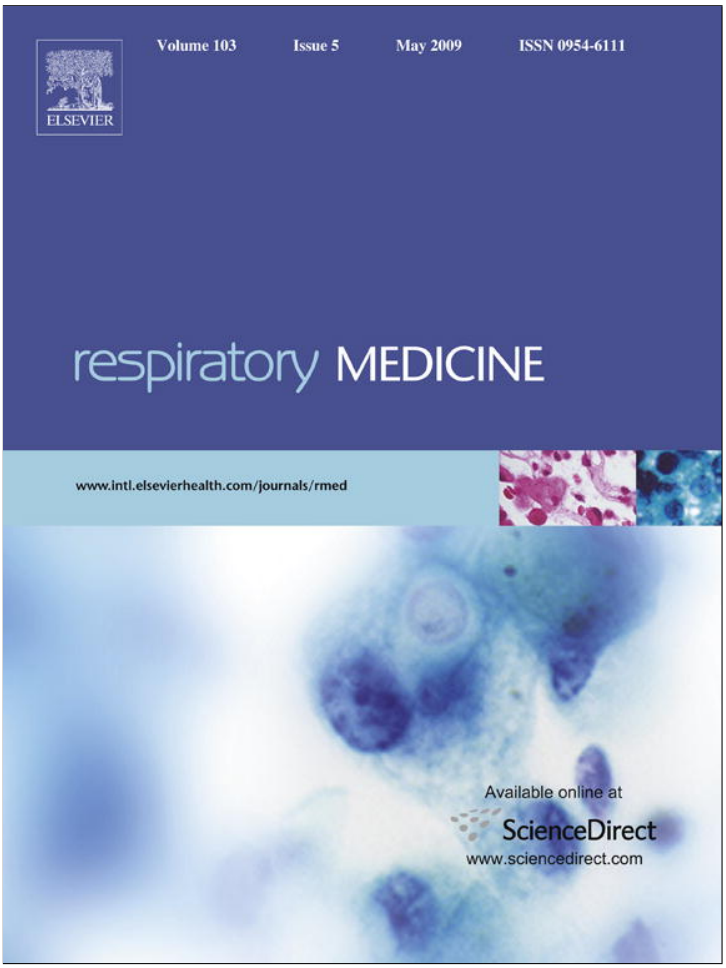

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REVIEW

A systematic review of integrated use of disease-management interventions in asthma and COPD

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Systematic review;
Disease management;
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Summary
Background: The effectiveness of multiple interventions in asthma and chronic obstructive pulmonary disease (COPD) is unclear.
Objective: To examine the effectiveness of multiple interventions as compared to single interventions or usual care on health outcomes and health care utilisation within the context of integrated disease management in asthma and COPD.
Methods: MEDLINE and the Cochrane Library (1995–May 2008) were searched for controlled trials. Two reviewers independently extracted data and assessed study quality. Meta-analyses were performed on quality of life and health care utilisation data. Furthermore, the effects of multiple interventions versus single interventions and usual care were assessed qualitatively.
Results: Of the 36 studies included, 17 targeted double interventions (patient-related and organisational interventions); 19 studies performed triple interventions (patient-related, professional-directed and organisational interventions). They were heterogeneous in terms of (combinations of) interventions, outcomes measured, study design and setting. Pooled data showed that studied disease management programmes significantly improved quality of life on several domains. Patients within triple intervention programmes had less chance of at least one hospital admission compared with usual care. No significant effects were found in number of emergency department visits. Qualitative analyses revealed positive trends on process improvements and satisfaction. Inconclusive results were reported on symptoms; no effects were found in lung function.

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Conclusion: In spite of the heterogeneity of disease management studies in asthma and COPD care, this review showed promising improvements in quality of life and reductions in hospitalisations, especially for triple intervention programmes.

Contents

Background

Chronic conditions account for more than 50% of the global disease burden, and this figure is projected to rise.[1] Among the most common chronic diseases worldwide are asthma and chronic obstructive pulmonary diseases (COPD). These respiratory diseases represent an enormous burden on individuals, families and societies, by their impact on quality of life and health resource utilisation, as well as mortality.[2,3] Yet, health care systems are often not organised to provide effective and efficient care for chronic health problems.[4] The causes of chronic conditions are complex and responses to patients' needs therefore should be multifaceted and multi-institutional.[5] Disease management has been introduced as the answer to these demands.[6–8]

Disease management is a concept by which care delivery is better coordinated through the integration of several components across the entire delivery system and the application of tools specifically designed for the population in question, e.g. guidelines, education, information systems.[9] The Disease Management Association of America (DMAA)[10] defined disease management as: ''a system of coordinated health care interventions and communications for populations with conditions in which patient self-care efforts are significant''. There are high expectations for disease management; it is expected to improve quality and efficacy of care for patients with chronic diseases. Disease management supports the use of multiple interventions, defined as combinations of at least two of three types of intervention: patient-related, professional-directed and organisational interventions, according to Cochrane Effective Practice and Organisation of Care (EPOC).[11,12] Key to disease management is therefore to involve the implementation and integration of combined interventions.[13] But evidence on the effectiveness of combined interventions in the care continuum is scattered and an overview on the state of the art in asthma and COPD is lacking. The question addressed in this paper is: ''what is the effect of the use of multiple interventions within the context of integrated disease management in asthma and COPD''.

Current literature contains evidence implying improvements in health care as a result of multiple interventions. Grol[14] concludes that multifaceted strategies — combining different approaches and targeting different barriers to improvement — are in general more effective than individual approaches. He assumes this will probably hold for disease management too. The chronic care model (CCM)[15,16] also emphasises a multifaceted approach, supposedly leading to healthier patients, more satisfied professionals and lower costs.[6,17] Several systematic reviews across a number of chronic diseases (e.g. diabetes, heart failure) confirm positive effects on quality of care.[18–22] But, many studies have focused on the effects of interventions solely directed either at the patient[23–26] or the professional.[27–32] So far, these interventions have only been partly successful. Weingarten and colleagues[33] conclude from a meta-analysis that most disease management programmes directed at either professionals or patients are associated with improvements in care. However, this analysis solely covered single interventions within disease management programmes; the effectiveness of the combined interventions was left out of consideration. A systematic review on the

Table 1 Observed EPOC definitions of interventions in asthma and COPD care.

Patient education: Interventions designed to promote increased understanding of a target condition or to teach specific prevention or treatment strategies, or specific in-person patient education (e.g., individual or group sessions with diabetes nurse educator; distribution of printed or electronic educational materials). Interventions with patient education were included only if they also included at least 1 other strategy related to clinician or organisational change.	Expansion or revision of professional roles: Changes to the structure or organisation of the primary health care team: • Adding a team member or ''shared care,'' e.g., routine visits with personnel other than the primary physician (including physician or nurse specialists in COPD care, pharmacists). • Expansion or revision of professional roles (e.g., nurse or pharmacist plays more active role in patient monitoring).
Professional education: Interventions designed to promote increased understanding of principles guiding clinical care or awareness of specific recommendations for a target condition or patient population (e.g. educational meetings, active distribution of educational materials, and educational outreach visits).	Case management: Any system for coordinating diagnosis, treatment, or ongoing patient management (e.g., arrangement for referrals, follow-up of test results) by a person or multidisciplinary team in collaboration with or supplementary to the primary care clinician.

effectiveness of the CCM in COPD patients focussed on interventions including one or more components, but did not look at combinations of interventions. Studies with two or more components had lower health care use compared with controls. Although previous reviews cover a wide range of interventions, little is known about the effectiveness of combined disease management components in asthma and COPD care. This review aims to understand the effectiveness of multiple disease management interventions in improving care and cost-effectiveness for patients with asthma or COPD.

