Effectiveness of Chronic Disease Self Management Support to Stimulate Healthy Active Lifestyle in Primary Care; a Systematic Review

Self management support for cardiovascular diseases, asthma and COPD, diabetes mellitus type 2, and osteoarthritis.

Emmylou Beekman MSc[1], Cor Zagers[2,3]

Supervisors:

Philip van der Wees, PT, PhD[1,3,4]

Tim Takken, PhD[2]

[1] Maastricht University, CAPHRI Research School, Department of Epidemiology, Centre for Evidence Based Physiotherapy, Maastricht

[2] Utrecht University, Clinical Health Science, Department of Physiotherapy Science, Utrecht

[3] Royal Dutch Society for Physical Therapy (KNGF), Amersfoort

[4] Scientific Institute for Quality of Healthcare (IQ Healthcare), Radboud University Nijmegen Medical Centre, Nijmegen

Words: 5772 (511 abstract)
Tables: 2
Appendices: 2

Abstract

Background

A sedentary lifestyle is a common risk factor for patients with chronic diseases, like asthma, chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD), Diabetes Mellitus (DM) type II and osteoarthritis. This specific group of patients' in primary care are at risk for reduced mobility and activity. Regular physical activity improves ability to perform their daily activities, and might enhance their quality of life. Stimulation of a healthy active lifestyle is an important element of primary care to gain health benefits related to the specific medical condition, quality of life and well-being of patients with chronic disease.

Objectives

The objective of this study was to assess the effectiveness of self management support interventions aimed at patients' adherence to healthy active lifestyle on health outcomes in patients' with asthma and COPD, CVD, DM-II, and osteoarthritis. This article focuses on health-related quality of life measured using the Chronic Respiratory Questionnaire (CRQ) in patients with asthma and COPD only.

Methods

Studies were identified from searches in MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), DocOnline, PEDro database, PsycINFO and ERIC. Reference lists were searched. Searches were current from 1985 until June 2010. Selection criteria were (randomized) controlled trials including self management support interventions to stimulate healthy active lifestyle in primary care in patients with chronic diseases. Two reviewers independently assessed study eligibility, methodological quality and extracted data.

Main results (part one: Asthma and COPD)

The reviewers found 1171 potential articles and included seven studies involving 669 patients with asthma and COPD after checking eligibility. Self management support to stimulate healthy active lifestyle was associated with increased subjective rating of quality of life measured with the CRQ total in patients with COPD only in comparison with usual care (MD 3.95; 95% CI -0.17,8.08) and in patients with asthma and COPD combined (MD 3.33; 95% CI -0.55,7.22). The effects were not statistically significant.

Comparisons for the CRQ subscales showed an overall effect in patients with COPD only (MD 1.28; 95% CI 0.93,1.63) and in patients with asthma and COPD combined (MD 1.17; 95% CI 0.85,1.50).
On the disease specific CRQ total, differences did not reach statistical significance for self management support as an add-on treatment to exercise in comparison with exercise alone (MD 1.89; 95% CI -2.32, 6.11). Overall mean difference for the CRQ subscales was 0.00 (95% CI -0.06, 0.06).

Authors' conclusions

Evidence from small studies of moderate methodological quality suggests that self management support to stimulate healthy active lifestyle is associated with improved quality of life measured with the CRQ. Self management support as an add-on treatment to exercise did not result in significant differences. Stimulation of healthy active lifestyle is recommended for patients with asthma and COPD because it might enhance quality of life. It is not clear why self management support as an add-on treatment to exercise is not superior to exercise alone. There is still much to be learned about self management programs in asthma and COPD. More research in large studies is required to gain insight in the mechanisms in health behaviour in patients with a chronic disease, such as asthma or COPD.

Background

A sedentary lifestyle is a risk factor and a prognostic factor for many illnesses. Especially specific groups of patients with chronic diseases in primary care are at risk for reduced mobility and activity, including cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), asthma, Diabetes Mellitus type II (DM-II), osteoarthritis and overall, frail elderly with multi-morbidity (Stevens, 2000; Chorus, 2003; Chodosh 2005; Orozco, 2008; Nelson, 2007; Hilsdon, 2005; Boezen, 2006a and 2006b; VWS, 2008a; Blokstra, 2007; Hoeymans, 2008). Regular physical activity has been linked consistently and reliably to a reduction in all-cause mortality and lower rates of cardiovascular disease and several other debilitating conditions. In addition to the beneficial effects of physical activity on health, regular physical activity also improves older adults' ability to perform daily activities (Stevens, 2000). Encouraging healthy active living is therefore an important element of care to gain health benefits related to the specific medical condition, quality of life and well-being of chronic disease patients. Integration of physical activity, healthy active lifestyle counselling and encouragement into routine primary care service requires involvement and collaboration of health care practitioners, including physicians and physical therapists.

Self-management support

Self-management support is an important component of chronic disease care management to stimulate healthy active living. Chronic care management, programmes in their wide-ranging definition, are typically based on the Chronic Care Model (CCM), (Wagner, 1998 and 2001). This model is an integrative multi-component framework that emphasizes active monitoring of the disease in a defined population of patients, care delivery according to clinical guidelines, education of patients about their disease and self-care techniques, and proactive patient outreach to assist patients in managing their disease (Wagner, 1998, 2001). An essential component of the CCM, *self management support*, encompasses activities that empower and prepare patients to manage their health care. This component reflects the pre-condition of the patient's central role in care and treatment and stresses use of self management support core elements, including goal setting, assessment, action planning, problem solving and follow-up (Estabrook, 2006, Von Korff, 1997).

There is a growing enthusiasm for self management programmes, either as stand-alone programme or as integral components in chronic care models and clinical practice guidelines, in controlling and preventing chronic disease complications. Despite this enthusiasm, there is no agreed definition of what constitutes “chronic disease self management support”. Current research shows slightly positive, but also conflicting results of self management support on active living in chronic disease patients (Hillsdon, 2005; Lorig, 1999 and 2001; Chodosh, 2005). No up-to-date overview of results of self management support on healthy active lifestyle in primary care on CVD, COPD, asthma, DM-II and osteoarthritis exists. One problem of an overview of self management interventions is that there is no general agreed definition of self management; it is often used as an umbrella concept for different phases, core elements, strategies and pre-conditions (Mesters, 2010). Another problem, besides heterogeneity, is that exact descriptions of self management support interventions in articles are lacking and remain often a black box. It is unknown which elements are used for an optimal design to support chronic disease self management. Consequently, it is unknown what form and content of self management education programmes can be optimally integrated in chronic care management in primary care for CVD, COPD, asthma, DM-II and osteoarthritis (Coleman, 2008; Chodosh, 2005; Effing, 2009; VWS, 2008a). The lack of consistency in the use of the term increases inconsistencies to review and compare self management support interventions. Furthermore, it serves as a barrier to identify elements (form and content) necessary for an optimal design to support chronic disease self management. Therefore, by not solely addressing the effectiveness of self management support, but also looking at the blue print of the interventions, this review tried to identify what the actual elements of a self management supporting intervention are. An accepted single, albeit wide-ranging definition of self management given by Barlow (Barlow, 2002) is: “Self management refers to the individual’s ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition. Efficacious self management encompasses ability to monitor one’s condition and to affect the cognitive, behavioural and emotional responses necessary to maintain a satisfactory quality of life. Thus, a dynamic and continuous process of self-regulation is established”. However, not self management in itself, but the *support* by caregivers in primary settings, as defined above, is the topic of this review.

A conceptual model

An explanatory theory of how patient-related, chronic disease self management support, provided as one of the pillars of chronic disease management, affects the outcomes of care is presented in the framework for evaluation of chronic disease self management support interventions (Figure 1). This review focuses on healthy active lifestyle; therefore, health behaviour in the figure concerns physical activity. However, generally speaking, diet adjustments or smoking cessation can also be placed in this model.

The framework starts at baseline with a patient that has specific characteristics (e.g. age) and chronic disease (e.g. COPD). Since self management support interventions are focussed on patients' concerns and problems, a detailed needs assessment (input) must be done for each new disease and group of patients (Lorig, 2003). Patient-provider interaction is an important overlapping core element, as can be seen in Figure 1. Patient-centred can be defined as "care which *(a)* explores the patients' main reason for the visit, concerns, and need for information; *(b)* seeks an integrated understanding of the patients' world – that is, their whole person, emotional needs, and life issues; *(c)* finds common ground on what the problem is and mutually agrees on management; *(d)* enhances prevention and health promotion; and *(e)* enhances the continuing relationship between the patient and the provider" (Little, 2001; Stewart, 2001). The circle in which patient-provider interaction takes place covers the full input and process and reaches out until the patient goes home and starts to manage him/ herself in everyday live (in this review: intermediate outcomes). Within the input, a self management support intervention, core elements and relating strategies that enhance collaborative management can be identified: (1) a collaborative definition of problems (ASSESS and ADVISE); (2) targeting, goal setting and planning (AGREE); (3) creation of a continuum of self management training and support service (ASSIST); and (4) active, sustained follow-up (ARRANGE) (Von Korff, 1997; Estabrooks, 2003). The effects of a self management programme on outcomes concerning health status and healthcare utilization are hypothesized to result from the intermediates behavioural change and self management skills (self-monitoring; interpretation; decision to act or not to act; and self-evaluation. These in turn, can be caused by enhanced self-efficacy together with personalised and self-tailored goal setting (SMART), taking into account two more self management skills (decision-making and action-planning). Perceived self-

efficacy is defined by Bandura (Bandura,1997) as “referring to beliefs in one’s capabilities to organize and execute the courses of actions required to produce given attainments”. Psychosocial mediators (including skills how to find and utilize resources), knowledge, outcome expectations and self management skills can subsequently influence self-efficacy. No core self management skills, which are expected to be necessary for self management, can be viewed as isolated actions, but as a continuum of actions. Therefore, the whole framework (Figure 1) can be read from the left to the right and from the right to the left. Moreover, active follow-up and feedback, arranged by the health care provider, is necessary to succeed an self management support intervention (Lemmens, 2008; Bandura, 1997 and 2000; Mesters, 2002; Lorig, 2003).

Learning and behavioural theories support the core assumptions of the chronic disease self management model. In this review the evaluation framework (Figure 1) was used to identify essential elements and strategies (form and content) of chronic disease self management support interventions and the mechanisms behind them, making valid comparison feasible (Lemmens, 2008).

Based on the above-mentioned models of chronic care management and the framework, presented in Figure 1, the aim of this review is to examine the effectiveness of self management support on healthy active lifestyle in primary care on CVD, COPD, asthma, DM-II and osteoarthritis.

Objectives

The objective of this review is to assess the effectiveness of self management support interventions aimed at patients’ adherence to healthy active lifestyle on health outcomes in patients with chronic disease, diagnosed with asthma, COPD, CVD, DM-II or osteoarthritis.

This paper presents the results of a review of studies in patients with asthma and COPD in primary care settings using the CRQ as outcome measure for health-related quality of life.

