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The Netherlands

Reducing the chronic disease burden in China: tailoring a self-management intervention among Chinese people with chronic lung disease

Song, X.

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Chapter 3

The effect of blended self-management interventions on disease burden in chronic obstructive pulmonary disease and asthma patients: A systematic review and meta-analysis

Song XY, Hallensleben C, Zhang WH, Jiang ZL, Shen HX, Gobbens JJ R, Van der Kleij R, Chavannes NH, and Versluis A, "Blended self-management interventions to reduce disease burden in patients with chronic obstructive pulmonary disease and asthma: systematic review and meta-analysis," Journal of Medical Internet Research, vol. 23, no. 3, Mar, 2021. doi: 10.2196/24602.

Abstract

Background

There is a high prevalence of and high disease burden in Chronic Obstructive Pulmonary Disease (COPD) and asthma. Blended self-management interventions, which combine eHealth with face-to-face interventions, could help to reduce the disease burden.

Objectives

This systematic review and meta-analysis was performed to examine the effectiveness of blended self-management interventions on health-related effectiveness and process outcomes for people with COPD or asthma.

Methods

PubMed, Web of Science, COCHRANE Library, Emcare and Embase were searched in December 2018 and updated in November 2020. Study quality was assessed using the Cochrane risk of bias (ROB)2 and the Grading of Recommendations Assessment, Development, and Evaluation.

Results

Fifteen COPD and seven asthma randomized controlled trials were included. The meta-analysis of COPD studies found that the blended intervention showed a small improvement on exercise capacity (standardized mean difference [SMD] = 0.48, 95% CI: 0.10-0.85), and a significant improvement on the quality of life (QoL) (SMD = 0.81, 95% CI: 0.11-1.51). Blended intervention also reduced the admission rate (Relative Ratio (RR) = 0.61, 95% CI: 0.38-0.97). In the COPD systematic review, on the exacerbation frequency, both studies found the intervention reduced exacerbation frequency (RR = 0.38, 95% CI: 0.26-0.56). A large effect was found on body mass index (d = 0.81, 95% CI: 0.25-1.34); however, the effect was inconclusive because only one study was included. On medication adherence, two of three studies found a moderate effect (d = 0.73, 95% CI: 0.50-0.96), and one study reported a mixed-effect. On self-management ability, one study reported a large effect (d = 1.15, 95% CI: 0.66-1.62), and no effect was reported in the one study. No effect was found on the other process outcomes. The meta-analysis of asthma studies found that blended intervention had a small improvement on lung function (SMD = 0.40, 95% CI: 0.18-0.62) and QoL (SMD = 0.36, 95% CI: 0.21-0.50), and a moderate improvement on asthma control (SMD = 0.67, 95% CI: 0.40 to 0.93). A large effect was found on body mass index (d = 1.42, 95% CI: 0.28-2.42) and exercise capacity (d = 1.50, 95% CI: 0.35-2.50), yet one study was included per outcome. There was no effect on other outcomes. Furthermore, the majority of twenty-two studies showed some concerns about the risk of bias, and the quality of evidence varied.

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Conclusions

In COPD patients, the blended self-management interventions had mixed effects on health-related outcomes, with the strongest evidence found for exercise capacity, QoL and admission rate. Furthermore, the review suggested that the intervention resulted in small effects for lung function and QoL and a moderate effect on asthma control in asthma patients. To conclude, there is some evidence for the effectiveness of blended self-management interventions for COPD and asthma patients; yet more research is needed.

Introduction

Chronic lung diseases are the leading cause of disability and death worldwide ¹⁴⁷. Of all chronic lung diseases, chronic obstructive pulmonary disease (COPD) and asthma are the most prevalent ones ¹⁴⁸. There were approximately 251 million cases of COPD globally in 2015, and COPD is predicted to become the third leading cause of death by 2030 ¹⁴⁹. Around 300 million people have asthma worldwide, with a projected increase of an additional 100 million people by 2025 ¹⁴⁹. The impact of a health problem, measured by financial cost, morbidity and other indicators, is called disease burden. It is often quantified in terms of disability-adjusted life years (DALYs) or quality-adjusted life years (QALYs) ¹⁴⁷. In 2017, the loss of DALYs was the first for COPD and the second for asthma ¹⁴⁷. Additionally, a loss in health-related quality of life (QoL) is seen in many patients (e.g., a decline in health, increased hospital admissions, and high medication costs). The World Health Organization estimates the cost of a QALY for COPD ranges from \$6700 to \$13400 due to exacerbations and medication. In asthma patients, the annual costs vary from less than \$150 to \$3000 ¹⁵⁰⁻¹⁵². There is increased awareness that self-management represents a promising strategy to decrease disease burden ¹⁵⁰⁻¹⁵². Self-management could improve patient outcomes and decrease disease burden by supporting the patients to positively adapt their health behaviors and develop skills to manage their diseases ¹⁵³.

Self-management refers to an individual's ability to manage their symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent to life with a chronic condition ¹⁵⁴. In traditional face-to-face self-management interventions, COPD and asthma patients are equipped with the knowledge and skills to manage their health condition successfully ¹⁵⁵. Previous studies have found these self-management interventions to be effective on disease knowledge and self-efficacy ^{156,157}. These face-to-face self-management interventions are, however, limited by their accessibility (e.g., lower accessibility for patients who are more distant to the healthcare provider or when the healthcare provider lacks time) ¹⁵⁸.

eHealth is an alternative to traditional face-to-face interventions. The most cited definition of eHealth is: "health services and information delivered or enhanced through the Internet and related technologies" ²⁴. Compared with traditional face-to-face interventions, eHealth interventions can be cost and time saving and offer better accessibility and flexibility ^{159,160}. Moreover, eHealth interventions can help to optimize the therapeutic process, increase treatment efficiency, and decrease costs by enhancing (online) communication possibilities between healthcare providers and patients ^{159,160}. There have been promising results with eHealth self-management interventions ¹⁶¹. A meta-analysis has shown that, for COPD patients, eHealth self-management programs (e.g., web-based phone calls, online interventions) led to a significant improvement on the symptoms ¹⁶¹. However, eHealth interventions typically allow for limited tailoring to patients' needs and lower patient

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engagement¹⁶². There have also been concerns about reliability, security, confidentiality, and lack of education and training¹⁶³. These factors can negatively impact the implementation and effectiveness of these interventions.

The most recent development is the blended intervention. There are different definitions of blended interventions^{25,164}. We use the definition by Erbe *et al.*: “Treatment programs that use elements of both face-to-face and internet-based interventions, including both the integrated and the sequential use of both treatment formats.”²⁵. Blended interventions could retain the positive aspects of face-to-face interventions and eHealth by mitigating their negative aspects. Furthermore, blended intervention could diminish the number of face-to-face contacts needed and provide the support that is available at all times¹⁶⁵. With eHealth, patients can also monitor their health condition throughout the day and convey their health information to healthcare providers without the time and distance limitation. Patients can also get quick assistance during critical periods of care facilitated by real-time alerts and reminders, which could help patients adhere to their action plan. For COPD and asthma patients, blended interventions can include varied elements^{28,29} (e.g., training, education and action plans) with different blended intervention components (e.g., internet-based phone calls and individual face-to-face intervention, web platform combined with individual face-to-face intervention)^{22,23}. Some studies have shown that blended self-management interventions are effective in improving QoL for COPD and asthma patients^{166,167}.

