Effectiveness of E-health interventions on improving adherence to treatments and health behaviors for patients with COPD: a systematic review

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English summary

Introduction: Poor adherence to treatment of patients with chronic obstructive pulmonary disease (COPD) is a worldwide issue. E-health is a promising mean to address the relatively poor adherence to therapy. The aim of the current systematic review was to investigate the effectiveness of a broad range of e-health interventions on improving adherence to medication and exercise in patients with COPD.

Method: A systematic literature search was conducted in the databases of Cochrane library, PsychINFO, PubMed, and Embase, in order to identify randomized controlled trials conducted in adult COPD populations. The risk of bias of included studies was examined with seven items of the Cochrance Collaboration's Risk of Bias tool.

Results: 9 studies met the inclusion criteria, of which four studies investigated the effect of a particular e-health intervention on medication adherence and five studies investigated the effect of a particular e-health intervention on exercise adherence. In all studies, the effects on clinical outcomes were also investigated. Findings were mixed, with some studies demonstrating positive effects of e-health interventions on medication and exercise adherence respectively, whereas other studies did not find any significant effects. Furthermore, some studies demonstrated positive clinical effects of e-health interventions, although not exclusively in the studies that reported positive effects on the medication or exercise adherence.

Discussion: In conclusion, the use of e-health adherence interventions in COPD might improve medication and exercise adherence, but it is unclear under which circumstances it would do so. Its efficacy seems to be influenced by many factors such as the operationalization of outcome measures and type of intervention.

1. Introduction

In 2013, the Dutch National Healthcare Institute started a program focusing on providing appropriate healthcare ('*Zinnige zorg*'). All available Dutch healthcare interventions that are offered as part of the Dutch basic healthcare insurance package are systematically screened. The aim of the program is to identify and remove inefficient and unnecessary care, in order to enhance the quality of care, improve health, and reduce unnecessary costs. As part of this program, the healthcare institute aims to examine the role of E-health in improving patient adherence to treatments for lung diseases asthma, chronic obstructive pulmonary disease (COPD), and obstructive sleep apnea syndrome (OSAS).

The current report focusses specifically on patients with COPD. More specifically, the aim of the current report was to investigate the effectiveness of a broad range of e-health interventions on improving adherence to medical treatments and health behaviors in patients with the lung disease COPD, by means of a systematic review.

2. Methods

2.1 Search strategy

Alongside the current report, there are two additional reports that focus on E-adherence interventions in obstructive sleep apnea syndrome and in asthma. The search strategy for the three lung diseases was pooled into one search strategy. To identify relevant studies, a systematic literature search was conducted in the electronic databases of Cochrane library (Wiley), PsychINFO (EBSCO), PubMed, and Embase. Numerous terms related to 1) E-health technology, 2) patient adherence, and 3) the target population (i.e. OSAS, asthma, COPD) were combined using both free-text and index terms (for full search string, see Appendix 1). In addition, reference lists of the included studies as well as systematic reviews on the research topic were checked for potential relevant additional studies.

2.2 Study selection

Study inclusion criteria were: 1) target population: patients with COPD, 2) target age: ≥ 18 years, 3) study investigated the effects of an e-health intervention on at least one quantitative measure of patient adherence to the health behavior or treatment under investigation, 4) health behavior or treatment under investigation comprised medication (oral and inhaler) or self-management behaviors (e.g. exercising), 5) adherence measure(s) were statistically compared between study groups, 6) experimental intervention delivered by means of e-health technology, including Information and communications technology (ICT), such as telephone calls, telemedicine (e.g. videoconferencing), websites, smartphone applications, short text messages (SMS). The delivery of the intervention was time- and place-independent, hence distance being a critical factor (i.e. video's delivered in a face-to-face session are not considered an e-health intervention), 7) (one of) the primary/main component(s) or the majority of the intervention was delivered by means of e-health technology, or, the e-health component was investigated as an add-on to usual, independent of whether this comprised a minor or major part of the intervention being studied, 8) study design was a randomized controlled trial, 9) publication date between January 2000 and March 18, 2018, 10) availability of full-text article in English or Dutch language.

Studies in which the control condition was an active and/or placebo control condition including the same e-health component as the experimental intervention were excluded since this would complicate measuring the effect of the e-health intervention on adherence. This would for example be the case when only the content of the interventions differed, such as general versus tailored short text messages.