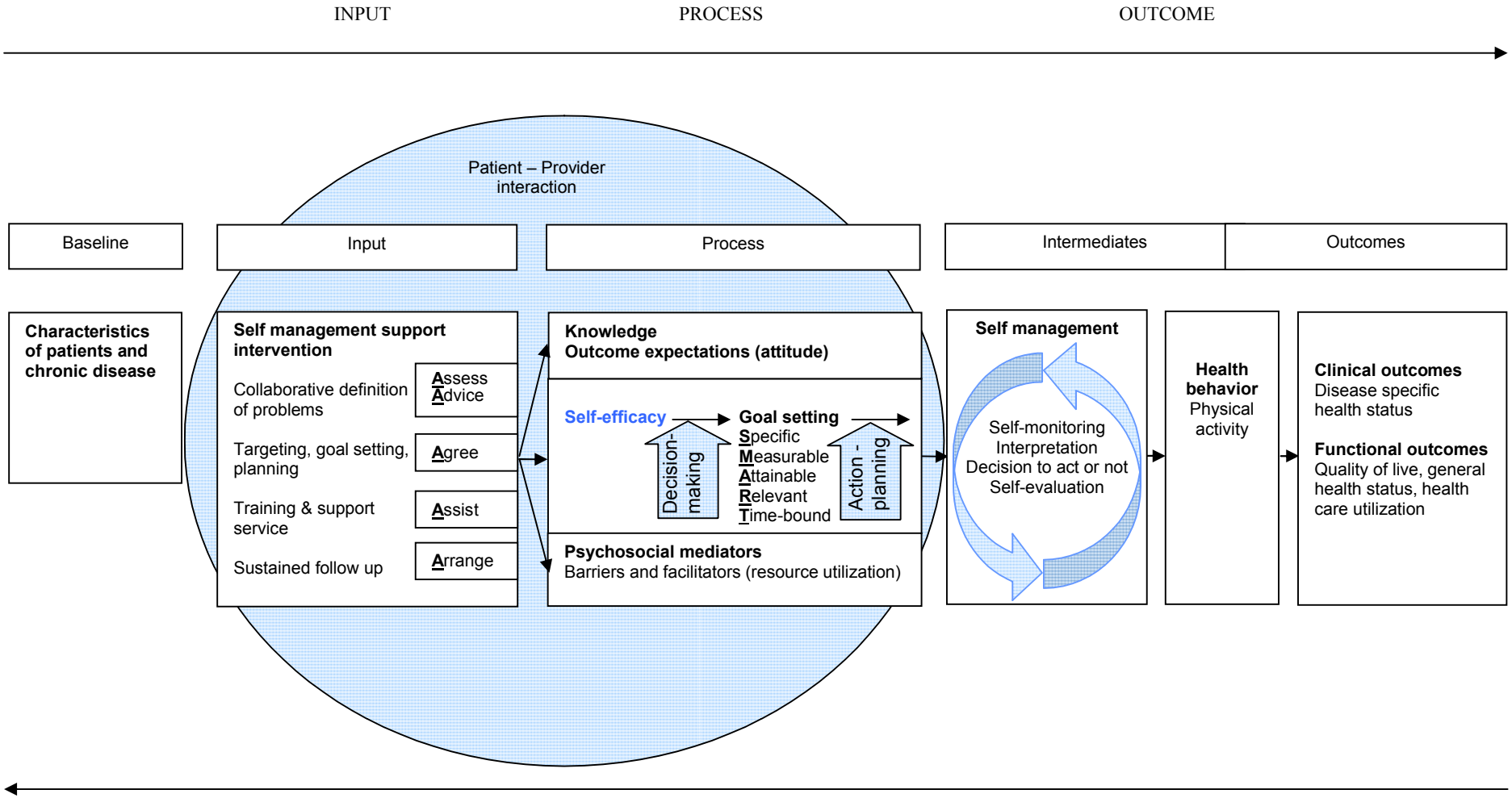


Figure 1: Framework for evaluation of chronic disease self management support interventions. Self-efficacy can be replaced by behavioural control.
Source: Integration of the Social Cognitive Theory (adapted from Bandura 2000), the Evaluation Model for Disease-Management Programmes (adapted from Lemmens 2008), the Health Counseling and Self management Models (adapted from Mesters 2002 and 2010), the Schematic to Direct Effective Physical Activity Promotion in a Primary Care Setting (adapted from Estabrooks 2003) and the theory on self management (adapted from Lorig 2003).

Methods

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) assessing the effectiveness of primary care self management support in CVD, COPD, asthma, DM-II and osteoarthritis were considered for this study. Also considered were controlled trials (CCT), using a pseudo-randomized treatment allocation. Studies published before 1985 were excluded since medicinal treatment of the mentioned chronic diseases prior to 1985 is not comparable with current practice and as a result, baseline populations would not be comparable (Effing, 2009). Studies published in English, German or Dutch were considered for this review. Full-text articles until June 2010 were considered for this study.

Types of participants

Chronic disease patients with a clinical diagnosis in of one of the following four categories of the International Statistical Classification of Diseases and Related Health Problems (10^{th} revision, version for 2007) of the WHO (WHO, 2007): (1) Diseases of the circulatory system: cardiovascular diseases (IX: I00-I99); (2) Diseases of the respiratory system: COPD (X: J40-J44), asthma (X: J45-J46); (3) Diseases of the musculoskeletal system and connective tissue: osteoarthritis/ osteoarthrosis (XIII: M15-M19, M47); and (4) Endocrine, nutritional and metabolic diseases: diabetes mellitus type 2 (IV: E10-E14). These chronic disease categories are conforming the present Dutch situation, as these are the frequently occurring diseases in primary care as highlighted by the Ministry of Health, Welfare and Sport (VWS, 2008a and 2008b).

This review does not focus solely on older populations (65> years of age), since self management support cannot only be addressed as a curative intervention, but also as a secondary preventive intervention. Studies including patients of 40 years of age and older were considered for this study, as different chronic diseases are almost exclusively present above the age of 40 (Gosselink, 2001; Verheij, 2009; CBS,

2009a,b,c). If studies included both patients older and younger than 40 years of age, only the first category of patients was of interest.

Types of intervention

The interventions were categorised according to whether or not they involved patient education and/or self management or self-regulation support components (i.e. goal setting, action planning, follow-up, etc.) on healthy active lifestyle in primary care. The operational definition of chronic disease self management support and its major elements was defined in the background of this article. Selected were programmes conform the definition and/or one or more mentioned elements, which transfers information about the specific chronic disease and the influence of active behaviour and exercise on this chronic disease in any of the following forms: written, verbal, visual or audio. The self management components might be directed towards improving physical activity and healthy active lifestyle and if necessary in combination with coping with activities of daily living. Interventions only addressing self-treatment guidelines directed towards medicinal intake, inhalation techniques, injection techniques, smoking cessation, nutrition, self management of exacerbations or a combination of these were not considered in this review. If one of these interventions was combined with improving physical activity it was included in this review. Patient education was distinguished in minimal and maximal education. Minimal education included the provision of written material alone or a short structured verbal interaction between a health-care provider and a patient. Maximal education included extensive education and an physical activity programme plus advices to continue with sports or other active behaviour in the home situation. It had to be imbedded in primary care where the ultimate goal was to improve the activity level of the patient in daily life and to improve knowledge and understanding of the influence and importance of active behaviour on the chronic disease condition. In this review self management was approached from the provider's perspective, not from the patient's perspective, since it focussed on support of self management in primary care practice, and not on the process addressed to the patients implementation of self management at home.

Types of outcome measures

Any of the following outcomes were used for inclusion in this study, independent of the chronic disease condition: health-related quality of life scores, symptom scores,

hospital admission, emergency room visits, use of other health care facilities/resources, days lost from work, exercise capacity, weight, courses of oral steroids or antibiotics, rescue medication (short-term). Intermediate outcome measures were: health behaviour as in physical activity, self-efficacy, knowledge, expectation, goal setting, self-tailoring, decision-making, action planning, self-monitoring, interpretation by the patient, patient's decision to act or not to act, self-evaluation, problem-solving and patient-provider/ professional interaction.
At least one of the following outcome measures were used for inclusion in this study, dependent of chronic disease condition:
CVD: blood pressure; *COPD / asthma:* number or severity exacerbations, dyspnea, lung function; *DM-II:* haemoglobin A1c level, fasting blood glucose level; *osteoarthritis:* pain, function (questionnaire or symptoms e.g. swelling).
In part one: Health-related quality of life scored by the CRQ in patients with asthma and COPD only.

Search methods for identification of studies

The following databases were searched from January 1985 to June 2010: MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Central Register of Controlled Trials (CENTRAL), DocOnline, PEDro database, PsycINFO and ERIC. Reference lists were searched for additional studies.
All records in the Specific Register coded as 'RCTs and/or CCTs' were searched using the following terms:
lung disease*, obstructive or COPD or pulmonary disease or asthma or asthma; arthritis or osteoarthritis or artrosis or osteoartrosis; diabetes mellitus* or type 2 or diabetes or diabetic or DM or DM-II; heart disease* or ischemic heart disease* or myocardial infarct* or heart infarct* or heart attack* or coronary disease* or peripheral vascular disease* or cardiovascular disease* or congestive heart failure or heart failure or arteriosclerosis or stroke.
All records in the Specific Register coded as 'CVD', 'COPD', 'asthma', 'DM-II' or 'osteoarthritis' were searched using the following terms:
educat* or selfmanag* or self-manag* or self manag* or self-regulat* or self regulat* or selfcar* or self-car* or self car* or self-effica* or self effica* or self-monit* or self monit* or self-control* or self control* or self-evaluat* or self evaluat* or self-tailor* or

self tailor* or train* or instruct* or patient-cent* or patient cent* or patient-focus* or patient focus* or patient-education or patient education or management plan* or management program* or patient-centered or patient centered or patient-centered medical home* or patient-centered care* or PCMH or patient-empower* or patient empower* or exercise* or physiotherap* or physical therap* or physical activit* or motor activit* or active lifestyle or active behavio* or demand manage* or action plan* or action-plan* or goal-setting or goal setting or problem-solving or problem solving or decision-making or decision making or coping-plan* or coping plan* or coping.

Data collection and analysis

Selecting of studies

From the title, two reviewers (EB and CZ) reviewed literature according to the above searches based on the abstract/ keywords/ title and identified potentially relevant trials for full review. Two investigators (EB and CZ) independently assessed study eligibility: study design, chronic disease diagnosis and intervention type (first screening). Of the selected references, the full-text article was retrieved for final assessment (second screening). Two reviewers (EB and CZ) made the final selection using a selection form. Agreement was examined; disagreement was resolved if possible by consensus, and otherwise by consultation with a third reviewer (PW). Articles were included if they were randomized or controlled clinical trials of CVD, COPD, asthma, DM-II or osteoarthritis self management support interventions, with usual care as a control group or placebo or other intervention serving as a control group, and reported relevant outcomes. The specific selection criteria for reviewing the effectiveness of self management interventions in patients with asthma and COPD were: 1. RCT/ CCT; 2.Patients diagnosed with asthma or COPD; 3. Population: 40+ years; 4. Self management support intervention for healthy active lifestyle; 5. Primary care setting; 6. Control group: usual care or placebo or other intervention; 7. Outcome: HRQoL with the CRQ.

Assessment of the methodological quality

Two reviewers (CZ and EB) assessed the methodological quality independently. The tool used in this review to assess risk of bias is a domain-based evaluation, which is recommended by the Cochrane Collaboration, instead of a scale or a checklist. In

this evaluation, critical assessments were made separately for six different domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and 'other issues' (Table 1) (Higgins, 2009). Annex 2 shows the specification of the criteria from Table 1. A description of what was reported in the study was made.

Table 1: The Cochrane Collaboration's tool for assessing risk of bias

Domain	**Description**	**Review authors' judgement**
Sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Was the allocation sequence adequately generated?
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Was allocation adequately concealed?
Blinding of participants, personnel and outcome assessors *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Was knowledge of the allocated intervention adequately prevented during the study?
Incomplete outcome data	Describe the completeness of outcome data for each main	Were incomplete outcome data adequately

Assessments should be made for each main outcome (or class of outcomes).	outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	addressed?
Selective outcome reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Are reports of the study free of suggestion of selective outcome reporting?
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Was the study apparently free of other problems that could put it at a high risk of bias?

We used the information gleaned from this process as a basis for judging the risk of bias for each domain ('Yes' indicates low risk of bias, 'No' indicates high risk of bias, and 'Unclear' indicates unclear or unknown risk of bias).

Data collection

Two reviewers (CZ and EB) extracted the data independently using a data-extraction form. This form contained study design, demographics (population/ age/ gender/ Tiffenau/ FEV1), setting of intervention, intervention parameters, control group, and primary and secondary outcome. Disagreement was resolved by a consensus procedure, followed, if necessary scrutiny from a third reviewer (PW).

Dealing with missing data

An attempt was made to contact authors to complete missing data.

Assessment of heterogeneity

Variation between study findings was explored using the chi-square statistics and subsequently the I-square statistical measurement (Higgins, 2003). Where I-square, which describes the percentage of total variation across studies that is due to heterogeneity rather than chance, was >30%, the data was considered clinically heterogeneous. If significant heterogeneity existed, subgroup analyses were to be done. A sensitivity analysis was conducted by pooling data with a random effects model if the studies or subgroups of studies were considered clinically heterogeneous, otherwise where appropriate a fixed effects model was used to pool the outcomes (Higgins, 2009).