Current reviews suggest that blended interventions could be effective^{25,164}, but these reviews are limited for several reasons. First, the reviews focus on mental health, not chronic lung diseases²⁵. Second, the reviews focus on health-related effectiveness outcomes and not on process outcomes^{25,164}. Third, the reviews do not specifically focus on self-management interventions^{25,164}. To conclude, a comprehensive overview or meta-analysis of the effect of blended self-management interventions on the disease burden of COPD and asthma patients, including process outcomes and health-related effectiveness outcomes, is missing. Therefore, a systematic review will be performed to assess the effectiveness of blended self-management interventions in COPD and asthma patients. When appropriate, a meta-analysis will be conducted. Internet-based, telephone, and SMS delivered interventions are included because all of these are parts of eHealth²⁴. Thus, this study aims to investigate the effectiveness of blended self-management interventions in COPD and asthma patients.

Methods

This review follows the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines¹⁶⁸. The review was registered in PROSPERO (number 2019: CRD42019119894).

Search strategy

A search strategy was set up in collaboration with a certified librarian to identify relevant studies of blended self-management interventions in COPD and asthma patients. Five electronic databases (i.e., PubMed, Web of Science, COCHRANE Library, Emcare and Embase) were searched on December 28th, 2018 and updated on November 30th, 2020. There were search terms related to four areas: (1) COPD or asthma, (2) eHealth, (3) face-to-face intervention, and (4) blended intervention (see **Multimedia Appendix 1**). The search terms related to COPD or asthma and blended intervention were first combined and resulted in 84 studies. Due to the limited number of studies, the search terms associated with COPD or asthma were combined with terms about eHealth and face-to-face interventions. In every database, the search was limited to peer-reviewed publications. The search strategy was not restricted based on publication year, as we aimed to provide a comprehensive overview of how blended intervention can be used in COPD and asthma patients. Additionally, reference lists of the included studies and previous reviews were searched to identify additional studies that might be eligible for inclusion.

Eligibility criteria

The PICOS (patient, intervention, comparison, outcome, study design) tool was used to develop an effective search strategy and determine the inclusion and exclusion criteria ¹⁶⁹. The following inclusion criteria were used to identify the studies: (1) Participants: adults (≥ 18 years old) with COPD or asthma, (2) Intervention: blended self-management intervention (consisting of an eHealth component combined with a face-to-face component), (3) Comparison: eHealth intervention with or without usual care (UC), face-to-face intervention with or without UC or only UC, (4) Outcome measures: health-related effectiveness or process outcomes, and (5) Individual randomized controlled trials (RCTs). Studies were excluded if: (1) The participants were Children or adolescent, (2) The eHealth applications were only used to collect data, (3) Outcomes were not about the health-related outcomes, and (4) studies were cluster RCTs.

Study selection

After the removal of duplicates, the identified titles and abstracts were screened for eligibility. If insufficient information was described, the full-text paper was screened. When a full-text paper was not available, a request was sent to the authors. Studies that did not meet the inclusion criteria were excluded. Screening the titles, abstracts, and full-texts was performed by two reviewers independently (Song and Jiang). Any disagreements between the two authors were resolved by a third reviewer (Hallensleben).

Data collection & coding

Data collection was performed with a standardized data extraction form. It included: (1) study characteristic (e.g., first author, publication year, country, number and age of patients, percentage of female patients, disease severity/diagnosis, setting (i.e., home, primary or secondary care), intervention and follow-up duration), (2) intervention characteristic (i.e., category and functionality of the eHealth and face-to-face component), (3) behaviour change techniques (BCTs) used in the blended self-management intervention, and (4) the health-related effectiveness and process outcomes. Information was extracted from each publication by Song and Jiang. Inter-rater reliability, as assessed with Cohen's kappa, indicated that there was strong agreement (kappa value of .90) ¹⁷⁰.

Classification of COPD severity was based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria ¹⁷¹. Patients were considered to have COPD when the ratio between forced expiratory volume in 1s (FEV1) and full forced vital capacity (FVC) is smaller than < 0.70 . The degree of obstruction was defined as follows: (1) GOLD I: $FEV1 \geq 80\%$ predicted (mild); (2) GOLD II: $50\% \leq FEV1 < 80\%$ predicted (moderate); (3) GOLD III: $30\% \leq FEV1 < 50\%$ predicted (severe), and (4) GOLD IV: $FEV1 < 30\%$ predicted (very severe). There was not a standard classification of severity for asthma patients.

As mentioned above, different intervention characteristics were extracted from the publications. First, the eHealth component of the intervention was categorized as a mobile application (e.g., phone call or SMS), an internet-assisted intervention (e.g., web page, chat room), or multiple component interventions with multiple eHealth technologies. Second, the function of the eHealth application was categorized into informing, instructing, displaying, guiding, reminding/alerts, and communicating (i.e., between provider and patients) ¹⁷². Third, face-to-face interventions were classified as an individual (e.g., home visits, primary/secondary care visits) or as a group-based intervention (e.g., group pulmonary rehabilitation). Fourth, the function of the face-to-face intervention was classified as (1) education: introduction of disease-related information and how to use eHealth; (2) training: provide information about self-management; (3) consultation: discuss individual action plan; (4) assessment: test and assess the patient's performance, or (5) monitoring: provide reminders to improve intervention adherence ^{173,174}.

Outcome indicators were classified into health-related effectiveness outcome or process outcome indicators. Health-related effectiveness outcome indicators included outcomes related to disease status and health condition (i.e., exercise capacity, dyspnea, lung function, QoL, admission, mortality, exacerbation frequency and BMI). Process outcome indicators included intermediate outcomes during the implementation process (e.g., visits, satisfaction, costs, smoking, self-management ability, physical activity, medication and therapy adherence, psychosocial, symptom

management, nutrition and alcohol). A positive effect was ascribed when there was a significant positive effect of the intervention on the outcome measure compared to the control group (CG). When the outcome measure did not significantly differ between the intervention group (IG) and CG, it was rated as 'no effect'. A mixed effect was ascribed when multiple measures were used to measure a similar outcome, and the effect on the measures was in different directions (e.g., in the study by Garcia²⁹, there was a significant positive effect on inhaler treatment adherence. At the same time, there was no effect on oral treatment adherence).

Quality assessment

Study quality was assessed using the Cochrane risk of bias (RoB)2¹⁷⁵. The tool assessed five domains of potential bias including (1) randomization, (2) deviations from the intended interventions (effect of assignment to intervention), (3) missing outcome data, (4) the measurement of the outcome, and (5) the selection of the reported result. Each domain had a few signalling questions. Based on the authors (Song and Jiang)' responses to the signalling questions, a judgment on the risk of bias ('low', 'some concerns' or 'high') for each domain could be made to assess the bias that might confound the study findings¹⁷⁵. The quality of the clinical evidence was critically appraised using the Grading of Recommendations Assessment, Development, and Evaluation system (GRADE)¹⁷⁶, which evaluated the risk for bias, inconsistency, indirectness, and imprecision for each outcome. Four categories were used to define the quality of evidence: high quality of evidence (the true effect lies close to that of the effect estimate), moderate quality of evidence (the true effect is likely to be close to the effect estimate, but there is a possibility that it is substantially different), low quality of evidence (the true effect may be substantially different from the effect estimate), very low quality of evidence (the true effect is likely to be substantially different from the effect estimate)¹⁷⁷. The quality assessment was done by author Song and Jiang, and any disagreements were resolved through discussion. Inter-rater reliability, as assessed with Cohen's kappa¹⁷⁰, indicated that there was strong agreement between raters (kappa value of .80).

