). Exclusion of two small studies [37,50] with considerable, but non-significant, differences in baseline scores reduced heterogeneity ( $I^2 = 0\%$ ). Improvements on the SGRQ total scores within the five remaining studies were

only marginally significant ( $P = 0.06$ , Table 3). All five studies consisted of three components, combining SMS and DSD with DS ( $n = 4$ ) or CIS ( $n = 1$ ).

Subgroup analyses for study quality showed significant improvements ( $P = 0.01$ ) with no heterogeneity ( $I^2 = 0\%$ ) for good study quality; where moderate quality studies did not improve significantly (Table 3). No effects were found for length of follow-up. Subgroup analysis could not be performed for the number of components as all five included studies had three components. Meta-regression analysis was used to identify whether the variables were associated with the effect as no heterogeneity between studies had to be explained ( $I^2 = 0\%$ ). The meta-regression showed that the quality of studies and length of follow-up are not associated with the effect of chronic care management on quality of life ( $P > 0.05$ ).

### Hospitalizations

A variety of outcome measures is used for all-cause hospitalization as well as COPD hospitalization (e.g. at least one hospitalization,

**Table 1** Summary of reviews

Author, year of publication	No. of studies included/ analysis type	Concept/definition of chronic care programmes	Inclusion criteria	Exclusion criteria	Author's conclusion
Adams <i>et al.</i> 2007 [1]	<i>n</i> = 32 (20 RCTs; five CCTs; Seven pre-post) Descriptive review	CCM including self-management support, delivery system design, decision support and clinical information systems.	(1) Intervention(s) with at least 1 CCM component; (2) a control or comparison group or at least 1 outcome measured at 2 points; and (3) had relevant outcome(s).	Specific therapeutic measures, such as oral or inhaled bronchodilator therapy, pulmonary rehabilitation, and supplemental oxygen therapy (= usual care).	Poolled data demonstrated that COPD patients who received interventions with $\geq 2$ CCM components had lower rates of hospitalizations and emergency/unscheduled visits and a shorter length of stay compared with control groups.
Lemmens <i>et al.</i> 2009 [14]	<i>n</i> = 21 (18 RCTs; three CCTs)	Disease management programmes, which include a combination of patient-related, professional-directed and/or organizational interventions.	(1) $\geq 2$ interventions; (2) patients >16 years; (3) principal diagnosis of asthma or COPD; (4) RCTs, CCTs or time series designs; (5) control group with usual care or single intervention; (6) reported any objective measure of outcomes reflecting the primary goals of disease management.	Studies on the effects of single interventions.	In spite of the heterogeneity of disease management studies in COPD care, this review showed promising improvements in quality of life and reductions in hospitalizations, especially for triple intervention programmes.
Niesink <i>et al.</i> 2007 [25]	<i>n</i> = 10 (all RCTs) Descriptive review	Integrated care: (1) multidisciplinary care team (2) clinical pathway (3) clinical follow-up (4) case management, or (5) self-management or patient education.	(1) RCTs or controlled trials; (2) clinical diagnosed COPD (stable); (3) outpatient integrated care programme, including 1 $\geq$ component(s): multidisciplinary care team, clinical pathway, clinical follow-up, case management and self-management or patient education (of at least 8 weeks); and (4) measuring general or disease-specific QoL.	Specific methods of case finding, prevention strategies, provider education or provider feedback.	Results on HRQoL were inconclusive. All chronic DMP for people with COPD involving primary care improved QoL. In most of the studies, aspects of chronic disease management were applied to a limited extent.

