Accepted Article

DR SIMEN A. STEINDAL (Orcid ID : 0000-0002-7676-8900)

PROFESSOR ANNERS LERDAL (Orcid ID : 0000-0002-7144-5096)

Article type : Review

Full title:

Effectiveness of nursing interventions for breathlessness in people with chronic obstructive pulmonary disease: A systematic review and meta-analysis

Running head:

The effectiveness of nursing interventions for breathlessness in COPD

Author details:

Simen A. STEINDAL, RN, PhD, associate professor, Lovisenberg Diaconal University College, Oslo, Norway.

Henny TORHEIM, CCN, MScN, assistant professor, Department of Health Sciences Ålesund, Faculty of Medicine and Health Sciences, NTNU-Norwegian University of Science and Technology, Ålesund, Norway.

Trine OKSHOLM, RN, PhD, associate professor, Faculty of Health Studies, Campus Haraldsplass, VID Specialised University, Oslo, Norway.

Vivi L. CHRISTENSEN, RN, PhD, associate professor, Lovisenberg Diaconal University College, Oslo, Norway.

Kathryn LEE, RN, PhD, FAAN, professor emerita, Department of Family Health Care Nursing, San Francisco, USA.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jan.13902

This article is protected by copyright. All rights reserved.

Accepted Article

Anners LERDAL, RN, PhD, professor, University of Oslo, Faculty of Medicine, Institute of Health and Society, Department of Nursing Science, Oslo, Norway and

Research Director, Lovisenberg Diaconal Hospital, Department for Patient Safety and Research, Oslo, Norway.

Heidi Øksnes MARKUSSEN, CCN, MScN, PhD candidate, The Norwegian National Advisory Unit on Longterm Mechanical Ventilation, Department of Thoracic Medicine, Haukeland University Hospital, Bergen, Norway and Department of Global Public Health and Primary Care, University in Bergen, Bergen, Norway.

Gerd GRAN, RN, MScN, Helse Bergen HF, Haukeland University Hospital, Bergen, Norway.

Marit LEINE, RN, MScN, Lovisenberg Diaconal Hospital, Oslo, Norway.

Christine Råheim BORGE, RN, PhD, senior researcher, Department for Patient Safety and Research, Oslo, Norway and postdoctoral fellow, Department of Health Science, University of Oslo, Oslo, Norway.

Corresponding author:

Simen A. Steindal, RN, PhD, Associate Professor

Lovisenberg Diaconal University College

Lovisenberggata 15B, 0456 Oslo

Telephone: +47 926 60 422

E-mail: simen.alexander.steindal@ldh.no

Twitter username: @SSteindal

Acknowledgement:

This article is protected by copyright. All rights reserved.

Accepted Article

Funding:

This research received funding from the Norwegian Nurses Organization's group of lung nurses regarding language editing of the article.

Conflict of interest

No conflict of interest has been declared by the authors.

Abstract

Aim: To critically review and synthesize the findings of studies that evaluated the effectiveness of nursing interventions for improving breathlessness in adults with chronic obstructive pulmonary disease.

Background: Systematic reviews of nursing interventions for breathlessness in people with chronic obstructive pulmonary disease have not been specifically addressed.

Design: Systematic review with meta-analysis.

Data sources: A systematic search of Medline, CINAHL, PsycINFO and Embase was performed for studies published between January 2000 - June 2017.

Review methods: Risk of bias, data extraction and meta-analysis were conducted using Cochrane methodology. The quality of evidence was assessed using the GRADE approach.

Results: Twenty papers were included. A meta-analysis of interventions performed at home, including two trials, showed a significant effect in favour of experimental groups for the symptom score of the St. George Respiratory Questionnaire compared with controls. A meta-analysis of interventions performed in clinics with home follow-up showed a significant effect in favour of experimental groups for the mastery and fatigue scores of the Chronic Respiratory Questionnaire compared with controls. In this category of intervention, an additional meta-analysis showed a significant effect in favour of experimental groups for the symptom, activity and total scores of the

This article is protected by copyright. All rights reserved.

St. George Respiratory Questionnaire compared with controls. The quality of evidence was assessed to be very low to moderate.

Conclusion: The results are equivocal as to whether nursing interventions performed at home and nursing interventions performed in hospital with follow-up improve breathlessness in people with chronic obstructive pulmonary disease.

KEYWORDS

Breathlessness, COPD, dyspnoea, literature review, meta-analysis, nursing intervention, shortness of breath, systematic review

Why is this review needed?

- Breathlessness is a highly common and distressing symptom in people with chronic obstructive pulmonary disease (COPD) and leads to limitations in daily life as well as emotional and psychological distress.
- Interventions to control breathlessness in people with COPD are often delivered, coordinated, or led by nurses.
- Prior systematic reviews have focused primarily on the effectiveness of pharmacological and non-pharmacological interventions, such as self-management support and rehabilitation, without specifically addressing nursing interventions.

What are the key findings?

- In COPD, most nursing interventions to control breathlessness are associated with pulmonary rehabilitation programmes and/or self-management support.

This article is protected by copyright. All rights reserved.

Accepted Article

- This systematic review found equivocal results whether nursing interventions performed in hospital with home follow-up improve breathlessness in people with COPD.

How should the findings be used to influence policy, practice, research and education?

- The findings could be used to justify further development and implementation of nursing interventions for breathlessness in people with COPD.
- The findings could be used to educate nursing students and nurses about the effectiveness and advantages of nursing interventions for breathlessness in people with COPD.
- More randomized controlled trials are needed to strengthen the body of knowledge regarding nursing interventions to manage the symptom of breathlessness in people with COPD.

1 INTRODUCTION

People with chronic obstructive pulmonary disease (COPD) experience a high symptom burden (Global Initiative for Chronic Obstructive Lung Disease, 2017) and breathlessness is their most common and debilitating symptom (Bausewein et al., 2010; Christensen et al., 2016; Gardiner et al., 2010). Breathlessness is "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity and therefore can only be perceived by the person experiencing it" (Parshall et al., 2012). In people with COPD, the experience of breathlessness may be uncomfortable or painful and may be experienced as a constant struggle. The symptom can impose great restrictions on everyday life by impairing the ability to eat, walk and socialize (Disler et al., 2014; Ek, Sahlberg-Blom andershed & Ternestedt, 2011; Gysels, Bausewein & Higginson, 2007). Breathlessness can lead to anxiety, loss of control and fear of dying (Barnett, 2005; Dunger et al., 2015; Gysels & Higginson, 2011).

This article is protected by copyright. All rights reserved.

Accepted Article

People with COPD are often dependent on healthcare professionals to treat and resolve breathlessness when their usual strategies to control the symptom fail (Fraser et al., 2006; Lomborg & Kirkevold, 2005). Even though interventions to control breathlessness take a multidisciplinary approach for COPD patients, these interventions are often delivered, coordinated, or led by nurses. Nurses meet people with COPD in different situations, such as homecare, in clinics or outpatient clinics and in rehabilitation. Because they care for people with COPD at all hours and in various situations, nurses play an important role in the management of breathlessness. Nurses also play an important role in improving care for people with other chronic conditions (Jonsdottir, 2008). Therefore, it is important to have knowledge about which nursing interventions are most effective in managing breathlessness in clinical practice.

1.1 Background

Previous systematic reviews of breathlessness in people with COPD have evaluated the effectiveness of pharmacological interventions (Ekstrom et al., 2015; Han et al., 2013; McCarthy et al., 2015) and non-pharmacological interventions (Coyle et al., 2014; Liao et al., 2015; Lundell et al., 2015; McCarthy et al., 2015; Tang et al., 2010; Uronis et al.,2015; Zwerink et al., 2014).

Pharmacological interventions, such as administration of inhaled long-acting bronchodilators to patients with stable COPD can improve breathlessness (Han el al., 2013). Furthermore, continuous oxygen during exertion can reduce breathlessness in mildly or non-hypoxemic patients with COPD (Uronis et al., 2015).

Non-pharmacological interventions, such as rehabilitation programmes and self-management support, can help to improve breathlessness (McCarthy et al., 2015; Zwerink et al., 2014). For example, resistance training (Liao et al., 2015) and walking programmes (Tang et al., 2010) in people COPD reduces breathlessness. However, one systematic review found that home-based telehealth

This article is protected by copyright. All rights reserved.

Accepted Article

care for people with COPD did not improve breathlessness (Lundell et al., 2015). This show that several interventions may improve breathlessness in COPD. However, these systematic reviews do not specifically address nursing interventions.

Although published research has reported on nursing interventions applied to people with COPD, we were unable to identify any systematic reviews on the effectiveness of nursing interventions directed at breathlessness in people with COPD. We conducted a systematic review of this topic to provide a broader understanding of the effectiveness of specific tasks applied by nurses and interventions that could be implemented in clinical practice.

2 THE REVIEW

2.1 Aims

The aim of this systematic review was to critically evaluate and synthesize findings from studies that reported on the effectiveness of nursing interventions on breathlessness in people with COPD.

2.2 Design

This systematic review used the Cochrane guidelines for systematic reviews (Higgins & Green, 2015). This systematic review specifically examined the study design, methods and outcome measures of relevant published research and includes a meta-analysis with results from two or more studies to obtain a pooled result. These pooled results are more generalizable than an individual study's findings and improve the evidence-based knowledge for clinical practice. The protocol for this systematic review has not been registered or published.

Accepted Article

This article is protected by copyright. All rights reserved.

2.3 Search method

A systematic search was performed in June 2017 using the databases Medline, CINAHL, PsycINFO and Embase for studies published between January 2000 - June 2017. The following search strategy was used in Medline using the Medical Subjects Headings terms and keywords and was adopted for the other three databases: Lung diseases OR Respiratory diseases AND Nursing OR Nursing and practical AND Dyspnea OR Dyspne* OR Dyspnoea* OR Shortness of breath OR Breathlessness OR Sob OR Quality of life. Because symptoms are often measured or understood under the concept "quality of life" (Bausewein et al., 2007; Osoba, 2007; Wilson & Cleary, 1995), the keyword "quality of life" was included in the search strategy to be able to identify studies that used disease-specific breathlessness tools to evaluate the effectiveness of interventions on breathlessness. Symptoms such as breathlessness may be seen as a part of the concept of quality of life (Bausewein et al., 2007; Bentsen et al., 2008; Osoba, 2007). In Medline, the limitations "humans", "all adult" and "language" restricted to the German, Danish, Swedish, Norwegian and English language were used. A manual search was also conducted to screen the reference lists of the included papers. For further details of the search, see Appendix 1.

2.4 Inclusion and exclusion criteria

To critically examine the quality of the published nursing interventions, we included both randomized controlled trials (RCTs) and non-RCTs (Higgins & Green, 2015). Studies with an RCT, two-group pre–post design, or pre–post study design published between 1 January 2000 and 29 June 2017 in the German, Scandinavian, or English language in peer-reviewed journals were included if they met the following criteria: 1) included adults diagnosed with COPD regardless of stage; 2) reported non-pharmacological interventions conducted by nurses or nurse-led non-pharmacological interventions in collaboration with other healthcare professionals to control breathlessness; 3) included any kind of comparator; 4) evaluated perception of breathlessness or other similar concepts

This article is protected by copyright. All rights reserved.

Accepted Article

such as dyspnoea and shortness of breath; and 5) collected data using a standardized instrument for measuring breathlessness or disease-specific breathlessness tools that report breathlessness symptoms.

Studies were excluded if 1) participants with lung diseases other than COPD were included; 2) interventions to control breathlessness were conducted by healthcare professionals other than nurses; 3) the person conducting the intervention was not described; 4) the intervention comprised mechanical ventilation, non-invasive ventilation, oxygen treatment, or pharmacological treatment; 5) the study included a proxy evaluation of breathlessness by healthcare professionals or next of kin; 6) breathlessness or a conceptually similar symptom was not mentioned in the introduction, methods, or discussion; and 7) the data were published as a doctoral thesis, report, or conference abstract.