Data analysis

When an outcome was assessed using different measurements in one study, data from the most specific disease-related questionnaire was used. For example, in the study by Garcia²⁹, QoL was measured with both the Saint-George's Respiratory Questionnaire (SGRQ), a specific QoL questionnaire, and Euroqol, a generic health-related QoL questionnaire. SGRQ was selected and analyzed in the meta-analysis because it was the most specific disease-related questionnaire.

First, a systematic review was conducted to present the result. For continuous data, Cohen's d was recommended to calculate the effect size^{170,178} (i.e., Cohen's $d > .2$ = small effect, Cohen's $d > .5$ = moderate effect, Cohen's $d > .8$ = large effect). For dichotomous data, Relative Ratio (RR) was

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calculated to assess the effect size. An RR greater than 1 indicates a increased likelihood that the stated outcome is achieved in the IG. If the RR is less than 1, there is a decreased likelihood the outcome is achieved in the IG. A ratio of 1 indicated no difference (i.e., the outcome was just as likely to occur in the IG as it is in the CG) ¹⁷⁹.

When three or more studies reported on the same outcome measure, this outcome was included in the meta-analysis ¹⁸⁰. For continuous data, the standardized mean difference (SMD) accounted for the same outcomes measured with different assessment tools (e.g., QoL was assessed using SGRQ, COPD assessment test (CAT), and chronic respiratory questionnaire (CRQ)). SMDs were used to standardize the results of the studies to a uniform scale before they could be combined in the quantitative synthesis. SMDs and associated 95% CIs were used to calculate the mean difference and standardized deviation difference between the change in the intervention group and the change in the control group for each study. When the mean or SD was not mentioned, the author was contacted for the missing information. Cohen *d* was used to interpret the data ^{170,178}. For dichotomous data, RR was calculated to assess the effect size ¹⁸¹. Publication bias was tested if more than ten studies report on the same outcome measure ¹⁸¹. $P < .05$ was considered significant for the effect estimate.

A random-effect model was used because the variance of study populations and intervention designs was anticipated as heterogeneity across included studies ¹⁸². The heterogeneity was assessed using chi-square tests and I^2 statistics ¹⁸³. A P value of $< .1$ indicates statistically significant heterogeneity. The I^2 statistic was used to quantify the size of the heterogeneity between studies: 25%, 50%, and 75% can be considered small, medium, and substantial heterogeneity ¹⁸⁴. Outliers were identified using the value of the standardized residual ¹⁸⁵. The study whose standardized residual was equal to or larger than 1.96 were identified as an outlier and were excluded from the meta-analysis. No subgroup analysis was planned due to the limited studies. All analyses were performed using the software packages Review Manager (RevMan version 5.4; The Cochrane Collaboration) and Stata version 14.0 (StataCorp, College Station, USA) ¹⁸⁶.

Results

Search Results

The literature search identified a total of 4495 potentially eligible records, and 2657 records remained after duplicates were excluded. After screening the titles and abstracts, an additional 2531 records were excluded for other reasons (see **Figure 1**). The full texts of the remaining 126 studies were assessed, and twenty-two RCTs ^{28,29,166,167,187-204} were included in this review. Two of twenty-two RCTs were pilot RCT study ^{187,193}, and one was feasibility RCT ¹⁹⁰. These studies were included because they followed the Consolidated Standards of Reporting Trials checklist ^{187,193}, and they were

small sample size RCTs^{190,193}. Fifteen RCTs focused on COPD patients^{29,166,187-199} and of these studies, eleven were included in the meta-analysis^{29,166,187,189,190,192,193,196-199}. The remaining four studies^{188,191,194,195} were excluded because no available means and SDs were reported or obtained after contacting the authors. Seven studies focused on asthma patients^{28,167,200-204}. Five of seven asthma studies with available data were pooled into meta-analysis^{167,200,202-204}. The other two studies were not included in the meta-analysis because of the lack of means and SDs after contacting the authors.

Study Characteristics

The fifteen COPD studies^{29,166,187-199} were published between 2006 and 2020, and were conducted were conducted in China (n = 5)^{190,196-199}, United States (n = 2)^{166,193}, Denmark (n = 2)^{191,194}, Canada (n = 1)¹⁹⁵, England (n = 1)¹⁸⁷, Spain (n = 1)²⁹, Germany (n = 1)¹⁹², Australia (n = 1)¹⁸⁸, and one in both Spain and Belgium¹⁸⁹. The sample size ranged from 39 to 242 (with a total sample size of 1477). The average age of COPD patients ranged from 64.10 to 73.50 years. Eight of the fifteen COPD studies had UC as a CG^{29,166,188,189,191,196,198,199}, five had a ‘visit’ as CG (meaning that the healthcare provider visited the patients’ home or patients visited the primary or secondary care)^{187,190,193,194,196}, and two studies had both UC and/or visits in the CG^{192,195}. The setting was home and secondary care (n = 9)^{29,166,188,189,195-199}, home (n = 2)^{187,190} and home and primary care (n = 4)¹⁹¹⁻¹⁹⁴. The duration of the blended self-management interventions ranged from 4 to 48 weeks, with a mean of 22.13 weeks (SD = 16.20). Follow-up duration ranged from 17 to 48 weeks.

The seven asthma studies^{28,167,200-205} were published from 2003 to 2020, and were conducted in the Netherlands (n = 3)^{167,203,204}, Germany (n = 1)²⁰¹, England (n = 1)²⁸, United States (n = 1)²⁰² and China (n = 1)²⁰⁰. Study sample size ranged from 16 to 200 (with a total N = 527). The mean age of asthma patients ranged from 24.80 to 52.00 years old. CG included UC (n = 4)^{28,167,202,204}, visits (n = 3)^{200,201,203}. The duration of the blended self-management interventions ranged from 3 to 48 weeks, with a mean of 15.88 weeks (SD = 13.48). Follow-up duration ranged from 36 to 120 weeks. An overview of the study characteristics is shown in **Table 1**.