Methods

Identification of studies

We included studies that evaluated the effectiveness of disease management programmes consisting of multiple interventions targeted at patients aged $\geq$16 years with a principal diagnosis of asthma or COPD. Studies were included if they met the following methodological criteria: experimental, randomised controlled trials (RCTs) and controlled clinical trails (CCTs), or quasi-experimental, controlled before and after studies (CBAs) or time series designs (ITS). The control group needed to have been provided usual care or single intervention. Studies were included if they reported any objective measure of outcomes reflecting the primary goals of disease management, i.e. to promote, maintain and enhance the health of patients. Studies therefore needed to provide details on clinical outcomes, quality of life, health care utilisation, and/or patient satisfaction.[10]

According to EPOC,[11] an intervention was classified as 'patient' when targeting patient behaviour, such as patient education, or self-management interventions; 'professional' when aiming at professional practice behaviour, for example professional education, audit and feedback; 'organisational' when interfering in the structure or organisation of care, for instance revision of professional roles, or arrangements for follow-up (Table 1). Since the focus of the study was on *multiple* interventions within the context of *disease management*, studies on the effects of single interventions versus usual care were excluded. Moreover, pulmonary rehabilitation programmes were defined as single intervention, since they already are a part of the organisational structure of care, and therefore excluded.

Literature search

Searches of MEDLINE (1995—May 2008) and the Cochrane Library (1995—May 2008) were undertaken. Studies published before 1995 were not considered for inclusion, as it was not until 1995 before disease management appeared frequently in the medical literature.[13] The following key words (Medical Subject Headings) were entered: disease management, disease state management, delivery of integrated health care, comprehensive health care, patient care planning, primary health care, patient care team, critical pathways, case management, continuity of patient care, practice guidelines, guidelines, clinical protocols, patient education, self-care, reminder systems, health education, health promotion, community health planning, ambulatory care, feedback, reminder or monitoring[33] in combination with asthma and COPD specific terms. These all aimed to identify studies evaluating the effectiveness of multiple interventions.

Methods of the review

Potentially relevant studies retrieved from the electronic searches were independently screened for eligibility (KL and AN). Next, three reviewers (KL, AN and RH) independently reviewed the selected studies and extracted data with the use of a standardised abstraction form. Data were collected which described the interventions, methods, sample size, population characteristics, setting, and measures of programme effects on processes and outcomes of care from unmasked articles that met the inclusion criteria. Where possible, data were tabulated in terms of means $\pm$ SD for patient outcomes and proportions for process measures; other data were presented as reported in the original sources. Any discrepancies between reviewers were resolved by discussion.

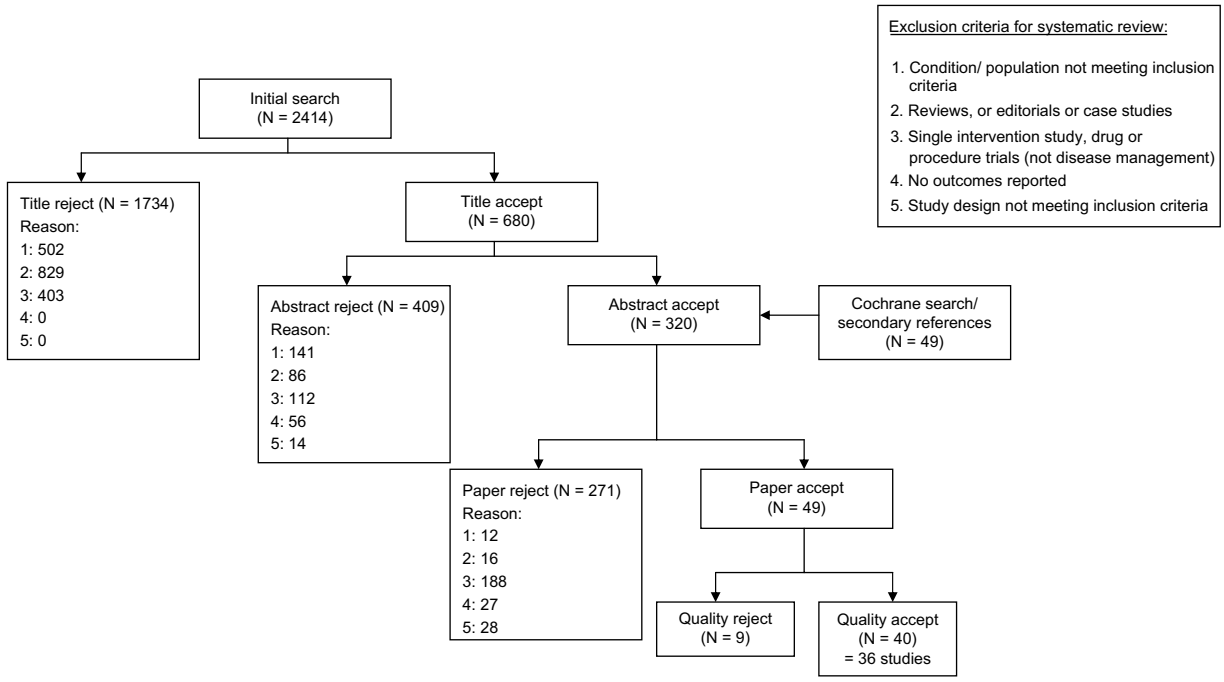

Figure 1 Selection process for including studies in systematic review.

Study quality was assessed with the Health Technology Assessment-Disease Management (HTA-DM) instrument developed by Steuten et al.[34] The scope of this instrument comprises quasi-experimental and experimental studies as well as controlled, uncontrolled and observational studies.[34] The instrument includes four components, namely, study population, description of the intervention, measurement of outcomes, and data analysis/presentation of data. Methodological quality is scored between 0 and 100 points with scores <50 points indicating inferior quality and ≥ 70 points indicating good quality.[35] Studies of inferior quality were excluded from this review. The HTA-DM is a reliable instrument for methodological quality assessment of HTA of disease management.[34]

Data analysis

Given the likely heterogeneity of the studies, we performed a qualitative assessment of the effects of studies, based upon the combination of interventions, study quality and population differences. Potential differences were analysed by preparing tables to examine the size of observed effects relative to these variables. When possible, meta-analyses were performed, using RevMan 4.2.[36] Data were pooled for the Asthma Quality of Life Questionnaire (AQLQ) in pharmacist disease management programmes, and the St. George's Respiratory Questionnaire (SGRQ), emergency department visits and hospital admissions in COPD disease management programmes. Outcomes were analysed as continuous variables using standard statistical techniques (weighted mean difference (WMD)) and with dichotomous outcomes pooled odds ratios (OR) were calculated. Both combined with a fixed effect model and 95% confidence intervals were calculated as appropriate. Statistical variation between study findings was explored using the I^2 statistical measurement.[37]

Results

Description of studies

Fig. 1 shows the flow of papers through the review. Overall, 2414 references published from January 1995 to May 2008 were identified; 680 were accepted for further screening. After reading titles and abstracts 409 papers were excluded, leaving 271 articles for a full-text review. Screening of the Cochrane Library and references resulted in another 49 potentially relevant articles. Of all 320 articles, 271 (85%) did not meet the inclusion criteria. Another nine studies were excluded due to inferior methodological quality.[38–46] Eventually, 36 studies[47–86] (40 papers) were identified as multiple intervention studies on asthma and/or COPD; 18 of which focused on COPD, 16 on asthma, and two on both diseases. Fourteen studies had 'good' methodological quality (≥ 70 points)[51–53,58,60,63,70,73,77,79,82,84–86]; 22 scored between 50 and 69 points and were therefore considered of 'moderate' quality.[47–49,54–56,61,62,64,65,67–69,71,72,74–76,78,80,81,83]

We present results based on combinations of interventions as outlined in the protocol. Seventeen studies used both patient-related and organisational interventions[51,55,56,61,63,64,67,70,72,73,75,77,78,81–84] and another 19 used triple interventions (patient-related, professional-directed, and organisational).[47–49,52–54,58,60,62,65,68,69,71,74,76,79,80,85,86] No studies that combined patient-related and professional-directed or professional-directed and organisational interventions passed the selection criteria (Table 2). As expected, the intervention groups were generally compared to control patients receiving 'usual care'. Control patients in three studies received patient education[55,78,81]; another two studies used two control groups: one given usual care and one given patient education.[54,86]

Most studies reported quality of life and health care utilisation measures. Instruments for measurement of

Table 2 Key Features of Studies Included in a Systematic Review of Multiple Interventions in Patients with Asthma and COPD