**Table 1** *Continued*

Author, year of publication	No. of studies included/analysis type	Concept/definition of chronic care programmes	Inclusion criteria	Exclusion criteria	Author's conclusion
Peytremann-Bridevaux <i>et al.</i> 2008 [15]	<i>n</i> = 13(9 RCTs; one CCT; three pre-post) Descriptive review and meta-analysis	DMP: 'an approach to patient care that emphasizes coordinated, comprehensive care along the continuum of disease and across health care delivery systems.' Patient counselling, education, coordination and standardization of care are key components	(1) $\geq 2$ different components (e.g. physical exercise, self-management, structured follow-up); (2) $\geq 2$ actively involved health care professionals; (3) patient education; (4) and at least one component of the intervention lasted $\geq 12$ months.	Programmes offered only in the hospital or targeting patients receiving palliative care or with end-stage COPD were excluded.	COPD DMPs modestly improved exercise capacity, health-related quality of life and hospital admissions, but not all-cause mortality.
Sin <i>et al.</i> 2003 [26]	<i>n</i> = 8 (all RCTs) Descriptive review	DMP which include any combination of patient education, enhanced follow-up and/or self-management.	RCT with at least 3 months follow-up and at least one of these clinical outcomes: health-related quality of life, COPD exacerbations or death.	Not specified.	Data on DMPs were heterogeneous, but overall, no effect was observed on survival or risk of hospitalization. On average, these programmes appear to improve health status of patients.
Steyten <i>et al.</i> 2009 [27]	<i>n</i> = 17 (14 RCT, two CCT and one pre-post)	Multicomponent disease management or chronic care programmes ( $\geq 2$ components as defined by the disease management association of America (DMAA) or the CCM).	(1) At least two components of disease management as defined by the DMAA or the CCM; (2) studies included a control or comparison group or at least one outcome measured at two points in time (before/after designs); and (3) evaluated relevant process, intermediate or end outcomes.	Specific therapeutic regimens, such as different forms of bronchodilator therapy, pulmonary rehabilitation, oxygen therapy, etcetera	There is little evidence for significant improvements in process and (intermediate) outcomes, except for increased provision of patient self-management education and improved disease-specific knowledge. But programmes containing $\geq 3$ components show lower relative risks for hospitalization. Estimations of potential cost effectiveness can, in the absence of 'perfect data', support timely decision making regarding these programmes.

<p>Taylor <i>et al.</i> 2005 [28]</p>	<p><math>n = 9</math> (all RCTs) Descriptive review and meta-analysis</p>	<p>Interventions aimed at improving the management of COPD as a chronic disease, which are led, coordinated and delivered (at least in part) by nurses.</p>	<p>Clinical service interventions or packages of care aimed at improving the management of patients with COPD in the community: inpatient, outpatient or community-based interventions that were either nurse led, nurse coordinated or largely delivered by nurses.</p>	<p>Drug trials, hospital at home or early discharge schemes for patients with acute exacerbations, educational interventions directed solely at other health care providers, and studies in which a substantial proportion of patients did not have COPD.</p>	<p>There is little evidence to date to support the widespread implementation of nurse-led management interventions for COPD, but the data are too sparse to exclude any clinically relevant benefit or harm arising from such interventions.</p>
<p>Tinker and While 2006 [29]</p>	<p><math>n = 26</math> (12 RCTs; one CCT; two pre-post; 11 other) Descriptive review</p>	<p>Key nursing interventions: smoking cessation; dyspnea management; exercise; hospital at home; palliative care; meta-analyses.</p>	<p>(1) State-of-the-art nursing care in relation to management of COPD, supporting the NICE guideline; (2) Patients with diagnosed moderate to severe COPD; and (3) observation studies and RCTs.</p>	<p>Narrative reviews.</p>	<p>NICE guidelines provide a key source of evidence for the delivery of evidence-based care in COPD. Good evidence for promoting smoking cessation. Hospital at home is attractive to policy makers because of relative cheapness. Low peak flow and oxygen dependency and low BMI are indicators of end-stage disease requiring palliative care</p>

CCM, chronic care model; DMP, disease management programme, RCT, randomized controlled trial, CCT, clinical controlled trial, COPD, chronic obstructive pulmonary disease, QoL, quality of life; HRQoL, health-related quality of life.

**Table 2** Summary of primary papers

Author, year of publication	Inclusion	Exclusion	Population (mean age I(C); % male I(C); severity (% FEV1 predicted))	Intervention	Control	Components SMS, DSD, CIS, DS	Follow-up (months)	Quality score study design
Aiken <i>et al.</i> 2000 [30]	(1) ≥18 years; (2) oxygen saturations <88% or baseline pO2 <55 and to be on continuous oxygen; (3) marked limitation of physical functioning; (4) exhibited recent exacerbation of their conditions (an emergency department, urgent care facility or hospital within the 3 months prior to enrolment); (5) have a telephone and (6) speak English or have a translator present	Not explicitly stated	Total: 68.5 (NR); Total: 36; NR	Intensive home-based case management provided by registered nurse case managers	Usual care provided by the managed care organization, including medication and technical treatment	SMS, DSD, DS	9	60
Barnett 2003 [31]	Patients that have been admitted to hospital repeatedly and have a moderate to severe COPD with less than 60% predicted FEV1	Not explicitly stated	NR; NR; ≤ 60%	COPD outreach team/active management plan	None	SMS, DSD, DS	24	30
Bourbeau <i>et al.</i> 2003 [32]	(1) Stable COPD (respiratory symptoms and medication unchanged for at least 4 weeks before enrolment); (2) at least 50 years of age; (3) current or previous smoker; (4) 25<%FEV1 <70; (5) history of hospital admission for at least one exacerbation in the preceding year	(1) Previous diagnosis of asthma, CHF, terminal disease, dementia or psychiatric illness; (2) previous participation in rehabilitation programme; (3) long-term facilities stays	69.4(6.5)/69.6(7.4); 52/69; 25–70%	A comprehensive patient education programme administered to weekly visits by trained health professionals over a 2-month period with monthly telephone follow-up	Usual care (managed by specialists or GPs and maintenance of usual access by health programmes	SMS, DSD, DS	12	75



