Identifying potentially cost effective chronic care programs for people with COPD

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Objective: To review published evidence regarding the cost effectiveness of multi-component COPD programs and to illustrate how potentially cost effective programs can be identified.
Methods: Systematic search of Medline and Cochrane databases for evaluations of multi-component disease management or chronic care programs for adults with COPD, describing process, intermediate, and end results of care. Data were independently extracted by two reviewers and descriptively summarized.
Results: Twenty articles describing 17 unique COPD programs were included. 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. Overall, the COPD programs generate end results equivalent to usual care, but programs containing ≥3 components show lower relative risks for hospitalization. There is limited scope for programs to break-even or save money.
Conclusion: Identifying cost effective multi-component COPD programs remains a challenge due to scarce methodologically sound studies that demonstrate significant improvements on process, intermediate and end results of care. Estimations of potential cost effectiveness of specific programs illustrated in this paper can, in the absence of 'perfect data', support timely decision-making regarding these programs. Nevertheless, well-designed health economic studies are needed to decrease the current decision uncertainty.
Keywords: chronic care management, COPD, cost-effectiveness, review

Introduction

Chronic care programs for people with chronic obstructive pulmonary disease (COPD), such as the chronic care model[1] and disease management programs[2] are increasingly implemented in daily health care[3,4] in response to the growing burden of COPD on societies worldwide.[5] The aim of these programs is, generally, to improve processes and outcomes of care whilst making a more efficient use of scarce health care resources, or even generate cost savings.

The disease management approach as described by the Disease Management Association of America (DMAA) highlights three components: the central care delivery and leadership roles of the primary care physician; the critical importance of patient activation, involvement and personal responsibility; and the patient focus and capacity expansion of care coordination provided through wellness, disease and chronic care management programs.[2] The chronic care model (CCM) identifies essential components that encourage high-quality chronic disease care, involving the community and health system and including self-management support, delivery system design, decision support, and clinical information systems.[6]

Notwithstanding the intuitive appeal of these approaches, the current evidence regarding their efficacy, effectiveness and cost effectiveness is severely limited by the amount and quality of well-designed studies and the evidence that has been published

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so far reveals results that are far below expectations.[7] Indeed, the systematic reviews of Weingarten,[8] Ofman,[9] and Mattke[10] consistently show that disease management is less effective for COPD than it is for chronic conditions such as diabetes, congestive heart failure and depression.

By specifically focussing on COPD, however, the systematic review of Adams and colleagues[11] demonstrated that patients who received two or more CCM components had lower rates of hospitalizations and emergency/unscheduled visits, and shorter length of hospital stay compared with control groups. This may indicate that, despite earlier less encouraging findings, a scope for COPD care programs to generate the necessary improvements in COPD care does exist, providing these packages are truly comprehensive, multifaceted and well co-ordinated. However, since even the proven effective but less comprehensive disease management and chronic care programs struggle to demonstrate their economic benefits,[7,9–11] and because more comprehensive programs are likely to come at an even higher opportunity cost than the less comprehensive ones, the need for rigorous studies and timely economic evaluations can hardly be underestimated. Furthermore, with innovative industries and health care practices greatly outpacing academic research in this area and considering the mounting health care costs, there is a need to estimate the potential cost effectiveness of COPD care programs, even in the absence of the 'ideal' clinical and economic data.[12] This study therefore first provides an update of the published evidence regarding the effectiveness and cost effectiveness of multi-component COPD care programs (ie, programs consisting of ≥2 components of disease management or the chronic care model). Secondly, we illustrate how the likely short and long term cost effectiveness of a particular program can be estimated with limited data available; the latter mainly with the aim to support timely decision-making, rather than providing the most precise estimates possible.[13,14]

Methods
Literature search
Medline and Cochrane databases were electronically searched for English-language articles published between January 1995 and September 2007 describing evaluations of disease management or chronic care model interventions for adults with mild, moderate, severe, or very COPD.

Search terms included combinations of MeSH terms and text words, as described in Table 1. The search was further expanded by hand searching the references of identified articles.

Study selection and data extraction
Two reviewers (KL and LS) independently selected studies for inclusion based on the following predetermined criteria: (1) interventions included at least two components of disease management as defined by the DMAA[2] or the CCM as described by Wagner[1] and Bodenheimer and colleagues; [15,16] (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 (ie, number of scheduled follow-up contacts with care providers and medication prescribing patterns); intermediate (ie, patients' disease-specific knowledge, self-efficacy and self-management skills, medication compliance, and social support) or end outcomes (ie, mortality, quality of life, exacerbations, lung function, dyspnoea, symptoms, overall clinical condition, hospital admissions, readmissions and bed days, emergency care admissions, unscheduled outpatient visits, health-related quality of life (HRQL), days off work, COPD-related health care resource use and total costs for COPD-related care). Agreement was examined and disagreements resolved by consensus. Articles describing the impact of specific therapeutic regimens, such as different forms of bronchodilator therapy, pulmonary rehabilitation, oxygen therapy etcetera, were excluded because these interventions are individual parts of clinical guidelines and therefore beyond the scope of this review. Two reviewers (KL and AN) independently extracted the data using a standardized form created for this review; assessed methodological quality of the articles with the so called 'HTA-DM instrument,'[17] and scored this on a 0 to 100 scale with a score < 50 points indicating poor quality, whilst 50 to 69 points was considered as moderate quality and ≥70 points as good quality. Articles of poor quality were excluded from the review.