Data synthesis

For continuous outcomes, Weighted Mean Differences (WMD) with 95% - confidence intervals were calculated as appropriate. For dichotomous outcomes Relative Risks (RR), or, if not applicable, odds ratio's (OR) were calculated. Further analysis was done by using a hierarchal rating system of the included studies, the GRADE approach, which entails an assessment of the quality of a body of evidence for each individual outcome by specifying four levels of quality:

Underlying methodology	Quality rating
Randomized trials; or double-upgraded observational studies.	High
Downgraded randomized trials; or upgraded observational studies.	Moderate
Double-downgraded randomized trials; or observational studies.	Low
Triple-downgraded randomized trials; or downgraded observational studies; or case series/case reports.	Very low

The quality of the studies involved consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The highest quality rating is for randomized trial evidence. Review authors could, however, downgrade or upgrade the evidence from all RCTs or CCTs to moderate, low, or even very low quality evidence, depending on the presence of the five factors (Higgins, 2009). A funnel plot was constructed to identify possible asymmetry suggesting publication bias.

Results: (Part one) Asthma and COPD

Description of studies

See: Characteristics of included studies; characteristics of excluded studies

Results of the search

Our search strategy identified 1171 titles and abstracts describing potentially relevant studies of self management support interventions in patients with asthma or COPD. 755 titles and abstracts were unique. We judged that 35 of these were potentially eligible for inclusion, and two studies were supplemented by the third reviewer, because there was no consensus. Eventually we retrieved the full-text versions of 37 papers for extensive assessment about the self management support interventions to enhance physical activity in asthma and COPD. Two reviewers (EB and CZ) independently assessed them and excluded 30 studies. Seven randomized controlled trials met the inclusion criteria of this review, part one (Behnke, 2000; Cambach, 1997; Carrieri, 1996; Maltais, 2008; Moore, 2009; Norweg, 2005; Ries, 2003).

Included studies

Participants and setting

A total of 669 patients were randomized in the seven included studies. 543 patients completed these studies. The drop-out rates ranged from 14% to 35%. All patients were treated in primary care settings.

Interventions

The content of the self management support interventions described in the seven studies included:

- Education (n=7, 100%)
- Stimulation physical exercise in group or recreational (n=7, 100%)
- Breathing exercises/ relaxation techniques (n=4)
- Reinforcement good behaviour [telephone calls and visits at home] (n=4)
- Written action plans (n=3)
- Videotape (n=2)

Comparisons

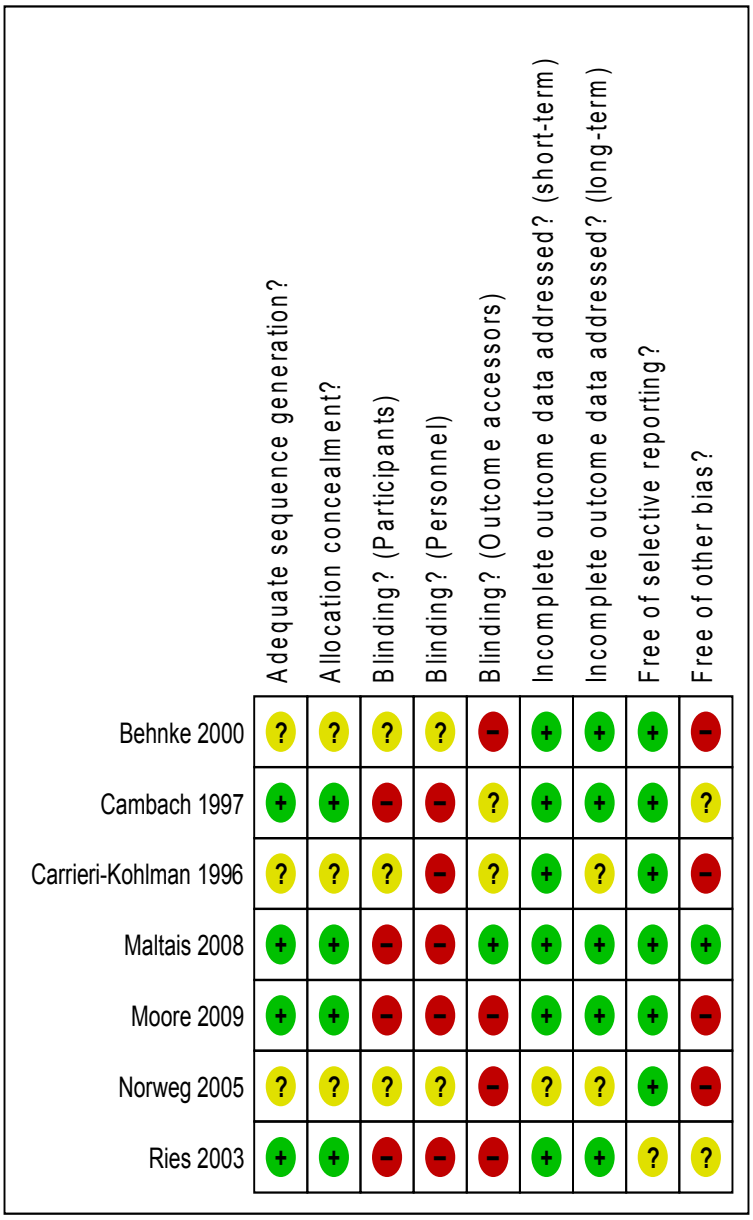
The seven studies were grouped by type of comparison, as follows:

1. Four studies described a self management support intervention aimed at active lifestyle versus usual care (Behnke, 2000; Cambach, 1997; Moore, 2009; Ries, 2003).
2. Three studies described a self management support intervention aimed at active lifestyle plus exercises versus exercises only (Carrieri, 1996; Maltais, 2008; Norweg, 2005).

Excluded studies

Thirty studies were excluded for the following reasons: the intervention type of the studies were not aimed at physical active lifestyle (n=11); the studies did not assess the appropriate outcome (n=8); the articles were not full-text available (n=2); the study was published twice (n=2); the article was a report of a conference (n=2); the study did not take place in primary care (n=2); the design was not a controlled trial (n=1); the language was not in English, Dutch or German (n=1); the study had different patient characteristics, less than 30% were patients with lung disease (n=1).

Risk of bias in included studies



The two reviewers scored 0.60 on Cohen's Kappa for 3 categories measuring the methodological quality. In three studies the third reviewer (PW) forced in 5 cases, all concerning the blinding, the final score.

Effects of interventions

Specific Health-Related Quality of Life (HRQoL) measurements differ widely among studies. The results in this review are presented for the Chronic Respiratory Questionnaire (CRQ) as a specific outcome measure to evaluate the effectiveness of

self management support interventions in the seven described studies for the two comparisons identified: (a) self management support versus usual care and (b) self management support plus exercise versus exercise only.

All studies presented one or more subscales of the CRQ. Six of the seven studies (Behnke, 2000; Cambach, 1997; Moore, 2009; Ries, 2003; Maltais, 2008; Norweg, 2005) used the total scale of the CRQ. We calculated the pooled mean difference for the CRQ total score as well as for subscales of the CRQ. In addition we calculated an overall score for the CRQ subscales in each of the two comparisons. The forest plots of the results are presented in figure 2 to 7.

Comparison 1: Self management support healthy active lifestyle versus usual care.

Self management support intervention to stimulate healthy active lifestyle showed a strong positive trend for health-related quality of life in patients with COPD only (MD 3.95; 95% CI -0.17,8.08), and asthma and COPD combined (MD 3.33; 95% CI -0.55,7.22). All four studies (Behnke, 2000; Cambach, 1997; Moore, 2009; Ries, 2003) provided data in patients with COPD, which could be included in a meta-analysis (figure 2) for the CRQ total in patients with COPD only. One study (Cambach, 1997) reported outcome data for asthma and COPD combined, and three others (Behnke, 2000; Moore, 2009; Ries, 2005) for COPD only. Another forest plot was made for asthma and COPD together (figure 3) for the CRQ total. This forest plot showed also a positive trend for the self management support intervention.

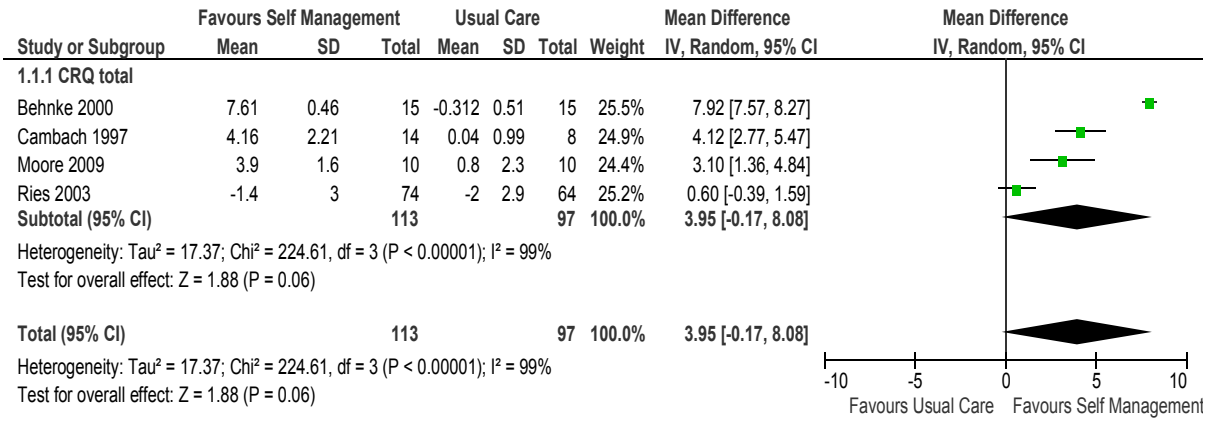


Figure 2: Self management support healthy active lifestyle versus usual care measured with the CRQ total score for COPD only

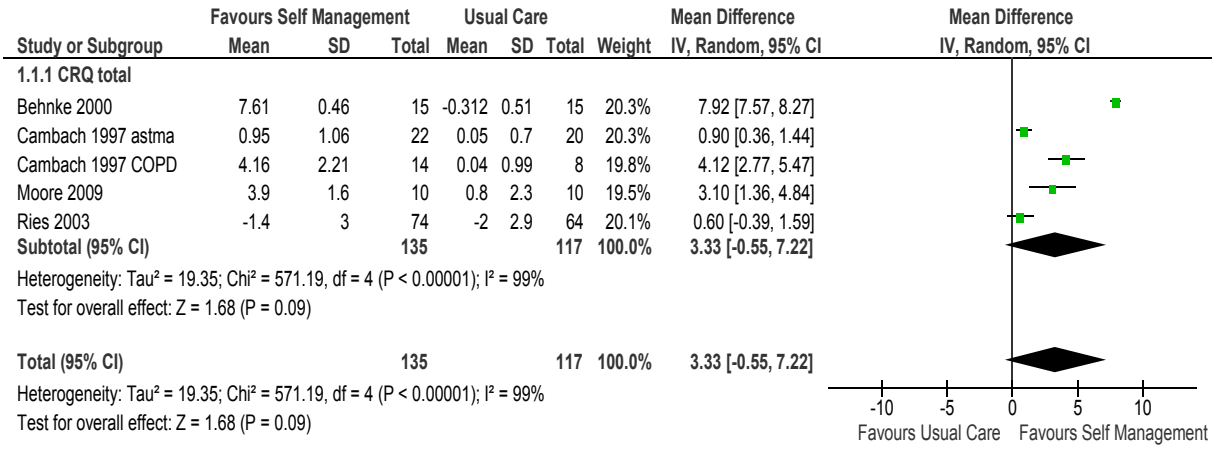


Figure 3: Self management support healthy active lifestyle versus usual care measured with the CRQ total score for asthma and COPD

Three studies (Behnke, 2000; Cambach, 1997; Moore, 2009) in this comparison provided data on the CRQ subscales that could be included in a forest plot for patients with COPD only, and asthma and COPD combined. Self management support intervention increased subjective rating of HRQoL in patients with COPD in three of the four subscales for patients with COPD only (figure 4). The overall MD was 1.28 [95% CI 0.93,1.63], only the mastery scale was not statistically significant MD 1.02 [95% CI -0.52,2.56]. For asthma and COPD combined the overall MD was 1.17 [95% CI 0.85,1.50] (figure 5). Again the mastery scale showed no statistical significance, MD 0.96 [95% CI -0.23, 2.14].