Author	Inclusion criteria	Exclusion criteria	Intervention	Comparison	Outcomes	Quality
Cambach <i>et al.</i> 1997 [33]	(1) Evidence of dyspnoea and decreased exercise tolerance as a result of obstructive lung disease; (2) age 18–75 years; (3) ability to travel independently to the physiotherapy practice; (4) medication prescribed by a pulmonary doctor; (5) no manifest cardiac complaints or locomotor disabilities; (6) absence of hypercapnia, arterial carbon dioxide tension (Pa,CO <sub>2</sub> ) >6.0 kPa (45 mmHg) and/or hypoxia; arterial oxygen tension (Pa,O <sub>2</sub> ) <8.7 kPa (65 mmHg) during rest and/or maximal bicycle exercise testing; (7) motivation to improve self-care; and (8) informed consent	After medical examination, patients were excluded because of (1) hypoxemia (2) not meeting diagnostic criteria of COPD	Rehabilitation programme, comprising techniques of breathing retraining and evacuation of mucus, exercise training, patient education, relaxation techniques and recreational activities	Drug treatment only	62(5)/62(9); 47/75; 59% (16)/60% (23)	SMS, DS 3 70
Casas <i>et al.</i> 2006 [34]	A previous episode of exacerbation requiring hospitalization for >48 hours	(1) Not living in the health care area; (2) severe co-morbid conditions; (3) logistical limitations due to extremely poor social conditions; and (4) being admitted to a nursing home	(1) A comprehensive assessment of patient at discharge; (2) an educational programme on self-management; (3) shared agreement on an individually tailored care plan between specialized nurse case manager and primary care team; (4) accessibility of specialized nurse to patients/carers and primary care professionals through an ICT platform	Usual care: patients discharged from hospital by the attending doctor who decided on the outpatient control regime	70 (9)/72(9); 77/88; <80% / 43% (20)/ 41% (15)	SMS, DSD, CIS, DS 12 80
Coultas <i>et al.</i> 2005 [35]	(1) >45 years; (2) COPD-related diagnosis code (September 2000 to August 2001); (3) current or former smoker with at least a 20-pack-year smoking history; (4) at least one respiratory symptom during past 12 months; (5) airflow obstruction (FEV <sub>1</sub> /FVC ratio <70% and FEV <sub>1</sub> <80% predicted	Not explicitly stated	Nurse-assisted collaborative management	1: nurse-assisted medical management 2: usual care	70.1(7.0)/68.3(6.6) or 68.8(10.4); 32.7/42.9 or 53.8*; <80%	SMS, DSD, DS 6 55