2.5 Search outcome and data extraction

Our primary outcome was breathlessness, which is a subjective experience that can be captured through interview and self-report. Breathlessness can be assessed by the patient's report using a unidimensional tool, breathlessness-specific tool, or disease-specific breathlessness tool (Bausewein et al., 2007; Osoba, 2007). A unidimensional tool measures the general severity of breathlessness at a specific time. A numeric rating scale (NRS) and visual analogue scale (VAS) are frequently used unidimensional tools (Bausewein, Booth & Higginson, 2008). A disease-specific tool covers a broader aspect of breathlessness affecting a person with COPD (Bausewein et al., 2007). For instance, one disease-specific breathlessness tool, the St. George Respiratory Questionnaire (SGRQ), has four scores: a total score, a symptom score that also includes breathlessness, an activity score and an impact score (Jones et al., 1991, Bausewein et. al. 2007). Other studies have used the SGRQ to measure breathlessness in people with COPD (Bentsen et al., 2008). Another example of a disease-specific breathlessness tool is the Chronic Respiratory Questionnaire (CRQ), which includes four domains: dyspnoea, fatigue, emotional function and mastery (Guyatt et al., 1987). The meta-analyses

This article is protected by copyright. All rights reserved.

Accepted Article

included studies that used either SGRQ or CRQ since these tools were used in several studies with study design that was possible to include in meta-analyses. Because breathlessness is a complex symptom affecting many dimensions of the patients' life (Bausewein et. al. 2007), we included studies that used tools that covered different dimensions of breathlessness and not only unidimensional tools.

Two authors independently assessed whether the titles, abstracts and full-text papers met the inclusion criteria in each database. A third author conducted an independent assessment when there was doubt about whether a study met the inclusion criteria. The data were independently extracted by two authors using a standardized data collection form. The extracted data included the name of the first author, year of publication, country of origin, intervention for each group, sample sizes for intervention and control groups, duration of the follow-up and outcomes for breathlessness that included the mean and standard deviation (SD) for each group.

2.6 Quality assessment

The risk of bias of the included studies was rated independently by two authors using the Cochrane Effective Practice and Organisation of Care (EPOC) (2015) risk of bias criteria, which have been adapted for different study designs. The following criteria were assessed in each paper: random sequence generation, allocation concealment, similar baseline outcome measurements, similar baseline characteristics, incomplete outcome data, knowledge of the allocated intervention adequately prevented during the study, protection against contamination, selective reporting and other bias. A high risk of bias was indicated by a negative sign (red colour) and a low risk of bias was indicated by a positive sign (green colour). Papers with no information about the criteria were marked as unclear (yellow colour) (Higgins & Green, 2015).

This article is protected by copyright. All rights reserved.

Accepted Article

The quality of the evidence was assessed by two authors using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) system and GRADEpro software. The following criteria were assessed for each outcome included in the meta-analysis: risk of bias, imprecision, inconsistency, indirectness and publication bias (BMJ BestPractice, 2017).

2.7 Data analysis

Before conducting the meta-analysis, two authors categorized the nursing interventions used in each of the 20 studies. The description of each intervention was read, coded and discussed. The type of nursing intervention was based on where the intervention took place: home, a mix of clinic and home, or clinic. The mean difference (MD) was calculated using the mean and SD for each outcome in each study regardless of the study design.

Because of heterogeneity in the different measurement tools, we chose not to pool all the outcome measures on breathlessness into one meta-analysis. Even though the standardized MD is recommended for pooling results from studies using different tools, some of the tools measured different concepts related to breathlessness. For instance, the symptom domain of the SGRQ and the dyspnoea domain of the CRQ do not address the same concept. The activity domain of the SGRQ is more related to the dyspnoea domain of the CRQ (Rutten-van Mölken, Roos, & Van Noord, 1999). Therefore, including outcome measures from similar tools may provide more relevant information about the effects of different nursing interventions. When possible, we included in the meta-analysis RCTs and studies using a two-group pre–post design using similar tools and similar outcome measures using RevMan (version 5.3). We excluded one-group design studies from the pooled analyses (Higgins & Green, 2015). Using the mean and SD for each outcome, the MD with 95% confidence interval (95% CI) was calculated as the common metric in the meta-analysis. A p-value < .05 was considered to be significant.

This article is protected by copyright. All rights reserved.

We considered fixed-effects models; however, because of heterogeneity between studies, we used only random-effects models. The I^2 statistic was used to evaluate heterogeneity between studies. The I^2 is a measure of variation across studies and an $I^2 > 50\%$ is interpreted as substantial heterogeneity (Higgins & Green, 2015, p. 278).

3 RESULTS

The database searches yielded 1433 publications. After 458 duplicates were removed, titles and abstracts for 975 papers were screened. Based on the inclusion and exclusion criteria, the full text of a total of 63 publications was read and 43 papers were excluded. The final sample for this review included 20 published studies: 11 RCTs, six studies with a two-group pre–post design and three studies with a one-group pre–post design (Figure 1). The sample sizes in these 20 studies ranged from 23-165. The characteristics of the included studies are shown in Table 1.

3.1 Quality assessment

A summary of the risk of bias summary is shown in Figure 2 and a graph of the risk of bias is shown in Figure 3. The quality of evidence according to the GRADE assessment is shown in Table 2 and 3. The quality of evidence was assessed to be very low to moderate.

3.3 Nursing interventions performed at home

Eight studies evaluated nursing interventions performed at home. The studies were conducted in Turkey (Akinci & Olgun, 2011), Australia (Cooke et al., 2009; Wood-Baker et al., 2012), Iceland (Ingadottir & Jonsdottir, 2010), China (Liu et al., 2013), Japan (Moriyama et al., 2015), Korea (Oh, 2003) and the Netherlands (Utens et al., 2012) and included a total sample size of 363 participants.

This article is protected by copyright. All rights reserved.

Accepted Article

The main content of these interventions was self-management support that included education/information on COPD and treatment, performance of breathing exercises, physical training, smoking cessation and early assisted discharge. The interventions were delivered to individual patients by nurses during regular home visits, telephone calls, mail contact, or video-based supervision. The duration of the interventions ranged from 4 days to 12 months.

In this category, one RCT was identified (Liu et al., 2013) and two studies with a two-group pre–post design (Akinci & Olgun, 2011; Moriyama et al., 2015). These three studies used the SGRQ and included an online video-based breathing programme (Liu et al., 2013), education about COPD and performance of breathing exercises and physical training (Akinci & Olgun, 2011), or a nurse-led self-management educational programme that included an interactive workbook, learning materials and journal for self-monitoring (Moriyama et al., 2015). One study reported a positive effect in favour of the experimental group (MD = 15.6–18.2, $p < .05$) for all of the SGRQ scores (Liu et al., 2013). However, this study reported very small SDs (0.2–1.2) compared with the other studies using the SGRQ. After not receiving any answers from the authors about the SDs, we excluded this study from the meta-analysis. Therefore, only two studies were included in the meta-analysis (Akinci & Olgun, 2011; Moriyama et al., 2015). The random-effects model analysis showed a significant effect in favour of the experimental group for the SGRQ symptoms score (MD = 20.2, 95% CI 5.3 to 35.0, I^2 = 56%, $p = .0008$). No effects were found using random-effect models for the SGRQ activity (MD = 15.3, 95% CI –4 to 34.5, I^2 = 82%, $p = .1$), impact (MD = 11.0, 95% CI –9.3 to 31.2, I^2 = 84%, $p = .3$) and total scores (MD = 11.0, 95% CI –6.4 to 28.3, I^2 = 83%, $p = .2$), (see Figures 4–7).

An RCT to test early assisted discharge with home care delivered to individual patients by community nurses reported no difference in scores (MD = 0.29, $p = .09$) on the clinical COPD questionnaire (CCQ) between groups (Utens et al., 2012). For the two-group pre–post studies, one involved a home-based pulmonary rehabilitation programme using the Chronic Respiratory Disease Questionnaire (CRDQ) and the Borg Dyspnoea Scale and this study reported a significant effect in

This article is protected by copyright. All rights reserved.

Accepted Article

favour of the experimental group compared with controls for the Borg Dyspnoea Scale (MD = –3.1, p = .04) and the CRDQ (MD = 20, p = .03) (Oh, 2003). Another two-group pre–post study of a mentoring programme delivered to individual patients by community nurses found no group difference (MD = –0.07, p = .3) using the Medical Research Council (MRC) dyspnoea scale (Wood-Baker et al., 2012). One of the two one-group pre–post studies evaluated partnership-based nursing practice for people with COPD and found an improvement in SGRQ scores over time (MD = 3.9–20.2, p = .04 to < .0001) for all the SGRQ subscores and total score (Ingadottir & Jonsdottir, 2010). The other one-group pre–post study evaluated home-based pulmonary rehabilitation and found no improvement over time in SGRQ scores (MD = –0.02 to –3.39, p = not reported) (Cooke et al., 2009).

3.4 Nursing interventions performed in clinics with home follow-up

Six studies evaluated nursing interventions performed in clinics with home follow-up. The studies were conducted in the Netherlands (Bischoff et al., 2012), Taiwan (Kuo et al., 2013), Korea (Song et al., 2014), England (Sridhar et al., 2008) and China (Wang et al., 2014; Yu et al., 2014) and included a total sample of 473 participants. The main content of the interventions was self-management education about living with COPD, COPD management, management of exacerbations, motivational interviewing and pulmonary rehabilitation. These interventions were delivered to the individual patient by nurses in a hospital or general practice and included a follow-up with home visits and telephone calls. The duration of the interventions ranged from 5 weeks to 24 months.

Two RCTs in this category used the CRQ and could be included in the meta-analysis (Bischoff et al., 2012; Sridhar et al., 2008). One intervention was a comprehensive self-management programme comprising tailored sessions in general practice with ongoing telephone support at home (Bischoff et al., 2012). The other was a pulmonary rehabilitation programme with follow-up home visits and telephone calls (Sridhar et al., 2008). No group differences were found for dyspnoea scores (MD = –0.1, 95% CI –0.5 to 0.2, I^2, p = .4) emotional scores (MD = –0.1, 95% CI –0.4 to 0.1, I^2 = 0%, p = .3), or

This article is protected by copyright. All rights reserved.

the total score (MD = –0.7, 95% CI –2.7 to 1.3, I^2 = 85%, p = .5). There was a significant effect favouring the intervention group compared with controls for mastery (MD = –0.5, 95% CI –0.8 to –0.2, I^2 = 0%, p = .0009) and fatigue (MD = –0.4, 95% CI –0.6 to –0.1, I^2 = 0%, p = .01) (see Figures 8–12).

An additional meta-analysis was performed and included two studies that used the SGRQ. One was an RCT (Song et al., 2014) and the other had a two-group pre–post design (Yu et al., 2014). The RCT tested the effects of inpatient and outpatient sessions using motivational interviews and telephone follow-up (Song et al., 2014) and the two-group study tested the effects of a structured hospital-based self-management education programme and telephone follow-up (Yu et al., 2014). There was a significant effect in favour of the experimental group for the SGRQ symptom score (MD = 16.5, 95% CI 7.6 to 25.4, I^2 = 36%, p < .0003), activity score (MD = 11.5, 95% CI 3.3 to 19.6, I^2 = 29%, p = .006) and total score (MD = 10.8, 95% CI 4.9 to 16.7, I^2 = 0%, p = .0004). No effect was found for the SGRQ impact score (MD = 9.9, 95% CI –6.6 to 26.3, I^2 = 86%, p = .24) (see Figures 13–16).