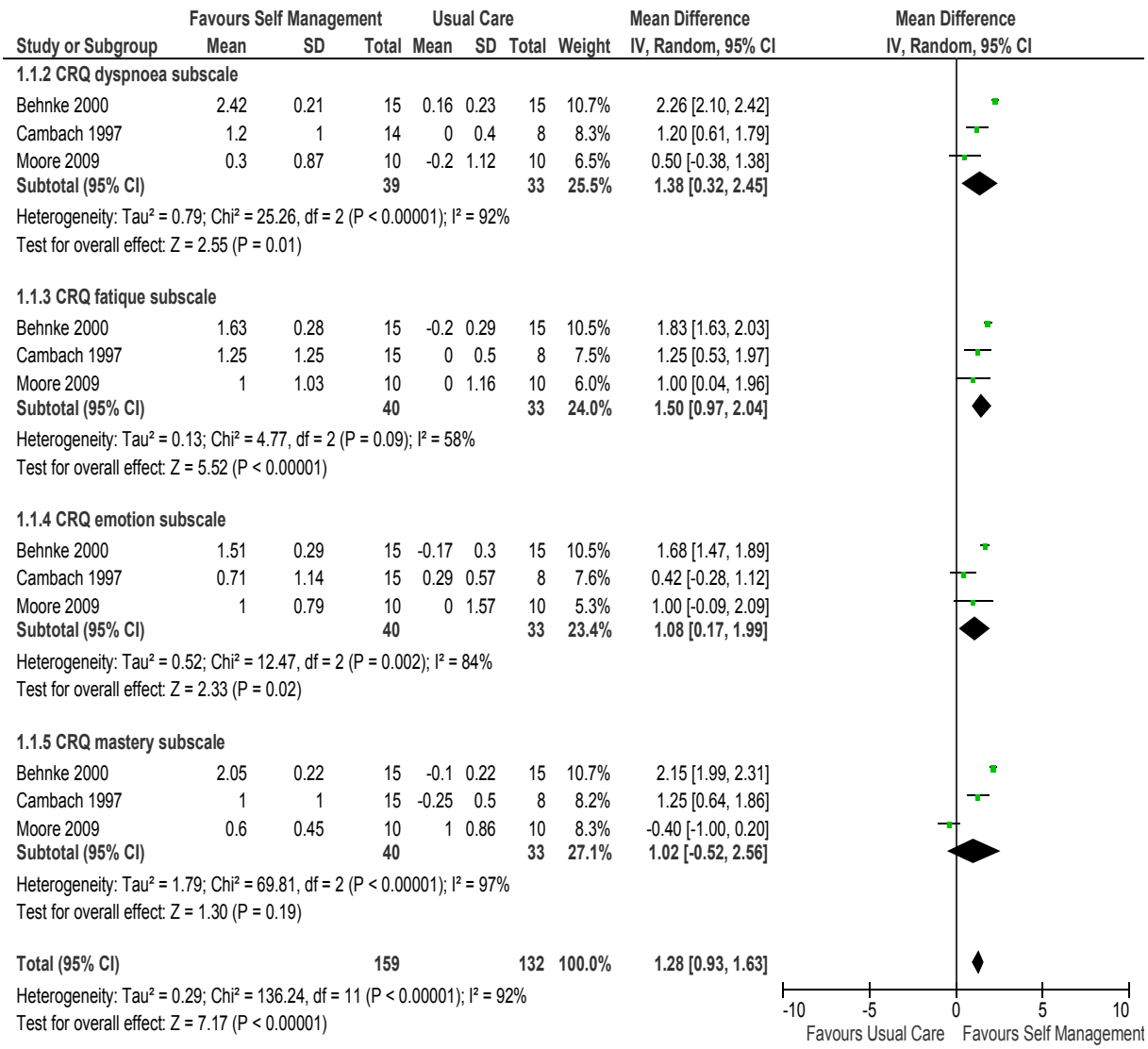


Figure 4: Self management support healthy active lifestyle versus usual care measured with the CRQ (4 subscales) in patients with COPD only.

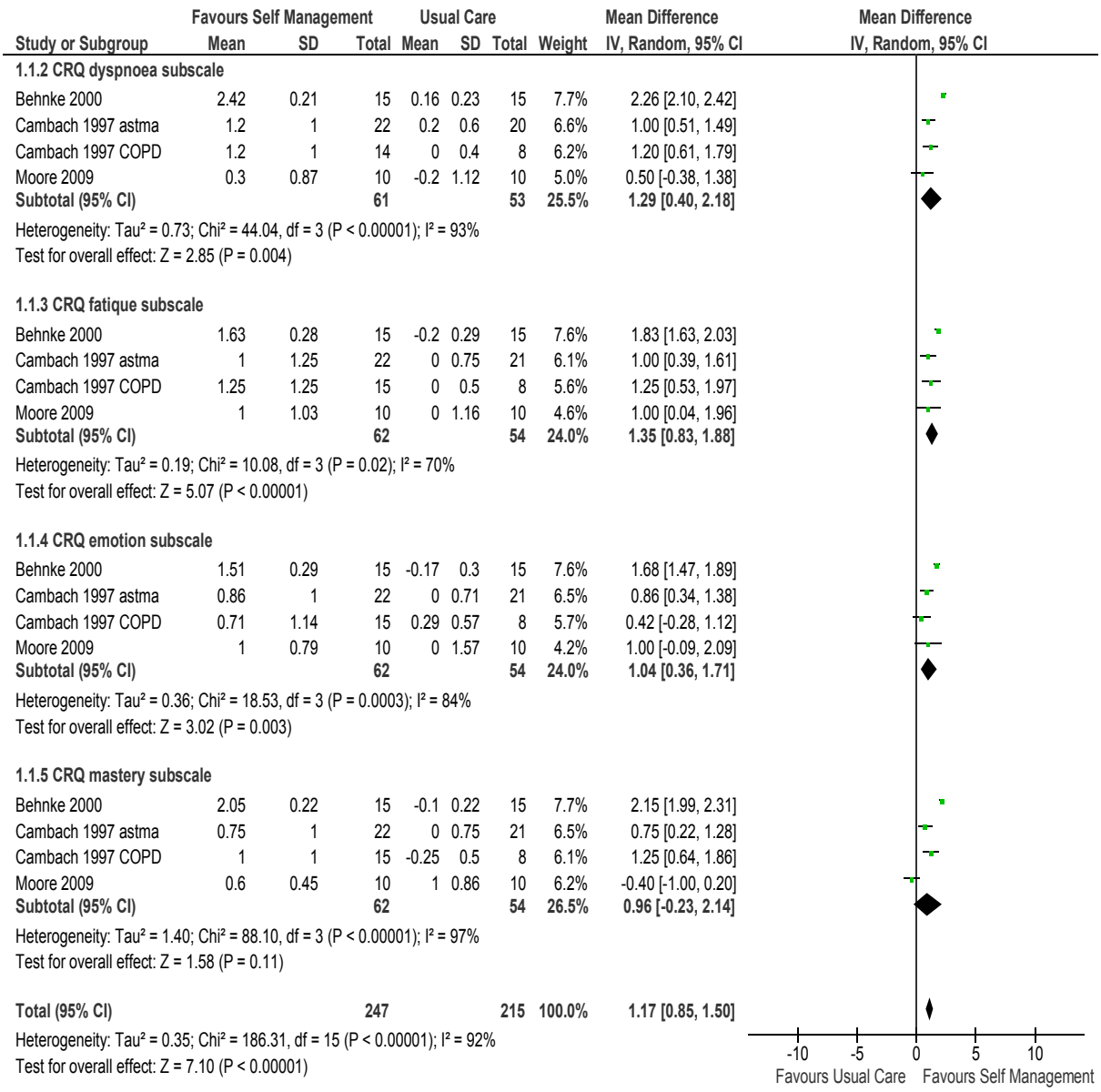


Figure 5: Self management support healthy active lifestyle versus usual care measured with the CRQ (4 subscales) in patients with asthma and COPD.

Comparison 2: Self management support intervention plus exercise versus exercise only.

Self management support as an add-on treatment to exercise was not superior to exercise alone. Three studies provided data in patients with COPD, which could be included in a meta-analysis. Two studies provided data on the CRQ total and all CRQ subscales. One study provided data on the CRQ subscale dyspnea only. Self management support as an add-on treatment did not change subjective rating of HRQoL in patients with COPD on the CRQ total scale (MD 1.89; 95% CI -2.32, 6.11) (figure 6). Also none of the CRQ subscales scored a significant result. This resulted in an overall CRQ score from the CRQ subscales in MD 0.00 [95% CI -0.06, 0.06] (figure 7).

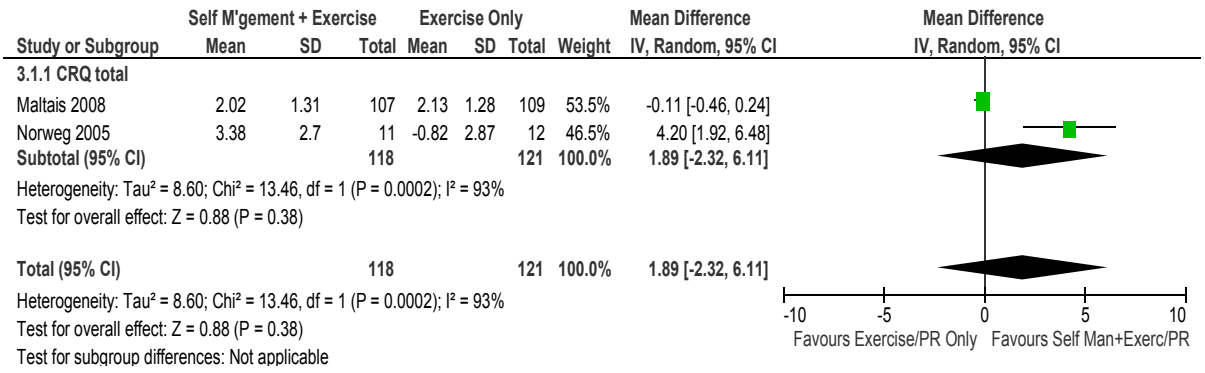


Figure 6: Self management plus exercises versus exercises only measured with the CRQ total in patients with COPD