Study	Setting	Study[a] design/quality	Interventions	Follow-up (months)[b]	Outcome[c]/process indicators[d]	Results[e]
Multiple interventions versus usual care						
Aiken et al., 2005 ''Intensive Home-based Case Management''	COPD patients in a hospice >18 years with an estimated 2 year life-expectancy, Phoenix, Arizona (U.S.)	RCT Moderate	I: Provider education, patient education, continuity of care (case management) ($N=33$) C: Usual care ($N=28$)	9	QOL: SF36 (8 domains) HCU: ED PROCESS: Behaviour; Knowledge	Sign. better on 3 domains: Physical functioning, General health and Vitality NS Sign. better outcomes on self-management of illness and knowledge on illness
Armour et al., 2007 ''Pharmacy Asthma Care Programme''	Asthma patients 18–75 registered in a pharmacy in New South Wales, Victoria and Queensland (Australia)	RCT Moderate	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) ($N=191$) C: Usual care ($N=205$)	6	LUNG: FEV_1 SYMP: Perceived Control of Asthma (PCAQ) QOL: AQLQ (4 domains) PROCESS: Knowledge; Technique; Behaviour	NS Sign. better asthma control Sign. more beneficial effects in Total score Sign. more asthma knowledge; Sign. increase of correct inhalation technique and usage action plan (*no data control*)
Barbanel et al., 2003 ''Community Pharmacist-based Programme''	Adults, 18–65, with a general practitioner diagnosis of asthma who regularly visited the pharmacy for collection of prescribed medication (U.K.)	RCT Moderate	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) ($N=12$) C: Usual care ($N=12$)	3	SYMP: North of England Symptoms Questionnaire	Sign. better symptom score

Bourbeau et al., 2003 Gadoury et al., 2005 Bourbeau et al., 2006 ''Multi-component self-Management Programme''	COPD patients ≥50 years in 7 hospitals with advanced COPD with at least 1 hospitalisation for exacerbation in the previous year (Canada)	RCT Good	I: Patient education, continuity of care (case management) ($N=96$) C: Usual care ($N=95$)	12	LUNG: FEV_1 QOL: SGRQ (4 domains) SYMP: 6MWT; MRC; Sputum; Exacerbations HCU: Hosp; ED; Cost	NS Sign. better on Impact domain, other domains NS NS; NS; NS; Borderline sign. more decrease in No. of exacerbations Sign. more reduction in No. of hospitalisations (acute exacerbations/all cause), frequency hospitalised, No. of hospital days; Reduction in emergency visits (acute exacerbations) and scheduled GP visits; cost savings with increased patient caseload and rising costs of hospitalisation.
				24	HCU: Hosp; ED	Stat. sign. and clinically relevant reduction in all-cause hospitalisations and in all-cause emergency visits
Casas et al., 2006 ''Integrated Care''	COPD patients recruited in two tertiary hospitals immediately after the patients' hospital discharge for an exacerbation >48 hours (Spain and Belgium).	RCT Good	I: Provider education, self-management, continuity of care (case management; follow-up) ($N=65$) C: Usual care ($N=90$)	12	HCU: Readm; Visits	Significantly lower No. of readmissions, rate of readmission, and mean No. of readmissions; NS

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Table 2 (*continued*)

Study	Setting	Study[a] design/quality	Interventions	Follow-up (months)[b]	Outcome[c]/process indicators[d]	Results[e]
Cordina et al., 2001 ''Community Pharmacist-based Programme''	Patients ≥16 registered at the asthma clinic cared for by community pharmacies (Malta)	RCT Good	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) (*N*=86) C: Usual care (*N*=66)	12	LUNG: PEFR QOL: SF36 (8 domains); LWAQ (11 domains) SYMP: Wheeze QOC: Satisfaction HCU: Hosp; Days off PROCESS: Technique; Compliance	NS Sign. better on Vitality domain, other domains NS; Borderline sign. better Total score Sign. more patients reported no wheezing Sign. more patients reported approachable pharmacist/questioned their pharmacist Sign. fewer self-reported hospitalisations; NS Sign. higher improved inhaler technique; NS
Coultas et al., 2005 ''Nurse-Assisted Home Care''	COPD patients in primary care clinics associates with an urban academic health center, aged ≥45 cared for by primary care physicians (U.S.)	RCT Moderate	I: Provider education, patient education, continuity of care (follow-up) (*N*=72) C: Usual care (*N*=73)	6	QOL: SF36; SGRQ; Illness intrusiveness scale HCU: ED; Hosp; Visits	NS; NS; Sign. more improvement in perceived illness intrusiveness NS; NS; NS
Egan et al., 2002 ''Nursing-Based Case Management''	COPD patients ≥18 years, admitted to a major private hospital (Australia)	RCT Moderate	I: Patient education, continuity of care (case management) (*N*=33) C: Usual care (*N*=33)	1,5	QOL: SGRQ (4 domains); HADS (2 domains) SYMP: SWB HCU: Readm PROCESS: Support	Sign. better on Activity domain, other domains NS; Sign. less anxiety *(not sustained)*, depression NS NS NS NS
Garcia-Aymerich et al., 2007 ''Integrated care intervention''	COPD patients recruited in a tertiary hospitals immediately after the patients' hospital discharge for an exacerbation >48 hours (Spain).	RCT Good	I: Provider education, self-management, continuity of care (case management; follow-up) (*N*=44) C: Usual care (*N*=69)	12	LUNG: FEV_1 QOL: SGRQ; EQ-5D SYMP: Dyspnoea PROCESS: Knowledge; Compliance; Behaviour	NS NS; NS NS All variables related to knowledge and behaviour were better, mostly sign.; Compliance NS

Herborg et al., 2001 ''Community-Based Programme for Pharmaceutical Care''	Asthma patients aged 16–60 who purchased medication at the participating community pharmacies in the area (Denmark)	CBA Good	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring)/monitoring system ($N=264$) C: Usual care ($N=236$)	12	LUNG: PEFR QOL: NHP; LWAQ SYMP: Asthma Symptom Status QOC: Satisfaction HCU: ED; Hosp; Visits PROCESS: Knowledge; Compliance	NS Sign. more improvement on both measures Sign. better improved asthma status NS NS; NS; Clinically relevant less use of services Sign. more knowledge on asthma (medications); Sign. less inhalation errors
Hermiz et al., 2002 ''Home-Based Care by Community Nurse''	COPD patients in Health Services 30–80 years, attended to ED or admitted to the hospitals (Australia)	RCT Moderate	I: Patient education, continuity of care (follow-up) ($N=84$) C: Usual care ($N=93$)	3	QOL: SGRQ QOC: Satisfaction HCU: Hosp; ED PROCESS: Knowledge; Behaviour; Follow	NS Sign. more satisfied with their care NS; NS Sign. greater knowledge of COPD; NS; Sign. more follow-up
Hernandez et al., 2003 ''Home Hospitalisation''	COPD patients with exacerbations admitted to ER or two tertiary hospitals (Spain)	RCT Moderate	I: Provider education, self-management, continuity of care (follow-up) ($N=121$) C: Usual care ($N=101$)	2	QOL: SGRQ (4 domains) QOC: Satisfaction HCU: Readm; ED; LOS; Cost PROCESS: Knowledge; Compliance	Sign. higher improvement in Total score Sign. higher satisfaction NS; Sign. less ED admissions; Sign. lower LOS; Sign. lower overall health care cost per patient Sign. more improvement in knowledge and compliance to inhalation technique
Hesselink et al., 2004 ''Education Programme''	Patients aged 16–75 from GP practices in with asthma or COPD (The Netherlands)	RCT Good	I: Patient education, team changes (professional roles; nurse) ($N=139$) C: Usual care ($N=137$)	12 24	QOL: QOL-RIQ SYMP: MRC PROCESS: Efficacy; Technique; Coping; Compliance; Behaviour QOL: QOL-RIQ SYMP: MRC PROCESS: Efficacy; Technique; Coping; Compliance; Behaviour	NS NS NS; Inhalation technique was significantly better; NS; NS; NS NS NS NS; Inhalation technique was significantly better; NS; NS; NS

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Table 2 (*continued*)