One RCT was a self-regulation intervention delivered to individual patients in hospital with telephone follow-up at home and showed no effect using the Borg Dyspnoea Scale (MD = 1.5, p = .07) (Kuo et al., 2013). In another RCT based on the health belief model, the effect was significant in favour of the experimental group (MD =1.4, p < .001) using the MRC Dyspnoea Scale (Wang et al., 2014).

3.5 Nursing interventions performed in clinics

Six studies evaluated nursing interventions performed in clinics. The studies were conducted in the USA (Alexander & Wagner, 2012; Carrieri-Kohlman et al., 2001), Sweden (Efraimsson et al., 2008), Ireland (Wilson et al., 2008), Korea (Kyung & Chin, 2008) and China (Liu et al., 2015) and included a total of 310 participants. One RCT involved nurse-monitored exercise using video tapes on relaxation and breathing strategies and this study found no differences between groups (MD = –4.0, p =.1) using the Shortness of Breath Questionnaire (Carrieri-Kohlman et al., 2001). Another RCT on smoking

This article is protected by copyright. All rights reserved.

cessation reported no differences between groups (individual support + usual care (MD = 0.07, p = .80)) and group support + usual care (MD = 0.02, p = .10) using the Modified MRC Dyspnoea Scale (Wilson et al., 2008). The third RCT tested the effects of a structured educational intervention programme at a nurse-led primary health clinic and found a significant effect (MD = 3.4–25.2, p = .03–.0004) in favour of the intervention group for all SGRQ scores (Efraimsson et al., 2008). Another RCT evaluated the effectiveness of pulmonary rehabilitation exercise and harmonica playing and reported no difference between groups (MD = –3.7, p = .6) using the Shortness of Breath Questionnaire (Alexander & Wagner, 2012). A two-group pre–post study evaluated the effects of rehabilitation guidance (Liu et al., 2015) and reported significantly lower MRC scores after treatment in the experimental group than in controls (MD = not reported, p = < .05). Finally, a one-group pre–post study tested an intervention delivered to a group of patients in a pulmonary rehabilitation programme (Kyung & Chin, 2008) and found positive changes over time using the Borg Dyspnoea Scale (MD = 0.65, $p < .001$) and VAS Dyspnoea Scale (MD = 1.3, p = .01).

4 DISCUSSION

This systematic review with meta-analyses critically reviewed and synthesized data in published studies that evaluated the effectiveness of nursing interventions on breathlessness in people with COPD.

Our results show that nurses are involved in a diverse range of interventions to manage breathlessness in people with COPD. These include education, providing information, instruction on breathing and physical exercises and mentoring and implementing frameworks or models for nursing practice. Nurses need to have the appropriate knowledge and skills to manage breathlessness in patients. Evidence implies that most people with COPD are given pharmacological treatment for breathlessness, but some do not receive any advice about managing breathlessness in daily life (Gysels & Higginson, 2011). This underlines the importance of interventions that teach patients

This article is protected by copyright. All rights reserved.

Accepted Article

strategies for managing their breathlessness in daily life. The nurse's role in patient education has been emphasized (Bailey et al., 2013). In our systematic review, most of the nursing interventions to control breathlessness in COPD patients were associated with various types of inpatient or outpatient pulmonary rehabilitation and self-management support. Previous systematic reviews have shown that both pulmonary rehabilitation programmes and self-management support are efficient interventions for improving breathlessness in people with COPD (McCarthy et al., 2015; Zwerink et al., 2014). Although traditionally provided by physiotherapists, nurses are increasingly assuming key roles in pulmonary rehabilitation (Vincent & Sewell, 2014).

Our systematic review found that three studies in the category of interventions performed at home showed significant effects on the SGRQ subscores and total score in favour of the experimental group compared with controls (Akinci & Olgun, 2011; Ingadottir & Jonsdottir; Liu et al., 2013). In contrast to our findings, some studies included in an integrated review of home-based respiratory care showed a significant difference in favour of the experimental groups for activity and impact scores on the SGRQ, but no significant differences between groups for the symptom score or total score (Jonsdottir, 2008). Our meta-analysis of interventions performed at home revealed a significant effect in favour of the experimental group only for the SGRQ symptom score compared with controls. The other SGRQ subscores and total score did not differ between groups; this lack of difference is similar to the findings of a meta-analysis of studies using the SGRQ to evaluate nurse-led COPD management with home visits (Taylor et al., 2005). However, other reviews have used health-related quality of life as the outcome of interest rather than the symptom of breathlessness (Jonsdottir, 2008; Taylor et al., 2005).

The main content of interventions performed at home was education and breathing exercises, which are the core elements among several elements in self-management support in people with COPD (Bourbeau & Nault, 2007). Self-management education aims to ensure that people acquire the confidence and skill (e.g. breathing techniques) needed to manage their disease in daily life at home

Accepted Article

This article is protected by copyright. All rights reserved.

(Bourbeau & Nault, 2007). For people with severe COPD, coping with everyday activities (e.g. walking, dressing and eating) may be a priority for self-management skill building (Pinnock et al., 2016). The opportunity to observe people with COPD in the context of their everyday life at home may enhance the nurse's ability to identify important problems or issues with disease management and then individualize the patient's self-management education. Nurse-led consultations may also increase the amount of self-management advice received by adults with COPD (Fletcher & Dahl, 2013).

Evidence suggests that any improvements arising from a short-course pulmonary rehabilitation programme diminish with time (Foglio et al., 1999; Griffiths et al., 2000). The diminished effect may reflect non-adherence to continuing exercising after completion of the programme. For instance, individuals with COPD may lack motivation to follow advice at home or fail to recall the exact recommendations of their healthcare provider (Brooks et al., 2002). Our meta-analysis indicates that interventions performed in the clinic with home follow-up were effective in improving breathlessness in people with COPD. Home follow-up appears to be an effective intervention for maintaining a longer-term positive effect of hospital-based self-management/rehabilitation. Home follow-up may also help people with chronic diseases to overcome barriers to active self-management and to increase their self-efficacy (Jerant et al., 2005). Home visits and telephone calls may be an effective way to meet individual needs and to deliver an individualized, tailored intervention. When combined with shared decision making, tailored interventions are beneficial for adults with chronic diseases and may also be useful for adults with COPD (Durand et al., 2014). In contrast to our findings, a RCT that evaluated a telephone-based 12-month maintenance programme after pulmonary rehabilitation in patients with chronic lung disease found no differences between groups for breathlessness at 12 and 24 months (Ries et al., 2003).

This article is protected by copyright. All rights reserved.

Several of the interventions in our systematic review can be performed by nurses, alone or in collaboration with a multidisciplinary team. Nurses who have frequent contact with people diagnosed with COPD are uniquely positioned to assess breathlessness and to initiate interventions to prevent or minimize this symptom. Given the long-standing published recommendations for nurses to follow-up patients diagnosed with COPD (Barnett, 2008; Stallard, 2007), it was surprising to find so few published nursing intervention studies. Nevertheless, because of the multidimensional nature of breathlessness and difficulty managing the symptom, comprehensive and multiple interventions with multidisciplinary approaches may be warranted (Kuzma et al., 2008; Parshall et al., 2012). In a multidisciplinary approach, complementary roles and contributions from team members, including social workers, dietitians, physicians, exercise specialists and nurses, are critical to providing the highest quality of patient care (Kuzma et al., 2008).

We included studies that used unidimensional tools, breathlessness-specific tools and disease-specific breathlessness tools in our systematic review. Unidimensional tools, such as the VAS and the NRS and breathlessness-specific tools, such as the modified MRC, are frequently used to measure the frequency and intensity of breathlessness. Disease-specific breathlessness is not limited to frequency and intensity but covers various aspects related to breathlessness such as the patient's perception of breathlessness and its impact on daily life (Bausewein et al., 2007). Because breathlessness can have a major effect on daily life (Disler et al., 2014; Ek et al., 2011; Gysels et al., 2007), a broader understanding of breathlessness and the effects of nursing interventions are needed. For instance, the intervention by Song and colleagues (2014) contained self-care support for different self-management strategies for daily life. The authors reported a positive significant effect on all of the SGRQ scores but not on the Borg Dyspnoea Scale score. The reason may be that the SGRQ scores capture

This article is protected by copyright. All rights reserved.

breathlessness in a broader sense than the Borg Dyspnoea Scale score and our results support the finding that breathlessness is improved in a broader sense.

The quality of the evidence was assessed as moderate to very low. We included non-RCTs in the meta-analyses and potential biases are more likely to occur in non-RCTs than in RCTs (Reeves, Deeks, Higgins & Wells, 2015). Lack of randomization and allocation concealment lead to a high risk for selection bias for included non-RCTs. However, non-RCTs are more likely to reflect clinical practice in real life because of their longer follow-up time, broader range of participants and lower cost than RCTs. To generate evidence to guide healthcare decisions, it is important to incorporate data from non-RCTs to complement RCTs (Faber, Ravaud, Riveros, Perrodeau, & Dechartres, 2016). Only two studies were included in each meta-analysis and the sample size ranged from 62 to 232. Evidence suggests that small trials are more likely to report larger beneficial effects than are larger trials. This can partly be explained by the lower methodological quality of smaller trials (Zhang, Xu, & Ni, 2013).

The meta-analyses of interventions performed in clinics with home follow-up showed significant differences for more of the SGRQ scores than CRQ scores. This suggests that the SGRQ is more responsive to changes than the CRQ. However, prior research is inconclusive about which instrument is the most responsive to changes in people with COPD (Puhan et al., 2007; Rutten-van Mölken et al., 1999). Other explanations include differences in study design, sample characteristics, interventions, duration of interventions and follow-up time between the studies included in the meta-analyses in this category.

In our systematic review, potential sources of heterogeneity include the different measurement tools, diversity of the interventions and differences in the duration of the interventions and data collection time points. The difference in study populations in terms of the stage of COPD is a possible source of heterogeneity. Two studies included people with COPD regardless of stage (Sridhar et al., 2008; Yu et al., 2014), one study included people

This article is protected by copyright. All rights reserved.

Accepted Article

with moderate COPD (Song et al., 2013) and another study excluded people with very severe COPD (Bischoff et al., 2012).

4.1 Strength and limitations

Studies that used disease-specific breathlessness tools were excluded if quality of life was the only concept of interest. Our systematic search of publications in the databases was performed with some language restrictions. We did not include doctoral theses, reports, or conference abstracts and we did not contact researchers in this field to clarify whether they had any unpublished material. Therefore, our results may be limited by publication bias. However, a strength of our study was that the search of publications was not restricted to only papers published in English language.

We also excluded publications that did not explicitly state who performed the intervention. It is plausible that we may have excluded studies where the intervention was performed by nurses. These choices may have limited the number of studies and types of interventions identified by our search strategy and included in the study selection process. Another limitation of our systematic review could be that our study protocol was not pre-registered.

We excluded the home-based study of Liu et al. (2013) because of their reported SD values. Including this study in the meta-analysis with their published SDs showed a highly significant effect for SGRQ subscores and total score that favoured the experimental group compared with controls. The small SDs of this study contributed to the highly significant effect. We chose to take a cautious approach and to exclude this study to avoid including a possible false-positive effect. In addition, we included in our review studies with different durations of intervention, small sample sizes and non-RCTs. Therefore, the results should be interpreted with caution. Finally, a random-effects model is considered to be a more cautious approach for estimating the effects of different types of

This article is protected by copyright. All rights reserved.

Accepted Article

interventions in the same meta-analysis. However, we also used a fixed-effects model in the presence of low heterogeneity and found similar results.