Table 2 Continued

Author, year of publication	Inclusion	Exclusion	Population [mean age (I/C); % male (I/C); severity (% FEV1 predicted)]	Intervention	Control	Components SMS, DSD, CIS, DS	Follow-up (months)	Qualityscore studydesign
Egan <i>et al.</i> 2002 [36]	(1) aged 18 years or older; (2) history of bronchitis, emphysema, chronic airway obstruction, chronic asthma or a combination of these; (3) FEV1 available; (4) adequate cognitive function; (5) admission to respiratory unit bed within 72 hours of admission to hospital; (6) informed consent	Not explicitly stated	67.2(NR)/67.8(NR); 36/60*; 35-50%	Nursing-based case management. The case manager conducted a comprehensive nursing assessment and coordinated care utilizing a clinical pathway, and facilitated communication between patient and caregiver.	Usual care	SMS, DSD, CIS, DS	3	60
Garcia-Aymerich <i>et al.</i> 2007 [37]	COPD patients admitted because of an episode of exacerbation requiring hospitalization for more than 48 hours.	(1) Not living in the health care area or living in nursing home; (2) lung cancer or other advanced malignancies; (3) logistic limitations: extremely poor social conditions, illiteracy, or no phone at home; (4) extremely severe neurological or cardiovascular co-morbidities.	72(1)/73(9); 80/80; NR	Integrated care intervention with self-management, specialized nurse (case manager), tailored care plan, scheduled follow-up and web-based call centre	Usual care: discharge from the hospital by the attending doctor. Pharmacological prescriptions followed the standard protocols	SMS, DSD, CIS, DS	12	80
Gourley <i>et al.</i> 1998 [38]	(1) Ambulatory COPD patient; (2) received pulmonary function test to diagnose COPD; (3) has COPD according to ATS; (4) received pharmacotherapy including metered dose inhalers (MDI); (5) mentally and physically able to use MDI; (6) read/write English; (7) signed informed consent; (8) able to comprehend to study procedures; (9) $\geq 40$ years	(1) History of severe life-threatening COPD; (2) hospitalized or ED visits in the last 2 weeks; (3) lung infection in last 2 weeks; (4) heart failure; (5) other respiratory disease; (6) drug or alcohol abuse; (7) participate in drug trial; (8) refusal informed consent	69.3(5.9)/69.3(9.2); 100/100; NR	Patient-centred pharmaceutical care model (employing standardized care) implemented by clinical pharmacy residents	Usual care: non-standardized care	SMS, DSD	6	60
Hermiz <i>et al.</i> 2002 [39]	All patients aged 30-80 years who attended the hospital emergency department or were admitted to the hospitals with COPD between September 1999 and July 2000	Patients (1) that resided outside the region; (2) had insufficient English speaking skills; (3) were resident in a nursing home; (4) or were confused or demented	67.1(NR)/66.7(NR); 49/46; NR	Home visits by community nurse at 1 and 4 weeks after discharge giving verbal and written education and monitoring progress and preventive general practitioner care plan made by nurse for GP	Usual care: discharge to general practitioner care with or without specialist follow-up	SMS, DSD, CIS	3	65

Author	Study	Inclusion criteria	Study population	Intervention	Comparison	Outcomes
Hernandez <i>et al.</i> 2003 [40]		(1) COPD exacerbation as a major cause of referral to the ER; (2) absence of any criteria for imperative hospitalization as stated by the British Thoracic Society (BTS) guidelines	(1) Not living in the health care area or admitted from a nursing home; (2) lung cancer and other advanced neoplasms; (3) extremely poor social conditions; (4) severe neurological or cardiac co-morbidities; (5) illiteracy; (6) no phone at home	71.0(9.9)/70.5(9.4); 97/97; 43%/41%	Assessment on ER admission by specialized team. Treatment at discharge: Pharmacological therapy of COPD and co-morbidities; No pharmacological treatment (e.g. education, training, smoking cessation, etcetera). Home hospitalization and 8-week follow-up	SMS, DSD 2 65
Hesselink <i>et al.</i> 2004 [41]		(1) A clinical diagnosis of asthma, COPD or mixed disease; (2) age 16–75 years; (3) treated by the GP; (4) absence of other specific pulmonary or terminal diseases; (5) use of asthma or COPD medication; and (6) experienced disease symptoms in the past year	Not explicitly stated	49.9(14.2)/44.7 (13.6); 35/28; 81.9% (22.6)/84.7% (23.4)	Taylor-made education conducted by a general practice assistant and focusing on a patients' technical skills and coping with the disease	SMS, DSD 24 80
Jeffs <i>et al.</i> 2005 [42]		All patients with COPD	Not explicitly stated	67.6(NR)/67.4(NR); 36/36; NR	Post-acute respiratory outreach service	SMS, DSD 12 55
Lee <i>et al.</i> 2002 [43]		(1) Patients $\geq 65$ ; (2) present resident of a nursing homes; (3) main diagnosis of COPD; (4) at least one hospital admission in the previous 6 months; (5) soon to be discharged to nursing home	(1) Patients with terminal illness; (2) communication problems.	81.1(16.0)/79.7(16.5); 56/49; 30.6% (10.1)/31.1% (13.3)	A care protocol was provided by community nurses to nursing home staff. Training of community nurses	SMS, DSD, DS 6 65
Meulepas <i>et al.</i> 2007 [44]		(1) patients >40 years with (2) a documented lung condition and (3) using inhalation medicines	Not explicitly stated	59(12)/58(10); 42/48; NR	A primary care model: structured follow-up including logistic support to the practice through a patient register and recall system and education and counselling	SMS, DSD 24 50
Neff <i>et al.</i> 2003 [45]		(1) A primary or secondary home health care diagnosis of COPD; (2) age 62 or older with Medicare as the primary insurer; (3) alert and oriented; (4) English speaking; (5) able to respond to questions	Persons with advanced COPD who were considered terminal and receiving primarily palliative care	75.5(7.3); 39; NR	Patients with COPD in the intervention group received services from pulmonary care RN/LPNs who were supervised and directed by a cardiopulmonary care APN specialist: home visits, telephone contacts and a nurse specialist available by phone 24 hours a day and clinical consultation	SMS, DSD, DS <3 45