Study	Setting	Study[a] design/quality	Interventions	Follow-up (months)[b]	Outcome[c]/process indicators[d]	Results[e]
Jeffs et al., 2005 ''Post Acute Respiratory Outreach Service''	All patients with COPD in a regional hospital (Australia)	CBA Moderate	I: Patient education, continuity of care (follow-up) ($N=28$) C: Usual care ($N=25$)	12	HCU: ED; Hosp; LOS	NS; NS; Sign. higher increase in hospital bed days
Johnson et al., 2005,2007 ''Disease Management''	Patients in the McKesson Asthma Care Support Advisor program (U.S.)	CBA Moderate	I: Provider education, self-management, continuity of care (case management) ($N=196$) C: Usual care ($N=196$)	12	HCU: ED; Hosp; LOS; Adm PROCESS: Compliance	Sign. fewer ED visits, hospitalisations, bed days, and asthma-related admissions. Sign. higher rates of medication usage
Knoell et al., 1998 ''Outpatient Pharmaceutical Care''	Adult asthma patients referred to a specialty outpatient clinic (U.S)	CBA Moderate	I: Patient education, team changes (professional roles/ pharmacist) ($N=45$) C: Usual care ($N=55$)	3	QOL: SF12; AQLQ QOC: Satisfaction HCU: Hosp; ED; Visits; Cost PROCESS: Compliance; Process	NS; sign. more improvement in quality of life Sign. more satisfaction with care NS: NS; NS; NS Sign. more compliant and better informed patients
Kritikos et al., 2007 ''Interactive Small-group Education in a Community Pharmacy Setting''	Asthma patients $\geq$16 registered in a pharmacy in the Central Sydney Area (Australia)	RCT Moderate	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) ($N=16$) C: Usual care ($N=16$)	3	SYMP: Asthma control QOL: AQLQ PROCESS: Knowledge; Technique; Compliance	Sign. less patients in the severe asthma/poor control category Sign. more improvement in quality of life Sign. higher asthma knowledge scores; Sign. more increase of correct inhalation technique; NS
Lee et al., 2002 ''Care Protocol by Community Nurses''	COPD patients $\geq$65, resident of 45 nursing homes in Hong Kong (China)	RCT Moderate	I: Provider education, self-management, continuity of care (follow-up) ($N=48$) C: Usual care ($N=41$)	6	LUNG: FEV_1 QOL: GHQ (4 domains); Barthel Index (BI) QOC: Satisfaction HCU: ED; Hosp; LOS	NS Sign. less anxiety and insomnia and sign. improved overall psychological well-being; NS Sign. more increase in level of satisfaction NS; NS; NS

McLean et al., 2003 ''Community Pharmacy Programme''	Uncontrolled asthma patients in from pharmacies in the community (Canada)	RCT Good	I: Patient education, team changes (professional roles/ pharmacist) ($N=191$) C: Usual care ($N=214$)	12	LUNG: PEFR QOL: AQLQ (4 domains) SYMP: Dyspnoea; cough; wheeze; phlegm HCU: ED; Hosp; Days off; Visits PROCESS: Knowledge; Compliance	Sign. improvement in mean PEFR Sign. greater improvement in all domains Sign. greater improvement in all symptoms NS; NS; NS; Sign. reduction in No. of medical visits Sign. greater improvement in knowledge and compliance
Mehuys et al., 2008 ''Pharmacist Intervention for Asthma Control''	Asthma patients 18–50 registered in pharmacies, located in diverse areas of Flanders (Belgium)	RCT Moderate	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) ($N=107$) C: Usual care ($N=94$)	6	QOL: AQLQ SYMP: Asthma Control Test (control, rescue medication, awakenings); Exacerbations PROCESS: Compliance; Technique; Knowledge; Behaviour	NS NS, Sign. higher reduction in need of rescue medication, Sign. less night-time awakenings; NS Sign. higher adherence to controller medication; Sign. better inhalation technique; NS; NS
Meulepas et al., 2007 ''Integrated primary care management model''	COPD patients $\geq$40 in general practice (The Netherlands)	CBA Moderate	I: Patient education, team changes (professional roles; nurse) ($N=137$) C: Usual care ($N=123$)	24	SYMP: Exacerbations PROCESS: Process; Technique; Compliance	NS Sign. more improvement of No. of planned visits and periodical lung function measurement; Sign. more improvement in correct inhalation technique; NS
Pilotto et al., 2004 ''Nurse-Run Asthma Clinics''	Asthma patients aged $\geq$18 years attended nurse-run asthma clinics (Australia)	RCT Good	I: Patient education, continuity of care (follow-up) ($N=80$) C: Usual care ($N=90$)	9	LUNG: FEV_1 QOL: SGRQ (4 domains) HCU: ED; Hosp; Days off; Visits PROCESS: Behaviour	NS NS NS; NS; Sign. less time off work; Sign. more hospital outpatient department visits NS

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Table 2 (*continued*)

Study	Setting	Study[a] design/quality	Interventions	Follow-up (months)[b]	Outcome[c]/process indicators[d]	Results[e]
Poole et al., 2001 ''Case Management''	All patients who had been admitted to Auckland hospital for COPD for ≥4 in the previous 2 years (with ≥2 in the previous 12 months) (New Zealand)	CBA Moderate	I: Provider education, self-management, continuity of care (follow-up) ($N=16$) C: Usual care ($N=16$)	12	QOL: CRQ (4 domains) HCU: Hosp; LOS	Clinically relevant improvement in all CRQ scores and stat. sign. for total and fatigue for theintervention group (*no data control*) NS; Sign. more decrease in LOS
Premaratne et al., 1999 ''Nurse specialists in asthma management''	All registered asthma patients aged 15—50 years of 41 general practices in Greenwich with a practice nurse (U.K.)	RCT Moderate	I: Patient education, team changes (professional roles; nurse) ($N=43436$) C: Usual care ($N=57932$)	36	QOL: AQLQ HCU: ED; Hosp PROCESS: Compliance	NS NS; NS NS
Rea et al., 2004 ''Chronic Disease Management''	COPD patients from four general practices (New Zealand)	RCT Moderate	I: Patient education, continuity of care (case management) ($N=83$) C: Usual care ($N=52$)	12	LUNG: FEV_1 QOL: SF36; CRQ (4 domains) SYMP: SWT HCU: Hosp; LOS PROCESS: Compliance	Stat. but not clinically sign. improvement NS; Stat. and clinically sign. improvement in 2 domains (fatigue, mastery) NS NS; NS NS
Rootmensen et al., 2008 ''Additional Pulmonary Nurse Care''	Asthma and COPD patients ≥18 from the pulmonary outpatient clinic at the Academic Medical Centre in Amsterdam (the Netherlands)	RCT Good	I: Patient education, continuity of care (case management) ($N=97$) C: Usual Care ($N=94$)	6	QOL: SGRQ; SF36 SYMP: Exacerbations QOC: Outpatient satisfaction PROCESS: Knowledge; Behaviour; Technique	NS; NS NS NS Sign. higher increase in knowledge; NS; NS
Schonlau et al., 2005 ''Quality Improvement Collaborative''	Asthma patients of 6 rural and urban asthma clinics (U.S.)	CBA Good	I: Provider education, self-management, continuity of care (case management) ($N=101$) C: Usual care ($N=64$)	12	QOL: SF12 QOC: Satisfaction HCU: ED; Days off PROCESS: Knowledge; Behaviour; Compliance; Process	NS Sign. more likely to be satisfied with clinician NS; NS NS; Sign. better self-management; NS; Sign. Process improvement