Two reviewers (J.A. and L.L.) independently screened all titles and abstracts for eligibility criteria. Disagreements were resolved by discussion. Hereafter, the same two reviewers independently screened the full-text articles of the selected papers in order to determine eligibility for the current review and extracted individual study data accordingly. The online systematic review software Covidence (www.covidence.org) was used to manage the screening process (both title and abstract, and full-text screening), and risk of bias assessment.

2.3 Data extraction

Two reviewers (J.A. and L.L.) extracted the following data of all eligible studies: 1) study reference (authors, year of publication), 2) study design characteristics (country in which study was conducted, study design and sample size, type of control condition, study aim), 3) study population characteristics (age, gender, target population and recruitment strategy, eligibility criteria, diagnostic procedure), 4) E-health intervention characteristics (type of technology, type of intervention, duration and frequency of intervention components), 5) outcome characteristics (assessment of adherence, operationalization of adherence, measurements), 6) results (means and standard deviations of outcome(s) for each study condition, significance test (*p*-value)), 7) source of funding and competing interest, 8) study limitations and other comments.

2.4 Quality assessment

The Cochrane Collaboration's Risk of Bias tool (Higgins et al., 2011) was used to assess the quality of all included studies. Two reviewers (J.A. and L.L.) independently evaluated the following dimensions of risk of bias: 1) adequacy of random sequence generation, 2) adequacy of concealment of allocation sequence to personnel, 3) blinding of study participants and personnel, 4) blinding of outcome assessors, 5) adequacy of handling of incomplete outcome data, 6) selective outcome reporting, and 7) potential other sources of bias. Each study was rated on each dimension as "low risk", "high risk", or "unclear risk". Disagreements were resolved by discussion.

3. Results

3.1 Search and screening

Figure 1 presents the PRISMA flowchart, which describes the process of literature screening and selection for the three different lung diseases. The systematic search resulted in 3049 potentially relevant articles after duplicates had been removed (n = 723). After title and abstract screening, a total of 123 studies were selected for further full-text screening to check for eligibility in the current systematic review. Of these, 24 targeted COPD. Assessment of the eligibility criteria as well as the results of the corresponding included studies is summarized in the following sections.

3.2 Results for COPD

3.2.1 Study characteristics

Full-text eligibility screening of 24 studies led to the exclusion of 15 studies (for more details, see Table 1), and inclusion of 9 studies accordingly. Table 2 and Table 3 provide an overview of the relevant characteristics of each of the studies. All of the included studies focused on adults with COPD who were prescribed medication or who were offered self-management interventions for their disease. The mean age in study conditions ranged from 63.9 (Wei et al., 2014) to 73.0 (Garcia-Aymerich et al., 2007). All but one study (Pinnock et al., 2013) included a (slight) majority of females (range percentage of females: 6.3 – 46.0%).

Four studies investigated the effects of e-health technology on medication adherence (see Table 1; Farmer et al., 2017; Garcia-Aymerich et al., 2007; Pinnock et al., 2013; Wei et al., 2014), whereas five studies focused on exercise behavior (see Table 2; Moy et al., 2016; Nguyen et al., 2008, 2013; Petty et al., 2006; Tabak, Vollenbroek-Hutten, Van Der Valk, Van Der Palen, & Hermens, 2014). We separately review these two types of studies in the following subsections.

3.2.2 Quality assessment

Figure 2 shows the averaged risk of bias across all included studies, whereas Figure 3 presents the results of the risk of bias assessment separately for each individual study and each type of bias. One study met none of the seven criteria in terms of low risk of bias, three studies met two criteria, one study met four criteria, and finally, four studies met five criteria.

Not a single study was rated as having low risk of bias on all seven assessment dimensions. This was largely due to ratings of high risk of bias on the "blinding of participants and personnel" dimension in all seven studies. Such a high risk of bias rating is common for (at least partially) person-delivered interventions where blinding participants and personnel to whether they receive or provide a treatment is often not possible (Higgins & Green, 2011).

Most of the studies adequately generated a random sequence (7 out of 9 studies). With respect to the other type of selection bias, being allocation concealment, five studies were rated as low risk of bias, whereas for the other four studies this quality dimension was rated as unclear as no information was provided on concealment of the allocation of care.