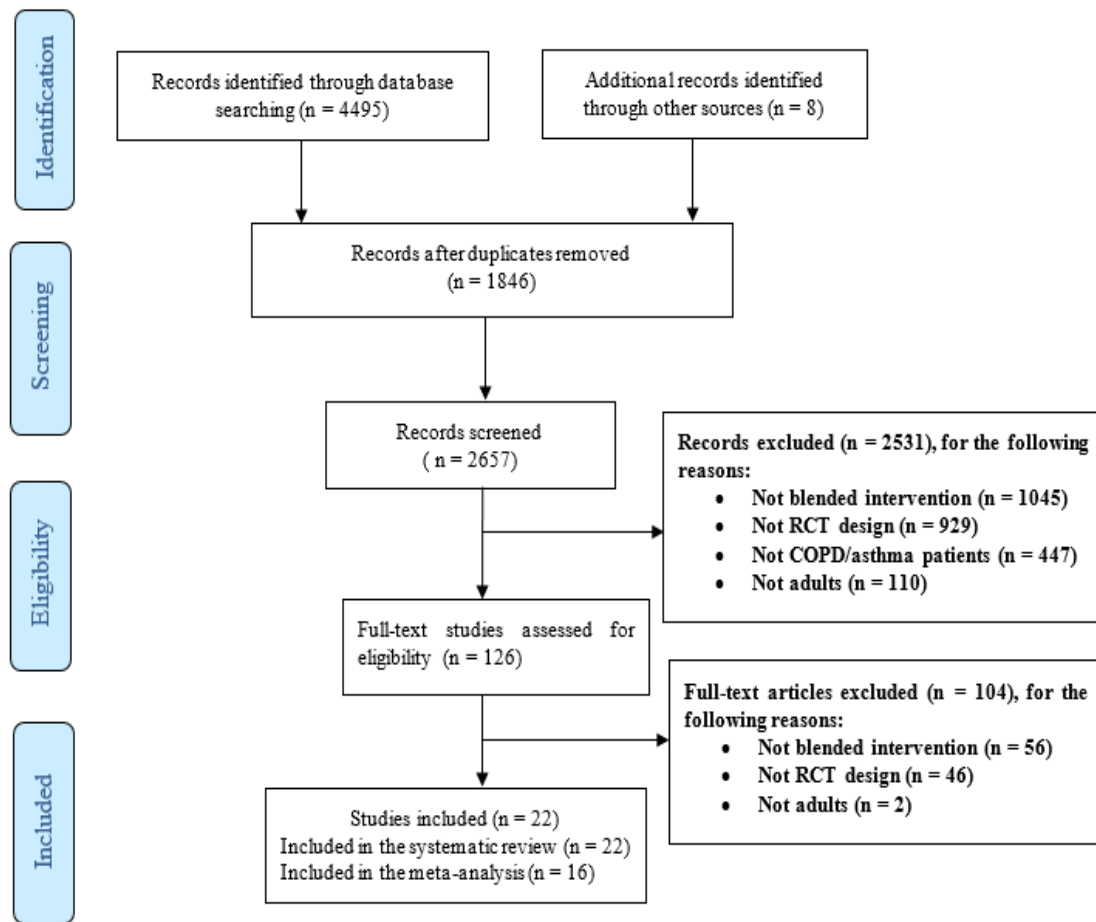


Figure 1. PRISMA flowchart of the systematic review and meta-analysis.

Quality assessment

Methodological quality

The risk of bias was summarised in Table 2. Among the fifteen COPD studies, the risk of bias rated as “some concerns” in ten studies ^{29,188,189,191,194-199}, and as “high” in five studies ^{166,187,190,192,193}. Besides, two studies had some concerns in randomisation process ^{190,192}, and thirteen studies showed a low risk of bias in the randomisation process ^{29,166,187-189,191,193-199}. The majority of the studies showed some concerns ^{29,187-189,191,193-199} while three studies showed high risk from intended intervention ^{166,190,192}. Low risk of bias due to missing outcome data was found in fourteen studies ^{29,166,187,188,190-199}, while one showed some concerns ¹⁸⁹. The risk of bias in the measurement of the outcome was some concerns in thirteen studies ^{29,166,187,188,190-193,195-199} and low risk of bias in two studies ^{189,194}. Low risk of bias in the

selection of the reported result was found in the majority studies ^{29,166,188-192,194-199}, and two had some concerns ^{187,193}.

In asthma studies, the overall risk of bias was some concerns in four studies ^{28,167,203,204} and high risk in three studies ²⁰⁰⁻²⁰². Four studies showed a low risk of bias in the randomization process ^{28,167,203,204}, and three showed some concerns ²⁰⁰⁻²⁰². All studies indicated some concerns due to deviations from intended intervention ^{28,167,200-204}. Six studies showed a low risk of bias outcome data ^{28,167,201-204}, and one had some concerns due to missing outcome data ²⁰⁰. All studies showed some concerns in the measurement of the outcomes and low risk of bias in the selection of the reported result ^{28,167,200-204}.

Quality of evidence

In COPD studies, there were nineteen different outcome measures included (i.e., exercise capacity, dyspnea, lung function, QoL, admission rate, exacerbation frequency, mortality, BMI, visits, satisfaction, costs, smoking, medication adherence, self-management ability, physical activity, psychosocial, symptom management, nutrition and alcohol). Two outcome measures were rated as high quality of evidence (i.e., exercise capacity and mortality), one measure had a moderate quality of evidence (i.e., admission rate), six had a low quality of evidence (i.e., dyspnea, lung function, QoL, visits, satisfaction and physical activity), and the other ten showed the very low quality of evidence (exacerbation frequency, BMI, adherence, self-management ability, smoking, costs, psychosocial, symptom management, nutrition and alcohol). In asthma studies, there were ten different outcome measures included (i.e., admission rate, BMI, exercise capacity, asthma control, lung function, QoL, asthma knowledge, adherence, visits and exacerbation frequency). Seven of the ten outcomes were rated as very low quality of evidence (i.e., admission rate, BMI, exercise capacity, asthma knowledge, adherence, visits and exacerbation frequency). Asthma control, lung function and QoL were rated as the moderate quality of evidence (see **Multimedia Appendix 2**).

Table 1. Study characteristics of COPD and asthma studies.

Study ^a	Country	N (IG/CG) ^b	Setting ^c	Age mean (SD) ^d (IG/CG)	Gender (% female) ^e	Severity ^f	CG ^g	Intervention/ Follow-up (weeks)
COPD (Included in the meta-analysis)								
Bentley et al. (2014)	England	25/23	Home	67.20 (11.60) 65.90 (9.40)	—	—	Home visits	8/32
Chau et al. (2012)	China	22/18	Home	73.50 (6.10) /72.20 (6.10)	3	II-IV	Home visits	8/—

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Casas et al. (2006)	Spain & Belgium	65/90	Home & SC	70.00 (90.00) /72.00 (90.00)	23	I-IV	UC	4/48
Garcia et al. (2007)	Spain	21/41	Home & SC	73.00 (6.00) /74.00 (8.00)	13	_____	UC	48/_____
Jehn et al. (2013)	Germany	32/30	Home & PC	64.10 (10.90) /69.10 (9.20)	23	II-IV	UC + PC visits	36/_____
Koff et al. (2009)	USA	20/20	Home & SC	66.60 (9.10) /65.00 (8.20)	53	III-IV	UC	12/_____
Nguyen et al. (2008)	USA	19/20	Home & PC	68.00 (8.30) /70.90 (8.60)	44	_____	Home visits	24/_____
Wang et al. (2017)	China	55/65	Home & SC	69.30 (7.80) /71.90 (8.10)	53	II-IV	UC	24/48
Wang et al. (2020)	China	39/39	Home & SC	63.20 (7.50)/ 64.40 (7.00)	30	II-IV	SC visits	48/_____
Wei et al. (2014)	China	42/45	Home & SC	65.20 (8.10)/ 63.90 (6.20)	33	I-IV	UC	24/48
Xin et al. (2016)	China	114/ 113	Home & SC	64.20(14.20) /64.60 (14.50)	62	_____	UC	48/_____
COPD (Not included in the meta-analysis)								
Cameron et al. (2016)	Australia	35/30	Home & SC	68.00 (9.90) /70.00 (6.80)	60	I-IV	UC	8/17
Haesum et al. (2017)	Denmark	47/43	Home & PC	70.20 (9.00) 69.50 (10.10)	52	I-IV	UC	4/40
Sorknaes et al. (2013)	Denmark	121/ 121	Home & PC	71.00 (10.00) 72.00 (9.00)	_____	I-IV	PC visits	12/26
Stamenova et al. (2020a)	Canada	41/41	Home & SC	71.98 (9.52)/ 71.76 (7.28)	41	II-IV	SC visits	24/_____
Stamenova et al. (2020b)	Canada	41/40	Home & SC	71.98 (9.52)/ 72.78 (9.16)	46	II-IV	UC	24/_____