5 CONCLUSION

Three categories of nursing interventions that focused on breathlessness in people with COPD were identified: those performed at home, in a clinic with home follow-up, or in a clinic. We found equivocal results about whether interventions performed at home were effective in improving breathlessness in people with COPD. Interventions in this category were effective in improving the SGRQ symptom score but not the other SGRQ subscores and total score. We found equivocal results about whether interventions performed in hospital and as a follow-up improve breathlessness. Interventions in this category were effective in improving two of five CRQ scores and three of four SGRQ scores. However, the results related to the SGRQ scores should be interpreted with caution because of the low quality of evidence. Furthermore, three of six studies suggested that nursing interventions performed in clinics may improve breathlessness. Because of the high and/or unclear risk of bias in the included studies and because few nursing interventions studies were found, more RCTs are needed to increase the body of knowledge about nursing interventions for breathlessness management in adults with COPD.

Author Contributions

All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE*):

1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;

2) drafting the article or revising it critically for important intellectual content.

* http://www.icmje.org/recommendations/

This article is protected by copyright. All rights reserved.

Accepted Article

REFERENCES

Akinci, A. C., & Olgun, N. (2011). The effectiveness of nurse-led, home-based pulmonary rehabilitation in patients with COPD in Turkey. *Rehabilitation Nursing, 36*(4), 159–165.

Alexander, J. L., & Wagner, C. L. (2012). Is harmonica playing an effective adjunct therapy to pulmonary rehabilitation? *Rehabilitation Nursing, 37*(4), 207–212.

Bailey, P. H., Boyles, C. M., Cloutier, J. D., Bartlett, A., Goodridge, D., Manji, M., & Dusek, B. (2012). Best practice in nursing care of dyspnea: The 6th vital sign in individuals with COPD. *Journal of Nursing Education and Practice, 3*, 108.

Barnett, M. (2005). Chronic obstructive pulmonary disease: A phenomenological study of patients' experiences. *Journal of Clinical Nursing, 14*(7), 805–812.

Barnett, M. (2008). Nursing management of chronic obstructive pulmonary disease. *British Journal of Nursing, 17*(21), 1314–1318.

Bausewein, C., Booth, S., Gysels, M., Kuhnbach, R., Haberland, B., & Higginson, I. J. (2010). Understanding breathlessness: Cross-sectional comparison of symptom burden and palliative care needs in chronic obstructive pulmonary disease and cancer. *Journal of Palliative Medicine, 13*(9), 1109–1118.

Bausewein, C., Booth, S., & Higginson, I. J. (2008). Measurement of dyspnoea in the clinical rather than the research setting. *Current Opinion in Supportive and Palliative Care*, *2*(2), 95–99.

Bausewein, C., Farquhar, M., Booth, S., Gysels, M., & Higginson, I. J. (2007). Measurement of breathlessness in advanced disease: A systematic review. *Respiratory Medicine, 101*(3), 399–410.

Bentsen, S. B., Henriksen, A. H., Wentzel-Larsen, T., Hanestad, B. R., & Wahl, A. K. (2008). What determines subjective health status in patients with chronic obstructive pulmonary disease:

Accepted Article

This article is protected by copyright. All rights reserved.

Importance of symptoms in subjective health status of COPD patients. *Health and Quality of Life Outcomes, 6*(1), 115.

Bischoff, E. W., Akkermans, R., Bourbeau, J., van Weel, C., Vercoulen, J. H., & Schermer, T. R. (2012). Comprehensive self management and routine monitoring in chronic obstructive pulmonary disease patients in general practice: Randomised controlled trial. *BMJ,* 345, e7642. doi: https://doi.org/10.1136/bmj.e7642

BMJ BestPractice. (2017). What is GRADE? Retrieved from http://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/

Bourbeau, J., & Nault, D. (2007). Self-management strategies in chronic obstructive pulmonary disease. *Clinics in Chest Medicine, 28*(3), 617–628.

Brooks, D., Krip, B., Mangovski-Alzamora, S., & Goldstein, R. (2002). The effect of postrehabilitation programmes among individuals with chronic obstructive pulmonary disease. *European Respiratory Journal, 20*(1), 20–29.

Carrieri-Kohlman, V., Gormley, J. M., Eiser, S., Demir-Deviren, S., Nguyen, H., Paul, S. M., & Stulbarg, M. S. (2001). Dyspnea and the affective response during exercise training in obstructive pulmonary disease. *Nursing Research, 50*(3), 136–146.

Christensen, V. L., Holm, A. M., Cooper, B., Paul, S. M., Miaskowski, C., & Rustoen, T. (2016). Differences in symptom burden among patients with moderate, severe, or very severe chronic obstructive pulmonary disease. *Journal of Pain and Symptom Management, 51*(5), 849–859.

Cooke, M., Moyle, W., Griffiths, S., & Shields, L. (2009). Outcomes of a home-based pulmonary maintenance program for individuals with COPD: A pilot study. *Contemporary Nurse, 34*(1), 85–97.

Coyle, M. E., Shergis, J. L., Huang, E. T., Guo, X., Di, Y. M., Zhang, A., & Xue, C. C. (2014). Acupuncture therapies for chronic obstructive pulmonary disease: A systematic review of

This article is protected by copyright. All rights reserved.

Accepted Article

randomized, controlled trials. *Alternative Therapies in Health and Medicine Journal, 20*(6), 10–23.

Disler, R. T., Green, A., Luckett, T., Newton, P. J., Inglis, S., Currow, D. C., & Davidson, P. M. (2014). Experience of advanced chronic obstructive pulmonary disease: Metasynthesis of qualitative research. *Journal of Pain and Symptom Management, 48*(6), 1182–1199.

Dunger, C., Higginson, I. J., Gysels, M., Booth, S., Simon, S. T., & Bausewein, C. (2015). Breathlessness and crises in the context of advanced illness: A comparison between COPD and lung cancer patients. *Palliative & Supportive Care, 13*(2), 229–237.

Durand, M.-A., Carpenter, L., Dolan, H., Bravo, P., Mann, M., Bunn, F., & Elwyn, G. (2014). Do interventions designed to support shared decision-making reduce health inequalities? A systematic review and meta-analysis. *PloS one, 9*(4), e94670. https://doi.org/10.1371/journal.pone.0094670

Effective Practice and Organisation of Care (EPOC). Suggested risk of bias criteria for EPOC reviews; 2015. Retrieved from https://epoc.cochrane.org/sites/epoc.cochrane.org/files/public/uploads/Resources-for-authors2017/suggested_risk_of_bias_criteria_for_epoc_reviews.pdf

Efraimsson, E. O., Hillervik, C., & Ehrenberg, A. (2008). Effects of COPD self-care management education at a nurse-led primary health care clinic. *Scandinavian Journal of Caring Sciences, 22*(2), 178–185.

Ek, K., Sahlberg-Blom, E. andershed, B., & Ternestedt, B. M. (2011). Struggling to retain living space: patients' stories about living with advanced chronic obstructive pulmonary disease. *Journal of Advanced Nursing, 67*(7), 1480–1490.

Ekstrom, M., Nilsson, F., Abernethy, A. A. & Currow, D. C. (2015). Effects of opioids on breathlessness and exercise capacity in chronic obstructive pulmonary disease. A systematic review. *Annals of the American Thoracic Society, 12*(7), 1079–1092.

This article is protected by copyright. All rights reserved.

Accepted Article

Accepted Article

Faber, T., Ravaud, P., Riveros, C., Perrodeau, E., & Dechartres, A. (2016). Meta-analyses including non-randomized studies of therapeutic interventions: A methodological review. *BMC Medical Research Methodology, 16*(1), 35.

Fletcher, M. J., & Dahl, B. H. (2013). Expanding nurse practice in COPD: Is it key to providing high quality, effective and safe patient care? *Primary Care Respiratory Journal, 22*, 230–233.

Foglio, K., Bianchi, L., Bruletti, G., Battista, L., Pagani, M., & Ambrosino, N. (1999). Long-term effectiveness of pulmonary rehabilitation in patients with chronic airway obstruction. *European Respiratory Journal, 13*(1), 125–132.

Fraser, D. D., Kee, C. C., & Minick, P. (2006). Living with chronic obstructive pulmonary disease: insiders' perspectives. *Journal of Advanced Nursing, 55*(5), 550–558.

Gardiner, C., Gott, M., Payne, S., Small, N., Barnes, S., Halpin, D., … Seamark, D. (2010). Exploring the care needs of patients with advanced COPD: An overview of the literature. *Respiratory Medicine, 104*(2), 159–165.

Global Initiative for Chronic Obstructive Lung Disease (2017). Global strategy for the diagnosis management and prevention of chronic obstructive pulmonary disease. Retrieved from http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/

Griffiths, T. L., Burr, M. L., Campbell, I. A., Lewis-Jenkins, V., Mullins, J., Shiels, K., Turner-Lawlor, G., … Lonescu, A. (2000). Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: A randomised controlled trial. *The Lancet, 355*(9201), 362–368.

Guyatt, G. H., Berman, L. B., Townsend, M., Pugsley, S. O., & Chambers, L. W. (1987). A measure of quality of life for clinical trials in chronic lung disease. *Thorax, 42*(10), 773–778.

Gysels, M., Bausewein, C., & Higginson, I. J. (2007). Experiences of breathlessness: A systematic review of the qualitative literature. *Palliative & Support Care, 5*(3), 281–302.

This article is protected by copyright. All rights reserved.

Gysels, M. H., & Higginson, I. J. (2011). The lived experience of breathlessness and its implications for care: a qualitative comparison in cancer, COPD, heart failure and MND. *BMC Palliative Care, 10*, 15. https://doi.org/10.1186/1472-684X-10-15

Han, J., Dai, L., & Zhong, N. (2013). Indacaterol on dyspnea in chronic obstructive pulmonary disease: A systematic review and meta-analysis of randomized placebo-controlled trials. *BMC Pulmonary Medicine, 13*, 26. https://doi.org/10.1186/1471-2466-13-26

Higgins, J. P. T., & Green, S. (editors) (2015). Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Collaboration book series. Wiley-Blackwell, England.

Ingadottir, T. S., & Jonsdottir, H. (2010). Partnership-based nursing practice for people with chronic obstructive pulmonary disease and their families: Influences on health-related quality of life and hospital admissions. *Journal of Clinical Nursing, 19*(19–20), 2795–2805.

Jerant, A. F., von Friederichs-Fitzwater, M. M., & Moore, M. (2005). Patients' perceived barriers to active self-management of chronic conditions. *Patient Education and Counseling, 57*(3), 300–307.

Jones, P. W., Quirk, F., & Baveystock, C. (1991). The St George's respiratory questionnaire. *Respiratory Medicine, 85*, 25–31.

Jonsdottir, H. (2008). Nursing care in the chronic phase of COPD: A call for innovative disciplinary research. *Journal of Clinical Nursing, 17*(7b), 272–290.

Kuo, C. C., Lin, C. C., Lin, S. Y., Yang, Y. H., Chang, C. S., & Chen, C. H. (2013). Effects of self-regulation protocol on physiological and psychological measures in patients with chronic obstructive pulmonary disease. *Journal of Clinical Nursing, 22*(19–20), 2800–2811.

Kuzma, A. M., Meli, Y., Meldrum, C., Jellen, P., Butler-Lebair, M., Koczen-Doyle, D., ... Brogan, F. (2008). Multidisciplinary care of the patient with chronic obstructive pulmonary disease. *Proceedings of the American Thoracic Society, 5*(4), 567–571.

This article is protected by copyright. All rights reserved.

Accepted Article

Kyung, K. A., & Chin, P. A. (2008). The effect of a pulmonary rehabilitation programme on older patients with chronic pulmonary disease. *Journal of Clinical Nursing, 17*(1), 118–125.