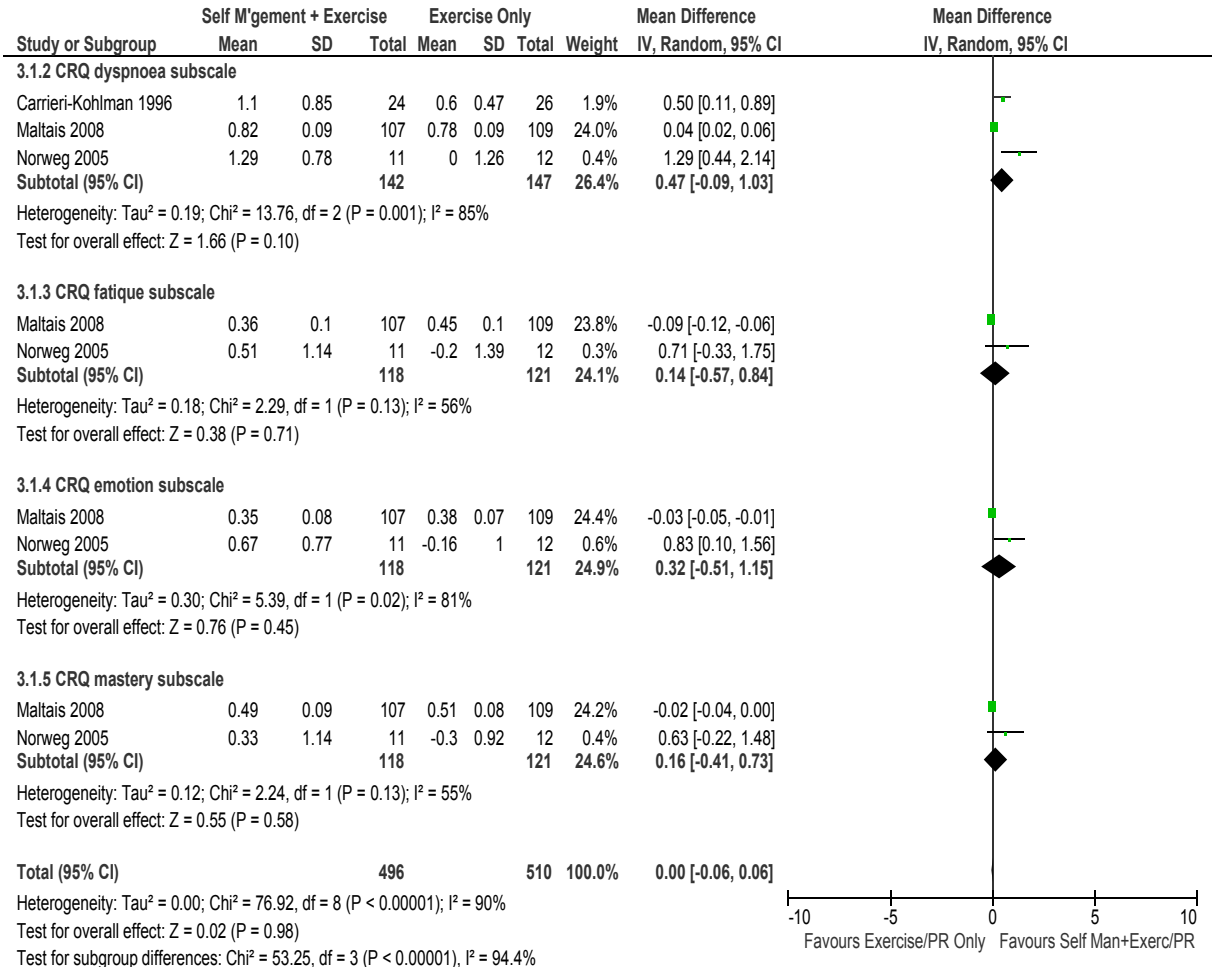


Figure 7: Self management plus exercises versus exercises only measured with the CRQ (4 subscales) in patients with COPD

Discussion

This review identified seven RCT's examining the effectiveness of chronic disease self management support interventions to stimulate healthy active living in primary care in 669 patients with asthma and COPD. Interventions differed in onset, but we recognized two comparisons: self management support interventions versus usual care, and self management support interventions plus exercise versus exercise only. Health-Related Quality of Life (HRQoL) is an important outcome in chronic disease studying self management (Effing, 2007; Turnock, 2009; Foster, 2009). The Chronic Respiratory Questionnaire (CRQ) is a specific measurement instrument used in patients with lung diseases and is often used in clinical research. The minimal clinical

important difference (MCID) in the CRQ is 0.5 point on each CRQ subscale (Jaeschke, 1989; Redelmeier, 1996).

In the first comparison, self management support intervention in patients with COPD only, and asthma and COPD combined, positive significant effects in HRQoL were measured by the CRQ in three of the four subscales. Only the mastery subscale was not statistical significant in both comparisons. The overall scores from the subscales were statistical significant for all subscales in patients with COPD only, and for patients with asthma and COPD in favour of the self management support intervention. The CRQ total scores were not significant. In the CRQ total data from Ries (Ries, 2003) were added, because only CRQ total scores were available. This study had no significant score in favour of the intervention and influenced the CRQ total score.

A study about self management education showed similar findings in HRQoL measured with the St. George's Respiratory Questionnaire (SGRQ) (Effing, 2009). In this study a significant improvement was seen in HRQoL, but this was too small to be clinically relevant. Our conclusion is based on three studies with small sample sizes and moderate methodological quality. The fourth study (Ries, 2003) had a large sample size (n=138). All showed a positive trend for the self management support intervention and were clinical relevant for three studies (Behnke, 2000; Cambach, 1997; Moore, 2009) in all the subscales except Cambach in patients with COPD only in CRQ subscale emotion and Moore in CRQ subscale mastery. There were many studies with asthma as a topic, mostly concerned on medical adherence or inhalation techniques, but just one on self management support to stimulate active healthy lifestyle as above mentioned. The outcome did not differ much from the analysis with the studies with patients with COPD only.

Within the comparison of self management support intervention plus exercise versus exercise only, there were no significant differences. Participants in both groups, intervention and control group, showed similar positive effects of treatment. However, this conclusion is based on three studies only (Carrieri, 1996; Maltais, 2008; Norweg, 2005) of which one (Maltais, 2008) with a larger sample size of 216 patients and weighted for almost 96% in the overall rating from the CRQ subscales. Just two studies (Maltais, 2008; Norweg, 2005) scored the CRQ total score and was not significant. It seemed that exercise training formed a major component of these studies in both the intervention as the control group. A study protocol by Chang

describing a RCT with two intervention groups, Pulmonary Rehabilitation and a self management program against usual care in improving HRQoL amongst people with COPD (Chang, 2008) would give some answers in these question in nearby future.
A limitation of this study is the heterogeneity of the studies. Despite dealing strictly with in- and exclusion criteria on patient characteristics, intervention type, outcome measure there is a high level of heterogeneity. In the first comparison I^2 varied from 58 to 97% in COPD only and from 70 to 97% in asthma and COPD in the CRQ subscales. Especially the study of Behnke (Behnke, 2000) had a very small Confidence Interval and a large effect size resulting in more weight in the overall effect. Even with a random effects model, for more equal distribution because of the high percentage of I^2, the heterogeneity is enormous. Probably this is due to the starting point of the patients short after an exacerbation versus stable patients in the other studies (Cambach,1997; Moore, 2009; Ries, 2003). Patients in the study of Behnke were in a worse condition and had a bigger opportunity to recover than the patients in the other studies. In the second comparison there was also heterogeneity (I^2 >55% in CRQ subscales and I^2 >93% in the CRQ total score). In the study of Maltais (Maltais, 2008) small Confidence Intervals were debit in a high heterogeneity. In this case the non-inferiority design of the intervention was of great interest. In both groups, control and intervention group, there was an increase in HRQoL measured with the CRQ. The minimum clinically important difference (MCID) on the CRQ subscale dyspnea was reached in both groups after 3 months. The home intervention at 3 months and 1 year was non-inferior to the out-patient intervention. So there were no significant differences between both groups. This resulted in non significant outcomes in comparison two, self management support intervention plus exercise versus exercise only.
Although education was present in all studies it was not in all cases behavioural education by physical therapists to promote physical activity. Especially physical therapists could promote safe and healthy physical activity according to a study of Verhagen (Verhagen, 2009). General Practitioner's and other caregivers alike should become aware of this. Another study (Sheedy, 2000) examined the impact of behavioural interventions by physiotherapists to promote physical activity for primary prevention purposes. There were clear improvements to undertake physical activity promotion.
The funnel plots for comparison one and two showed little inconsistency in

the triangle meaning there was publication bias.

Authors' conclusions

Implications for practice

Self management support interventions to stimulate healthy active lifestyle is associated with improvement in HRQoL as measured with the CRQ in patients with asthma and COPD in comparison to usual care. Self management support as an add-on treatment to exercise is not superior to exercise alone. However, due to heterogeneity in interventions and different outcome measures, we could not formulate clear recommendations for effective self management support to stimulate healthy active lifestyle.

Implications for research

Further research with more homogeneity in interventions and equal outcome measures is required to determine the effect of self management support interventions to stimulate healthy active lifestyle. When HRQoL is one of the outcomes long-term follow-up data would benefit the value for drawing conclusions.

Acknowlegements

We are grateful to dr. Sylvia van den Heuvel, researcher form the Netherlands Paramedic Institute (NPi) for her assistance in constructing the search strategies for the different databases.

We thank Carolien Bastiaenen and Ilse Mesters, researchers at Maastricht University for help with the construction of the framework for evaluation of chronic disease self management support interventions.

We thank the study authors who responded to our queries: J. Shackelford, R Cruz-Correia, Y. Dhein.

We thank Cas Kruitwagen, statician of the University Utrecht for his comments on the heterogeneity in this review.

Reviewers

Cor Zagers (CZ)

Emmylou Beekman (EB)

Philip van der Wees (PW)

References

References to studies included in this review

Behnke 2000 ***{published data only}***

Behnke M, Taube C, Kirsten D, Lehnigk B, Jörres RA, Magnussen H. Home-based exercise is capable of preserving hospital-based improvements in severe chronic obstructive pulmonary disease. *Respiratory medicine* 2000; 94:1184-1191.

Cambach 1997 ***{published data only}***

Cambach W, Chadwick-Straver RV, Wagenaar RC, van-Keimpema AR, Kemper HC. The effects of a community-based pulmonary rehabilitation programme on exercise tolerance and quality of life: a randomized controlled trial. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology* 1997; 10:104-113.

Carrieri-Kohlman 1996 ***{published data only}***

Carrieri-Kohlman V, Gormley JM, Douglas MK, Paul SM, Stulbarg MS. Exercise training decreases dyspnea and the distress and anxiety associated with it. Monitoring alone may be as effective as coaching. *Chest* 1996; 110(6):1526-1535.

Maltais 2008 ***{published data only}***

Maltais F, Bourbeau J, Shapiro S, Lacasse Y, Perrault H, Baltzan M Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: A randomized trial. *Annals of Internal Medicine* 2008; 149(12):869-878.

Moore 2009 ***{published data only}***

Moore J, Fiddler H, Seymour J, Grant A, Jolley C, Johnson L Effect of a home exercise video programme in patients with chronic obstructive pulmonary disease. *Journal of Rehabilitation Medicine* 2009; 41(3):195-200.

Norweg 2005 ***{published data only}***

Norweg AM, Whiteson J, Malgady R, Mola A, Rey M. The effectiveness of different combinations of pulmonary rehabilitation program components: a randomized controlled trial. *Chest* 2005; 128(2):663-672.

Ries 2003 ***{published data only}***

Ries AL, Kaplan RM, Myers R, Prewitt LM. Maintenance after pulmonary rehabilitation in chronic lung disease: a randomized trial. *Am J Respir Crit Care Med* 2003; 167(6):880-888.

References to studies excluded from this review

Carrieri-Kohlman 2001 ***{published data only}***

Carrieri-Kohlman V, Stulbarg MS, Cuenco D, Demir DS, Nguyen H. The long term effects of dyspnea self-management education and three "doses" of exercise on the anxiety related to dyspnea. *European Respiratory Journal* 2001;18:173s.

Carrieri-Kohlman 2005 ***{published data only}***

Carrieri-Kohlman V, Nguyen HQ, Donesky-Cuenco D, Demir-Deviren S, Neuhaus J, Stulbarg MS. Impact of brief or extended exercise training on the benefit of a dyspnea self-management program in COPD. *Journal of Cardiopulmonary Rehabilitation* 2005 Sep;25(5):275-84.

Ciaccio 2009 ***{published data only}***

Ciaccio CE, Portnoy JM. Self-management improves asthma. Current Allergy and Asthma Reports 2009;9(6):411.

Clark 2007 ***{published data only}***

Clark NM, Gong ZM, Wang SJ, Lin X, Bria WF, Johnson TR. A randomized trial of a self-regulation intervention for women with asthma. *Chest* 2007;132:88-97.

Cox 1993 {*published data only*}

Cox NJ, Hendricks JC, Binkhorst RA, van-Herwaarden CL. A pulmonary rehabilitation program for patients with asthma and mild chronic obstructive pulmonary diseases (COPD). *Lung* 1993;171:235-44.

Davis 2006 {*published data only*}

Davis AHT, Carrieri-Kohlman V, Janson SL, Gold WM, Stulbarg MS. Effects of Treatment on Two Types of Self-Efficacy in People with Chronic Obstructive Pulmonary Disease. *Journal of Pain and Symptom Management* 2006 Jul;32(1):60-70.

De Blok 2006 {published data only}

De Blok BMJ, De Greef MHG, Ten Hacken NHT, Sprenger SR, Postema K, Wempe JB. The effects of a lifestyle physical activity counseling program with feedback of a pedometer during pulmonary rehabilitation in patients with COPD: A pilot study. *Patient education and counseling* 2006 Apr;61(1):48-55.

Donesky-Cuenco 2007 {*published data only*}

Donesky-Cuenco D, Janson S, Neuhaus J, Neilands TB, Carrieri-Kohlman V. Adherence to a home-walking prescription in patients with chronic obstructive pulmonary disease. *Heart and Lung: Journal of Acute and Critical Care* 2007 Sep;36(5):348-63.