Schulz et al., 2001 ''Pharmaceutical Asthma Care Services''	Asthma patients registered in a pharmacy in the city of Hamburg (Germany)	CBA Moderate	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) ($N=191$) C: Usual care ($N=205$)	12	LUNG: FEV_1; PEFR SYMP: Dyspnoea QOL: SF36 (2 domains); LWAQ (11 domains) PROCESS: Knowledge; Technique; Efficacy	NS; NS NS Sign. more improvement in mental scale, physical scale NS; Sign. more improvement in summary and all subscales Sign. more improvement in knowledge, inhalation technique and self-efficacy
Smith et al., 2005 ''Home-Based Nurse-led Psycho Educational Intervention''	Adult patients registered at the asthma clinic (U.K.)	RCT Good	I: Patient education, continuity of care (follow-up) ($N=47$) C: Usual care ($N=45$)	12	QOL: SF36 (2 domains); LWAQ SYMP: Asthma Symptom Status PROCESS: Behaviour; compliance	Sign. more improvement in mental health score, physical functioning NS; Sign. better asthma quality of life score NS NS; Sign. more increase in PEF monitoring
Solomon/Gourley 1998 ''Pharmaceutical Care Model''	Ambulatory COPD patients >40 years of 10 departments of Veterans Affairs medical centres and 1 academic medical centre (U.S.)	RCT Moderate	I: Patient education, team changes (professional roles/ pharmacist) ($N=43$) C: Usual care ($N=55$)	6	QOL: HSQ SYMP: Dyspnoea QOC: Satisfaction HCU: ED; Hosp; Visits PROCESS: Compliance; Knowledge; Process	NS NS Sign. better satisfaction NS; NS; NS NS; NS; NS
Sridhar et al., 2008 ''Nurse-led intermediate care package''	COPD patients previously admitted to community and hospital care in west London (U.K.)	RCT Good	I: Patient education, continuity of care (follow-up) ($N=61$)10. C: Usual care ($N=61$)	24	SYMP: Mortality QOL: CRQ (4 domains) SYMP: Exacerbations HCU: Hosp; Visits; Cost PROCESS: Behaviour	Sign. lower No. of COPD-related deaths NS NS NS; Sign. less unscheduled GP contacts; NS Sign. better self-management of exacerbations

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Table 2 (*continued*)

Study	Setting	Study[a] design/quality	Interventions	Follow-up (months)[b]	Outcome[c]/process indicators[d]	Results[e]
Vrijhoef et al., 2007	Patients with previously documented COPD attending the respiratory outpatient clinic (The Netherlands)	RCT Good	I: Provider education, patient education, team changes (professional roles; nurse), continuity of care (follow-up) (N= 91) C: Usual Care (N=83)	9	LUNG: FEV_1; FVC	NS; Sign. more improvement in mean FVC
''Transfer of Care''					QOL: SGRQ; COOP/WONCA	NS; NS
					QOC: Satisfaction	Sign. better satisfaction
					HCU: Visits	NS
					PROCESS: Behaviour; Knowledge	Self care behaviour was mostly NS with exception of sign. better coping and sign. lower condition maintenance; Sign. bigger improvement of knowledge
Weinberger et al., 2002	Asthma and COPD patients >18 years with reactive airways disease at 36 community drugstores in Indianapolis (U.S)	RCT Good	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) (N=447) C: Usual care (N=303)	12	LUNG: PEFR	Sign. higher peak flow rates
''Pharmaceutical Care Programme''					QOL: CRQ; AQLQ	NS (COPD); NS (asthma)
					QOC: Satisfaction	Sign. more satisfied with pharmacist
					HCU: ED; Hosp	NS; NS (COPD); Sign. more breathing-related ED and hospital visits (asthma)
					PROCESS: Process	NS
Multiple interventions versus single intervention						
Donald et al., 2008	Adults aged 18–55 years admitted to one or both of two metropolitan Melbourne (Victoria) teaching hospitals with a primary diagnosis of asthma (Australia)	RCT Moderate	I: Patient education, continuity of care (follow-up) (N=36) C: Patient education (N=35)	12	LUNG: Morbidity	NS
''Telephone based Asthma Management''					HCU: ED; Readm; Visits	NS; Sign. less readmissions; NS
Coultas et al., 2005	COPD patients in primary care clinics associates with an urban academic health center, aged ≥45 cared for by primary care physicians (U.S.)	RCT Moderate	I: Provider education, patient education, continuity of care (follow-up) (N=72) C: Patient education (N=72)	6	QOL: SF36; SGRQ; Illness intrusiveness scale	NS; NS; NS
''Nurse-Assisted Home Care''					HCU: ED; Hosp; Visits	NS; NS; NS

Schatz et al., 2006 ''Care Manager''	Asthma patients 18–56 of the San Diego Kaiser Permanente Medical Care Programme (U.S.)	RCT Moderate	I: Patient education, continuity of care (follow-up/case management) ($N=31$) C: Patient education ($N=31$)	12	QOL: AQLQ SYMP: Symptom free days PROCESS: Knowledge	NS NS Sign. better rating of asthma knowledge
Smith et al., 1999 ''Respiratory Home Nurse Intervention''	Patients >40 years with severe COPD attending a teaching hospital (Australia)	RCT Moderate	I: Patient education, continuity of care (follow-up) ($N=48$) C: Patient education ($N=48$)	12	LUNG: FEV_1 QOL: COOP HCU: Hosp; Visits; LOS	Sign. deterioration (*no data control*) Sign. improvement in total quality of life (*no data control*) NS; NS; NS
Weinberger et al., 2002 ''Pharmaceutical Care Programme''	Asthma and COPD patients >18 years with reactive airways disease at 36 community drugstores in Indianapolis (U.S)	RCT Good	I: Provider education, patient education, expansion or revision of professional roles (pharmacist plays more active role in patient monitoring) ($N=447$) C: Patient education ($N=363$)	12	LUNG: PEFR QOL: CRQ; AQLQ QOC: Satisfaction HCU: ED; Hosp PROCESS: Process	NS NS (COPD); NS (asthma) Sign. more satisfied with pharmacist NS; NS NS

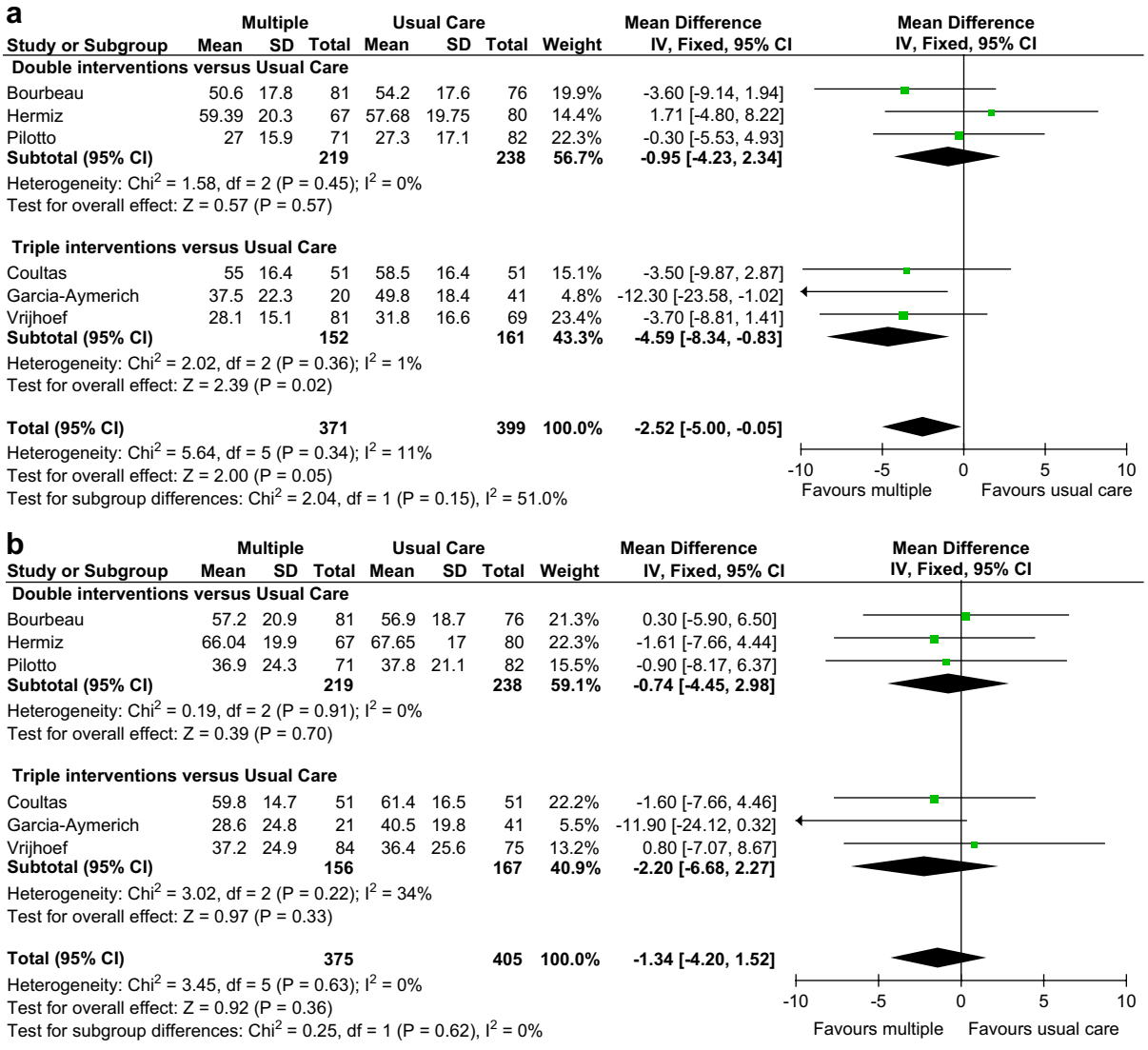
[a] *Research designs*: RCT: Randomised Controlled Trial; CBA: Controlled Before-After study.
[b] When the follow-up period is longer then 12 months, the 12-months results as well as the final results are presented.
[c] *Outcome indicators*: Main: LUNG = lung function; QOL = quality of life; SYMP: symptoms; QOC: quality of care; HCU: health care utilisation. Measures: FEV_1=forced expiratory volume in 1 second; PEFR=peak expiratory flow rate; MRC=Medical Research Council; Exacerbations = number of exacerbations; SWB=Subjective Well-Being; 6MWD=6-Minute Walking Distance; SWT=Shuttle Walk Test; CRQ=Chronic Respiratory Questionnaire; SGRQ=St. George's Respiratory Questionnaire; QWB=Quality of Well-being Scale; SF36/12=Short-Form 36/12; NHP=Nottingham Health Profile; COOP/WONCA=; LWAQ = Living With Asthma Questionnaire; QOL-RIQ=Quality-of-life for Respiratory Illness Questionnaire; AQLQ=Asthma Quality of Life Questionnaire; GHQ = General Health Questionnaire; HSQ = Health Status Questionnaire; VAS=Visual Analogue Scale; EQ-5D=Euro-Quol-5D; HADS=Hospital and Anxiety Depression Scale; ED = number of emergency department visits; Hosp=number of hospitalisations; Days off = number of days off work/school; Visits=number of visits to health care services; (Re)adm = number of (re)admissions; LOS=length of stay; Cost = costs.
[d] *Process indicators*: Main: PROCESS=Process indicators. Measures: Behaviour = self-management behaviour; Compliance = (medication) compliance; Knowledge=patient knowledge; Efficacy=self-efficacy; Technique=inhalation technique; Support=social support; Process=process performed; Follow=follow-up.
[e] All results are presented compared to ''usual care''.