Liao, W. H., Chen, J. W., Chen, X., Lin, L., Yan, H. Y., Zhou, Y. Q., & Chen, R. (2015). Impact of resistance training in subjects with COPD: a systematic review and meta-analysis. *Respiratory care*, respcare-03598.

Liu, F., Cai, H., Tang, Q., Zou, Y., Wang, H., Xu, Z., … Cui, J. (2013). Effects of an animated diagram and video-based online breathing program for dyspnea in patients with stable COPD. *Patient Preference and Adherence, 7*, 905–913. https://doi.org/10.2147/PPA.S43305

Liu, J., Meng, G., Ma, Y., Zhang, X., Chen, D., & Chen, M. (2015). Influence of COPD Assessment Text (CAT) evaluation and rehabilitation education guidance on the respiratory and motor functions of COPD patients. *Open Medicine, 10*(1): 394–398.

Lomborg, K. & Kirkevold, M. (2005). Curtailing: Handling the complexity of body care in people hospitalized with severe COPD. *Scandinavian Journal of Caring Sciences, 19*(2), 148–156.

Lundell, S., Holmner, A., Rehn, B., Nyberg, A., & Wadell, K. (2015). Telehealthcare in COPD: A systematic review and meta-analysis on physical outcomes and dyspnea. *Respiratory Medicine, 109*(1), 11–26.

McCarthy, B., Casey, D., Devane, D., Murphy, K., Murphy, E., & Lacasse, Y. (2015). Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev, 2*, CD003793.

Moriyama, M., Takeshita, Y., Haruta, Y., Hattori, N., & Ezenwaka, C. E. (2015). Effects of a 6-month nurse-led self-management program on comprehensive pulmonary rehabilitation for patients with COPD receiving home oxygen therapy. *Rehabilitation Nursing, 40*(1), 40–51.

Oh, E.-G. (2003). The effects of home-based pulmonary rehabilitation in patients with chronic lung disease. *International Journal of Nursing Studies, 40*(8), 873–879.

This article is protected by copyright. All rights reserved.

Accepted Article

Osoba, D. (2007). Translating the science of patient-reported outcomes assessment into clinical practice. *Journal of the National Cancer Institute Monographs, 2007*(37), 5–11.

Parshall, M. B., Schwartzstein, R. M., Adams, L., Banzett, R. B., Manning, H. L., Bourbeau, J., … O'Donnell, D. E. (2012). An official American Thoracic Society statement: update on the mechanisms, assessment and management of dyspnea. *American Journal of Respiratory and Critical Care Medicine, 185*(4), 435–452.

Pinnock, H., Steed, L., & Jordan, R. (2016). Supported self-management for COPD: making progress, but there are still challenges. *European Respiratory Journal, 48*(1):6–9.

Puhan, M. A., Guyatt, G. H., Goldstein, R., Mador, J., McKim, D., Stahl, E., ... & Schünemann, H. J. (2007). Relative responsiveness of the Chronic Respiratory Questionnaire, St. Georges Respiratory Questionnaire and four other health-related quality of life instruments for patients with chronic lung disease. *Respiratory Medicine, 101*(2), 308–316

Ries, A. L., Kaplan, R. M., Myers, R. & Prewitt, L. M. (2003). Maintenance after pulmonary rehabilitation in chronic lung disease: A randomized trial. *American Journal of Respiratory and Critical Care Medicine, 167*(6), 880–888.

Reeves BC, Deeks JJ, Higgins JPT, Wells GA. Chapter 13: Including non-randomized studies. In: Higgins JPT, Green S (editors), *Cochrane handbook for systematic reviews of interventions*. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Retrieved from www.cochrane-handbook.org.

Rutten-van Mölken, M., Roos, B., & Van Noord, J. A. (1999). An empirical comparison of the St George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Disease Questionnaire (CRQ) in a clinical trial setting. *Thorax*, *54*(11), 995–1003.

This article is protected by copyright. All rights reserved.

Accepted Article

Song, H. Y., Yong, S. J., & Hur, H.K. (2014). Effectiveness of a brief self-care support intervention for pulmonary rehabilitation among the elderly patients with chronic obstructive pulmonary disease in Korea. *Rehabilitation Nursing, 39*(3), 147–156.

Sridhar, M., Taylor, R., Dawson, S., Roberts, N. J., & Partridge, M. R. (2008). A nurse led intermediate care package in patients who have been hospitalised with an acute exacerbation of chronic obstructive pulmonary disease. *Thorax, 63*(3), 194–200.

Stallard, L. (2007). Chronic obstructive pulmonary disease: A non-pharmacological approach. *Nursing Older People, 19*(6), 32–37.

Tang, C. Y., Taylor, N. F., & Blackstock, F. C. (2010). Chest physiotherapy for patients admitted to hospital with an acute exacerbation of chronic obstructive pulmonary disease (COPD): A systematic review. *Physiotherapy, 96*(1), 1–13.

Taylor, S. J., Candy, B., Bryar, R. M., Ramsay, J., Vrijhoef, H. J., Esmond, G., … Griffiths, C. J. (2005). Effectiveness of innovations in nurse led chronic disease management for patients with chronic obstructive pulmonary disease: Systematic review of evidence. *BMJ, 331*(7515), 485. https://doi.org/10.1136/bmj.38512.664167.8F

Uronis, H. E., Ekstrom, M. P., Currow, D. C., McCrory, D. C., Samsa, G. P., & Abernethy, A. P. (2015). Oxygen for relief of dyspnoea in people with chronic obstructive pulmonary disease who would not qualify for home oxygen: A systematic review and meta-analysis. *Thorax, 70*(5), 492–494.

Utens, C. M., Goossens, L. M., Smeenk, F. W., Rutten-van Mölken, M. P., van Vliet, M., Braken, M. W., ... & van Schayck, O. C. (2012). Early assisted discharge with generic community nursing for chronic obstructive pulmonary disease exacerbations: results of a randomised controlled trial. BMJ open, 2(5), e001684.

Vincent, E., & Sewell, L. (2014). The role of the nurse in pulmonary rehabilitation. *Nursing Times, 110*(50), 16.

This article is protected by copyright. All rights reserved.

Accepted Article

Wang, Y., Zang, X. Y., Bai, J., Liu, S. Y., Zhao, Y., & Zhang, Q. (2014). Effect of a health belief model-based nursing intervention on Chinese patients with moderate to severe chronic obstructive pulmonary disease: A randomised controlled trial. *Journal of Clinical Nursing, 23*(9-10), 1342–1353.

Wilson, I. B., & Cleary, P. D. (1995). Linking clinical variables with health-related quality of life: A conceptual model of patient outcomes. *Journal of the American Medical Association, 273*(1), 59–65.

Wilson, J. S., Fitzsimons, D., Bradbury, I., & Elborn, J. S. (2008). Does additional support by nurses enhance the effect of a brief smoking cessation intervention in people with moderate to severe chronic obstructive pulmonary disease? A randomised controlled trial. *International Journal of Nursing Studies, 45*(4), 508–517.

Wood-Baker, R., Reid, D., Robinson, A. & Walters, E.H. (2012). Clinical trial of community nurse mentoring to improve self-management in patients with chronic obstructive pulmonary disease. *International Journal of Chronic Obstructive Pulmonary Disease, 7*(4), 407–413.

Yu, S.-H., Guo, A.-M., & Zhang, X.-J. (2014). Effects of self-management education on quality of life of patients with chronic obstructive pulmonary disease. *International Journal of Nursing Sciences, 1*(1), 53–57.

Zhang, Z., Xu, X., & Ni, H. (2013). Small studies may overestimate the effect sizes in critical care meta-analyses: A meta-epidemiological study. *Critical Care, 17*(1), R2.

Zwerink, M., Brusse-Keizer, M., van der Valk, P. D., Zielhuis, G. A., Monninkhof, E. M., van der Palen, … Effing, T. (2014). Self management for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev, 3*, CD002990.

Accepted Article

This article is protected by copyright. All rights reserved.

Table 1 Characteristics of the included studies

Author Year Country	**Design**	**Intervention group (sample) and control group (sample)**	**Group category in analysis**	**Outcomes on breathlessness**	**Results**
Akinci & Olgun (2011) Turkey	Two group pre-post	*IG: Nurse led home based pulmonary rehabilitation* with two to three times visits during three months containing education, breathing exercises and aerobic exercises (n=16) *CG: NR* (n=16)	At home	SGRQ: symptoms, impact, activity and total scores BDI	Positive significant difference in favour of IG for all SGRQ scores (MD = 13.0 - 26.0, *p* = .004 - .001) and BDI score (MD = -2.9, *p* = .001)
Alexander & Wagner (2012) USA	RCT	*IG: Pulmonary rehabilitation exercise* twice a week for eight to ten weeks (16 session) and harmonica playing twice a week during eight to nineteen weeks study period (n=16) *CG: Only exercise* as described above (n=16)	In clinics	University of California at San Diego SOBQ	No difference between groups (MD = -3.7, *p* = .6). The whole sample improved significantly on SOBQ over time (*p* = .002).
Bischoff et al. (2012) Netherlands	RCT	*IG1: Self-management program* with four tailored session in general practice and on-going telephone calls with information covering disease knowledge, drugs, breathing techniques, managing exacerbation, healthy life style, managing stress, anxiety and home exercise (n=55) *IG2: Routine monitoring* with two to four structured consultation during twenty-four months study period based on COPD guidelines (n=55) *CG: Usual care* (n=55)	In clinics with home follow-up	CRQ dyspnoea	Positive significant difference in favour of IG2 (MD = -0.40 to 0.19) compared with CG) (*p* = .04). No other effects
Carrierri-Kohlman et al. (2001) USA	RCT	*IG: Nurse monitored exercise* with twelve sessions during four to eight weeks of using a video tape on relaxation and breathing strategies before and after treadmill exercise (n=24) *CG: Nurse coached experience* with only treadmill exercise (n=21)	In clinics	SOB VAS dyspnoea	No significant difference between groups or no significant change in groups (MD = -4,0, *p* = .1)
Cooke et al.	One group	*Home based pulmonary rehabilitation* for twelve months with	At home	SGRQ:	No significant change in-group over time

This article is protected by copyright. All rights reserved.

Accepted Article

(2010) Australia	Pre-post Pilot study	maintenance program containing; strength training, goal setting, regular telephone calls every week from community respiratory nurse and home visits by physiotherapist (n=29)		symptoms, impact, activity and total scores MRC Dyspnoea Scale	(MD = -0.02 to -3.39, *p* = not reported)
Efraimsson et al. (2008) Sweden	RCT	*IG: Visits to nurse-led primary health clinic* in a period of three to five months containing education on self-care and on how to cope with disease and treatment (n=26) *CG: Usual care* (n=26)	In clinics	SGRQ: symptoms, impact, activity and total scores	Positive significant difference in favour of IG for all SGRQ scores (MD = 3.4 - 25.2, *p* = .0.03 - .0004)
Ingadottir & Jonsdottir (2010) Iceland	One group Pre-post	*Partnership as nursing practice at home* for six months with participatory comprehensive, long term and dynamic tailored follow ups to meet individual patient-family needs with a six months and twelve months follow ups (n=50)	At home	SGRQ: symptoms, impact, activity and total scores	Positive significant change over time for all SGRQ scores (MD = 3.9 - 20.2, *p* = .04 - < .0001)
Kuo et al. (2013) Taiwan	RCT	*IG: Self-regulation intervention* protocol for four weeks containing education on COPD, controlling symptom, implement self-regulation in daily life, how to use guidebook in hospital with telephone follow up at the first, second and fourth week at home (n=33) *CG: Reading the self-regulation guidebook* containing self-monitoring, self-judgment and self-reaction guidelines (n=31)	In clinics with home follow-up	Borg dyspnoea scale	No significant at 5 weeks, but positive significant different at 9 weeks and 13 weeks in favour of IG for the Borg dyspnoea scale (MD = 1.5, *p* = .07 at 5 weeks)
Kyung & Chin (2008) Korea	One group pre- post	*Pulmonary rehabilitation* for four weeks containing breathing exercise, upper limb exercises and inspiratory muscle training (n=20)	In clinics	Borg dyspnoea VAS- dyspnoea	Positive significant difference for the BORG dyspnoea scale (MD = 0.65, *p* < .001) and the VAS dyspnoea scale (MD = 1.3, *p* = .01)
Liu et al. (2013) China	RCT	*IG: Online pulmonary rehabilitation program* after discharge from hospital for four months containing breathing exercises in four stages (n=30) *CG: Instructed of respiratory nurse* at discharge (n=30)	At home	SGRQ: symptoms, impact, activity and total score	Positive significant difference in favour of IG for all the scores on SGRQ (MD = 15.5 - 18.2, *p* < .05)
Liu et al.	Two group	*IG: Rehabilitation education guidance* containing breathing training	In clinics	MRC	IG significant lower MRC score than CG

This article is protected by copyright. All rights reserved.