Table 2 Continued

Author, year of publication	Inclusion	Exclusion	Population [mean age (I/C); % male (I/C); severity (% FEV1 predicted)]	Intervention	Control	Components SMS, DSD, CIS, DS	Follow-up (months)	Qualityscore studydesign
Poole <i>et al.</i> 2001 [46]	(1) Admitted to hospital 4 >in previous 2 years (2 >previous 12 months)	Overwhelming co-morbidities such as severe cardiac failure or cancer or were institutionalized.	70.0(NR)/75.4(NR)*; 63/66; 26% (10)/NR	Clinical nurse and a social worker, education about COPD and use of medicines, smoking cessation and recognition and management of exacerbations. Weekly telephone calls, discharge planning, home exercise programme/pulmonary rehabilitation.	No specific intervention	SMS, DSD	12	55
Rea <i>et al.</i> 2004 [47]	Diagnosis of COPD by ICD-9-CM codes and GP diagnosis of moderate to severe COPD	(1) Chronic asthma; (2) bronchiectasis; (3) co-morbidity; (4) prognosis <12 months, long-term oxygen therapy or unwell; (5) no informed consent; (6) deceased	Total: 68 (44-84); Total: 41; 51.8%/50.0%	A disease management programme, with a COPD management guideline, a patient-specific care plan and collaboration between patients, GPs, practice nurses, hospital doctors and nurse specialists	Usual care, no care plan, not seen by a respiratory doctor or nurse specialist	SMS, DSD, CIS, DS	12	75
Rootmensen <i>et al.</i> 2008 [48]	(1) Diagnosed having asthma or COPD by a pulmonary doctor; (2) age >18 years; (3) understood Dutch sufficiently to answer the questionnaires; and (4) never had consulted a pulmonary nurse.	Not explicitly stated	60(15)/61(15); 47/39; 57% (19)/64% (26)	A protocol-based nursing care programme in the treatment of asthma and COPD patients at a pulmonary outpatient clinic	Pulmonary doctor care	SMS, DSD	6	80
Sridhar <i>et al.</i> 2008 [51]	(1) Discharged COPD patients having been due to an acute exacerbation	(1) Significant co-morbidity such as severe heart disease or cancer, or any condition that would preclude participation in the physical therapy component of a pulmonary rehabilitation programme	69.9 (9.6)/69.68 (10.4); 49.2/49.2; 42.9% (15.5)/48.9% (18.7)	A care package incorporating initial pulmonary rehabilitation and self-management education, provision of a written, personalized COPD action plan, monthly telephone calls and three monthly home visits by a specialist nurse for a period of 2 years	Usual care from their primary care doctor, or secondary care and/or the respiratory nursing service as appropriate	SMS, DSD	24	75
Smith <i>et al.</i> 1999 [49]	(1) >40 years; (2) FEV1/FVC <60%; (3) no other active major illness; (4) stable; (5) speak/write English	Not explicitly stated	70.0(1.2)/69.8(1.2); 56/65; 33%/NR	*Respiratory home-based nursing intervention* (HBNL). Discharge planning; home visits; education and counselling for smoking cessation, referral to GP for nicotine replacement. Nurse aimed to identify exacerbations early.	Usual care and education from outpatient clinics and GP services	SMS,DSD	12	80