Interventions were categorized based on (1) the setting in which they were carried out (ie, community, primary care, secondary care, tertiary care or a combination of these); (2) the population of COPD patients included (ie, at risk, mild, moderate, severe or very severe); (3) the type and number of intervention components (ie, self-management [SMAN]; delivery system design [DSYS]; decision support [DSUP]; clinical information systems [CIS]). As regards the latter we also noted whether the article explicitly named the intervention as being a disease management program or a CCM intervention. If the intervention was stated to be a disease management program and encompassed a clinical

Table I Search strategy

Combinations of MeSH and text words searched
1. "Disease management" [MeSH]
2. "Disease management"
3. "Disease state management"
4. "Delivery of Health Care, Integrated" [MeSH]
5. "Comprehensive Health Care" [MeSH:NoExp]
6. "Patient Care Planning" [MeSH] NOT "Advance Care Planning" [MeSH]
7. "Primary Health Care" [MeSH] NOT "Refusal to Treat" [MeSH]
8. "Patient Care Team" [MeSH:NoExp]
9. "Critical Pathways" [MeSH]
10. "Case Management" [MeSH]
11. "Continuity of Patient Care" [MeSH]
12. "Practice Guidelines" [MeSH]
13. "Guidelines" [MeSH]
14. "Clinical Protocols" [MeSH:NoExp]
15. "Patient Education" [MeSH]
16. "Self Care" [MeSH:NoExp]
17. "Reminder systems" [MeSH]
18. "Health Education" [MeSH]
19. "Health Promotion" [MeSH:NoExp]
20. "Community Health Planning" [MeSH]
21. "Ambulatory Care" [MeSH]
22. (Patient OR providers) AND feedback
23. (Patient OR providers) AND reminder
24. (Patient OR providers) AND monitor$
25. OR/1–24
26. "Epidemiologic Research Design" [MeSH] NOT "Sensitivity and Specificity" [MeSH]
27. "Clinical Trials" [MeSH:NoExp]
28. "Controlled Clinical Trials" [MeSH]
29. "Randomized Controlled Trials" [MeSH]
30. "Multicenter Studies" [MeSH]
31. "Epidemiologic Studies" [MeSH] NOT "Seroepidemiologic Studies" [MeSH]
32. "Pilot Projects" [MeSH]
33. "Sampling Studies" [MeSH]
34. "Program Evaluation" [MeSH]
35. "Intervention Studies" [MeSH]
36. "Evaluation Studies" [MeSH:NoExp]
37. OR 26–36
38. Controlled Clinical Trial [pt]
39. Clinical Trial [pt]
40. Multicenter Study [pt]
41. Randomized Controlled Trial [pt]
42. Evaluation Studies [pt]
43. Meta-analysis [pt]
44. OR 38–43

(*Continued*)

Table I (*Continued*)

Combinations of MeSH and text words searched
45. 37 OR 44
46. AND "Pulmonary Disease, Chronic Obstructive" [MeSH]
47. 25 AND 45
48. Limit 47 to human
49. Limit 48 to yr 1995–2007
50. Limit 49 to English

information system, it was additionally registered whether this information system facilitated (a) population identification processes [PIP]; (b) process and outcome measurement, evaluation and management [MEM]; and/or (c) routine reporting and/or feedback loops [RFEED].[2]

Data analysis

Extracted data were entered into a spreadsheet (Excel®; Microsoft, Redmond (WA), US) and analysed in a descriptive way (ie, numbers, frequencies, and percentages). To determine the impact of the interventions, included studies were analysed for statistically significant differences (considering the p-value as applied in the study's analysis). In addition we noted whether the study was sufficiently powered (ie, $\beta \leq 0.2$) to detect a statistical significant difference of a 'meaningful' size on the primary study outcome (with 'meaningful' as determined by the authors of the included studies). Further, where the presented data allowed us to, we calculated relative risks (RRs) and their associated 95% confidence intervals for hospitalization, emergency department visits and other unplanned visits, and mortality. Finally, to illustrate the potential financial viability of the COPD programs, it was explored at what opportunity costs a program might be expected to demonstrate a cost effective use of resources (1) within one year; or (2) in the long term (ie, over the expected remaining life time of the patient population) from a health system's perspective. The exploration was carried out for a selection of programs that reported the necessary data for these analyses.

The short term cost effectiveness analysis was based on the reported changes in hospital and emergency department (re)admissions within one year of follow-up and the associated cost per hospital and/or emergency department (ED) admission. The long-term analysis was based on reported changes in survival and HRQL and evaluated against a range of societal willingness-to-pay (WTP) thresholds for one 'quality-adjusted life year'(QALY).[18,19]

Results

Study retrieval

The search identified 308 nonduplicative titles. After independent assessment of abstracts and full-texts by two reviewers regarding eligibility, 288 articles were excluded because these (1) did not concern disease or chronic care management in accordance with the definitions of the DMAA or Wagner and colleagues (n = 166); or (2) were single component interventions (n = 72); or (3) did not employ a control group or report more than one measurement (n = 42); or (4) were of poor methodological quality (n = 8). The 20 included articles described 17 unique COPD programs. Most articles originate from the US (n = 6; describing five programs)[20–25] followed by Australia (n = 4)[26–29] and New Zealand (n = 2);[30,31] Canada (n = 3; describing one program)[32–34] the Netherlands (n = 2);[35,36] Spain (n = 2;[37,38] one including a Belgian comparator group[38]); and China (n = 1).[39]

Study designs and methodological quality

The 17 studies include 14 randomized controlled trials (RCTs), two nonrandomized controlled trials[28,30] and one before–after study[36] (see Table 2). In 11 of the 14 RCTs randomization was performed on the patient level, whereas three RCTs randomized on the level of care delivery centres, ie, general practices,[31] nursing homes,[39] or drugstores.[25]

Although 15 studies report the impact of the intervention on resource use, only three evaluated this impact in monetary terms[34,36,37] and can therefore be considered an economic evaluation. Poole and colleagues[30] conducted a limited return-on-investment analysis by investigating the reduction in bed days per patient needed in order to pay off the salary costs of the main care providers involved in the program.