(2015) China	pre-post	and follow up visits at 2, 12 and 48 weeks and treated with combined bronchodilators and inhaled corticosteroids (n=35) *CG:* Treated with combined bronchodilators and inhaled corticosteroids (n=35)			after 48 weeks of treatment (MD = not reported, *p* < .05)
Moriyama et al. (2015) Japan	Two group pre-post	I*G: Nurse led home visits for stage IV COPD*, twice, monthly mail and telephone calls one every months for six months on self-management educational program. Contained: workbook, learning materials, daily journal of self-monitoring, management of signs, prevent shortness of breath, exercise, diet, infection control and smoking cession (n=15) *CG: Conventional education* with monthly visit at clinic (n=15)	At home	SGRQ: symptoms, impact, activity and total scores	No significant difference between groups or in groups (MD = 0.40 - 28.20, *p* = .2 - .6)
Oh (2003) Korea	Two group pre-post	*IG: Home based pulmonary rehabilitation* for eight weeks containing education, inspiratory muscle training, exercise training, psychosocial education and telephone calls (n=15). *CG: Educational advice* (n=8)	At home	CRDQ dyspnoea Borg dyspnoea	Positive significant difference in favour of IG on Borg dyspnoea score (MD = -3.1, *p* = .04). No difference in CRDQ dyspnoeal score (MD = 20,0, *p* = .03)
Song et al. (2014) Korea	RCT	*IG: Self-care support motivational interviews* containing living with COPD and self-management strategies with two inpatient sessions, one outpatient session and two telephone calls (over a period of two months) (n=20) *CG: NR* (n=20)	In clinics with home follow-up	SGRQ: symptoms, impact, activity and total scores BORG dyspnoea	Positive significant change in favour of IG for all the SGRQ scores (MD = 6.4 - 21.4, *p* = .02 - .003). No change in BORG dyspnoea score (MD = -0.8, *p* = .8)
Sridhar et al. (2008) England	RCT	IG: Hospital *based pulmonary rehabilitation monthly telephone calls and 3 monthly home visits by a specialist nurse* over 2 years (n=61) CG: Usual care (n=61)	In clinics with home follow-up	CRQ	Negative significant difference for dyspnoea score in both groups (MD = -1.85 to -0.20, *p* < .05)
Utens et al. (2012) Netherlands	RCT multicentre trial	IG: Early assisted discharge after three days with four days follow ups by home visit nurse (n=70) CG= Seven days in hospital (n=69)	At home	CCQ-total score	No difference in change in CCQ score (MD = 0.29, *p* = .09)
Wang et al.	RCT	*IG: Health belief model based nursing* for 20-30 minutes every	In clinics	MMRC	Positive significant change in favour of IG

This article is protected by copyright. All rights reserved.

(2013) China		second days during hospitalisation and 6 months of telephone and home visits follow-ups after discharge. The program contained learning susceptibility and severity of COPD, benefits of treatment, healthy behaviour applied and adverse action avoided, confidence in management and signals to monitor disease (n=42) *CG=Routine nursing care* (n= 46)	with home follow-up		(MD = 1.4, *p* < .001)
Wilson et al. (2008) Ireland	RCT	*IG1: Smoking cessation individual support (IS)* for five weeks with follow ups at 2,3,6,9 and 12 months (n=27) *IG2: Smoking cessation group support (GS)* for five weeks with follow ups at 2,3,6,9 and 12 months (n=29) *CG=Usual care* (n=35)	In clinics	MRC	No significant difference between groups or in groups (IS - CG MD = 0.07, *p* = .8, GS - CG MD = 0.02, *p* = .1)
Wood-Baker et al. (2012) Australia	Two group pre-post	*IG: Community nurse using motivational interview* on COPD self-management by two home visits and by regular telephone calls for twelve months, in addition to daily diary (n=36 completed of 55) *CG: Usual care* (n=33 completed of 51)	At Home	MRC	No significant difference between groups or in groups (MD = -0.07, *p* = .3)
Yu et al. (2014) China	Two group pre-post	*IG: Structured self-management education-program at hospital* containing education, respiratory techniques, medication tip and exacerbation recognizing by face to face sessions and telephone calls for six months (n=42) *CG: Usual care* (n=42)	In clinics with home follow-up	SGRQ: symptoms, impact, activity and total scores	Positive significant difference between three months and six months (MD = 6.40 - 21.40, *p* = .01 - .001).

BDI = Baseline Dyspnoea Index, CG = control group, CCQ = Clinical Chronic Questionaire, CRQ = Chronic respiratory questionnaire, MD = mean difference,

Obstructive Pulmonary Questionnaire, CRDQ = Chronic Respiratory Disease Questionnaire, IG = intervention group, MMRC = The Modified Medical Research Council Dyspnoea Scale, MRC = Medical Research Council Dyspnoea Scale, NR= not reported, SGRQ = St. George Respiratory Questionnaire, SOB = shortness of breath, SOBQ = Shortness of Breath Questionnaire, VAS = Visual Analogue Scale

This article is protected by copyright. All rights reserved.

Accepted Article

Table 2 Assessment of the quality using GRADE system: Nursing interventions performed at home

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	**Risk with Home based nursing**		
SGRQ symptom score Scale from: 0 to 100	The mean SGRQ symptom score was **-1.6** changed	The mean SGRQ symptom score in the intervention group was 20,17 changed higher (5,29 higher to 35,04 higher)	62 (2 observational studies (Two group pre-post design))	⊕◯◯◯ VERY LOW [1,2]
SGRQ activity score Scale from: 0 to 100	The mean SGRQ activity score was **-2.4** changed	The mean SGRQ activity score in the intervention group was 15,28 changed higher (3,95 lower to 34,51 higher)	62 (2 observational studies (Two group pre-post design))	⊕◯◯◯ VERY LOW [1,2]
SGRQ impact score Scale from: 0 to 100	The mean SGRQ impact score was **0.1** changed	The mean SGRQ impact score in the intervention group was 10,98 changed higher (9,2 lower to 31,16 higher)	62 (2 observational studies (Two group pre-post design))	⊕◯◯◯ VERY LOW [1,2]
SGRQ total score Scale from: 0 to 100	The mean SGRQ total score was **0.5** changed	The mean SGRQ total score in the intervention group was 10,93 changed higher (6,41 lower to 28,27 higher)	62 (2 observational studies (Two group pre-post design))	⊕◯◯◯ VERY LOW [1,2]

[1] Scored "serious" on risk of bias due to including two observational study in the same meta-analysis, [2] Scored "serious" on imprecision due to including only two studies in the meta analysis

Accepted Article

This article is protected by copyright. All rights reserved.

Table 3 Assessment of the quality using the GRADE system: Nursing interventions performed in clinics with home follow-up

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	**Risk with Mix of self-management/rehabilitation and home-based nursing**		
CRQ dyspnea Scale from: 1 to 7	The mean CRQ dyspnea was **0.4** changed	The mean CRQ dyspnea in the intervention group was 0,14 changed lower (0,45 lower to 0,16 higher)	232 (2 RCTs)	⨁⨁⨁◯ MODERATE [1]
CRQ emotion Scale from: 1 to 7	The mean CRQ emotion was **0.25** changed	The mean CRQ emotion in the intervention group was 0,13 changed lower (0,41 lower to 0,14 higher)	232 (2 RCTs)	⨁⨁⨁◯ MODERATE [1]
CRQ mastery Scale from: 1 to 7	The mean CRQ mastery was **0.3** changed	The mean CRQ mastery in the intervention group was 0,51 changed lower (0,81 lower to 0,21 lower)	232 (2 RCTs)	⨁⨁⨁◯ MODERATE [1]
CRQ fatigue Scale from: 1 to 7	The mean CRQ fatigue was **0.24** changed	The mean CRQ fatigue in the intervention group was 0,35 changed lower (0,61 lower to 0,08 lower)	232 (2 RCTs)	⨁⨁⨁◯ MODERATE [1]
CRQ total Scale from: 1 to 7	The mean CRQ total was **0.9** changed	The mean CRQ total in the intervention group was 0,7 changed lower (2,69 lower to 1,29 higher)	232 (2 RCTs)	⨁⨁◯◯ LOW [12]
SGRQ symptom score Scale from: 0 to 100	The mean SGRQ symptom score was **-7.85** changed	The mean SGRQ symptom score in the intervention group was 16,53 changed higher (7,63 higher to 25,42 higher)	124 (1 RCT and 1 observational studies (two group pre-post design))	⨁◯◯◯ VERY LOW [13]
SGRQ activity score Scale from: 0 to 100	The mean SGRQ activity score was **-13.5** changed	The mean SGRQ activity score in the intervention group was 10,44 changed higher (2,12 higher to 18,76 higher)	124 (1 RCT and 1 observational studies (two group pre-post design))	⨁◯◯◯ VERY LOW [13]
SGRQ impact score Scale from: 0 to 100	The mean SGRQ impact score was **4.4** changed	The mean SGRQ impact score in the intervention group was 9,38 changed higher (7,04 lower to 25,79 higher)	124 (1 RCT and 1 observational studies (two group pre-post design))	⨁◯◯◯ VERY LOW [123]
SGRQ total score Scale from: 0 to 100	The mean SGRQ total score was **-5.65** changed	The mean SGRQ total score in the intervention group was 10,84 changed higher (4,85 higher to 16,83 higher)	124 (1 RCT and 1 observational studies (two group pre-post design))	⨁◯◯◯ VERY LOW [13]