Asthma (Included in the meta-analysis)								
Cao et al. (2018)	China	37/30	Home & SC	39.10 (14.30)/ 41.40 (12.00)	78	_____	SC visits	12/_____
Ostojic et al. (2005)	USA	8/8	Home & PC	24.80 (6.30) 24.50 (7.00)	44	M	UC	16/_____
Türk et al. (2020a)	The Netherlands	7/10	SC	41.57(12.54)/ 41.90(8.58)	77	_____	SC visits	12/48
Türk et al. (2020b)	The Netherlands	14/10	SC	41.57(9.73)/ 41.90(8.58)	79	_____	SC visits	12/48
Van Meer et al. (2009)	The Netherlands	101/99	Home & SC	36.00 (19.00; 50.00)/ 37.00 (18.00; 50.00)	70	_____	UC	12/36
Van Gaalen et al. (2013)	The Netherlands	47/60	Home & SC	36.00 (8.70)/ 37.00 (8.00)	71	_____	UC	48/120
Asthma(Not included in the meta-analysis)								
Barbanel et al. (2003)	England	12/12	Home & SC	45.00 (17.00)/ 47.00 (17.00)	54	_____	UC	12/_____
Kohler et al. (2020)	Germany	41/41	Home & PC	49.00 (12.00)/ 52.00 (8.00)	37	_____	PC visits	3/_____

^a Study by Bentley et al. (2014) and Nguyen et al. (2008) were feasibility RCTs, and study by Chau et al. (2012) was a pilot RCT. There was one study including one intervention group and two control groups. i.e., studies by Stamenova et al.(2020). Study by Türk et al.(2020) included two intervention groups and one control group.

^b Sample size at post-intervention reported separately for the intervention group (IG) and control group (CG).

^c The setting was used to conduct the interventions including primary care (PC), secondary care (SC) and home.

^d Interquartile range was also reported and not the mean/SD (as this information was not reported in the publication).

^e _____ = not reported in the study.

^f COPD severity was classified according to GOLD classification. GOLD, Global Initiative for Chronic Obstructive Lung Disease. Asthma severity was classified by the physician diagnosis. M = moderate severity.

^g UC = usual care

Table 2. Risk of bias judgements for randomized controlled trials

Study	Bias arising from the randomization process ^a	Bias due to deviations from intended intervention	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall
COPD						
Bentley et al. (2014)	L	S	L	S	S	H
Cameron et al. (2016)	L	S	L	S	L	S
Casas et al. (2006)	L	S	S	L	L	S
Chau et al. (2012)	S	H	L	S	L	H
Garcia et al. (2007)	L	S	L	S	L	S
Haesum et al. (2017)	L	S	L	S	L	S
Jehn et al. (2013)	S	H	L	S	L	H
Koff et al. (2009)	L	H	L	S	L	H
Nguyen et al. (2008)	L	S	L	S	S	H
Sorknaes et al. (2013)	L	S	L	L	L	S
Stamenova et al.(2020)	L	S	L	S	L	S
Wang et al. (2017)	L	S	L	S	L	S
Wang et al. (2020)	L	S	L	S	L	S
Wei et al. (2014)	L	S	L	S	L	S
Xin et al. (2016)	L	S	L	S	L	S
Asthma						
Barbanel et al. (2003)	L	S	L	S	L	S
Cao et al. (2018)	S	S	S	S	L	H
Kohler et al. (2020)	S	S	L	S	L	H
Ostojic et al. (2005)	S	S	L	S	L	H
Türk et al. (2020)	L	S	L	S	L	S
Ver der Meer et al. (2009)	L	S	L	S	L	S
Ver Gaalen et al. (2013)	L	S	L	S	L	S

^a L = Low risk of bias; S = Some concerns; H = High risk of bias

Intervention characteristic

Category of the blended self-management intervention

In COPD studies, five blended self-management intervention combinations were discussed: (1) multiple component eHealth and an individual face-to-face intervention (n = 6)^{191-195,199}, (2) internet-assisted intervention and an individual face-to-face intervention (n = 5)^{29,187,189,190,196}, (3) multiple component plus an individual and group face-to-face intervention (n = 1)¹⁹¹, (4) mobile applications and an individual face-to-face intervention (n = 2)^{197,198}, and (5) mobile applications and an individual plus group face-to-face intervention (n = 1)¹⁸⁸.

In asthma studies, three blended self-management intervention combinations were discussed: (1) mobile application and the individual face-to-face intervention (n = 3)^{28,200,202} and (2) internet-assisted intervention and the group face-to-face intervention (n = 4)^{167,201,203,204}. Detailed information on the interventions in the COPD and asthma studies can be found in **Table 3**.

Table 3. Description of the blended self-management interventions in COPD and asthma studies.

Study	eHealth		Face-to-face	
	Category (details) ^a	Functionality	Category (details) ^b	Functionality
COPD (Included in the meta-analysis)				
Bentley et al. (2014)	IA (Telehealth-supported service)	Guide, remind, record	Individual (Home visits)	Training
Chau et al. (2012)	IA (Peripheral devices + mobile phone)	Guide, record, remind, display	Individual (Home visits)	Education, consultation
Garcia et al. (2007)	IA (Web-based call centre)	Guide, remind, record	Individual (SC & home visits)	Assessment, education, consultation
Jehn et al. (2013)	MC (Peripheral devices + mobile)	Display, record, remind	Individual (Outpatient visits)	Training, monitoring
Koff et al. (2009)	MC (Peripheral devices + web platform+ phone call)	Record, display, instruct, guide, remind, communication	Individual (Home visits)	Education, consultation; Training, assessment
Nguyen et al. (2008)	MC (Web modules + PDA)	Guide, remind, record,	Individual (Home & PC	Education, training, assessment

		communication	visits)	
Stamenova et al.(2020)	MC (Peripheral devices + web platform+ phone call)	Display, record, remind, guide, communication	Individual (SC visits)	Assessment, consultation
Wang et al. (2017)	IA (Web platform)	Guide, record, instruct, communication	Individual (SC visit)	Monitoring
Wang et al. (2020)	MA (web-based application)	Guide, communication	Individual (SC visits)	Education
Wei et al. (2014)	MA (Phone call)	Guide, remind, record, communication	Individual (PC visits)	Education, training, assessment
Xin et al. (2016)	MC (Phone call + web platform)	Guide, record, instruct, communication	Individual (SC visits)	Education, training
COPD (Not included in the meta-analysis)				
Cameron et al. (2016)	MA (Phone call)	Guide, communication	Individual + group (Exercise guidance)	Education, consultation
Casas et al. (2006)	IA (web-based application)	Display, record	Individual (SC & home visits)	Assessment, education, consultation
Haesum et al. (2017)	MC (Peripheral devices + web platform)	Guide, record, remind, communication	Individual + group visits	Training, monitoring
Sorknaes et al.(2013)	MC (Peripheral devices + web platform)	Guide, instruct, communication	Individual (PC visits)	Consultation
Asthma (Included in the meta-analysis)				
Cao et al. (2018)	MA (Wechat application)	Guide, remind, communication	Individual (SC visit)	Education
Ostojic et al. (2005)	MA (SMS)	Guide, display, record, communication	Individual (PC visits)	Education
Türk et al. (2020)	IA (Web platform)	Instruct, record, communication	Group (Unclear)	Education, training

Ver der Meer et al. (2009)	IA (Web platform)	Guide, remind, record, communication	Group (Unclear)	Assessment, education
Ver Gaalen et al. (2013)	IA (Web platform)	Guide, remind, communication	Group (Unclear)	Education, consultation
Asthma (Not included in the meta-analysis)				
Barbanel et al. (2003)	MA (Phone call)	Guide, remind, record	Individual (Unclear)	Education
Kohler et al. (2020)	IA (Web platform)	Guide, record, communication	Group (Unclear)	Education, training

^a eHealth categories (internet-assisted (IA), multiple component (MC), mobile application (MA)) and specific eHealth application were included. ^b Face-to-face categories and specific intervention were included. SC = secondary care, PC = primary care.