Reported study follow-up varies from eight weeks[37] to two years,[22,33,35] with most articles reporting a follow-up of 12 months (n = 9).[25,28–32,34,36,38] Study sample size at baseline varies from n = 32[30] to n = 453,[25] with a mean (±SD) sample size of n = 163 (±104) and a median of n = 155. Average proportion of patient follow-up is 81% (±14%) in intervention arms and 78% (±16%) in control arms. Six of the 17 included studies demonstrate at least 80% power for detecting a meaningful statistical significant change in their primary outcome measure[25,29,31,32–34,36,38] and four studies failed to include sufficient patient numbers as determined by their sample size calculations.[20,21,27,35] Seven studies did not mention whether their study was sufficiently powered,[22–24,26,28,30,37,39] but three of these studies include less than 40 patients in each study arm[26,28,30] and are most likely underpowered.

Methodological quality of studies is mostly moderate (see Table 2), with an overall mean (±SD) quality score of 67.6 (±9.4) points and a median of 65 points. The most frequently observed flaw in included articles is that information on the program itself and the characteristics of the region or institution in which the program has been implemented is lacking or described too briefly, herewith hindering the assessment of external validity of the findings. Further, the time horizon of the evaluations is in almost 50% of the studies considered too short (ie, less than one year) to adequately capture the potential benefits of essentially nonpharmacological interventions in a patient population suffering from an irreversible and progressing chronic condition.

Study setting and population

Most programmes are implemented in secondary care and three programs have been implemented across multiple settings (see Table 2).

The study settings reflect the subgroups of COPD patients enrolled in the program, as characterized by the staging system of Global Initiative for Chronic Obstructive Lung Disease (GOLD).[40] For example, all programs include patients with severe COPD (GOLD 3) who are commonly treated in secondary care, whereas multiple setting programmes encompass a broader range of patients (eg, GOLD 1 to 4).[28,35,36]

The mean age (±SD) of the included study samples ranges from 47.3 (±13.9)[28] to 80.4 (±6.3)[21] years. Across all included studies, the mean age is 66.4 (±7.9) with a median of 68.5 years.

Types of programs and included interventions

All programs include the components self-management and delivery system design. Five programs additionally encompass the component decision support[20,21,25,32–34,39] and four also include clinical information systems.[26,31,36,38] Of the four programs that are explicitly referred to as DMPs, three operate a clinical information system that serves to support process and outcomes measurement, evaluation and management.[26,31,36] In two of these programs this system also facilitates routine reporting and feedback loops,[26,36] and in one program[31] the system is further used for population identification processes.

Results on process measures

The majority of studies describing the number of scheduled outpatient visits and home visits reported no significant

Table 2 Characteristics of studies included in the systematic review (clustered where) describing unique COPD programs

Author (year of publication)	Location	Setting (CC; PC; SC; TC)#	Population		Program type (CCM; DMP; not explicitly stated)χ	No. (types) of components (2 to 4; (Types¶))	Study design	Study quality score (0–100)	Length of follow-up	Sample size at baseline		No completed	
			Mean age (yrs ± sd)	Gold stage						I_1/I_2*	C	I_1/I_2*	C
Aiken et al (2006)[20]	United States	TC	68.5 (±13.5)	3 and 4	Not stated	3 (SMAN, DSYS, DSUP)	RCT	60	18 mo	100	90	43	30
Bourbeau et al (2003 and 2006)[32,34]/Gadoury et al (2005)[33]	Canada	SC	69.5 (±7.0)	2 and 3	Not stated	3 (SMAN, DSYS, DSUP)	RCT	80 (both)/65	12 mo 24 mo	95	95	86[B] and 91[G]	79[B] and 84[G]
Casas et al (2006)[38]	Spain/Belgium	TC	71.2 (±9.0)	3 and 4	Not stated	4 (SMAN; DSYS, DSUP, CIS)	RCT	80	12 mo	65	90	48	72
Coultas et al (2005)[21]	United States	PC	69.0 (±8.2)	2 and 3	Not stated	3 (SMAN, DSYS, DSUP)	RCT	55	6 mo	72 72	73	51/49	51
Egan et al (2002)[26]	Australia	SC	67.5 (SD not stated)	1–3	DMP	4 (SMAN; DSYS, DSUP, CIS)	RCT	60	3 mo	33	33	25	28
Hermiz et al (2002)[27]	Australia	CC and PC	49.3 (SD not stated)	2 and 3	Not stated	2 (SMAN, DSYS)	RCT	65	3 mo	84	93	67	80
Hernandez et al (2003)[37]	Spain	SC and TC	70.8 (±9.7)	2 and 3	Not stated	2 (SMAN, DSYS)	RCT	65	8 wk	121	101	116	94
Hesselink et al (2004)[35]	The Netherlands	PC	47.3 (±13.9)	1–4	Not stated	2 (SMAN, DSYS)	RCT	80	24 mo	46	38	32	22
Jeffs et al (2005)[28]	Australia	SC	67.5 (SD not stated)	1–4	Not stated	2 (SMAN, DSYS)	CCT	55	12 mo	28	25	28	25
Lee et al (2002)[39]	China	TC	80.4 (±6.3)	1–3	Not stated	3 (SMAN, DSYS, DSUP)	RCT	65	6 mo	48	41	48	41
Poole et al (2001)[30]	New Zealand	SC	69.7 (±7.1)	3	Not stated	2 (SMAN, DSYS)	CCT	55	12 mo	16	16	15	13
Rea et al (2004)[31]	New Zealand	PC	68 (range 44–84)	2 and 3	DMP	4 (SMAN; DSYS, DSUP, CIS)	RCT	75	12 mo	83	52	71	46
Ries et al (2003)[22]	United States	TC	67.1 (±8.2)	3	Not stated	2 (SMAN, DSYS)	RCT	70	24 mo	87	87	82	73
Smith et al (1999)[29]	Australia	SC	69.9 (±1.2)	3	Not stated	2 (SMAN, DSYS)	RCT	80	12 mo	48	48	36	36