**Table 2 Continued**

Author, year of publication	Inclusion	Exclusion	Population [mean age (I/C); % male (I/C); severity (% FEV1 predicted)]	Intervention	Control	Components SMS, DSD, CIS, DS	Follow-up (months)	Qualityscore studydesign
Weinberger <i>et al.</i> 2002 [56]	(1) Prescription for methylxanthines, ICS, ...; (2) reported as having COPD; (3) >18 years; (4) >70% of medication from one pharmacy; (5) no significant impairment in vision, hearing, speech; (6) not reside in an institution (7) provided written consent	Not explicitly stated	62.2(11)/62.9(10) or 62.2(12); 36/34 or 33; 52.2% (21.1)/46.4% (19.8) or 48.1% (18.4)	The pharmaceutical care programme provided pharmacists with recent patient-specific clinical data, training, customized patient educational materials and resources to facilitate programme implementation	PEFR monitoring group: received a peak flow meter, instructions about its use and monthly calls to elicit PEFRs, but PEFR data were not provided to the pharmacist. Usual care: received neither peak flow meters nor instructions	SMS, DSD, CIS, DS	12	80
Wong <i>et al.</i> 2005 [57]	(1) Diagnosis of COPD;(2) not been diagnosed with ischaemic heart disease, musculoskeletal disorders or other disabling diseases that might limit rehabilitation; (3) able to speak Cantonese; (4) alert and oriented; and (5) contactable by phone	(1) Discharged to an old-age home; (2) serious abuse of alcohol or drugs or suffering from a psychiatric disease; (3) dying	I = 72.8(8.3); C = 74.4(7.4); 90/67; NR	A nurse-initiated telephone follow-up programme. The telephone follow-up was guided by a protocol developed and validated for this study	The control group received normal routine care without telephone follow-up	SMS, DSD	3	55
Zajac 2002 [58]	A pool of potential programme participants is typically identified based on diagnosis codes for COPD (chronic bronchitis and emphysema) appearing in claims history.	Not explicitly stated	Total: 68.9; Total: 50; NR	Disease management programme provides patient education, self-management tools and support, case management, and follow-up to members of contracted managed care organizations with asthma and COPD	None	SMS, DSD, DS	Various	35

\*Statistically different between I and C.  $P < 0.05$

NR, not reported; COPD, chronic obstructive pulmonary disease; I, intervention group; C, control group; SMS, self-management support; DSD, delivery system (re)design; DS, decision support; CIS, clinical information system; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; PaO<sub>2</sub>, partial pressure of oxygen in arterial blood; PaCO<sub>2</sub>, partial pressure of carbon dioxide in the arterial blood; kPa, kilo Pascal; ER, emergency room; CHF, chronic heart failure; RN, registered nurse; LPN, licensed practical nurse; APN, advanced practice nurse; PEFR, peak expiratory flow rate; GP, general practitioner; ATS, American Thoracic Society; ICD-9, international classification of diseases and related health problems.

**Table 3** Meta-analysis and meta-regression results.

	No. of studies	No. of participants (I/C)	MD (95% CI) I <sup>2</sup>	Explained heterogeneity (P-value)
<b>Quality of life</b>	5	442/438	-2.36 (-4.78, 0.06) 0%	
Number of components				NA
3	5	442/438	-2.36 (-4.78, 0.06) 0%	
Length of follow-up				No heterogeneity (0.5035)
<12 months	3	199/200	-2.17 (-5.57, 1.23) 0%	
≥12 months	2	243/238	-2.56 (-6.02, 0.89) 0%	
Quality				No heterogeneity (0.7215)
Moderate quality	2	118/131	-0.94 (-6.05, 4.16) 21%	
Good quality	3	324/307	-2.92 (-5.78, -0.06) 0%*	
<b>Emergency department visits</b>	6	308/274	-0.11 (-0.26, 0.04) 40%	
Number of components				100% (0.0183)
2	3	176/154	-0.23 (-0.41, -0.05) 21%*	
3	3	132/120	0.02 (-0.12, 0.17) 0%	
Length of follow-up				100% (0.0612)
<12 months	5	278/244	-0.11 (-0.20, -0.01) 34%	
≥12 months	1	30/30	-1.53 (-3.38, 0.32) NA	
Quality				30.9% (0.8070)
Low quality	1	30/30	-1.53 (-3.38, 0.32) NA	
Good quality	5	278/244	-0.10 (-0.24, 0.03) 34% RR (95% CI) I <sup>2</sup>	
<b>Hospitalizations</b>	10	621/597	0.93 (0.76, 1.14) 54%	
Number of components				100% (0.0022)
2	5	259/229	1.10 (0.90, 1.35) 19%	
3	3	214/226	0.89 (0.51, 1.55) 55%	
4	2	148/142	0.70 (0.55, 0.90) 0%*	
Length of follow-up				5.5% (0.6940)
<12 months	3	234/225	0.94 (0.61, 1.44) 19%	
≥12 months	7	387/372	0.93 (0.73, 1.18) 65%	
Quality				19.6% (0.2108)
Moderate quality	5	275/266	1.07 (0.83, 1.39) 11%	
Good quality	5	346/331	0.85 (0.64, 1.12) 68%	
<b>Mortality</b>	13	861/858 (1719)	0.92 (0.69, 1.24) 0%	
Number of components				No heterogeneity (0.1253)
2	7	421/387	0.75 (0.48, 1.18) 0%	
3	3	252/261	0.82 (0.44, 1.51) 0%	
4	3	188/210	1.16 (0.56, 2.43) 47%	
Length of follow-up				No heterogeneity (0.6492)
<12 months	3	277/267	0.85 (0.46, 1.59) 0%	
≥12 months	10	584/591	0.94 (0.67, 1.31) 4%	
Quality				No heterogeneity (0.3798)
Moderate quality	7	468/444	0.85 (0.53, 1.36) 0%	
Good quality	6	393/414	0.91 (0.56, 1.48) 39%	