quality of life differed widely among the studies. Reported clinical outcomes, lung function and symptoms, generally demonstrated no significant differences between intervention and control groups. But, studies directed at asthma patients frequently showed a significant decline in symptoms.[48,53,60,70,71] Various studies reported quality of care measures (satisfaction), a great variety of instruments found mostly significant beneficial differences for multiple interventions. Significant improvements on process measures were reported, as well. Improved compliance, enhanced knowledge, and inhalation technique were frequently found, often combined with significant improvement in quality of care.

Patient education in combination with case management (and professional education)

Nine studies examined patient education in combination with case management compared to usual care[51,56,61,64,73,77,78,82,84] showing mixed results. We noted an apparent variation in intensity and duration of the interventions, ranging from home visits after 1 and 4 weeks to weekly calls and monthly visits for 1 year. Similarly, duration of the follow-up period largely varied; from 6 weeks to 2 years.

Most of these studies reported quality of life parameters[51,56,61,73,77,82,84]; three studies reported significant beneficial differences for multiple interventions. Bourbeau et al.[51,57] found statistically and clinically significant differences on the SGRQ impact and total score at 4 months favouring the intervention group, whereas at 12 months only the impact score reached clinical significance. Egan et al.[56] showed significant improved scores for the activity domain of the SGRQ and the anxiety dimension of the HADS in the intervention group. Smith et al.[82] reported evidence of significant effects on asthma specific quality of life and SF-36 mental subscales at 12 months, no results were found on SF-36 physical subscales. Six studies evaluated the impact of the interventions in terms of changes in health care utilisation.[51,56,61,64,73,84] Only the study by Gadoury et al.[57] revealed strong indications for improvements in health care utilisation, i.e. statistically significant and



clinically relevant reduction of emergency room visits and hospitalisations over a 2 year period. None of the other studies detected statistical significant changes on these parameters.

Eleven studies examined patient education and case management in combination with professional education.[47,52,54,58,62,65,69,74,76,79,85] All but two studies concerned COPD care. Quality of life measures were reported in most studies. Four studies reported improvement on the SGRQ score in favour of the multiple intervention groups, however not constantly significant. Rea et al.[76] reported a significant improvement for two dimensions of the CRQ (fatigue and mastery), but no significant difference was found on the SF-36 score. Conversely, another study by Aiken et al.[47] showed better physical functioning, vitality and total function on the SF-36 in favour of the intervention group. Lee et al.[69] showed a significant greater improvement in psychological wellbeing (GHQ) in the intervention group. Of the ten studies reporting health care utilisation three studies[52,62,65] demonstrated significant reductions in readmissions and emergency department visits.

Overall, no significant differences between intervention and control groups were found on clinical outcomes, namely lung function and symptoms. Reports on satisfaction showed significant more increase in satisfaction in intervention groups compared to control groups. Processes measures also showed positive results: most studies reported significantly better scores on knowledge and self-management in the intervention groups.

Meta-analyses demonstrated statistically significant improvements on the SGRQ total and impact scores in favour of multiple interventions (Fig. 2). The differences on the SGRQ activity score reached statistical significance in the triple intervention studies. Pooled SGRQ data showed better effects in triple intervention compared to double intervention studies. Moreover, clinically relevant differences for triple interventions were found in SGRQ total, activity and impact scores. No significant difference or clinically relevant