(Continued)

Table 2 (*Continued*)

Author (year of publication)	Location	Setting (CC; PC; SC;TC)[#]	Population Mean age (yrs ± sd)	Gold stage	Program type (CCM; DMP; not explicitly stated)[X]	No.(types) of components (2 to 4;(Types[¶]))	Study design	Study quality score (0–100)	Length of follow-up	Sample size at baseline I₁/I₂*	Sample size at baseline C	No completed I₁/I₂*	No completed C
Solomon et al (1998)[23]/Gourley et al (1998)[24]	United States	SC	69.3 (±7.8)	3 and 4	DMP	2 (SMAN, DSYS)	RCT	60/60	6 mo	43	55	43	54
Steuten et al (2006)[36]	The Netherlands	PC and SC	61 (±14)	1–4	DMP	4 (SMAN; DSYS, DSUP; CIS)	CBA	70	12 mo	317	NA	222	NA
Weinberger et al (2002)[25]	United States	CC	62.4 (±11.1)	1–3	Not stated	3 (SMAN, DSYS, DSUP)	RCT	80	12 mo	185/130	138	149/105	111

Abbreviations: [#]CC, community care; PC, primary care; SC, secondary care; TC, tertiary care; [X]CCM, chronic care model; DMP, disease management program; SMAN, self-management; DSYS, delivery system design; DSUP, decision support; CIS, clinical information systems; PIP, population identification processes; MEM, process and outcome measurement, evaluation and management; RFEED, routine reporting and feedback loops. **Notes:** *I₁, I₂, the 2nd intervention for trials with three study arms; [B]denotes study of Bourbeau et al; [G]denotes study of Gadoury et al.

changes for general practitioner (GP), specialist or nurse visits (see Table 3). Medication prescribing patterns (ie, type and amount of COPD medication prescribed) also remained largely the same, except for one study that found a statistical significant lower cost for COPD prescriptions (31% lower) associated with the intervention.[37] The amount of patient education provided increased significantly in all studies reporting this process measure. Results for coordination of care were mixed, depending on how coordination was defined and measured, whereas one study reported improved accessibility of care.[36]

Results on intermediate outcomes

Disease-specific knowledge has been found to improve in four out of five studies measuring this.[20,27,36,37] Further, patient reported outcomes indicated advanced technical skills (inhalation technique) and self-efficacy in two studies,[27,37] whereas one study showed improved self-management and medication adherence.[36] The majority of studies, however, did not detect statistical significant changes as far as self-management behaviour, medication compliance, technical skills/self-efficacy and social support are concerned (see Table 3).

Results on end outcomes

For all reported end results, the dominating finding is that COPD care management programs generate equivalent outcomes in comparison to usual care and less intense forms of chronic care or disease management. Nevertheless, a few studies have detected a positive impact of their intervention on lung function (n = 2),[25,31] physical functioning (n = 3),[20,22,29] and mental functioning (n = 3).[22,29,39] Furthermore, eight[20,22,29–32,36,37] out of 15 studies reporting on HRQL find statistical significant improvements for (at least some aspects of) this parameter, although these are not always sustained in the longer term.[22,32] As regards health care utilization, seven studies (eight articles)[22,23,30,32,33,35,36,38] out of 15 studies (19 articles) report a decrease in exacerbation related health care utilization, including ED-visits, hospital (re)admissions and other unscheduled outpatient visits. Three studies[34,36,37] presented cost data and showed that differences were found on individual cost parameters including higher costs for prescriptions,[36,37] lower hospitalization-related costs[37] and lower sick leave costs.[37] However, none of these studies reported significant changes in total costs.

Negative findings associated with the interventions have also been reported. These include: deteriorated lung

Table 3 Reported intermediate and end outcomes: measures used and summary of findings