Regarding the dimension 'blinding of outcome assessment', two third of the studies (6 out of 9) were

rated as high risk of bias as adherence outcomes were based on patients' self-report, and patients were not blinded to the care they had received. As shown in Figure 3, three studies were rated as low risk of bias, because self-report information was checked against more objective dispensing information at pharmacies (Wei et al., 2014), or adherence was automatically assessed by means of pedometer data (Moy et al., 2016; Tabak et al., 2014).

Three studies (33.3%) conducted intention-to-treat analyses and therefore had low risk of attrition bias. Six studies had a risk of bias, of which five studies did not conduct intention-to-treat analyses and limited the analyses to study or intervention completers, hence only individuals with post-intervention data were taken into account (Farmer et al., 2017; Garcia-Aymerich et al., 2007; Moy et al., 2016; Petty et al., 2006; Tabak et al., 2014). A sixth study (Nguyen et al., 2008) was rated as high risk because of imputing missing data by the last-observation-carried-forward method. Research has demonstrated this method to lead to biased results (Lachin et al., 2006).

With respect to selective reporting, four studies (44.4%) had low risk of bias given that the research protocol was available and all adherence outcomes were reported on, whereas another three studies were rated as unclear as there was no protocol available. The study by Nguyen et al. (2008) was rated as high risk of reporting bias because not all pre-defined adherence outcomes as published in the protocol were reported on. Moreover, the primary outcome in the research protocol (i.e. exercise adherence) was different from the primary outcome as stated in the effectiveness paper (i.e. dyspnea with activities of daily living). The latter also applied to the study of Nguyen et al. (2013). Also, in the trial registration of the latter study (Nguyen et al., 2013) the exercise adherence outcome measure had not been operationalized a-priori.

Finally, seven studies (66.7%) had low risk of other sources of bias, whereas two studies were rated as high risk. The high risk of bias in these two studies was caused by differential participant attrition due to technical and usability challenges with the e-health application under investigation (Nguyen et al., 2008), and differential dropout rates (p = .01) between study conditions respectively (Petty et al., 2006).

3.3 Medication adherence

3.3.1 Study characteristics

The range of e-health technologies being used in the interventions included one or more of the following: tele-monitoring (Pinnock et al., 2013), telephone contacts (Farmer et al., 2017; Garcia-Aymerich et al., 2007; Pinnock et al., 2013; Wei et al., 2014), text messages (Garcia-Aymerich et al., 2007), an ICT platform including a web-based call center (Garcia-Aymerich et al., 2007), a fully automated Internet-linked tablet-based monitoring and self-management support platform including tailored video material (Farmer et al., 2017), and a Bluetooth-enabled pulse oximeter (Farmer et al., 2017). The telephone-based intervention of the study by Wei et al. (2014) was conducted by a pharmacist, who assessed treatment effects, clarified misconceptions about treatment, educated about side effects and reminded patients of their next clinical appointment. The telephone calls in the integrated care intervention of Garcia-Aymerich et al. (2007) were conducted by specialized nurses and focused on reinforcement of

self-management strategies as part of individually tailored COPD care plans. In addition, access to specialized nurses, caregivers, and primary care professionals was enabled by means of the ICT-platform including a web-based call center. Daily monitoring of COPD symptoms was conducted in two studies, one by means of touch-screen tele-monitoring equipment (Pinnock et al., 2013), and one by means of an Internet-linked tablet-based diary with Bluetooth-enabled pulse oximeter (Farmer et al., 2017). In both of these studies, a clinical team reviewed these data regularly and provided follow-up care by telephone (Pinnock et al., 2013, Farmer et al., 2017) or SMS (Farmer et al., 2017) in case of severe symptoms or non-adherence. In one of these studies (Farmer et al., 2017), the intervention furthermore comprised online self-management support modules including tailored videos on self-management strategies, such as inhaler techniques, pulmonary rehabilitation exercises, educational advice on managing COPD, smoking cessation, diet, and self-management techniques for breathlessness. The online modules also contained personalized self-management and treatment plans, and the facility to receive short messages from respiratory nurses.