\*P-value &lt;0.05, NA, not applicable.

CI, confidence interval; I<sup>2</sup>, statistical heterogeneity.

length of stay, mean number of hospitalizations or readmissions). Ten primary studies reported all-cause hospitalizations in a manner that could be pooled, that is, they all reported all-cause hospitalization as the number of hospital admissions [32,34,35,39,40,42,46,47,49,51]. The risk ratio (random) of chronic care management is 0.93 (95%CI: 0.76–1.14; I<sup>2</sup>:54%, Table 3). Subgroup analyses showed that ‘good quality’ studies had no significant effect similar to ‘moderate quality’ studies, heterogeneity was apparent. Subgroup

analyses showed no effects and heterogeneity on length of follow-up. Studies with four components ( $n=2$ ), without any heterogeneity (I<sup>2</sup>=0%), showed significant effects whereas two-component ( $n=5$ ) and three-component ( $n=3$ ) studies did not. Meta-regression showed no significant effects for study quality or length of follow-up on the relative risk of hospitalization. Yet, the number of components explained 100% of the variance ( $P=0.022$ ), which is in line with the subgroup analyses.

## Emergency department visits

The pooled results of the six primary studies that implemented chronic care programmes and reported a mean number of emergency department visits did not reach a significant reduction in these visits ( $-0.11$ ; 95%CI:  $-0.26-0.04$ ;  $I^2:40\%$ , Table 3) in the intervention groups compared with controls [30,35,40,43,52,57]. Subgroup analyses demonstrated no effects of studies of moderate or poor quality. No effects were found on length of follow-up. Studies including two components showed significant effects ( $P = 0.01$ ), whereas three-component studies did not. Meta-regression analysis showed that the number of components explained 100% of the variance ( $P = 0.018$ ). In contrast, quality of the study and length of follow-up did not explain heterogeneity.

## Mortality

Thirteen primary papers assessed mortality as an outcome measure [32,34,35,37,39,40,42,44,46,47,49–51]. However, none of them measured a significant improvement on mortality due to the chronic care management. The relative risk of mortality from the meta-analysis confirmed this finding; no significant improvement was found due to the implementation of chronic care programmes [0.89 (random effect); 95%CI: 0.69–1.24, Table 3]. Subgroup analyses showed comparable relative risk ratios. Heterogeneity was absent between studies ( $I^2 = 0\%$ ). Meta-regression analysis was performed to identify whether the variables were associated with the effect of chronic care management on mortality. The meta-regression analyses showed that the quality of studies, the length of follow-up and the number of components are not associated with the effect ( $P > 0.05$ ).

## Discussion

This study aimed to examine the effectiveness of chronic care management in COPD taking the various sources of heterogeneity of included studies into account; enabling the understanding of and the decision making about chronic care management strategies for COPD. Generally, the included reviews show positive results on quality of life and hospitalizations. Inconclusive effects were found on emergency department visits; no effects were reported on mortality. Meta-analyses on the primary papers revealed just no significant effects of decrease on emergency department visits and improvement in quality of life. Studies of good quality showed significant improvements in quality of life. Hospitalizations were not significantly reduced. Moderate statistical heterogeneity was at hand for hospitalizations and emergency department visits. Meta-regression showed that the number of components explained statistical heterogeneity for hospitalizations and emergency department visits. Methodological study quality and length of follow-up did not significantly explain heterogeneity.