Outcome (n, number of studies reporting the outcome)	Measures§	Summary of findings [study references]
Process measures		
Scheduled outpatient visits (n = 7)	Physician (GP) office visits[32,21,27,37,36]; Specialist/outpatient hospital visits[32,38,37,22,36]; Nurse home visits[38,27,37]	+[27 (nurse home visits), 36] =[32,38,21,27 (GP visits), 37,22 (12 month follow-up)] −[22 (24 month follow-up)]
Medication prescriptions (n = 5)	Total prescribed COPD-related medication[37,36]; new medications prescribed[23]; antibiotics[28,31]; oral steroids[28,31]; domiciliary oxygen[28]; inhaled bronchodilators[28]	+[37 (oxygen and nebulizer), 36] =[37,28,31,23]
Amount of patient education provided (n = 5)	Self-management education[20,36]; COPD education [20,21,27,24]	+[20,21,27,24,36]
Coordination of care (n = 2)	Number of GP-arranged follow-ups[27]; Patient assessed change in coordination of care[36]	+[36] =[27]
Accessibility of care (n = 1)	Patient assessed change in accessibility of care[36]	+[36]
Intermediate outcomes		
Disease specific knowledge (n = 5)	Deenen's respiratory knowledge questionnaire[M1,36]; Self-designed questionnaire (not validated)[20,27,37,24]	+[20,27,37,36] =[24]
Self-management behaviour (n = 4)	Self-designed questionnaire (not validated)[27,35,31,36]; Patient-reported smoking cessation[35,31,36]; physical activity[36]; influenza vaccination[27]; pneumococcal vaccination[27]	+[36] =[27,35,31]
Medication compliance (n = 4)	Self-designed questionnaire (not validated)[37,35,36,25]; Single-item[M2,25] and 4-point Likert scale questionnaire[M3,25]	+[36] =[37,35,25]
Technical skills/self-efficacy (n = 4)	COPD Self-Efficacy Scale[M4,21,35]; Coping style questionnaire[M5,35]; Inhalation checklist[M6,35]; Walking self-efficacy[M7,22]; Self-designed questionnaire (not validated)[37]	+[37,35 (inhalation)] =[21,35 (self-efficacy and coping), 22]
Social support (n = 2)	MOS social support survey[M8,21,26]	=[21,26 (tangible and emotional support, positive social interaction)] −[26 (affectionate support)]
End outcomes		
Lung function (n = 7)	Post bronchodilators FEV$_1$ (litres)[32,31,22,29]; FEV$_1$ (% predicted)[39,31,22,29,36]; FVC (litres)[32]; FEV$_1$/FVC (%)[32,36]; PEF rate (% predicted)[25]	+[31,25] =[32,39,36] −[22,29]
Dyspnoea (n = 7)	MRC dyspnoea questionnaire[M9,35]; CRQ-dyspnoea dimension[M10,30,31,25]; UCSD Shortness of Breath Questionnaire[M11,22]; Baseline and Transition Dyspnoea Indices (interview administered)[M12,22]; BORG scale[M13,23]; Self-developed questionnaire (not validated)[29]	=[35,30,31,29,23,25] −[22]
Symptoms (n = 9)	SGRQ-symptoms[M25,32,21,26,27,37]; Memorial Symptom Assessment Scale[M26,20]; General Health Questionnaire [M23,39]; Symptoms checklist[M27,35]; Self-developed questionnaire (not validated)[23]	=[20,32,21,26,27,37,35,39,23]
Physical functioning (n = 10) => Questionnaire based (n = 8)	SF-36 physical functioning[M14,20,21,31]; SF-12 physical functioning[M15,37]; Barthel Index[M16,39]; RAND-36 physical component[M17,22]; COOP (adapted physical functioning item)[M18,29]; Health Status Questionnaire[M19,24]	+ [20,29] =[21,37,39,31,22,24]

(*Continued*)

Table 3 (Continued)

Outcome (n, number of studies reporting the outcome)	Measures§	Summary of findings [study references]
=> Performance based (n = 2)	6-minute walk test[M20,32,22]; Shuttle Walk Test[M21,31]; Treadmill Test[22]	+ [22 (12 month follow-up)] − [32,31,22 (24 month follow-up)]
Mental functioning (n = 11)	SF-36 mental health[M14,20,21,31]; HAD[M22,26,30]; Health Status Questionnaire [M19,23]; SF-12 mental health [M15,37]; General Health Questionnaire [M23,39]; CRQ-emotion dimension [M10,30,31,25]; CED-Depression Scale [M24,22]; RAND-36 mental component [M17,22]; COOP emotion components [M18,29]	+ [39,22 (12 month follow-up), 29] − [20,21,26,37,30,31,22 (24 month follow-up), 29,23,25]
Health-related Quality of Life	SF-36[M14,20,21,31]; SGRQ-total[M25,32,21,26,27,37,36]; CRQ-total[M10,30,31,22,25]; Subjective Well Being Scale[M28,26]; Health Status Questionnaire[M19,23]; SF-12[M15,37]; QOL-RIO[M29,35]; General Health Questionnaire-total[M23,39]; Quality of Well Being Scale[M30,22]; COOP-total[M18,21]; EQ–5D[M31,36]	+ [20,32 (4 month follow-up), 37 (SGRQ), 30,31 (CRQ-fatigue and mastery), 22 (12 month follow-up), 29,36 (EQ-5D)] − [32 (12 month follow-up), 21,26,27,37 (SF-12), 35,39,31 (SF-36), 22 (24 month follow-up), 36 (SGRQ), 25]
Health care utilization and costs (n = 19)	Hospital (re)admission[32,33,38,21,26,27,37,28,39,30,31,29,23,36,25]; Hospital LOS[37,28,39,30,31,22]; ED-visits[20,32,33,21,27,37,28,39,31,22,29,23,25]; Unscheduled outpatient visits[32,38,21,37,22,29,23,36]; Prescriptions[37,28,31,23,36]; Home visits[38]; Phone calls[22]; Sick leave[36]; Total costs[34,37,36]	+ [37 (prescriptions), 28 (hospital LOS), 36 (prescriptions)] − [20,34,38,21,26,27,35 (outpatient visits), 28,39,30,31, 22 (ED-visits), 29,23,36 (total costs), 25] −− [32,33,38 (readmissions), 35,30 (hospital LOS), 22,23 (outpatient visits), 36]
Mortality (n = 14)	All causes death[20,32,34,33,38,21,27,37,35,30,31,22,29,25]	− [20,32,34,33,38,21,27,37,35,30,31,22,29,25]

Notes: §References to included studies that applied this measure are indicated numerically; References to papers describing the validity/reliability of the measure or questionnaire are indicated with *Mx*.