BCTs of the blended self-management intervention

In COPD studies, the number of BCTs used in the interventions ranged from three to ten, with a mean of 6.42 (SD = 1.99). “General information”, “Provide feedback on performance”, “Prompt self-monitoring/ tracking” and “Problem-solving/barrier” were included in fifteen studies^{29,166,187-199}. “Action planning”^{29,188,189,193-196,198,199} and “Motivational approach”^{29,166,188,189,192-194,196,197} were included in nine studies, respectively. “Prompt review of behavioural goals” were included in seven studies^{29,188,189,191,193,195,196}. “Goal setting” was used in five studies^{29,188,189,193,195,196}. “Social support” was in four studies^{29,189,193,197}, and “Emotional control training” was used in two studies^{188,193}.

In asthma studies, the number of BCTs ranged from four to ten, with a mean of 6.29 (SD = 2.63). “General information”, “Prompt self-monitoring/ tracking” and “Problem-solving/barrier” were used in all seven studies^{28,167,200-204}. “Provide feedback on performance” was used in six studies^{167,200-204}. “Action planning” and “Motivational approach” were used in four studies^{28,167,203,204}. “Goal setting” and “Prompt review of behavioural goals” were used in three studies^{167,203,204}, “Social support” was used in two studies^{203,204}, and “Emotional control training” was used in one study²⁰³. (Multimedia Appendix 3).

Effects of the interventions

Systematic review

In COPD studies, the following three health-related effectiveness outcomes were reported: mortality^{187,189,194}, exacerbation frequency^{192,199} and body mass index (BMI)²⁹. On the outcome mortality, all three studies reported no effect^{187,189,194}. On the outcome exacerbation frequency, both

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studies found the blended self-management intervention reduced the exacerbation frequency ($RR = 0.38$, 95% CI: 0.26 to 0.56). The study with BMI reported that the blended self-management intervention had a significant effect in BMI ($d = 0.81$, 95% CI: 0.25 to 1.34)²⁹. Eleven different process outcomes were studied: number of visits (including home visits, primary care visits and secondary care visits) ($n = 3$)^{189,190,192}, satisfaction with the intervention ($n = 3$)^{29,166,190}, medication adherence ($n = 3$)^{29,198,199}, costs ($n = 2$)^{166,187}, smoking ($n = 2$)^{29,188}, self-management ability ($n = 2$)^{193,197}, physical activity ($n = 2$)^{29,193}, nutrition ($n = 1$)¹⁸⁸, alcohol ($n = 1$)¹⁸⁸, psychosocial management ($n = 1$)¹⁸⁸ and symptom management ($n = 1$)¹⁸⁸. Two of three studies showed moderate effect ($d = 0.73$, 95% CI: 0.50 to 0.96)^{198,199} while the other one reported no effect on medication adherence²⁹. On the outcome of self-management ability, one reported large effect ($d = 1.15$, 95% CI: 0.66, 1.62)¹⁹⁷, and the other one showed no effect¹⁹³. No effect was found on the other process outcome indicators. In asthma studies, three health-related effectiveness outcomes were reported: admission²⁰², BMI²⁰³, and exercise capacity²⁰³. No effect was found in admission. Large effect was found in BMI ($d = 1.42$, 95% CI: 0.28 to 2.42) and exercise capacity ($d = 1.50$, 95% CI: 0.35 to 2.50). Three process outcomes were reported: asthma knowledge ($n = 2$)^{167,201}, visits ($n = 2$)^{167,202}, adherence (therapy and medication adherence) ($n = 2$)^{167,202}. No effect was found on process outcome indicators.

Meta-analysis

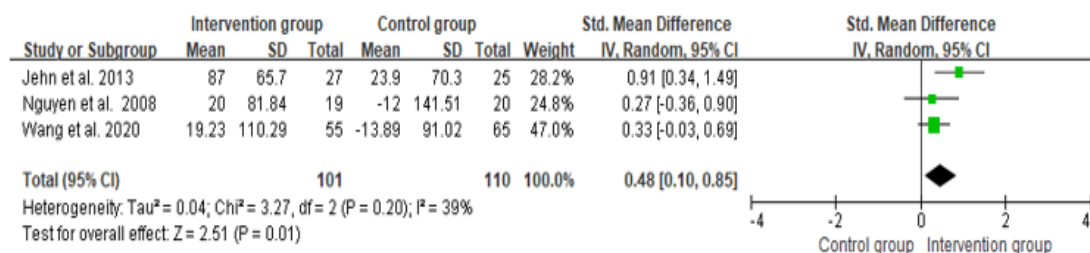
Eleven studies focusing on COPD patients were included in the meta-analysis^{29,166,187,190,192,193,195-199}. The following health-related effectiveness outcomes were included: exercise capacity, dyspnea, lung function, QoL and admission rate. Three studies reported walking distance as an indicator of exercise capacity^{192,193,196}. Blended self-management intervention showed a small effect on the walking distance without significant heterogeneity ($SMD = 0.48$, 95% CI: 0.10 to 0.85, chi-squared = 3.27, $P = .20$, $I^2 = 39\%$) (see **Figure 2**). No study was identified as an outlier. Dyspnea was reported in four studies^{29,190,193,196}. It was measured with the dyspnea subscale of the Chronic Respiratory Questionnaire^{190,193}, Medical Research Council²⁹ and Modified Medical Research Council¹⁹⁶. Lung function was measured with FEV1%^{190,192,196} and FEV1/FVC (%)²⁹ in four studies. No significant difference was found for dyspnea and lung function between the IG and the CG (see **Figure 2**). No study was identified as an outlier. QoL was reported in eight studies with SGRQ^{29,166,187,196}, CAT^{192,197,199} and CRQ¹⁹³. A large effect was found on QoL with substantial heterogeneity ($SMD = 0.81$, 95% CI: 0.11 to 1.51, chi-squared = 108.44, $P < .001$, $I^2 = 94\%$). The standardized residual identified one study as an outlier²⁹. Removal of this study resulted in an increased effect size without decreasing heterogeneity ($SMD = 0.90$, 95% CI: 0.15 to 1.65, chi-squared = 94.14, $P < .001$, $I^2 = 94\%$) (see **Figure 3**). Furthermore, blended self-management intervention reduced the admission rate with a

substantial heterogeneity ($RR = 0.61$, 95% CI: 0.38 – 0.97, chi-squared = 17.63, $P = .003$, $I^2 = 72\%$) (see **Figure 4**). No outliers were identified.