In particular, the number of components explained statistical heterogeneity in COPD chronic care management programmes. This was also suggested, however not grounded, in earlier reviews [14,24]. Four components showed significant effects on hospitalizations whereas two and three components did not. In contrast, two-component studies had the best results on emergency department visits, which could not be explained by the combination of

components. An explanation might be the limited number of studies included in the meta-regression analysis.

This study is the first in which a meta-regression analysis is performed to explain heterogeneity in the effectiveness of COPD care programmes. It utilized a strong evidence base due to an extensive search strategy following the internationally accepted definition of chronic care management (WHO) [60]. However, several limitations should be noted. The absence of publication bias cannot be guaranteed. Although, broad search strategies were defined, grey literature has not been searched.

Primary papers were selected through the reviews. This implies that the limitations of the included review also affect our results. Chronic care management programmes as well as 'usual care' are often poorly described, which makes comparison between studies difficult. Besides, results are frequently not fully reported, such as  $P$ -values and standard deviations, and therefore not used in the meta-analyses. Furthermore, the components of care programmes are frequently scarcely operationalized or reported. Moreover, it can be questioned whether three suboptimal components are more effective than two well-operated ones.

A quality instrument to assess the quality of the reviews as well as an instrument to assess the quality of trials for complex interventions like chronic care management is needed. The PRISMA checklist, which recently replaced the QUOROM statement, is a guideline for performing and reporting reviews and meta-analyses and includes several noteworthy changes (e.g. the methodological quality of included and selective reporting of outcomes of included studies). However, the PRISMA checklist is not developed for gauging the quality of systematic reviews [61,62]. To our knowledge, the HTA-DM instrument [18] is the only relevant and validated instrument for primary studies for chronic care management.

Although the variables for the subgroup analyses and meta-regression were selected based on the available evidence [14,15], heterogeneity between the studies regarding the effect on hospitalizations and emergency department visits might be caused by other variables than those measured, as for example the degree in which the components are implemented or usual care. Taking the nature of interventions into account, length of follow-up and study quality can only explain part of the statistical heterogeneity that characterizes the evidence base for COPD chronic care management. Moreover, further research is needed to elucidate the diversity between COPD chronic care management studies in terms of the effects measured and to identify successful intervention components.

The effectiveness of chronic care management for patients with COPD is most frequently assessed for quality of life, hospitalization, emergency department visits and mortality. Despite the premises of control of cost by chronic care programmes, most studies lack information on health care costs. Furthermore, although patient satisfaction, medication adherence, education and knowledge are measured, a great variety of instruments is used. More knowledge is needed on the underlying mechanisms and associations between chronic care programme implementation, behavioural changes and outcomes of care [63]. Absence of this evidence base is largely due to the strong position of the medical model in research of chronic care management [64]. As a result, medical outcomes of care prevail and conclusions could not be drawn with regard to important aspects such as behavioural changes, process changes, and health care costs.



The introduction of complex, multicomponent interventions, such as chronic care programmes, is essentially a process of social change [16]. The effectiveness of these programmes is sensitive to an array of influences, for example, details of implementation and context [65,66]. Although traditional (quasi-) experimental methods are important for learning whether improvement interventions change behaviour, they do not provide appropriate and effective methods for addressing the crucial pragmatic questions about improvement: what is it about the mechanism of a particular intervention that works, for whom, and under what circumstances? [67] Therefore, a wider range of scientific methodologies should be embraced. Evaluation should retain information on both mechanisms and contexts to be valuable for decisions to be made on local and national level [63]. Moreover, strict inclusion criteria should be avoided, since this impedes the population approach of chronic care programmes.

Practical implications of this study address the design and implementation of chronic care programmes. Chronic care programmes were designed to build on the interrelationships between care components, leading to practice redesign across various components. This study showed that an arbitrary selection of components is applied in most studies. Moreover, programmes were directed at specific populations (mostly rather severe COPD patients). Integrating multiple components and application of a population approach offer possibilities for an increase in quality and effectiveness of COPD care programmes. With regard to implementation, little attention is paid to implementation strategies and derived process measures. Implementation of complex programmes should be based on evidence-based change principles to guide improvements [9].

## Conclusion

COPD management programmes have the potential to significantly improve quality of life, and significantly reduce hospitalizations and emergency department visits. Absence of heterogeneity in quality of life makes it a robust outcome measure. Yet, this finding also implies quality of life is no useful outcome measure to identify the most effective chronic care management programme. Heterogeneity in hospitalizations and emergency department visits can be explained by the number of components of programmes. Further research is needed to elucidate the diversity between COPD chronic care management studies in terms of the effects measured and strengthen the support for chronic care management.

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