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function, increased dyspnoea, increased medication use and longer hospital length of stay in comparison with the control groups. An overview of results on end outcomes is presented in Table 3.

Relative risks for hospitalizations, emergency department/unscheduled visits, and mortality

The observed relative risks (RRs) for hospitalization of intervention patients versus control patients vary widely (from 0.64 to 1.50; see Table 4) and only three[31,32,38] are statistically significant at a 95% confidence interval (95% CI). The findings from these three studies all favour the intervention group. Moreover, these three programs include three[32] chronic care components (ie, DSUP on top of SMAN and DSYS) or four[31,38] (ie, DSUP and CIS in addition to SMAN and DSYS) components, whereas all other programs for which a RR could be calculated encompass SMAN and DSYS only. As regards ED and other unplanned outpatient visits, the RRs vary from 0.28 to 2.28 (see Table 4), with two studies[32,37] observing a statistical significant reduction in ED-visits favouring the intervention. The RRs for mortality vary from 0.31 to 1.20 (see Table 5), and none of these reach statistical significance at a 95% CI.

Illustration 1a: Potential short term cost effectiveness based on reduced hospital admissions only

In the study of Rea and colleagues, a RR for hospital admissions in the intervention group of 0.81 (95% CI: 0.59–0.83) was observed.[31] Also the mean length of hospital stay was reportedly shorter in the intervention group than in the control group (1.1 vs 4.0 days). The cost of a hospital bed

Table 4 Relative risks of hospitalization and emergency department (ED)/unscheduled visits for intervention patients versus control patients

Source	Study setting	Included GOLD-stages	Number of components	Relative risk of hospitalization (95% Confidence interval)	Relative risk of ED/ unscheduled visits (95% Confidence interval)
Bourbeau et al (2003)[32]	Secondary care	2 and 3	3	0.64 (0.45–0.91)	0.64 (0.48–0.86)
Casas et al (2006)[38]	Tertiary care	3 and 4	4	0.67 (0.49–0.91)	NA
Gourley et al (1998)[24]	Secondary care	3 and 4	2	NA	1.12 (0.44–5.43)
Hermiz et al (2002)[27]	Community and primary care	2 and 3	2	1.27 (0.66–2.43)	0.28 (0.06–1.27)
Hernandez et al (2003)[37]	Secondary and tertiary care	2 and 3	2	0.74 (0.45–1.21)	0.44 (0.22–0.86)
Jeffs et al (2005)[28]	Secondary care	1–4	2	1.50 (0.84–2.67)	NA
Poole et al (2001)[30]	Secondary care	3	2	1.08 (0.75–1.57)	NA
Rea et al (2004)[31]	Primary care	2 and 3	4	0.81 (0.59–0.83)	0.46 (0.16–1.37)
Smith et al (1999)[29]	Secondary care	3	2	1.01 (0.82–1.26)	2.28 (0.96–5.43)

day was approximately NZ$700 in 2003. From this it can be calculated that the average cost of hospitalization per COPD patient per year for the conventional care strategy would be:

$$4 * NZ\$ 700 = NZ\$ 2800$$

whereas the average annual cost of hospitalization per COPD patient in the intervention group would be:

$$0.81 * (1.1 * NZ\$ 700) = NZ\$ 623.7$$

Thus, based on the observed reduction in hospital admissions and hospital length of stay, and assuming all else equal, a cost effective use of resources from a health systems perspective for this program will be achieved if it can be delivered in a way that the incremental costs of the program are lower than NZ$ 2800 – NZ$ 623.7 = NZ$ 2176.3 per patient per year.

Illustration 1b: Potential short term cost effectiveness based on changes in hospital admission and ED visits

In the study of Hermiz and colleagues,[27] a RR for hospital admissions of 1.27 (95% CI: 0.66–2.43) and a RR for ED visits of 0.28 (95% CI: 0.06–1.27) was observed for the intervention group as compared for the controls. The cost of a hospital bed is approximately AUS$ 320 and the costs of an ED visit AUS$ 100.[41] Assuming the length of hospital stay is 2.4 days[41] and is equal in

COPD care management and usual care, the average cost of hospitalizations per patient per year in a usual care strategy would be:

$$2.4 * AUS\$ 320 = AUS\$ 768$$

Further, assuming an average of 0.5 ED visits per COPD patient per year,[41] the cost of ED visits in a usual care strategy would be:

$$0.5 * AUS\$ 100 = AUS\$ 50$$

In the COPD care program, the annual cost of hospitalizations per patient would be:

$$1.27 * (2.4 * AUS\$ 320) = AUS\$ 975.36$$

and the average annual cost of ED visits per COPD patient would be:

$$0.28 * (0.5 * AUS\$ 100) = AUS\$ 14$$

Based on the observed increase in hospital admissions and reduction in ED visits, and assuming all else equal, this COPD program would be considered cost effective from a health systems perspective if its incremental costs would be lower than AUS$ 818 – AUS$ 989.36 = − AUS$ 171.36 per patient per year. This means that on other aspects of the program savings of at least AUS$ 171.36 per patient per year should be generated in order to set off the additional hospitalization costs, and even more to potentially achieve a return on investment.[42]

Table 5 Relative risks of mortality for intervention patients versus control patients