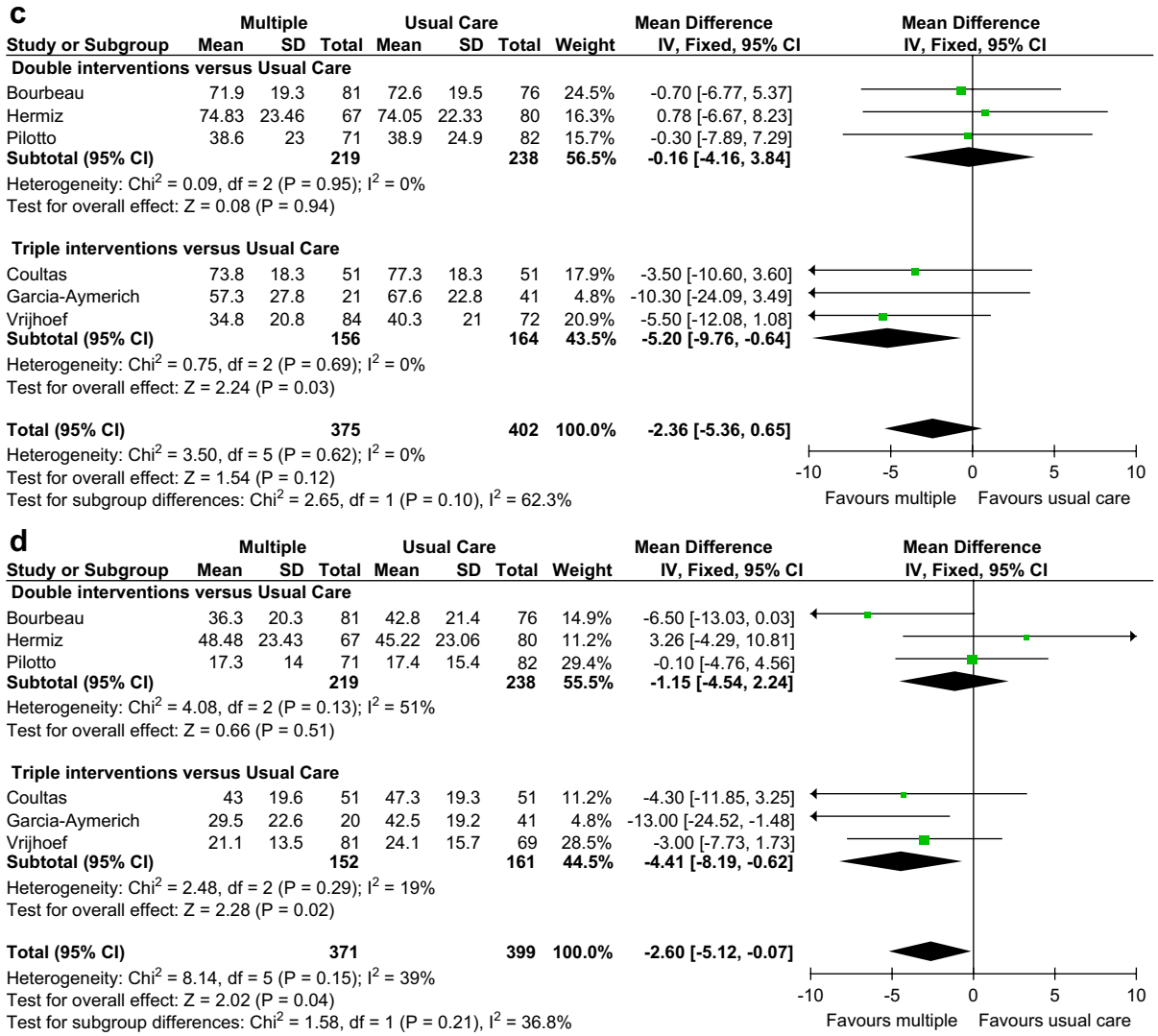


Figure 2 Multiple interventions including case management versus usual care, quality of life (SGRQ) post intervention (A: total; B: symptoms; C: activity; D: impact).

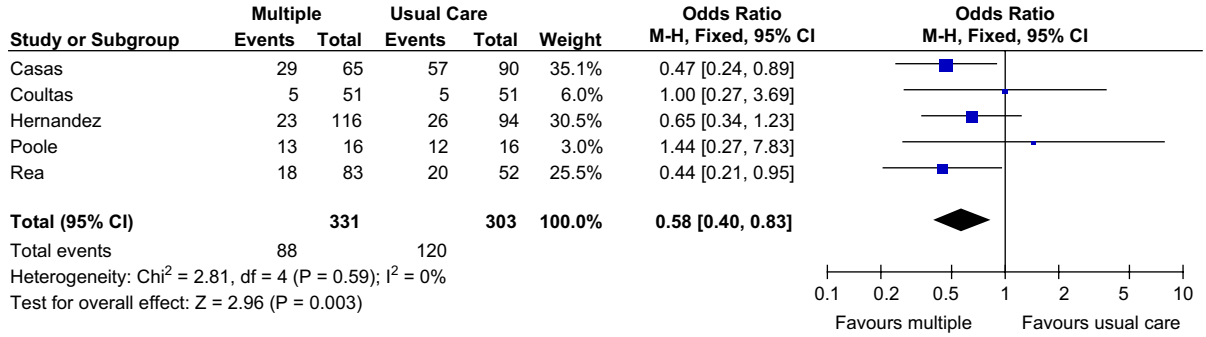


Figure 3 Multiple interventions including case management versus usual care, hospital admissions.

was found on the SGRQ symptom score. Nine studies reporting hospitalisations in COPD-care were pooled (Fig. 3). For a few studies standard deviations were not available,[56,62,77] however they did show similar mean scores.

There was a statistically significant reduction of the probability of at least one hospital admission among patients receiving multiple interventions compared to usual care. Data on double interventions showed statistical heterogeneity ($I^2 = 67.4\%$) and were therefore excluded from further analyses. Subgroup analyses of triple interventions revealed a significant effect. Meta-analysis of emergency department visits per person did not show a statistically significant effect in favour of treatment (Fig. 4). The level of statistical heterogeneity for this outcome was related to the outlying effect reported in Bourbeau[57] (only double intervention); its removal led to a lower I^2 statistic (93.7% versus 21.2%).

Patient education in combination with revision of professional roles (and professional education)

Six studies focussed on patient education as well as on revision of professional roles. Two forms of revision could be distinguished: substitution of physicians by nurses[63,72,75] and pharmacists providing (drug) counselling that was formerly provided by nurses and physicians.[67,70,83] Substitution of physicians by nurses was not associated with any significant benefits, other than process improvements mainly of inhalation technique. Of the studies involving a pharmacist, two studies[67,83] showed significantly more satisfaction with care. Knoell et al.[67] also reported significant between-group differences in quality of life and process measures. Moreover, McLean and colleagues[70] found significant improvements on clinical, quality of life and all process measures, but could not detect significant differences on health care utilisation between groups. They applied intense patient education: at least three 1-h appointments every 2 or 3 weeks, followed by 1-h sessions every 3 months.

Interventions in another eight studies constituted of professional and patient education in combination with pharmacists playing a more active role in patient monitoring.[48,49,53,60,68,71,80,86] All studies concerned asthma patients, apart from one study which focussed on both diseases. The numerous outcomes measured showed positive results: in the intervention groups significantly better symptom scores, quality of life scores and improvement in process indicators, such as knowledge and inhalation technique, were found in most studies. Overall, no significant improvements were found in lung function. Results on health care utilisation and satisfaction were ambiguous.

Meta-analysis of studies that included a pharmacist[67,70,71,86] demonstrated a significant improvement on the Asthma Quality of Life Questionnaire (AQLQ) (Fig. 5). However, statistical heterogeneity was apparent. Subgroup analyses showed a significant effect of double interventions.[67,70] Triple interventions[71,86] compared to usual care did not reach statistical significance. Yet, a qualitative comparison on all quality of life instruments and other outcomes suggest more significant effects of triple rather than double interventions. Data measured by the Living With Asthma Questionnaire (LWAQ)[53,60,80] could not be pooled due to instrument differences, caused by use of an adjusted version of the original; all studies reported significantly improved outcomes.

Multiple versus single interventions

In five studies multiple interventions were compared to single interventions.[54,55,78,81,86] Four studies reported

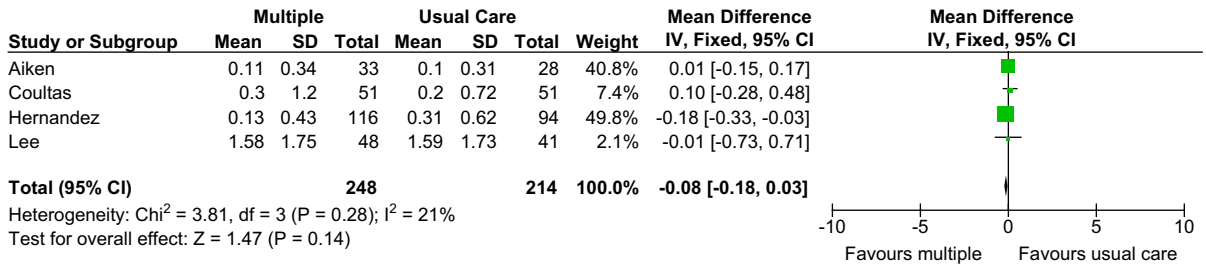


Figure 4 Multiple interventions including case management versus usual care, emergency department visits per person per year.