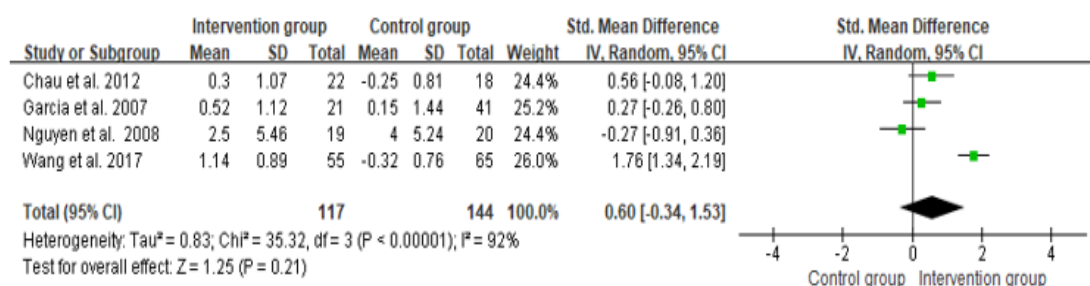
Five asthma studies were pooled in the meta-analysis^{167,200,202-204}. Three health-related effectiveness outcomes were included, that is lung function, QoL and asthma control. Lung function was reported with FEV1(%)^{200,203} and FEV₁¹⁶⁷. Blended self-management intervention showed a small effect on lung function without significant heterogeneity (SMD = 0.40, 95% CI: 0.18 to 0.62, chi-squared = 1.48, $P = .83$, $I^2 = 0\%$). No study was identified as an outlier. Three studies reported QoL with asthma quality of life questionnaire^{167,200,204}. There was a small effect size of the blended self-management intervention on QoL without significant heterogeneity (SMD = 0.36, 95% CI: 0.21 to 0.50, chi-squared = 0.76, $P = .68$, $I^2 = 0\%$). No study was identified as an outlier. Three studies reported asthma control with asthma control questionnaire^{167,200,204}. A moderate effect was found in the blended intervention self-management group without significant heterogeneity (SMD = 0.67, 95% CI: 0.40 to 0.93, chi-squared = 2.98, $P = .23$, $I^2 = 33\%$) (see **Figure 5**). No study was identified as an outlier.

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A. Forest plot for exercise capacity



B. Forest plot for dyspnea



C. Forest plot for lung function

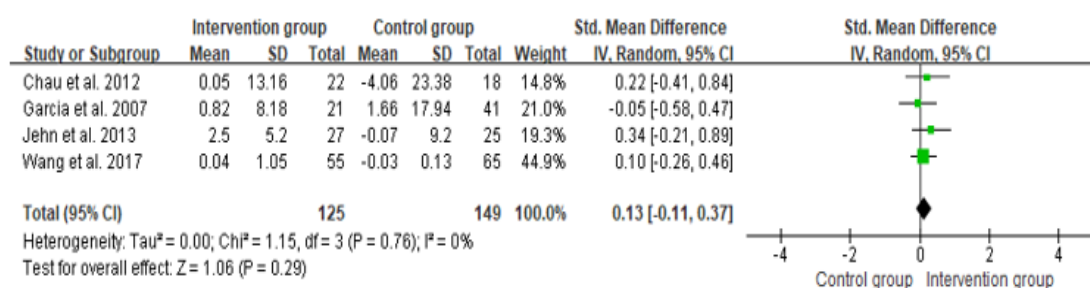


Figure 2. Forest plot for exercise capacity, dyspnea, and lung function in COPD studies.

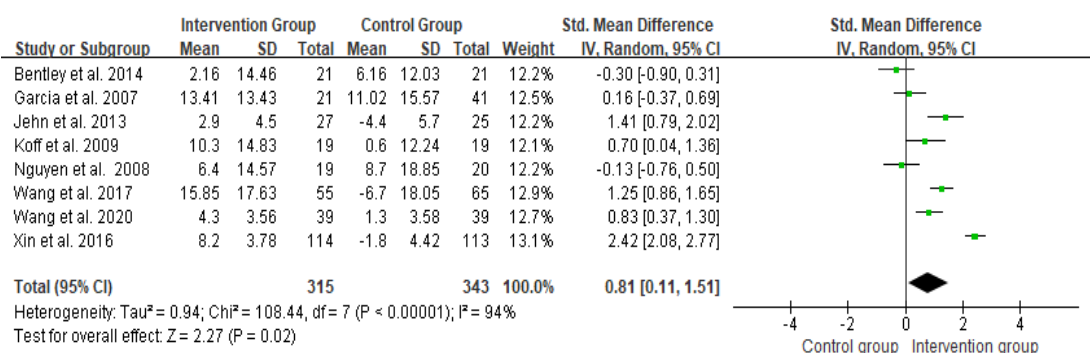


Figure 3. Forest plot for quality of life in COPD studies.

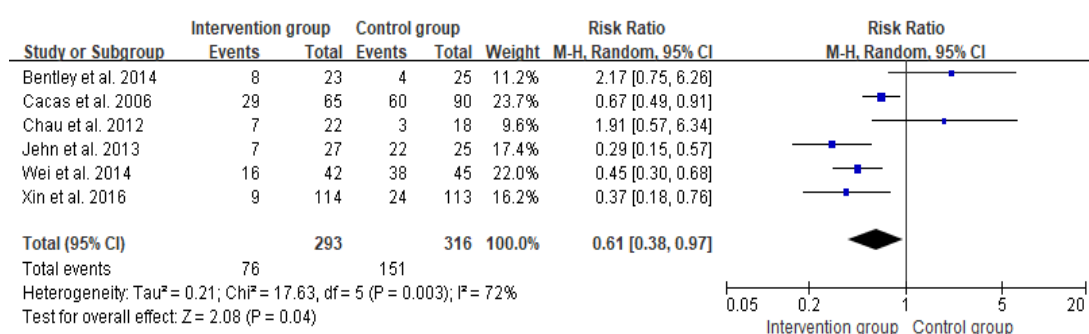
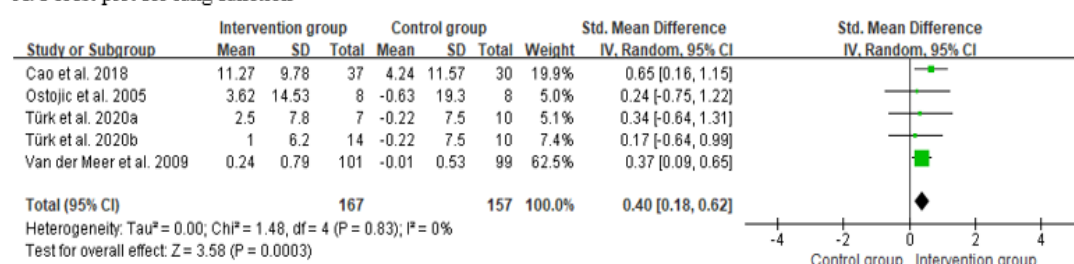
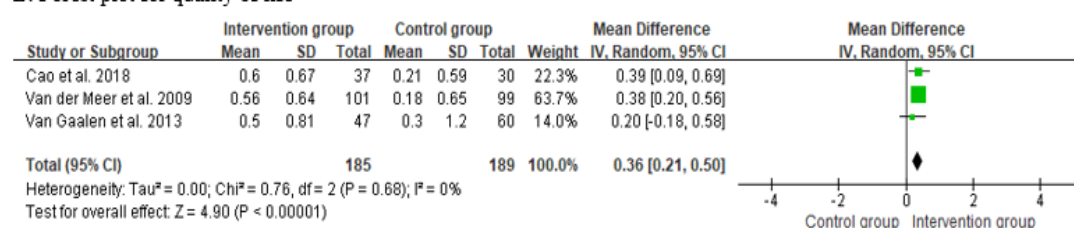


Figure 4. Forest plot for admission rate in COPD studies.

A. Forest plot for lung function



B. Forest plot for quality of life



C. Forest plot for asthma control

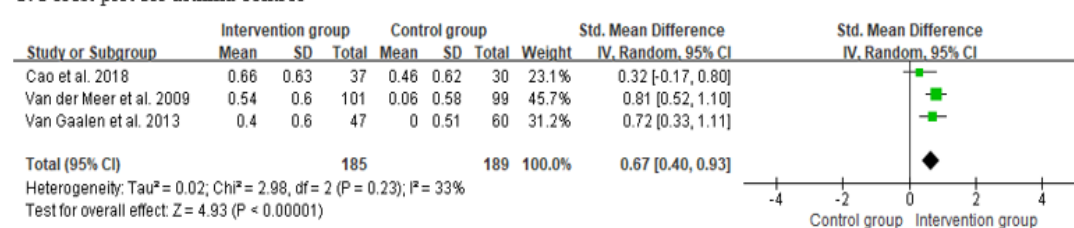


Figure 5. Forest plot for lung function, quality of life and asthma control in asthma studies.