The type and intensity of the interventions was quite similar for three interventions (Farmer et al., 2017, Garcia-Aymerich et al., 2007, Pinnock et al., 2013). More specifically, these three interventions all lasted for 12 months and included regular monitoring and telephone support. A fourth intervention (Wei et al., 2014) included regular telephone contacts over a period of 6 months, and additionally included a 6-month follow-up assessment.

Medication adherence was primarily assessed by means of self-report questionnaires (n = 3; Farmer et al., 2017, Garcia-Aymerich et al., 2007, Pinnock et al., 2013), whereas one study interviewed patients about their medication regimen and adherence patterns, which was subsequently checked against dispensing information of pharmacies (Wei et al., 2014). These assessments resulted in adherence outcomes operationalized as medication adherence scores, calculated percentages of adherers, or percentages of medication taken accordingly.

The care that was provided in the control groups varied in type and intensity (see Table 2). Control care ranged from pharmacological prescriptions at the discharge hospital (Garcia-Aymerich et al., 2007) and general counselling only (Wei et al., 2014), to more extensive usual care such as detailed personalized education and self-management plans (Farmer et al., 2017, Pinnock et al., 2013). On top of the latter, one study provided additional care in accordance to service models, which could comprise respiratory physiotherapy, weekday service or nurse specialist, or care as provided by one's GP (Pinnock et al., 2013).

3.3.2 Effects of e-health interventions on medication adherence

A summary of the included papers on the effect of e-health interventions on medication adherence can be found in Table 2. Investigating the post-intervention results, two studies found non-significant effects of the e-health interventions (Farmer et al., 2017, Pinnock et al., 2013), whereas one study found a significant effect (Wei et al., 2014), and one study found mixed results depending on how adherence was operationalized (Garcia-Aymerich et al., 2007). No effects on oral treatment as measured with the Medication Adherence Scale (MAS) were found, but there were significant effects on inhaled treatment

as measured with Inhaler Adherence Scale (IAS) and on observed correct inhaler maneuvers. Only one study conducted a follow-up assessment after the intervention period (Wei et al., 2014). Six months after receiving a 6-month telephone-based intervention by clinical pharmacists, including individualized face-to-face education and a series of telephone counseling sessions, participants were found to have greater medication adherence in terms of percentage of medication taken in comparison to control participants who only received general counseling.

When reviewing these results more closely by type of interventions and outcomes, the two interventions including both online monitoring and as-needed telephone contact (Farmer et al., 2017, Pinnock et al., 2013), were not found to have a significant impact on medication adherence, whereas the other two interventions that mainly comprised telephone-based counseling and education (Garcia-Aymerich et al., 2007, Wei et al., 2014), were found to significantly improve medication adherence in comparison to control conditions. Although the type of intervention may have impacted results, the operationalization of medication adherence may have also (partly) accounted for the different findings. That is, in the monitoring and as-needed telephone contact intervention studies (Farmer et al., 2017, Pinnock et al., 2013), medication adherence was determined by scores on the Medication Adherence Report Scale (MARS; range 5-25), whereas in the telephone-based interventions of the studies by Garcia-Aymerich et al. (2007) and Wei et al. (2014), percentage scores were used as outcome measures. Specifically, the proportion of adherers, the proportion of correct inhaler maneuvers, or the proportion of medication taken.

Predictors or subgroup analyses were conducted in three out of four studies (Farmer et al., 2017, Pinnock et al., 2013, Wei et al., 2014), however were limited to primary outcomes not including adherence measures.

3.3.3 Effects e-health medication adherence interventions on clinical outcomes

All four studies did not only assess the effectiveness of the e-health interventions in terms of medication adherence, but also included clinical outcomes as part of primary or secondary outcome measures. None of the studies (Farmer et al., 2017, Garcia-Aymerich et al., 2007, Pinnock et al., 2013, Wei et al., 2014) found significant effects on overall disease-specific health-related quality of life, although participants in the telephone-based intervention by pharmacists were found to have significant larger improvements on the symptom sub-scale scores and impact sub-scale scores as measured with the disease-specific St George's Respiratory Questionnaire compared to usual care (Wei et al., 2014). Findings with respect to generic health-related quality of life were mixed; an integrated care intervention including a web-based call center was not found to achieve better results in terms of quality of life as compared to usual care (Garcia-Aymerich et al., 2007), whereas a fully automated Internet-linked, tablet computer-based system of monitoring and self-management support modules did (0.076 difference on the EQ-5D, p=0.03; Farmer et al., 2017).