Effing 2009 {*published data only*}

Effing T, Kerstjens H, van der Valk P, Zielhuis G, van der PJ. (Cost)-effectiveness of self-treatment of exacerbations on the severity of exacerbations in patients with COPD: the COPE II study. *Thorax* 2009 Nov;64(11):956-62.

Efraimsson 2008 {*published data only*}

Efraimsson EO, Hillervik C, Ehrenberg A. Effects of COPD self-care management education at a nurse-led primary health care clinic. *Scandinavian Journal of Caring Sciences* 2008;22:178-85.

Elzen 2007 {*published data only*}

Elzen H, Slaets JPJ, Snijders TAB, Steverink N. Evaluation of the chronic disease self-management program (CDSMP) among chronically ill older people in the Netherlands. *Social Science & Medicine* 2007 May;64(9):1832-41.

Ford 1996 {*published data only*}

Ford ME, Edwards G, Rodriguez JL, Gibson RC, Tilley BC. An empowerment-centered, church-based asthma education program for African American adults. *Health & social work* 1996;21:70-5.

Ford 1997 {*published data only*}

Ford ME, Havstad SL, Tilley BC, Bolton MB. Health outcomes among African American and Caucasian adults following a randomized trial of an asthma education program. *Ethnicity & health* 1997;2:329-39.

Gallefoss 1999 {*published data only*}

Gallefoss F, Bakke PS, Rsgaard PK. Quality of life assessment after patient education in a randomized controlled study on asthma and chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine* 1999;159:812-7.

Gallefoss 2002 {*published data only*}

Gallefoss F, Bakke PS. [The effect of patient education in asthma, a randomized controlled trial]. *Tidsskrift for den Norske lægeforening : tidsskrift for praktisk medicin, ny række* 2002;122:2702-6.

Gallefoss 2004 {*published data only*}

Gallefoss F. The effects of patient education in COPD in a 1-year follow-up randomised, controlled trial. *Patient education and counseling* 2004;52:259-66.

Garcia-Aymerich 2007 {*published data only*}

Garcia-Aymerich J, Hernandez C, Alonso A, Casas A, Rodriguez-Roisin R,

Anto JM, Effects of an integrated care intervention on risk factors of COPD readmission. *Respiratory medicine* 2007 Jul;101(7):1462-9.

Kara 2004 {*published data only*}

Kara M, Asti T. Effect of education on self-efficacy of Turkish patients with chronic obstructive pulmonary disease. *Patient Educ Couns* 2004 Oct;55(1):114-20.

Maltais 2005 {*published data only*}

Maltais F, Bourbeau J, Lacase Y, Shapiro S, Perrault H, Penrod JR, et al. A Canadian, multicentre, randomized clinical trial of home-based pulmonary rehabilitation in chronic obstructive pulmonary disease: Rationale and methods. *Canadian Respiratory Journal* 2005 May;12(4):193-8.

Mancuso 2009 {*published data only*}

Mancuso CA, Wenderoth S, Wells MT, Charlson ME. Increasing lifestyle physical activity in asthma patients: a randomized trial [Abstract]. American Thoracic Society International Conference, May 15-20, 2009, San Diego 2009;A4081.

Monnikhof 2003 {*published data only*}

Monninkhof E, van der Valk P, Van Der Palen J, van HC, Zielhuis G. Effects of a comprehensive self-management programme in patients with chronic obstructive pulmonary disease. *European Respiratory Journal* 2003 Nov;22(5):815-20.

Nguyen 2009 {*published data only*}

Nguyen HQ, Gill DP, Wolpin S, Steele BG, Benditt JO. Pilot study of a cell phone-based exercise persistence intervention post-rehabilitation for COPD. *International journal of chronic obstructive pulmonary disease* 2009;4(pp 301-313):-313.

Petty 2006 {*published data only*}

Petty TL, Dempsey EC, Collins T, Pluss W, Lipkus I, Cutter GR, et al. Impact

of customized videotape education on quality of life in patients with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil* 2006 Mar;26(2):112-7.

Put 2003 ***{published data only}***

Put C, van den Bergh O, Lemaigre V, Demedts M, Verleden G. Evaluation of an individualised asthma programme directed at behavioural change. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology* 2003;21:109-15.

Scherer 1998 ***{published data only}***

Scherer YK, Schmieder LE, Shimmel S. The effects of education alone and in combination with pulmonary rehabilitation on self-efficacy in patients with COPD. *Rehabilitation nursing : the official journal of the Association of Rehabilitation Nurses* 1998;23:71-7.

Schott-Baer 1999 ***{published data only}***

Schott-Baer D, Christensen M. Research for practice. A pilot program to increase self-care of adult asthma patients. *MEDSURG Nursing* 1999 Jun;8(3):178-83.

Steele 2008 ***{published data only}***

Steele BG, Belza B, Cain KC, Coppersmith J, Lakshminarayan S, Howard J, et al. A Randomized Clinical Trial of an Activity and Exercise Adherence Intervention in Chronic Pulmonary Disease. *Archives of Physical Medicine and Rehabilitation* 2008 Mar;89(3):404-12.

Tuazon 2000 ***{published data only}***

Tuazon JA. Comparison of two adult asthma education programs in enhancing self-care behaviors and symptom control. *American journal of respiratory and critical care medicine* 2000;161:A54.

van der Meer 2010 ***{published data only}***

van der Meer V, Bakker MJ, van den Hout WB, Rabe KF, Sterk PJ, Kievit J, et

al. Self-management for asthma on the Internet: A randomized study. [Dutch]. *Nederlands Tijdschrift voor Geneeskunde* 2010 Mar 6;154(9):403-9.

Yang 2003 {*published data only*}

Yang ML, Chiang CH, Yao G, Wang KY. Effect of medical education on quality of life in adult asthma patients. *Journal of the Formosan Medical Association = Taiwan yi zhi* 2003;102:768-74.

Additional references

Bandura 1997

Bandura A. (1997). Self-Efficacy: The Exercise of Control (p. 3). New York: W.H. Freeman.

Bandura 2000

Bandura A. (2000.) Cultivate self-efficacy for personal and organizational effectiveness. In Locke EA (Ed.), The Blackwell handbook of principles of organizational behavior (pp.120-136). Oxford, UK: Blackwell.

Barlow 2002

Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. *Patient Educ Couns. 2002 Oct-Nov;48(2):177-87*

Blokstra 2007

Blokstra A, Verschuren WMM, Baan CA, Boshuizen HC, Feenstra TL, Hoogenveen R, Picavet HSJ, Smit HA, Wijga AH. Vergrijzing en toekomstige ziektelast: Prognose chronische ziektenprevalentie 2005-2025. RIVM rapport 260401004, 2007.

Boezen 2006a

Boezen HM (UMCG), Smit HA (RIVM), Postma DS (UMCG). Astma. In Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid.

Bilthoven: RIVM. Retrieved from <http://www.nationaalkompas.nl> Gezondheid en ziekte\ Ziekten en aandoeningen\ Ademhalingswegen\ Astma, 10 maart 2006.

Boezen 2006b

Boezen HM (UMCG), Smit HA (RIVM), Postma DS (UMCG). COPD. In Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid. Bilthoven: RIVM. Retrieved from <http://www.nationaalkompas.nl> Gezondheid en ziekte\ Ziekten en aandoeningen\ Ademhalingswegen\ COPD, 10 maart 2006.

CBS 2009a

Centraal Bureau voor de Statistiek (CBS). Gezondheid en zorg in cijfers 2009. Den Haag (NL): CBS, 2009.

CBS 2009b

Centraal Bureau voor de Statistiek (CBS). Persbericht PB09-020, 17-03-2009.

CBS 2009c

Centraal Bureau voor de Statistiek. Gezondheid en zorg in cijfers 2009. Den Haag/Heerlen, 2009. Retrieved from <http://www.cbs.nl/nl-NL/menu/themas/gezondheid-welzijn/publicaties/publicaties/archief/2009/2009-c156-pub.htm (21-02-2011).

Chang 2008

Chang A, Haines T, Jackson C,Yang I, Nitz J, Low Choy N, Vicenzino B. Rationale and design of the PRSM study: Pulmonary Rehabilitation or self management for chronic obstructive pulmonary disease (COPD), what is the best approach? *Contemporary Clinical Trials 29 (2008) 796-800*

Chodosh 2005

Chodosh J, Morton SC, Mojica W, Maglione M, Suttorp MJ, Hilton L et al. Meta-analysis: chronic disease self-management programmes for older adults. *Ann Intern Med* 2005; 143(6):427-438.

Chorus 2003

Chorus AM, Miedema HS, Boonen A, van der Linden S. Quality of Life and work in patients with Rheumatoid Arthritis and ankylosing spondylitis of working age. *Ann Rheum Dis. 2003 Dec;62(12):1178-84*

Coleman 2009

Coleman S, Briffa NK, Caroll G, Inderjeeth C, Cook N, McQuade J. Effects of self-management, education and specific exercises, delivered by health professionals, in patients with osteoarthritis of the knee. *BMC Musculoskeletal Disord. 2008 Oct 2;9:133.*

Effing 2009

Effing T, Monninkhof EEM, van der Valk PP, Zielhuis GGA, Walters EH, van der Palen JJ, Zwerink M. Self-management education for patients with chronic obstructive pulmonary disease (Review). *The Cochrane Collaboration, 2009*

Estabrooks 2003

Estabrooks PA. Glasgow RE, Dzewaltowski DA. Physical activity promotion through primary care. *JAMA.* 2003;289(22):2913-6.

Estabrooks 2006

Estabrooks PA. Glasgow RE. Translating effective clinic-based physical activity interventions into practice. *Am J Prev Med.* 2006;31(4S):S45-S56.

Foster 2009

Foster G, Taylor SJC, Eldridge S, Ramsay J, Griffiths CJ.
Self-management education programmes by lay leaders for people with chronic conditions (Review). *The Cochrane Collaboration, 2009*

Gosselink 2001

Gosselink R, Decramer M. Chapter 1. Chronic Obstructive Pulmonary Disease

(COPD). In Revalidatie bij chronisch obstructieve longziekten. (2001). Maarssen: Elsevier gezondheidszorg. p. 15.

Higgins 2003

Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-560.

Higgins 2009

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2 [updated September 2009]. The Cochrane Collaboration, 2009. Retrieved from www.cochrane-handbook.org (Section 8).

Hillsdon 2005

Hillsdon M, Foster C, Thorogood M. Interventions for promoting physical activity. *Cochrane Database Syst Rev.* 2005;(1):CD003180.

Jaeschke 1989

Jaeschke R, Singer A, Guyatt G. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clinical Trials, 1989*

Hoeymans 2008

Hoeymans N, Schellevis FC, Wolters I. Hoeveel mensen hebben een of meer chronische ziekten? Bilthoven, RIVM: Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid, 12 december 2008.

Lemmens 2008

Lemmens KM, Nieboer AP, van Schayck CP, Asin JD, Huijsman R. A model to evaluate quality and effectiveness of disease management. *Qual Saf Health Care. 2008 Dec;17(6):447-53*

Little 2001

Little P, Everitt H, Williamson I, Warner G, Moore M, Gould C, et al. Preferences

of patients for patient centred approach to consultation in primary care: observational study. *BMJ* 2001;322:468-72.

Lorig 1999

Lorig K, Sobel DS, Stewart AL, Brown BW, Bandura A, Ritter P, González VM, Laurent DD, Holman HR. Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial. Med Care 1999; 37(1):5-14.

Lorig 2001

Lorig K, Ritter P, Stewart A, Sobel D, Brown BW, Bandura A, González VM, Laurent DD, Holman H. Chronic disease self-management program. 2-year health status and health care utilization outcomes. Med Care 2001;39(11):1217-1223

Lorig 2003

Lorig KR, Halsted R, Holman MD. Self-Management Education: History, Definition, Outcomes, and Mechanisms. Annals of Behavioral Medicine:2003;26(1):1-7.

Mesters 2002

Mesters I, Creer TL, Gerards F. Chapter 6. Self-management and respiratory disorders: Guiding patients from health counseling and self-management perspectives. In Kaptein AA, Creer TL. (Eds.) (2002). *Respiratory disorders and behavioral medicine*. London: Martin Dunetz. P.143.