Discussion

Principal Findings

This systematic review and meta-analysis assessed the effectiveness of blended self-management interventions on health-related effectiveness and process outcome indicators in people with COPD or

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asthma. Twenty-two studies were included in the systematic review, of which fifteen were about COPD and seven were about asthma.

The studies focusing on COPD patients included three different health-related effectiveness outcome indicators, and mixed effects were observed. No effect was found on mortality. A positive effect was found on exacerbation frequency and BMI. Eleven different process outcome indicators were studied (e.g., medication adherence, self-management ability). Two of the three studies found a moderate effect on adherence. A positive effect was found in one of two studies on self-management ability. No effects were found on the other process outcomes. Eleven of the COPD studies were included in the meta-analysis. Blended self-management interventions did not have a significant effect on dyspnea and lung function. Still, they did result in a small improvement in exercise capacity and a moderate improvement on QoL and decreased the admission rate. Overall, the majority of studies had some concerns about the risk of bias assessment.

The asthma studies included four health-related effectiveness outcomes. Large effects were found in BMI and exercise capacity. There was no effect on the admission rate and exacerbation frequency. Three process outcomes were studied (i.e., visits, intervention and medication adherence and asthma knowledge). No effect was found on all the process outcomes. Five asthma studies were included in the meta-analysis. Blended self-management intervention showed a small effect on lung function and QoL, and a moderate effect was found on asthma control. Half of the studies reported some concerns, and others showed high risk in the risk of bias assessment.

The meta-analysis suggested that blended self-management interventions can effectively improve COPD patients' exercise capacity. This result was in line with another systematic review that examined the effect of COPD disease-management programs, including eHealth and face-to-face components³⁰. However, this finding was not consistent with the systematic review of the effect of telehealth in COPD patients²⁰⁶. That may be because the blended programs, contrary to the telehealth programs, were likely to promote exercise capacity using various BCTs, including providing information and instruction on the behavior, self-monitoring, and providing feedback on performance by eHealth and face-to-face intervention³⁰. This meta-analysis also showed that there was a positive effect of blended self-management interventions on QoL, which was in line with the findings of a meta-analysis that investigated the effect of COPD self-management interventions, including various self-management programs²⁰⁷. Blended self-management intervention significantly decreased the admission rate. This finding was consistent with the previous meta-analysis²⁰⁸, where the effect of integrated care from healthcare providers with or without eHealth was identified. That might be because patients increased self-management ability and acted on exacerbations more promptly if they received self-management intervention with multiple BCTs²⁰⁹. However, the blended self-

management interventions included in this meta-analysis did not improve dyspnea and lung function, and this was consistent with earlier systematic reviews, which investigated the implementation of eHealth or manual therapy in COPD patients ^{210,211}.

Blended self-management intervention showed an inconsistent impact on process outcomes in COPD patients. To illustrate, internet-assisted eHealth and individual face-to-face intervention showed a positive effect on self-management ability ¹⁹⁶, while no effect was found in the blended intervention, including multiple eHealth components and individual face-to-face intervention ¹⁹³. The findings in this study may show that certain combinations within the blended interventions may be more effective in some outcomes; however, more large-scale studies using different combinations are needed to provide insight into this. There are several potential explanations for the lack of effects in the COPD studies included in the systematic review. First of all, the length of the blended interventions varied in the included studies (i.e., ranged from 4 to 48 weeks). The short intervention duration might have been problematic because patients with mild to very severe COPD were included in the studies. Airway obstruction is usually irreversible in those patients, and the duration of the blended interventions might have been too short or not have encompassed enough training session to accommodate a change in health ²¹². Furthermore, it appeared that patients did not sufficiently adhere to blended interventions ²⁹. This lack of adherence might be because eHealth applications were unfamiliar to use for some patients ²¹³. We recommend that future studies educate patients on how to use eHealth because eHealth positively improved medication adherence.

In asthma studies, in line with other systematic reviews focusing on integrated asthma management (i.e., the cooperation of community pharmacist and general practitioner or eHealth and face-to-face intervention), the blended interventions had a positive effect on QoL and asthma control ^{214,215}. A previous review focusing on face-to-face interventions in asthma patients showed that face-to-face intervention could not improve QoL and asthma control ²¹⁶. The possible reasons for this improvement could be attributed to the integrated care provided by healthcare providers. Healthcare providers could update and refer patients for education, counselling, and guidance with eHealth and face-to-face intervention ^{214,215}. Unlike face-to-face interventions, blended interventions or integrated asthma management - where healthcare providers could refer patients for additional education, counselling, and guidance with eHealth and face-to-face intervention – are more effective. A positive effect was found on lung function. This finding was consistent with the meta-analysis focusing on aerobic exercise on asthma patients ²¹⁷. That may be because adequate exercise training was beneficial to lung function. However, due to limited studies included in the meta-analysis, more studies are needed to identify the effect. In this systematic review, limited studies investigated the effect of the

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blended intervention for asthma patients. The findings should, therefore, be interpreted cautiously, and future studies with larger sample sizes are needed.

Strengths and limitations

Several strengths of this review are worth mentioning. First, a detailed description of the interventions was provided, and a wide range of outcomes was included. The detailed information might provide a helpful direction for the development of effective blended self-management interventions. Second, GRADE was used to assess the quality of evidence about the true effect of the blended intervention on COPD and asthma patients. This quality of evidence assessment could provide a clear and pragmatic interpretation of the recommendations for clinicians and policymakers. And finally, we followed a strict study design and precise data analysis steps. By using a strict and precise process, we wanted to ensure the quality of the systematic review and meta-analysis.

Nevertheless, several limitations also needed to be addressed. First, there was a diversity in the intervention and outcome measurements, which made it difficult to compare the findings. As a consequence, there might be statistical heterogeneity in the true effect size. The significant heterogeneity potentially diluted the intervention effect ²¹⁸. Second, only a small number of studies reported the same outcome measure, and studies with a small sample size were included. These studies may be underpowered to detect a true effect, and this negatively impacted the validity of these studies. Third, the quality of the evidence ranged from very low to high on all the outcomes. The various quality of evidence in the outcomes may weaken the recommendation level for clinicians and researchers because the high heterogeneity among studies downgraded the quality of evidence. Fourth, we were not able to assess the risk of publication bias in the meta-analysis because few studies reported the same outcome ¹⁸¹. There might be a potential risk for publication bias. Fifth, not all studies reported a follow-up. The lack of this reporting made it impossible to examine the long-term intervention effect in a comprehensive way. The results should be interpreted with caution due to the mentioned limitations. Larger RCTs are required to provide more insights, especially RCTs examining the effect of blended interventions in asthma patients. Moreover, data reporting should be performed in an exact, standardized format to enable reliable extraction for future meta-analysis studies.

Conclusions

The studies focusing on COPD found mixed effects of blended self-management interventions on health-related outcomes, with the strongest evidence found for exercise capacity, QoL and admission rate. In asthma studies, small to moderate effects were found on asthma control, lung function and QoL. Overall, blended self-management interventions potentially improve health-related outcomes in COPD and asthma patients, and more studies are needed to evaluate their effectiveness.