Two studies did not find significant differences between e-health interventions and usual care in terms of COPD exacerbations (Farmer et al., 2017, Pinnock et al., 2013). However, Wei et al. (2014) found that participants receiving a telephone-based intervention by pharmacists demonstrated lower rates of

severe exacerbations resulting in hospitalization (20 hospitalizations vs. 46 hospitalizations) , as well as less days spent in the hospital during admissions (5.56 ± 9.68 days vs. 11.11 ± 18.16 days) , in comparison to control participants.

E-health interventions were not found to be superior to usual care in terms of functional COPD status as assessed by FEV1, FEV1/FVC, PaO2 (mmHg), PaCO2 (mmHg), or dyspnea (Garcia-Aymerich et al., 2007). Nor was superiority found with respect to comorbid symptoms of anxiety and depression (Farmer et al., 2017, Garcia-Aymerich et al., 2007, Pinnock et al., 2013) and smoking status or cessation (Farmer et al., 2017, Garcia-Aymerich et al., 2007).

Mixed results were found regarding patients' knowledge about COPD and self-management. The study by Garcia-Aymerich et al. (2007) found an increase in knowledge about COPD, the identification, and early treatment of COPD exacerbations in the intervention group compared to the usual care. Conversely, no such effects on knowledge were found in the tele-monitoring intervention with as-needed telephone calls (Pinnock et al., 2013).

Finally, it remains unclear whether e-health interventions have potential in reducing healthcare resource usage. Pinnock et al. (2013) found their e-intervention to actually increase the workload of health care professionals in terms of telephone calls and home visits not initiated by symptom alerts as part of e-monitoring. Farmer et al. (2017) found mixed results within their study. They found significantly fewer nurse contacts in the intervention compared to usual care (median difference -1.0, p=0.03), but no significant differences in the number of GP contacts.

Predictors or subgroup analyses on clinical outcomes were conducted in three out of four studies (Farmer et al., 2017, Pinnock et al., 2013, Wei et al., 2014), studying a range of demographic and clinical variables. Only the severity of COPD was found to be related to outcome in terms of the first hospital admission with an exacerbation of COPD (Pinnock et al., 2013). Although based on a small subsample of patients, the tele-monitoring intervention with as-needed telephone contact was found to be more effective for patients with severe or very severe COPD than for those with mild to moderate COPD.

3.3.4 Dropout

Study dropout rates were approximately 15% (Farmer et al., 2017), 20% (Pinnock et al., 2013), 26% (Wei et al., 2014), and 45% (Garcia-Aymerich et al., 2007), see Table 2. The reasons for patients being lost to follow-up were often unclear, although death was a commonly reported reason that accounted for between 17 (Wei et al., 2014) to 73% (Pinnock et al., 2013) of the total dropouts. Only one study investigated whether there were differences in any baseline characteristics between participants completing and dropping out of the study respectively (Garcia-Aymerich et al., 2007). Dropouts were found to a significant higher number of COPD admissions in the year before study initiation, as compared to those who completed the 12-month post-intervention assessment (p=0.003).

3.3.5 Acceptability/evaluation e-health interventions

Only one study briefly reported on the satisfaction of participants with the provided healthcare. In

comparison to pharmacological prescriptions and usual care as provided by standard treatment protocols, the development of an individually tailored care plan with reinforcing telephone calls and access to clinical care by a web-based call center, led to a similar proportion of individuals being satisfied with the provided care (Garcia-Aymerich et al., 2007).