Mesters 2010

Mesters I, Hoving C. Chapter 10. De chronische fase: nazorg, adaptatie en gedragsbehoud. In Lechner L, Mesters I, Bolman C. (2010). Gezondheidspsychologie bij patiënten. Assen: Koninklijke Van Gorcum BV.

Nelson 2007

Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC et al. Physical activity and public health in older adults: recommendation from the

American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc.* 2007; 39(8):1435-1445.

Orozco 2008

Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roqué i Figuls M, Richter B, Mauricio D. Exercise or exercise and diet for preventing type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2008, Issue 3.

Redelmeier 1996

Redelmeier D, Guyatt G, Goldstein R. Assessing the minimal important difference in symptoms: a comparison of two techniques. *J. Clin. Epidemiol. 1996*

Sheedy 2000

Sheedy J, Smith B, Bauman A, Barnett A, Calderan A, Culbert J, Jacka J. A controlled trial of behavioural education to promote exercise among physiotherapy outpatients. *Australian Journal of Physiotherapy 2000 Vol.46*

Stevens 2000

Stevens M, Lemmink KAMP, Greef de MHG, Rispens P. Groningen Active Living Model (GALM): Stimulating Physical Activity in Sedentary Older Adults; First Results. *Preventive Medicine* 2000;31:547–553.

Stewart 2001

Stewart M. Towards a global definition of patient centred care; The patient should be the judge of patient centred care *BMJ* 2001;322(7284):444–5.

Turnock 2009

Turnock AC, Walters EH, Walters JAE, Wood-Baker R. Action plans for chronic obstructive pulmonary disease (Review). *The Cochrane Collaboration, 2009*

Verhagen 2009

Verhagen E, Engbers L. The physical therapist's role in physical activity promotion. *Br. J. Sports Med. 2009;43;99-101*

Verheij 2009

Verheij RA; Van Dijk CE; Stirbu-Wagner I; Visscher S; Abrahamse H; Davids R; Braspenning J; Van Althuis T; Korevaar JC. Landelijk Informatienetwerk Huisartsenzorg. Feiten en cijfers over huisartsenzorg in Nederland. Utrecht/Nijmegen: NIVEL/IQ, 2009. Retrieved from <http://www.nivel.nl/oc2/page.asp?pageid=14039 (21-02-2011).

Von Korff 1997

Von Korff M, Gruman J, Schaefer J, Curry SJ, Wagner EH. Collaborative management of chronic illness. *Ann Intern Med* 1997;127:1097-102.

Wagner 1998

Wagner EH. Chronic disease management: What will it take to improve care for chronic illness? *Effect Clin Pract* 1998;1:2-4.

Wagner 2001

Wagner EH, Austin BT, Davis C, Hindmarsh M, Schaefer J, Bonomi A. Improving Chronic Illness Care: translating evidence into action. *Health Affairs* 2001;20(6):64-78.

WHO 2007

World Health Organisation (WHO). International Statistical Classification of Diseases and related Health Problems. 10th Revision. Version for 2007. Retrieved from <http://apps.who.int/classifications/apps/icd/icd10online/ (02-02-2010).

WVS 2008a

Letter "Programmatische aanpak van chronische ziekten". Ministry of Health, Welfare and Sport of The Netherlands (WVS). 13 June 2008.

WVS 2008b

Letter "De patiënt centraal door omslag naar functionele bekostiging". Ministry of Health, Welfare and Sport of The Netherlands (WVS). 22 December 2008.

Appendix 1:

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Behnke 2000

Methods	RCT – Self management active lifestyle versus usual care
Participants	Eligible: ? Randomized: 46 Completed: 30 Mean age: I:64 ± 1.9 C: 68 ± 2.2 Gender: M/F: I: 12/3 C: 11/4 FVC % pred.: I: 72.0 ± 3.8 C: 73.5 ± 3.4 FEV_1 % pred.: I: 34.1 ± 7.4 C: 37.5 ± 6.6 ITGV % pred.: I: 185.5 ± 44.9 C: 188.3 ± 32.2 CRQ: I: 79.3 ± 5.3 C: 79.5 ± 5.0
Interventions	I: Mode: conventional therapy (pharmacological therapy and 30 min daily breathing exercises [diaphragmatic and pursed lips breathing]) Content + duration: - individually tailored instruction to practice walking at home for 3 times a day at 125% of the best 6-min treadmill distance within 15 minutes - used diary collected monthly by post to record walking distance and time spent on walking - every two weeks a home visit by one of the researchers to check health status for 3 months, afterwards maintained by monthly phone calls C: conventional therapy and advice to perform exercise without specific instructions
Outcomes	CRQ

	6 MWD TDI Lung function
Notes	

Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Unclear	Described as randomized; other information not available
Allocation concealment?	Unclear	randomly allocated - further information not available from trial report
Blinding? (Participants)	Unclear	information not available from trial report
Blinding? (Personnel)	Unclear	information not available from trial report
Blinding? (Outcome accessors)	No	author was supervising coordinating physician
Incomplete outcome data addressed? (short-term)	Yes	missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Incomplete outcome data addressed? (long-term)	Yes	missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Free of selective reporting?	Yes	outcomes have been reported in the pre-specified way
Free of other bias?	No	potential source of bias related to the specific study design used

Cambach 1997

Methods	RCT with cross over design – Self management active lifestyle versus usual care

Participants	Eligible: 130 Randomized: 89 (I: 46 - C:43) Completed: 66 (43 Asthma + 23 COPD) Mean age: I: 49 ± 14 C: 55 ± 15 Gender: M/F: I: 11/26 C: 13/16 FEV_1 % pred.: I: 77 ± 22 C: 77 ± 23
Interventions	Rehabilitation program in local physiotherapy practices + drug treatment for 3 months followed by a 3 month control period drug treatment only. The other group underwent an initial 3 month control period of drug treatment alone followed by a 3 month rehabilitation program including drug treatment. The rehabilitation program consists, comprising techniques of breathing retraining and evacuation of mucus, exercise training (both for upper and lower extremities), patient education, relaxation techniques and recreational activities. In each physiotherapy practice, 3-4 participants attended group sessions 3 days a week for 90 min. Recreational activities were conducted once a week for 45 min. The purpose of these activities was to direct participants toward regular physical activities deemed essential essential to maintain benefits after rehabilitation.
Outcomes	CRQ Exercise tolerance (6 MWT + sub max ergometry)
Notes	Incremental cycle ergometer test T0 – only

Risk of bias table

	Judgement	**Description**
Adequate sequence generation?	Yes	randomly allocated in block randomization procedure with two times four closed envelopes
Allocation concealment?	Yes	sequentially closed envelopes

Blinding? (Participants)	No	no blinding of participants
Blinding? (Personnel)	No	study personnel were not blinded
Blinding? (Outcome accessors)	Unclear	study did not address this outcome
Incomplete outcome data addressed? (short-term)	Yes	reasons for missing outcome data unlikely to be related to true outcome (intention to treat)
Incomplete outcome data addressed? (long-term)	Yes	reasons for missing outcome data unlikely to be related to true outcome (intention to treat)
Free of selective reporting?	Yes	study protocol is available and all of the study's pre-specified outcomes that are of interest in the trial have been reported in the pre-specified way
Free of other bias?	Yes	insufficient information to assess whether risk of bias exists

Carrieri-Kohlman 1996

	RCT – Self management + exercises versus exercise only
Participants	Eligible: 90 patients (< 60% FEV_1 and Tiffenau < 60% after inhaling albuterol) Randomized: 58 Completed: 51 (after phase 1) and 50 (after phase 2) Mean age: ME: 66 $\pm$ 9 CE: 68 $\pm$ 7 Gender: M/F: ME: 12/15 CE: 14/10 FVC % pred.: ME: 62 $\pm$ 15 CE: 69 $\pm$ 16 FEV_1 % pred.: ME: 36 $\pm$ 10 CE: 40 $\pm$ 11 FEV_1/FVC %: ME: 43 $\pm$ 12 CE: 41 $\pm$ 11
Interventions	Both groups underwent in phase one 12 supervised treadmill exercise sessions in 4 to 6 weeks, in phase two patients underwent a 8-week

	period of home walking. Patients completed a daily dyspnea/ exercise log. ME: the monitored group exercised at self-selected levels of speed and up to 30 min, including 3 min. warm-up and cool-down at 0.5 mph. If patients questioned the nurse, she gave the American Heart Association recommendations that exercise should be maintained for 20 min. at 70 to 85% of the maximum predicted heart rate. CE: the coached group were thought in methods of increasing self-efficacy, i.e., self-confidence in performing a task. The coaching techniques provide successful performances, vicarious experience, verbal persuasion, and physiological feedback. The cognitive-behavioral interventions were described as "guided mastery" techniques and contained breathing and relaxation, feedback, demonstration, distraction, and encouragement. The patients viewed a video on relaxation and breathing strategies. At the beginning of each of the 12 sessions, the nurse coach helped CE patients set goals related to their prior performance and clinical status.
Outcomes	Exercise performance (6 MWT) Dyspnea in laboratory (WOB - SOB - DD - DA Dyspnea in ADL and self-efficacy for home walking (BDI/TDI - CRQ) Anxiety (STAI - TRANX)
Notes	

Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	No	insufficient information about the sequence generation process
Allocation concealment?	Unclear	not described.
Blinding? (Participants)	Unclear	insufficient information
Blinding? (Personnel)	No	no blinding - nurse conversation in both groups
Blinding? (Outcome accessors)	Unclear	insufficient information

Incomplete outcome data addressed? (short-term)	Yes	missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Incomplete outcome data addressed? (long-term)	Unclear	insufficient reporting of attrition/exclusions for long term
Free of selective reporting?	Yes	study protocol is available and all of the study's pre-specified outcomes that are of interest in the trial have been reported in the pre-specified way
Free of other bias?	No	baseline imbalance - prior education or PR for 16 patients

Maltais 2008

Methods	A parallel-group, randomized, non inferiority, multicenter clinical trial – Self management + exercises versus exercise only
Participants	Eligible: 631 Randomized: 252 Completed: 216 Mean age: outpatient group (OG): 66 ± 9 Home group (HG): 66 ± 9 Gender: M/F: OG: 72/54 HG: 68/58 FVC % pred.: OG: 81 ± 19 HG: 82 ± 18 FEV_1 % pred.: OG: 43 ± 13 HG: 46 ± 13 FEV_1 - FVC ratio %: OG: 43 ± 13 HG: 46 ± 12 FRC % pred.: OG: 153 ± 46 HG: 148 ± 39 CRQ: ?
Interventions	Both groups received the same educational program. This program is known under "Living Well With COPD". OG: Aerobic + strength training 3 times a week for 8 weeks. Aerobic training consisted 25 to 30 min. stationary leg cycling at 80% of peak

	work capacity and 30 min. strength training started with 1 set of 10 repetitions per exercise for a maximum of 3 sets. During training, a qualified exercise specialist closely supervised in a ratio of 4 to 5 participants for 1 trainer. HG: The home program was self-monitored and included aerobic and strength exercises 3 times a week for 8 weeks. After carefully instruction the patients trained at home. Aerobic training consisted 40 min. stationary leg cycling at 60% of peak work capacity. The strengthening exercises were the same as in the out-patient programma. The exercise trainer called weekly to reinforce the importance of exercise and patients kept a diary after each training session.
Outcomes	CRQ SGRQ 6 MWD
Notes	

Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Yes	computer number generator
Allocation concealment?	Yes	Use of a centrally administered, computer-generated permuted block randomization scheme using blocks of 2 stratified according to sex and participating site.
Blinding? (Participants)	No	no blinding participants
Blinding? (Personnel)	No	no blinding personnel
Blinding? (Outcome accessors)	Yes	blinding assessor - unaware of the patient group assignment (patients asked not to mention their group assignment) - only contact for evaluations
Incomplete outcome data addressed? (short-term)	Yes	missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups

Incomplete outcome data addressed? (long-term)	Yes	missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Free of selective reporting?	Yes	study protocol is available and all of the study's pre-specified outcomes that are of interest in the trial have been reported in the pre-specified way
Free of other bias?	Yes	no other bias