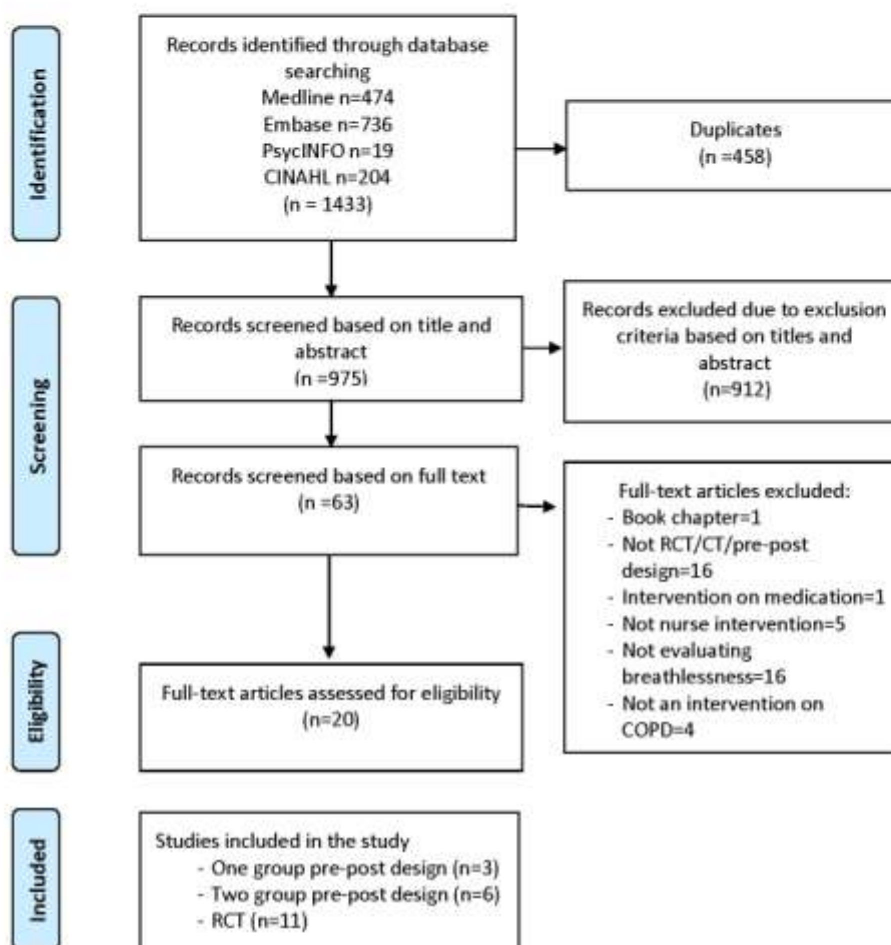
[1] Scored "serious" on imprecision due to including only two studies in the meta analysis, [2] Scored "serious" on inconsistency due different result in the studies, [3]Scored "serious" on risk of bias due to including one RCT and one observational study in the same meta analysis

Accepted Article

This article is protected by copyright. All rights reserved.

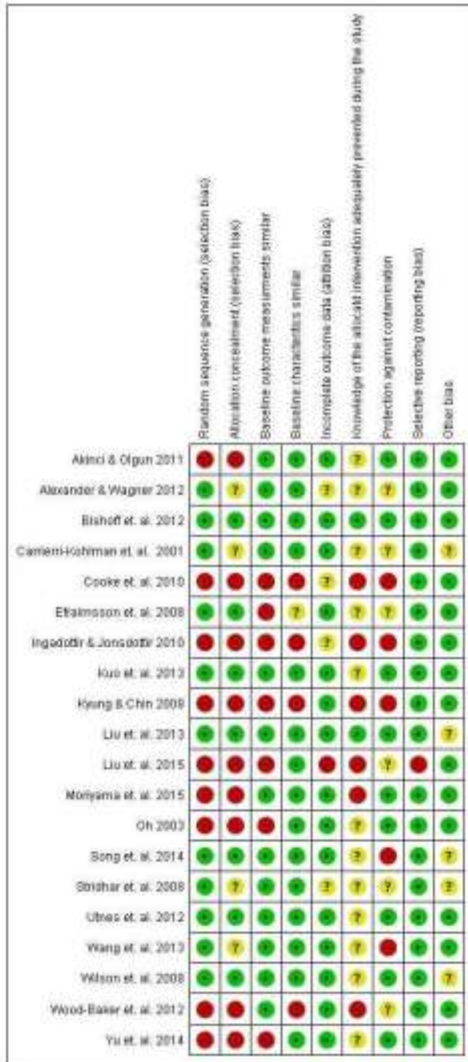
Accepted Article

Figure 1 Summary of the selection of studies



This article is protected by copyright. All rights reserved.

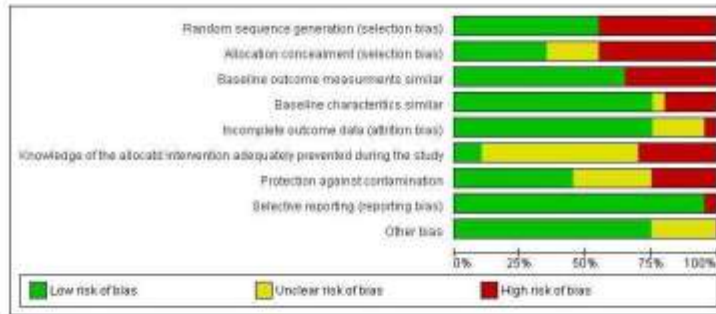
Figure 2 Risk of bias



This article is protected by copyright. All rights reserved.

Accepted Article

Figure 3 Summary of risk of bias



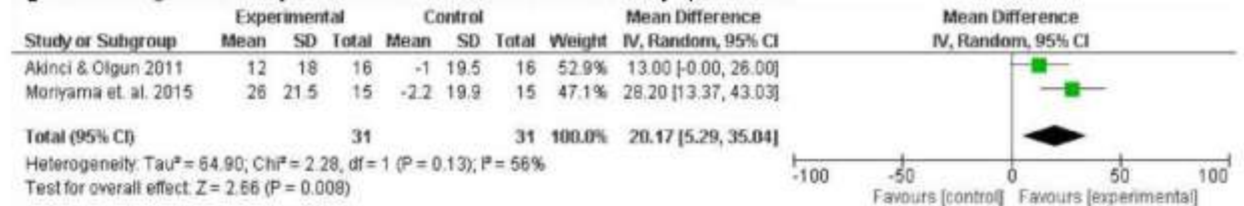
Accepted Article

This article is protected by copyright. All rights reserved.

Accepted Article

Figures 4-16

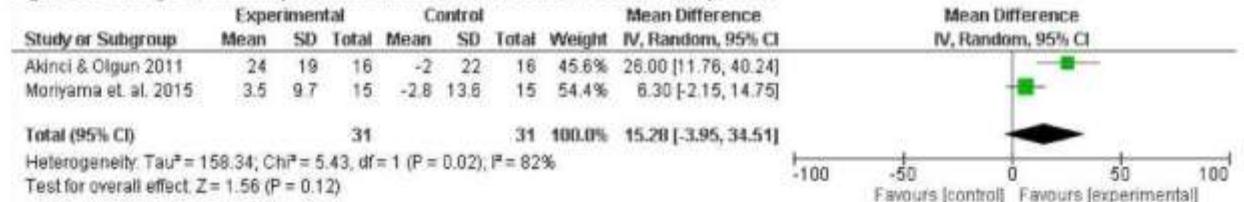
Figure 4. Nursing interventions performed at home versus control. SGRQ symptom score



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Akinci & Olgun 2011	12	18	16	-1	19.5	16	52.9%	13.00 [-0.00, 26.00]
Moriyama et. al. 2015	26	21.5	15	-2.2	19.9	15	47.1%	28.20 [13.37, 43.03]
Total (95% CI)			**31**			**31**	**100.0%**	**20.17 [5.29, 35.04]**

Heterogeneity: Tau² = 64.90; Chi² = 2.28, df = 1 (P = 0.13); I² = 56%
Test for overall effect: Z = 2.66 (P = 0.008)

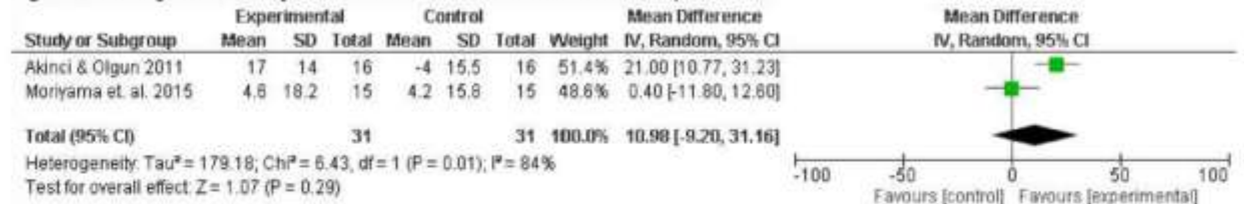
Figure 5. Nursing interventions performed at home versus control. SGRQ activity score



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Akinci & Olgun 2011	24	19	16	-2	22	16	45.6%	26.00 [11.76, 40.24]
Moriyama et. al. 2015	3.5	9.7	15	-2.8	13.6	15	54.4%	6.30 [-2.15, 14.75]
Total (95% CI)			**31**			**31**	**100.0%**	**15.28 [-3.95, 34.51]**

Heterogeneity: Tau² = 158.34; Chi² = 5.43, df = 1 (P = 0.02); I² = 82%
Test for overall effect: Z = 1.56 (P = 0.12)

Figure 6. Nursing interventions performed at home versus control. SGRQ impact score



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Akinci & Olgun 2011	17	14	16	-4	15.5	16	51.4%	21.00 [10.77, 31.23]
Moriyama et. al. 2015	4.6	18.2	15	4.2	15.8	15	48.6%	0.40 [-11.80, 12.60]
Total (95% CI)			**31**			**31**	**100.0%**	**10.98 [-9.20, 31.16]**

Heterogeneity: Tau² = 179.18; Chi² = 6.43, df = 1 (P = 0.01); I² = 84%
Test for overall effect: Z = 1.07 (P = 0.29)

This article is protected by copyright. All rights reserved.

Accepted Article

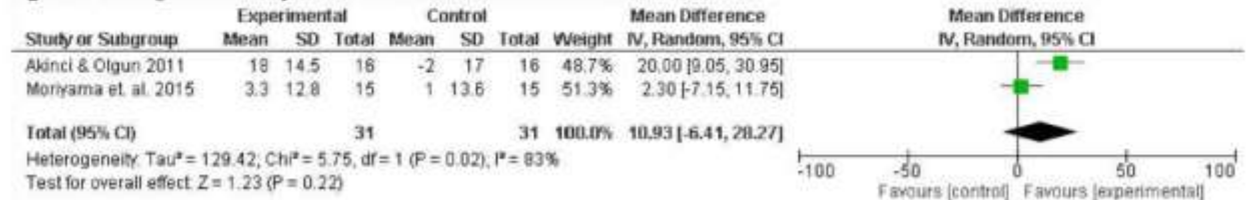


Figure 7. Nursing interventions performed at home versus control. SGRQ total score.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Akinci & Olgun 2011	18	14.5	16	-2	17	16	48.7%	20.00 [9.05, 30.95]
Moriyama et. al. 2015	3.3	12.8	15	1	13.6	15	51.3%	2.30 [-7.15, 11.75]
Total (95% CI)			**31**			**31**	**100.0%**	**10.93 [-6.41, 28.27]**

Heterogeneity: Tau² = 129.42; Chi² = 5.75, df = 1 (P = 0.02); I² = 83%
Test for overall effect: Z = 1.23 (P = 0.22)

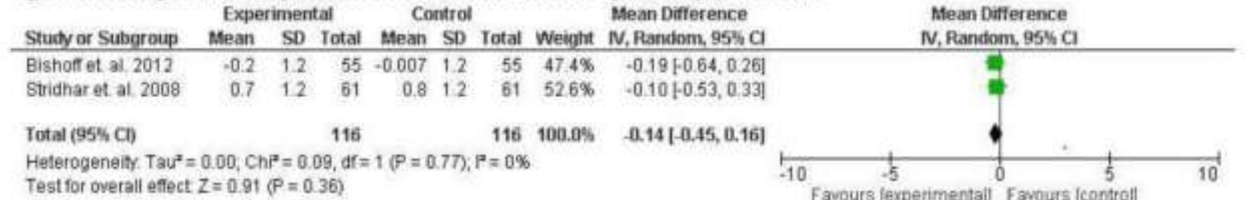


Figure 8. Nursing interventions performed in clinics with home follow-up. CRQ dyspnea score