3.4 *Exercise adherence*

3.4.1 Study characteristics

Five studies investigated the effectiveness of an e-intervention in terms of enhancing adherence to exercise behavior for individuals with COPD, see Table 3. Moy et al. (2016) studied an Internet-based mediated pedometer-based program, which incorporated individualized goal setting, educational and motivational content, self-monitoring of step counts by means of a pedometer, and an online community forum to enhance social support. Two other studies investigated the same Internet-based dyspnea self-management program (Nguyen et al., 2008, 2013). Patients receiving this program self-monitored respiratory symptoms and exercise behavior by means of a website and a Personal Data Assistant (PDA), and received individualized feedback and reinforcement of dyspnea strategies by e-mail. Furthermore, the program included interactive web modules delivering education and skills training. The content of these modules was reinforced further by live group chat sessions with peers. A study by Petty et al. (2006) comprised videotapes with pulmonary rehabilitation exercises and educational content, either with or without customization with respect to patients' disease level and motivational stage of change. Finally, the current review included a study on a tele-rehabilitation program (Tabak et al., 2014) which consisted of a smartphone application and web-based portal. The application served as activity coach; patients' activity level was registered by means of a pedometer, and automated feedback messages were sent for awareness and motivation. The web-based portal included a symptom diary for daily monitoring, and a decision-support system that automatically formed an advice to start medication in case of an exacerbation.

The duration of the interventions ranged from four weeks (Tabak et al., 2014) to one year (Moy et al., 2016, Nguyen et al., 2012). Adherence to exercise behavior was measured by means of self-report in three studies (i.e. frequency and duration of exercising; Nguyen et al., 2008, 2013, Petty et al., 2006), whereas the two studies used more objective step-count data (i.e. pedometers; Moy et al., 2016, Tabak et al., 2014).

As shown in Table 3, control conditions were either relatively low-intensity care such as daily wearing a pedometer, monthly uploading the data, and reporting adverse events (Moy et al., 2016), or verbal or written information by physician (Petty et al., 2006). On the other hand, several studies included relatively more intensive control care such as a face-to-face dyspnea self-management program including similar components as the Internet-based version as described above, except that content was primarily being delivered by face-to-face sessions or paper materials (Nguyen et al., 2008, 2013). A second control care condition in the study by Nguyen et al. (2013) comprised general health education as delivered by a home visit, monthly face-to-face classes, and regular phone calls.

3.4.2. Effects e-health interventions on exercise adherence

A summary of the included papers on the effect of e-health interventions on exercise adherence can be found in Table 3. In three of the five studies, no significant effects of the e-health interventions on exercise adherence were found (Nguyen et al., 2008, Nguyen et al., 2013, Tabak et al., 2014), whereas one study found significant effects on exercise adherence (Petty et al., 2006), and one study found mixed results depending on the operationalization and time point (Moy et al., 2016). Two studies conducted a follow up assessment (Moy et al., 2016, Petty et al., 2006), but only Moy et al. (2016) acquired sufficient data to perform the analyses. After an eight-month maintenance phase where participants were instructed to continue the intervention but without receiving novel content, there were no significant effects on exercise when looking specifically at the maintenance phase ($p=0.28$) or at the complete twelve-month study period ($p=0.82$).

When reviewing these results more closely by type of intervention and outcome, the use of internet-based platforms or portals (Moy et al., 2016, Nguyen et al., 2008, 2013, Tabak et al., 2014) did not significantly affect exercise adherence, whereas the use of customized videotapes that were send by e-mail positively affected exercise adherence (Petty et al., 2006). However, although different operationalizations of exercise adherence were used (self-report vs. pedometer), this did not seem to systematically affect the results since both positive (Moy et al., 2016, Petty et al., 2006) and negative results (Nguyen et al., 2008, 2013, Tabak et al., 2014) were found for both operationalizations.

Predictors or subgroup analyses were conducted in three out of five studies (Nguyen et al., 2008, 2013, Petty et al., 2006), but only two studies analyzed these with respect to adherence measures (Nguyen et al., 2008, 2013). In addition to analyzing the data according to intention-to-treat principles (all patients were analyzed according to randomization, regardless of adherence), Nguyen et al. (2013) also performed per-protocol analyses (i.e. only patients with a certain level of adherence), and 'completers'-analyses. The additional analyses did not lead to differences in results, indicating that the intervention also was not effective in subsamples with greater adherence. Nguyen et al. (2008) investigated the effect on factors that could potentially mediate treatment effects (e.g. knowledge and self-efficacy of symptom management, perception of perceived support, and satisfaction with the intervention). They did not perform mediation analyses, but also did not find an effect of the E-health intervention on these factors.