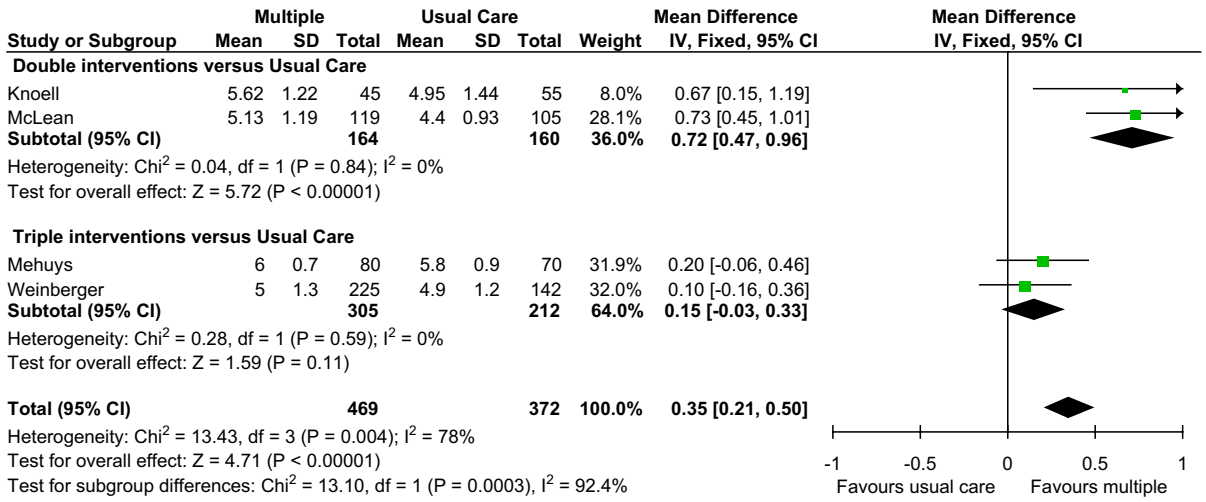


Figure 5 Multiple interventions including a pharmacist versus usual care, quality of life (AQLQ) at 6 months.

complete quality of life data, demonstrating better, however non-significant, quality of life in the multiple intervention group. Data on quality of life could not be included in a meta-analysis due to heterogeneity of instruments. Data reported on other outcomes in these studies was too diverse to interpret.

Discussion

This study was performed to understand the effectiveness of multifaceted disease management interventions in improving care or reducing costs for patients with asthma or COPD. Although relevant reports are limited in number and show great heterogeneity, some cautious conclusions can be drawn. The studies showed significant improvements on quality of life in pharmacist programmes and COPD care programmes. Qualitative analyses of other quality of life measures partially confirmed this finding. Meta-analyses on hospitalisations showed a significant reduction in the number of patients with one or more hospital admissions within triple interventions. No effects were found in emergency department visits per person. Qualitative assessment of the studies showed significant improvements in process measures in several studies. Moreover, for satisfaction, a positive trend was seen. Inconclusive results were reported on symptoms; no effects were found in lung function.

In particular, combining patient and professional education with an active role of the pharmacist in patient monitoring led to improvements in patient outcomes as compared with usual care. Bravata et al.[87] also reported statistically significant improvements in processes and outcomes when pharmacists were actively involved. Education provided by pharmacists rather than by nurses seemed to achieve better results. Taylor et al.[88] also found little evidence to support nurse-led management of COPD patients in the community. A factor contributing to this effect might be the lower intervention intensity of nurse education compared with pharmacist education. Overall the provision of education as a result of revision of roles seemed to have a positive impact on patient satisfaction.

This review included asthma as well as COPD studies; these differed in several respects. Asthma studies focused on adult patients from the age of 16 years; in some cases the population was constrained to a maximum age. Studies with regard to COPD patients, on the other hand, mostly restricted their populations to older patients, from the age of 30 years. All asthma studies were in community settings; COPD studies took place in various settings. Results on asthma seemed to achieve more favourable results of multiple interventions than COPD studies, albeit not consistently across all studies.

The multifaceted interventions also targeted various populations ranging from mild to severe patients. It was apparent that studies including more severe patients showed greater tendency to success on the short run. Another recurring theme was that studies that reported a positive effect on quality of life often concerned programmes with more intense interventions of longer duration. This supports the continuous character of disease management: multifaceted interventions should frequently interact with the patients therein; the chronic care model approach provides a promising manner to shape long-term care for chronic patients.

The complexity of multiple disease management interventions makes rigorous evaluation and determining their practical feasibility quite problematic. Although RCTs are the gold standard in clinical research, in organisational research it is difficult to set up RCTs.[89] In general, a design should be chosen that minimises potential bias (internal validity) and maximises generalisability (external validity).[90–92] Therefore, this review concentrated on quasi-experimental and experimental study designs. It was apparent that many studies that failed to meet the quality criteria on research methodology, concerned asthma disease management studies.[43–45] In these studies, participants were offered commercial disease management programmes. However, using total costs as the primary outcome measure to demonstrate programme effectiveness and return on investment poses a significant threat to the validity of outcomes in the evaluation of disease management.[93]

While almost all studies measure outcome parameters, less attention is paid to structure and process indicators. Since multifaceted interventions interfere in the structure and the process of care delivered, these are important aspects to be measured. Nevertheless, nine studies did not report process measures and merely one study reported structure measures. For example, geographical differences reflected in diverse organisational structures are considered to influence the design and performance of the programmes. We would like to make a plea for more attention to the use of structure and process parameters, as well as to considerable (minimum) duration of data collection. Although the major effects of disease management interventions may be expected to occur in the long-term, the follow-up period in 15 of 36 studies was less than 1 year after allocation of the subjects or start of the interventions. Sixteen studies lasted 12 months. No studies reported simulation models to extrapolate measurements over time.

Limitations of the study

As with all systematic reviews, this study has several limitations. Most importantly, it may be criticised for the widely ranging quality and heterogeneity of the original studies. These encompass a wide range in (combinations of) interventions used, process and outcome variables, and patient populations. Programme interpretation according to the EPOC criteria was hampered by the imprecise descriptions of the interventions. Next to that, lack of data impeded the determination of the incremental benefits of the various components of each intervention. Moreover, an informative description of each intervention is extremely important in disease management, because of the comprehensiveness and the complexity of disease management interventions. Furthermore, the intensity of the interventions was often unclear. When described, various interventions could be characterised as being of low intensity, in particular professional-directed interventions. In many cases the intervention consisted of a minimal level of education, which Grimshaw and colleagues advised against.[18] They concluded that occasional education had only short-term effects. From a methodological point of view, restrictions in search strategies, such as databases, could have influenced the study findings. Furthermore, the absence of publication bias cannot be guaranteed. Consequently, the effectiveness of combinations of interventions may appear too positive.

Practice and research implications

Measuring at outcome as well as process levels contributes to a better understanding of ways to improve quality of care. Measuring the process of care contributes to understanding heterogeneity in patient outcomes. In addition to outcomes measures, process measures should be collected in future research. Structure indicators are largely missing in this literature review. Since most multifaceted interventions involve some form of organisational change resulting in structural change, information about the structure of healthcare is essential. Future research should attempt to set up practical, multicentre clinical trials; a wider range of physicians and settings is bound to improve external validity.[94] International comparative studies can gain a better understanding of the effects of disease management in relation to the health care system.

A wide variety of indicators were used to evaluate the interventions. The indicators in the studies included in this review were frequently not related to the interventions that were evaluated. This holds true for process measures in particular: although present in many studies, they did not cover the degree of successful implementation of the interventions. A plea has been made, therefore, to choose process indicators that are sensitive to the specific interventions and are associated with the expected changes in outcomes of care.[35]

More research on the long-term effectiveness of multifaceted interventions is needed, as follow-up in most of the studies in the present review was short. Lack of hard evidence of effectiveness of multiple interventions may in part be due to inadequate length of follow-up. To deal with this issue, future studies need to evaluate sustainability of multiple interventions on the longer-term. Finally, as variation in follow-up periods and reporting of data complicate comparability of studies, we would recommend to standardising reporting periods and data sets.

Conclusions

Current evidence on disease management programmes in asthma and COPD shows improvements in quality of life and reductions in hospitalisations in triple interventions. No effects on emergency department visits were found. Qualitative analysis demonstrated small, albeit no consistent, improvements in process and outcome indicators. Estimates of the effectiveness of multifaceted interventions are limited by the wide range of outcomes measured, the diverging combinations of interventions, the different study designs and the many different settings in which care was delivered. Still, this review points at promising combinations of interventions. Improvement in comparison with usual care was notably found for interventions in which pharmacists can liase with the patient and the professional, provide education and play an active role in patient monitoring.

Authors' contributions

KL, AN and RH drew up the design and framework of this manuscript. Data extraction was done by KL, AN and RH. Statistical analysis was done by KL. All authors read and approved the final manuscript.

Conflict of interest statement

The author(s) declare that they have no conflict of interest.

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