Moore 2009

Methods	RCT with a concealed minimization strategy to match the groups for age (≤ 65 or > 65 years) and airway obstruction (≤ FEV_1 40% or > FEV_1 40%) – Self management active lifestyle versus usual care
Participants	Eligible: 40 COPD patients Tiffenau < 70% and FEV_1 < 60% on the waiting list for Pulmonary Rehabilitation Randomized: I: 14 C: 13 Completed: I: 10 C: 10 Mean age: I: 70.5 (57.5 to 78.5) C: 70 (13) Gender: M/F: I: 4/6 C: 6/4 FEV_1 % pred.: I: 41.5 (30 to 55) C: 40 (36.5 to 49) CRQ-dyspnea score: I: 2.7 (2 to 4.8) C: 3.3 (1.8 to 4.1)
Interventions	I: 19 min. video A (benefits of exercise in COPD + patients experience + rehabilitation team to provide motivation) and 30 min. video B (performance of exercise 4x/ week for 6 weeks) and diary + educational booklet about COPD. C: educational booklet COPD only + consultation physiotherapist
Outcomes	CRQ ISWT HADS

Notes	

Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	No	concealed minimiazation
Allocation concealment?	Yes	sealed envelopes
Blinding? (Participants)	No	all participants received individual consultation
Blinding? (Personnel)	No	study physiotherapist could equally discuss the COPD management in both groups
Blinding? (Outcome accessors)	No	no assessor blinding
Incomplete outcome data addressed? (short-term)	Yes	missing outcome data balanced in numbers across intervention groups
Incomplete outcome data addressed? (long-term)	Yes	no long term follow up
Free of selective reporting?	Yes	study protocol is available and all of the study's pre-specified outcomes that are of interest in the trial have been reported in the pre-specified way
Free of other bias?	No	a potential source of bias related to the specific study design

Norweg 2005

Methods	RCT – Self management + exercise versus exercise only
Participants	Eligible: 67 Randomized: 43 in 3 groups (18-10-15) Completed: 22 Baseline characteristics after 6 weeks reevaluation (n=33 and dropped out n=10) Mean age: 74,2 $\pm$ 6,6 dropped out (do): 79 $\pm$ 8,2

	Gender: M/F: 22/11 do: 8/2 FEV_1 % pred.: 55 ± 18 do:59 ± 17 CRQ total: 16,8 ± 3,8 do: 14,9 ± 3,6
Interventions	ETA (exercise training): 15 sessions exercise training 2 times a week for 20 to 30 min. mostly walking on a treadmill. Upper-body training using hand weights. Advise exercise at home unsupervised for at least 20 min, 2 to 3 times per week. ETAT (activity training): a behavioral intervention, controlled breathing combined with supervised exertion. 6 times for 1 hour concurrently with exercise training. ETLS (lecture series): once a week for 45 min. concurrently with exercise training for 8 weeks.
Outcomes	CRQ FDSQM CSES
Notes	

Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Unclear	a biased coin design/ probability table
Allocation concealment?	Unclear	insufficient information
Blinding? (Participants)	Unclear	insufficient information
Blinding? (Personnel)	Unclear	insufficient information
Blinding? (Outcome accessors)	No	data collector was not blinded to group assignment
Incomplete outcome data addressed? (short-term)	Unclear	insufficient information
Incomplete outcome data addressed? (long-term)	Unclear	insufficient information
Free of selective reporting?	Yes	study protocol is available and all of the study's pre-

		specified outcomes that are of interest in the trial have been reported in the pre-specified way
Free of other bias?	No	baseline imbalance - great number of dropouts - small sample size - low power

Ries 2003

Methods	RCT – Self management active lifestyle versus usual care
Participants	Eligible: 172 Randomized: 164 Completed: 131 Mean age: 67,1 $\pm$ 8,2 Gender: M/F: 89/75 FEV_1 , Lit.(% pred.): 1,06 $\pm$ 0,43 (45) CRQ total: 88,4 $\pm$ 17,3
Interventions	Both groups received a 8 week program, including components of education, physical and respiratory care instruction, exercise reconditioning, and psychosocial support. I: 12 months maintenance program, immediately after completion rehabilitation program, included (1) weekly telephone calls and (2) monthly supervised reinforcement sessions (review information previously thought, re-evaluate home treatment program, and provide encouragement and reinforcement . A session included 1,5 hours of supervised training, 1 hour of topic review, and 0,5 hour of social time. C: usual care: referral back to the patient's primary care provider for continued medical care with a letter outlining the recommended home care rehabilitation program. Subjects were invited to regular monthly alumni group meetings.
Outcomes	Lung Function Maximal exercise tolerance

	6 MWD UCSD Self-efficacy QoL: QWB, SF-36, CRQ VAS overall health status Health care use
Notes	

Risk of bias table

Item	Judgement	Description
Adequate sequence generation?	Yes	QBASIC random number generator
Allocation concealment?	Yes	Random allocation was accomplished using the Moses-Oakford assignment algorithm with an allocation ratio of 1:1 - assignments were sealed in sequentially numbered identical opaque envelopes and stored in a safe deposit box with access limited to the principal investigator and data coordinator
Blinding? (Participants)	No	no blinding
Blinding? (Personnel)	No	no blinding
Blinding? (Outcome accessors)	No	no blinding
Incomplete outcome data addressed? (short-term)	Yes	missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Incomplete outcome data addressed? (long-term)	Yes	missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Free of selective reporting?	Unclear	insufficient information
Free of other bias?	Unclear	insufficient information

Characteristics of excluded studies [ordered by study ID]

Carrieri - Kohlman 2005

Reason for exclusion	Same study as RM 222

Carrieri 2001

Reason for exclusion	Intervention type - no stimulation to physical activity

Ciaccio 2009

Reason for exclusion	full text not available - intervention type (medication adherence)

Clark 2007

Reason for exclusion	Intervention type - no stimulation to physical activity

Cox 1993

Reason for exclusion	no primary care

Davis 2006

Reason for exclusion	No RCT

de Blok 2006

Reason for exclusion	Outcome

Donesky 2007

Reason for exclusion	Outcome

Effing 2009

Reason for exclusion	Intervention - no stimulation to physical activity

Efraimsson 2008

Reason for exclusion	Intervention type - no stimulation to physical activity

Elzen 2007

Reason for exclusion	patient characteristics - <30% patients with lung disease

Ford 1996

Reason for exclusion	Intervention type - no stimulation to physical activity

Ford 1997

Reason for exclusion	no primary care

Gallefoss 1999

Reason for exclusion	Intervention type - no stimulation to physical activity

Gallefoss 2002

Reason for exclusion	nordic language

Gallefoss 2004

Reason for exclusion	Intervention type - no stimulation to physical activity

Garcia-Aymerich 2007

Reason for exclusion	Outcome

Kara 2004

Reason for exclusion	Outcome

Maltais 2005

Reason for exclusion	Same study as RM 804

Mancuso 2009

Reason for exclusion	Conference report

Meer 2010

Reason for exclusion	Intervention type - no stimulation to physical activity

Monninkhof 2003

Reason for exclusion	Outcome

Nguyen 2009

Reason for exclusion	Outcome

Petty 2006

Reason for exclusion	Outcome

Put 2003

Reason for exclusion	Intervention type - no stimulation to physical activity

Scherer 1998

Reason for exclusion	Intervention type - no stimulation to physical activity

Schott-Bear 1999

Reason for exclusion	Intervention type - no stimulation to physical activity

Steele 2008

Reason for exclusion	Outcome

Tuazon 2000

Reason for exclusion	Conference report

Yang 2003

Reason for exclusion	full text not available - intervention type? (abstract)

Appendix 2:

Criteria for judging risk of bias in the 'Risk of bias' assessment tool (Higgins, 2009)

SEQUENCE GENERATION **Was the allocation sequence adequately generated? [Short form: *Adequate sequence generation*?]**	
Criteria for a judgement of 'YES' (i.e. low risk of bias).	The investigators describe a random component in the sequence generation process such as: • Referring to a random number table; • Using a computer random number generator; • Coin tossing; • Shuffling cards or envelopes; • Throwing dice; • Drawing of lots; • Minimization*. *Minimization may be implemented without a random element, and this is considered to be equivalent to being random.
Criteria for the judgement of 'NO' (i.e. high risk of bias).	The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: • Sequence generated by odd or even date of birth; • Sequence generated by some rule based on date (or day) of admission; • Sequence generated by some rule based on hospital or clinic record number. Other non-random approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgement or some method of non-random categorization of participants, for example:

	• Allocation by judgement of the clinician; • Allocation by preference of the participant; • Allocation based on the results of a laboratory test or a series of tests; • Allocation by availability of the intervention.
Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Insufficient information about the sequence generation process to permit judgement of 'Yes' or 'No'.

ALLOCATION CONCEALMENT

Was allocation adequately concealed? [Short form: *Allocation concealment*?]

Criteria for a judgement of 'YES' (i.e. low risk of bias).	Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: • Central allocation (including telephone, web-based and pharmacy-controlled randomization); • Sequentially numbered drug containers of identical appearance; • Sequentially numbered, opaque, sealed envelopes.
Criteria for the judgement of 'NO' (i.e. high risk of bias).	Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: • Using an open random allocation schedule (e.g. a list of random numbers); • Assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered); • Alternation or rotation; • Date of birth;

	• Case record number; • Any other explicitly unconcealed procedure.
Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Insufficient information to permit judgement of 'Yes' or 'No'. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement – for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.
BLINDING OF PARTICIPANTS, PERSONNEL AND OUTCOME ASSESSORS **Was knowledge of the allocated interventions adequately prevented during the study? [Short form: *Blinding*?]**	
Criteria for a judgement of 'YES' (i.e. low risk of bias).	Any one of the following: • No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding; • Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken; • Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.
Criteria for the judgement of 'NO' (i.e. high risk of bias).	Any one of the following: • No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding; • Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken; • Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.

Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Any one of the following: • Insufficient information to permit judgement of 'Yes' or 'No'; • The study did not address this outcome.
INCOMPLETE OUTCOME DATA **Were incomplete outcome data adequately addressed? [Short form: *Incomplete outcome data addressed*?]**	
Criteria for a judgement of 'YES' (i.e. low risk of bias).	Any one of the following: • No missing outcome data; • Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); • Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; • For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; • For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; • Missing data have been imputed using appropriate methods.
Criteria for the judgement of 'NO' (i.e. high risk of bias).	Any one of the following: • Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; • For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to

	induce clinically relevant bias in intervention effect estimate; • For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; • 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomization; • Potentially inappropriate application of simple imputation.
Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Any one of the following: • Insufficient reporting of attrition/exclusions to permit judgement of 'Yes' or 'No' (e.g. number randomized not stated, no reasons for missing data provided); • The study did not address this outcome.

SELECTIVE OUTCOME REPORTING

Are reports of the study free of suggestion of selective outcome reporting? [Short form: *Free of selective reporting*?]

Criteria for a judgement of 'YES' (i.e. low risk of bias).	Any of the following: • The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; • The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).
Criteria for the judgement of 'NO' (i.e. high risk of bias).	Any one of the following: • Not all of the study's pre-specified primary outcomes have been reported; • One or more primary outcomes is reported using measurements, analysis methods or subsets of the data

	(e.g. subscales) that were not pre-specified; • One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); • One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; • The study report fails to include results for a key outcome that would be expected to have been reported for such a study.
Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Insufficient information to permit judgement of 'Yes' or 'No'. It is likely that the majority of studies will fall into this category.

OTHER POTENTIAL THREATS TO VALIDITY

Was the study apparently free of other problems that could put it at a risk of bias?

[Short form: *Free of other bias*?]

Criteria for a judgement of 'YES' (i.e. low risk of bias).	The study appears to be free of other sources of bias.
Criteria for the judgement of 'NO' (i.e. high risk of bias).	There is at least one important risk of bias. For example, the study: • Had a potential source of bias related to the specific study design used; or • Stopped early due to some data-dependent process (including a formal-stopping rule); or • Had extreme baseline imbalance; or • Has been claimed to have been fraudulent; or • Had some other problem.
Criteria for the judgement of	There may be a risk of bias, but there is either:

'UNCLEAR' (uncertain risk of bias).	• Insufficient information to assess whether an important risk of bias exists; or • Insufficient rationale or evidence that an identified problem will introduce bias.