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bishoff et. al. 2012	-0.2	1.2	55	-0.007	1.2	55	47.4%	-0.19 [-0.64, 0.26]
Stridhar et. al. 2008	0.7	1.2	61	0.8	1.2	61	52.6%	-0.10 [-0.53, 0.33]
Total (95% CI)			**116**			**116**	**100.0%**	**-0.14 [-0.45, 0.16]**

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 0.91 (P = 0.36)

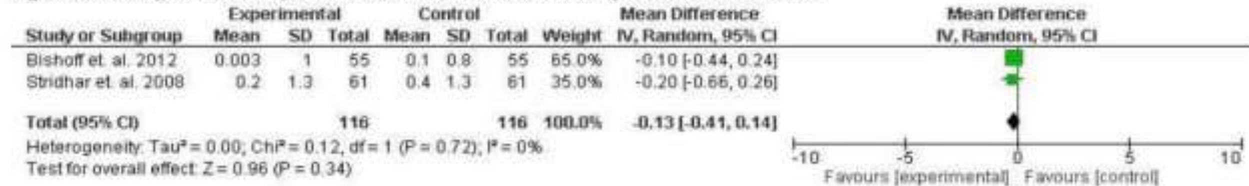


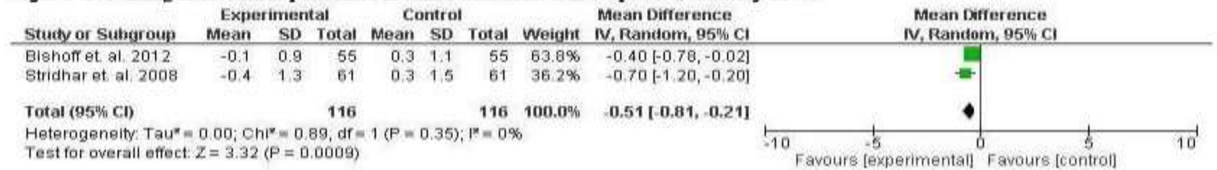
Figure 9. Nursing interventions performed in clinics with home follow-up. CRQ emotion score.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bishoff et. al. 2012	0.003	1	55	0.1	0.8	55	65.0%	-0.10 [-0.44, 0.24]
Stridhar et. al. 2008	0.2	1.3	61	0.4	1.3	61	35.0%	-0.20 [-0.66, 0.26]
Total (95% CI)			**116**			**116**	**100.0%**	**-0.13 [-0.41, 0.14]**

Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)

This article is protected by copyright. All rights reserved.

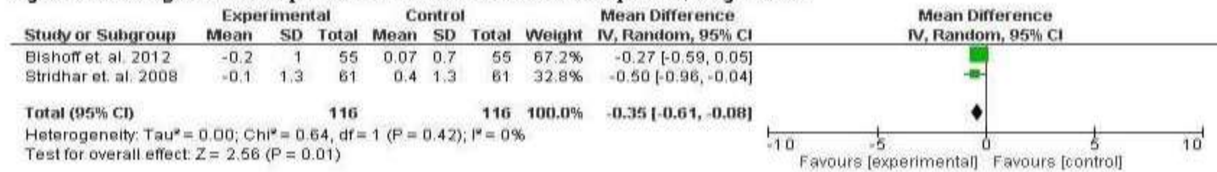
Figure 10. Nursing interventions performed in clinics with home follow-up. CRQ mastery score



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bishoff et. al. 2012	-0.1	0.9	55	0.3	1.1	55	63.8%	-0.40 [-0.78, -0.02]
Stridhar et. al. 2008	-0.4	1.3	61	0.3	1.5	61	36.2%	-0.70 [-1.20, -0.20]
Total (95% CI)			**116**			**116**	**100.0%**	**-0.51 [-0.81, -0.21]**

Heterogeneity: Tau² = 0.00; Chi² = 0.89, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 3.32 (P = 0.0009)

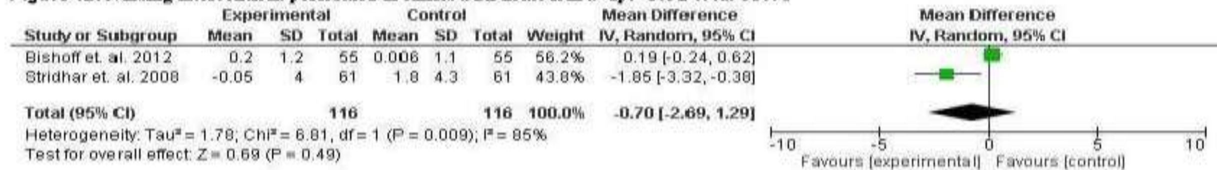
Figure 11. Nursing interventions performed in clinics with home follow-up. CRQ fatigue score



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bishoff et. al. 2012	-0.2	1	55	0.07	0.7	55	67.2%	-0.27 [-0.59, 0.05]
Stridhar et. al. 2008	-0.1	1.3	61	0.4	1.3	61	32.8%	-0.50 [-0.96, -0.04]
Total (95% CI)			**116**			**116**	**100.0%**	**-0.35 [-0.61, -0.08]**

Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 2.56 (P = 0.01)

Figure 12. Nursing interventions performed in clinics with home follow-up. CRQ total score



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bishoff et. al. 2012	0.2	1.2	55	0.006	1.1	55	56.2%	0.19 [-0.24, 0.62]
Stridhar et. al. 2008	-0.05	4	61	1.8	4.3	61	43.8%	-1.85 [-3.32, -0.38]
Total (95% CI)			**116**			**116**	**100.0%**	**-0.70 [-2.69, 1.29]**

Heterogeneity: Tau² = 1.78; Chi² = 6.81, df = 1 (P = 0.009); I² = 85%
Test for overall effect: Z = 0.69 (P = 0.49)

Accepted Article

This article is protected by copyright. All rights reserved.

Accepted Article

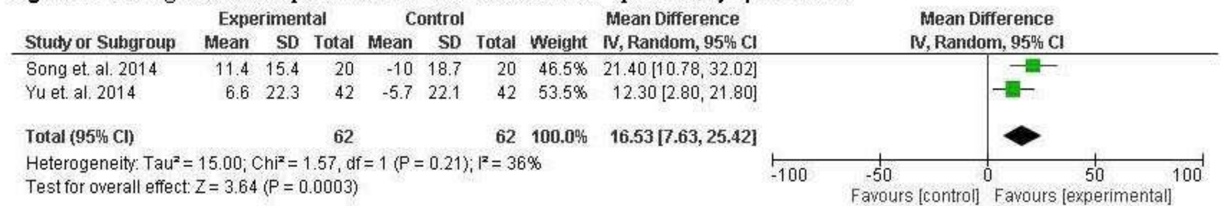


Figure 13. Nursing interventions performed in clinics with home follow-up. SGRQ symptom score

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Song et. al. 2014	11.4	15.4	20	-10	18.7	20	46.5%	21.40 [10.78, 32.02]
Yu et. al. 2014	6.6	22.3	42	-5.7	22.1	42	53.5%	12.30 [2.80, 21.80]
Total (95% CI)			**62**			**62**	**100.0%**	**16.53 [7.63, 25.42]**

Heterogeneity: Tau² = 15.00; Chi² = 1.57, df = 1 (P = 0.21); I² = 36%
Test for overall effect: Z = 3.64 (P = 0.0003)

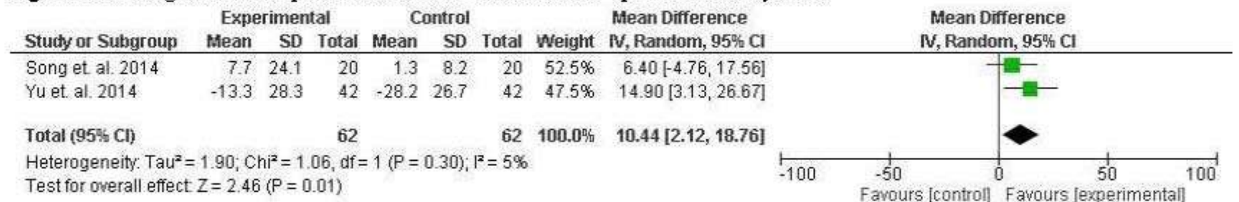


Figure 14. Nursing interventions performed in clinics with home follow-up. SGRQ activity score

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Song et. al. 2014	7.7	24.1	20	1.3	8.2	20	52.5%	6.40 [-4.76, 17.56]
Yu et. al. 2014	-13.3	28.3	42	-28.2	26.7	42	47.5%	14.90 [3.13, 26.67]
Total (95% CI)			**62**			**62**	**100.0%**	**10.44 [2.12, 18.76]**

Heterogeneity: Tau² = 1.90; Chi² = 1.06, df = 1 (P = 0.30); I² = 5%
Test for overall effect: Z = 2.46 (P = 0.01)

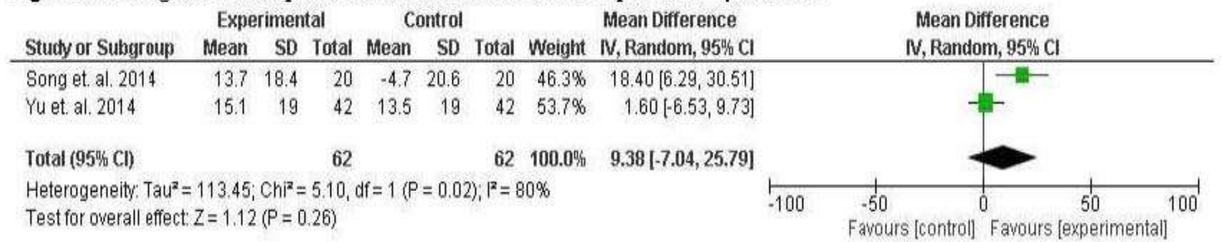


Figure 15 Nursing interventions performed in clinics with home follow-up. SGRQ impact score

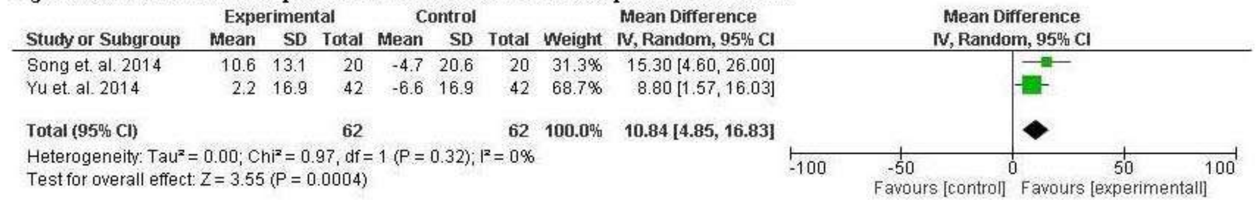
Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Song et. al. 2014	13.7	18.4	20	-4.7	20.6	20	46.3%	18.40 [6.29, 30.51]
Yu et. al. 2014	15.1	19	42	13.5	19	42	53.7%	1.60 [-6.53, 9.73]
Total (95% CI)			**62**			**62**	**100.0%**	**9.38 [-7.04, 25.79]**

Heterogeneity: Tau² = 113.45; Chi² = 5.10, df = 1 (P = 0.02); I² = 80%
Test for overall effect: Z = 1.12 (P = 0.26)

This article is protected by copyright. All rights reserved.

Accepted Article

Figure 16. Nursin interventions performed in clinics with home follow-up. SGRQ total score



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Song et. al. 2014	10.6	13.1	20	-4.7	20.6	20	31.3%	15.30 [4.60, 26.00]
Yu et. al. 2014	2.2	16.9	42	-6.6	16.9	42	68.7%	8.80 [1.57, 16.03]
Total (95% CI)			**62**			**62**	**100.0%**	**10.84 [4.85, 16.83]**

Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 3.55 (P = 0.0004)

This article is protected by copyright. All rights reserved.