Source	Study setting	Included GOLD-stages	Number of components	Relative risk (95% Confidence interval)
Aiken et al (2006)[20]	Tertiary care	3 and 4	3	1.20 (0.60–2.40)
Bourbeau et al (2003)[32]	Secondary care	2 and 3	3	0.56 (0.19–1.60)
Casas et al (2006)[38]	Tertiary care	3 and 4	4	1.19 (0.59–2.39)
Coultas et al (2005)[21]	Primary care	2 and 3	4	1.01 (0.21–4.86)*
Gadoury et al (2005)[33]	Secondary care	2 and 3	3	0.71 (0.37–1.38)
Hermiz et al (2002)[27]	Community and primary care	2 and 3	2	1.00 (0.43–2.33)
Hernandez et al (2003)[37]	Secondary and tertiary care	2 and 3	2	0.60 (0.20–1.82)
Poole et al (2001)[30]	Secondary care	3	2	0.33 (0.04–2.87)
Rea et al (2004)[31]	Primary care	2 and 3	4	0.31 (0.26–1.65)
Ries et al (2003)22	Tertiary care	3	2	0.98 (0.43–2.22)
Smith et al (1999)[29]	Secondary care	3	2	1.14 (0.45–2.90)

Note: *RR for case management versus usual care.

Illustration 2a: Potential long term cost effectiveness based on changes in health-related quality of life only

The study of Steuten and colleagues reports an increase in HRQL of 0.02 (from 0.67 at baseline to 0.69 at 12 months follow-up).[36] Assuming 1) no difference in mortality between usual care and the intervention; 2) an average life expectancy of 75 years (ie, plus 14 years from the sample's baseline age of 61 years); and 3) a sustained relative intervention effect on HRQL over the life time of a patient, then, all else equal, the incremental QALYs over the remaining life time of one patient in the intervention versus the control strategy would be:

$$14 * 0.02 = 0.28 \text{ QALYs}^{1*}$$

At a societal WTP of €30,000 per QALY this means that the program would be considered cost effective if its incremental costs do not exceed 0.28 * €30,000 = €8400 per patient over his/her remaining lifetime or on average €600 per patient per year (€8400/14). Similarly, if the WTP for a QALY would be €50,000 then the cost effectiveness gap for the program, given its incremental effectiveness on HRQL of 0.28, would be as high as €14,000 per patient over his/her remaining lifetime (or €1,000 annually) and at a WTP of €20,000 only €5600 over lifetime (or €400 per year).

Illustration 2b: Potential long term cost effectiveness based on changes in health related quality of life and survival

From the paper of Hernandez and colleagues,[37] it can be derived that the average score on the physical component of the Short Form 12 (SF-12) is 0.3770 in the intervention group and 0.3590 in the control group (scores converted from a 0–100 to a 0–1 scale). The incremental HRQL for the interventions group on the physical domain is thus +0.0180. On the mental domain of the SF12, the average scores are 0.4600 and 0.4395 in the intervention and control group respectively, thus an incremental HRQL for the intervention group of 0.0205 on the mental domain. It is assumed that the incremental and physical domains are additive.[43] Given that the average age of the study subjects is 71 years at baseline, the RR for mortality is 0.6 for intervention vs control group, and assuming an average life expectancy of 75 years when receiving conventional care (so +4 years from baseline), then, all else equal, the mean difference in QALYs over the remaining life time of one patient in the intervention versus the usual care strategy would be:

$$(4/0.6) * (0.0180 + 0.0205) = 6.66676 * 0.03085 = 0.256 \text{ QALYs}^{2*}$$

At a societal WTP of €30,000 per QALY this means that the program would be considered cost effective if its incremental

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1.*For reasons of simplicity, future benefits and costs are not discounted in this illustration.

2.*For reasons of simplicity, future benefits and costs are not discounted in this illustration.

costs would not exceed 0.256 * €30,000 = €7680 per patient over his/her expected lifetime of 6.7 years. At a WTP of €50,000 the cost effectiveness gap would be €12,800 and at a WTP of €20,000 this gap would be €5,120 per patient over the expected lifetime.

Discussion

Notwithstanding their relentless efforts and investments, the innovators behind chronic care programs for people with COPD keep struggling to articulate the value of these programs to patients, care providers and payers in terms of 'proof' rather than 'belief'. This study therefore aimed to update and critically review the current evidence base as regards the impact of multi-component COPD care programs on process, intermediate and end results of care. Further-more, in order to support timely decision-making regarding (further) investment in such programs, we illustrated how potentially cost effective programs can be identified, even in the absence of full-blown health economic evaluations.

Starting with the effectiveness of multi-component COPD programs on processes and intermediate outcomes of care, we find little evidence of significant improvements. Although significantly more patient self-management education is provided as part of the COPD programmes, and patient's disease-specific knowledge indeed improves as a result of this, on the whole there is little proof that this better knowl-edge actually translates into significant and sustained behav-ioural changes, as for example smoking cessation, or in better medication adherence and self-efficacy within one or two years follow-up. This finding is in accordance with results from previous reviews,[11,44] but nevertheless dissatisfying. Since smoking cessation is still regarded the most effective way to slow down the disease progression, more emphasis should be placed on other ways to encourage smokers to quit than purely providing education. Reimbursing the costs of smoking cessation therapy, for example, has been proven an efficacious[45] and cost effective[46] way to significantly increase the prolonged abstinence rate.

Also on end outcomes of care (including clinical outcomes, dyspnoea, symptoms and physical and mental functioning, HRQL, mortality, health care utilizations and costs), the COPD care programs merely demonstrate equivalence to usual care. As regards hospital (re)admissions, which are commonly the primary outcome of evaluation, it is worth noting that only for the three programs that encompass ≥3 components of chronic care management, the associated RRs for hospital readmission were statistically significant, and favoured the intervention strategy, whereas

for programs encompassing two components no statistical significant changes were detected. Given that the patient populations included in these studies were comparable to the other studies in terms of sample size, COPD severity and age, and that all programs encompassed the components 'delivery system design' and 'self-management support', this might suggest that programs that additionally encompass the components 'clinical information system' and/or 'decision-support' are more likely to be effective in reducing hospital (re)admissions than the more limited packages. Although this suggestion should be interpreted with caution since the programs were not compared head to head and RRs could only be calculated for nine of the 17 studies, this may start to shed more light on the important issues raised in the review of Adams and colleagues[11] about the relative value of each of the chronic care components for COPD, and the incremental value of combining more than two components in one COPD program. Further, the fact that the component 'decision-sup-port' is lacking in most programs might indicate that clinical guidelines, which have shown to reduce unjustified variety in care and improve delivery of cost effective care, are still underused. A possible explanation for this is that most guide-lines focus more on decision-making by individual profes-sionals than on such multi-disciplinary care processes.[47] As such, this points out the responsibility for health professionals and care managers to intensify their efforts for developing and implementing such multidisciplinary decision-support tools as part of their COPD programs.

As regards HRQL, about half of the studies reporting this outcome observed statistical significant improvements on (limited) aspects of quality of life, but it was not always clear whether these improvements exceeded the minimal clinically meaningful difference. Moreover, the studies of Bourbeau and colleagues[34] and Ries and colleagues[22] showed that the positive impact did not sustain over time. Neverthe-less, no studies reported a deterioration in HRQL and also there seemed to be no relation with the COPD severity of the included population or the setting in which the program was implemented. The latter is in contrast with a previous review of Niesink and colleagues,[48] concluding that improved HRQL resulting from COPD disease management is limited to programs that are (at least partly) implemented in primary care.

Since only three studies undertook a (partial) economic evaluation, and the programs differ largely in terms of their contents as well as in the way they are operated in daily practice, the extent to which COPD care programs deliver value-for-money could not convincingly be demonstrated

at the aggregate level. The provided illustrations on the potential cost effectiveness of specific COPD programs, however, may help to indicate whether there is sufficient opportunity for the program to be considered a worthwhile spending of scarce resources or to deliver a return on investment in the short or longer term. Although the illustrations are deliberately kept simple and therefore the figures should not be taken at face value, they do suggest that there is a fairly limited scope for the programs to save money or break-even. Again, similar observations have been published previously as well as reasons why this might be the case. Linden and Adler-Milstein[12] for example point out that "the main opportunity for chronic care programs to realize short-term medical cost savings is via reductions in costly and avoidable hospital admissions" and "a focus on avoiding the first admission during the intervention period is critical given that hospitalizations are relatively rare events for the majority of the population" and that "individuals may only experience one over the entire course of the program." Therefore, close patient monitoring and effective integrated care delivery across community, primary, secondary and tertiary care are crucial to pick up exacerbation signs more timely and respond more pro-actively to achieve the desired cost effectiveness target. However, when having a closer look at the programs included in this review, it can be seen that only three are characterized by some degree of integration between care settings, whereas the majority is aimed at secondary care only, and therefore after the first hospitalization. As regards the disease severity of the included populations a similar observation can be made: most programs focus on the sicker part of the population, ie, GOLD stage 3. Of course, in a sicker population with higher hospitalization rates, a relatively lower number of admissions need to be avoided for the program to break even. But, such a narrowly focused program addresses only a small part of the population in a too late stadium to achieve the long term goal of chronic care management, which is reducing the increasing burden of COPD on society.

Finally, a couple of limitations of this review have to be taken into account when interpreting its results. First, determining whether a program consisted of two or more components was complicated by the fact that some papers only provided a limited description of their intervention. In case of doubt the paper was excluded and this may conservatively have limited the sample of included papers. However, when comparing the number of included studies in our review (ie, 20 studies) with the review of Adams and colleagues[11] (n = 37) that also considered single component studies, the amount of included papers seems reasonable. Moreover, the multi-component programs included by Adams and colleagues[11] were also picked up by our search. Finally, the results of this review should be interpreted in the light of the moderate methodological quality of its underlying studies, including for example at least seven studies that were underpowered to detect meaningful and statistical significant changes, as well as the lack of economic evaluations in the existing evidence base. Although the currently published data can be used to provide some indication about the potential cost effectiveness of COPD care programs, more and better health economic information will be needed to reduce uncertainty regarding the real impact of COPD care programs in daily practice. To obtain this, well-designed but practical multicentre health economic studies including broad representative patient samples, should be performed across care settings.[49–50]

Conclusion

This systematic review shows that identifying potentially cost effective multi-component COPD care programs remains a challenge given the scarcity of methodologically sound studies that demonstrate significant improvements on process, intermediate and end results of care. Nevertheless, also in the absence of 'perfect data', decisions regarding (future) investments in such care programs have to be made, and will be made, with the information that is available today. Estimations of potential cost effectiveness of specific programs as illustrated in this paper might support decision-makers in doing so. Further research, however, is needed to, firstly, substantiate the finding of this study that programs including three or more chronic care components are likely to be more cost effective than programs that only include the components 'delivery system design' and 'self-management support'. Finally it is recommended to carefully investigate whether programs that are more strongly based on multidisciplinary guidelines will indeed deliver more value for money than the current COPD care programs, especially when implemented across care settings and including broader patient samples.

Acknowledgment

Disclosure

The authors report no conflicts of interest in this work.

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