3.4.3 Effects e-health exercise adherence interventions on clinical outcomes

All five studies also investigated the effects of E-health interventions on clinical outcomes as part of primary or secondary outcome measures. Two studies investigated the effect of dyspnea (Nguyen et al., 2008, 2013), but found no significant between-group differences in improvements in dyspnea. Of the four studies investigating health related quality of life (HRQL; Moy et al., 2016; Nguyen et al., 2008, 2013; Petty et al., 2006), only one study found significant between-group differences in improvements in HRQL (emotion functioning: $p=0.0489$, coping skills: $p=.005$; Petty et al. 2006). The other three studies found no between-group differences in improvements in HRQL (Moy et al., 2016, Nguyen et al., 2008, Nguyen et al., 2013) and one also found similar clinically relevant improvements (Moy et al.,

2016) in all study groups. Tabak et al. (2014) investigated the effect of E-health interventions on health status, but also did not find significant between-group differences in improvements.

Two studies reported COPD-related events during the study (Moy et al., 2016, Nguyen 2008). Moy et al. (2016) did not find between-group differences in acute exacerbations, emergency room visits or death. Nguyen et al. (2008) did not analyze between-group differences in exacerbations due to high heterogeneity in disease severity.

No significant effects of e-health interventions were reported regarding patients' knowledge about COPD self-management. More specifically, Nguyen (2008) found no between group differences in improvement in knowledge about the management of dyspnea at 3 months, which was sustained at 6 months. In addition, self-efficacy for managing dyspnea was found to be significantly improved, but without between-group differences (Nguyen et al., 2008, 2013). However, Nguyen (2013) found marginally significant between-group differences in self-efficacy for dyspnea management (p=.06), with the greatest improvement for the experimental group.

Predictors or subgroup analyses with respect to clinical outcomes were conducted in three out of five studies (Nguyen et al., 2008, 2013, Petty et al., 2006). Petty et al. (2006) investigated the association of age, gender and type of COPD on emotional functioning and coping skills with respect to quality of life. They only found a significant positive association between age and emotional functioning, meaning that emotional functioning increased with increasing age. As mentioned in the previous section, Nguyen et al. (2013) did not find different results when analyzing the data according to different principles (i.e. intention-to-treat, per-protocol, or completers), indicating that the intervention was not effective in subsamples with greater adherence. Furthermore, Nguyen et al. (2008) investigated the effect on factors that could potentially mediate treatment effects. They did not perform mediation analyses, but also did not find direct effects of the intervention on these factors.

3.4.4 Dropout

Study dropout rates were approximately 0.4% (Moy et al., 2014), 5.9% (Tabak et al., 2014), 12% (Nguyen et al., 2013), 18.7% (Petty et al., 2006), and 24% (Nguyen et al., 2008). The reasons for patients being lost to follow-up were often unclear. Only one study (Nguyen et al., 2013) reported that 3 of the 16 participants had been lost to follow-up due to death, but the other reasons remained unclear. Two studies investigated whether there were differences between participants completing and dropping out of the study respectively (Nguyen et al., 2008, 2013). Nguyen et al. (2013) found no differences between completers and dropouts. Although Nguyen et al. (2008) found no difference in demographics, COPD specific symptoms, or factors related to motivation to participate; they did find that dropouts reported more often to have no musculoskeletal problems, were less likely to have participated in any face-to-face support groups, and were less likely to have previously attended pulmonary rehabilitation. In addition, dropouts more often tended to be current smokers and female.

3.4.5 Acceptability and evaluation

Two of the five studies reported on the satisfaction of participants with the provided healthcare. In the

studies of both Nguyen et al. (2008) as well as Nguyen et al. (2013), participants reported high ratings of satisfaction with the intervention as assessed with by semi-structured interviews. In addition, participants reported they perceived the support of the study nurses necessary to either initiate or maintain the intervention program (Nguyen et al., 2008, 2013).

4. Discussion

The current review investigated the efficacy of a broad range of e-health interventions in improving adherence to medical treatments and exercise in patients with COPD. To this end, 9 studies were included, of which four studies investigated the effect of a particular e-health intervention on medication adherence (Farmer et al., 2017; Garcia-Aymerich et al., 2007; Pinnock et al., 2013; Wei et al., 2014), and five studies investigated the effect of a particular e-health intervention on exercise adherence (Moy et al., 2016; Nguyen et al., 2008, 2013; Petty et al., 2006; Tabak et al., 2014). Regarding medication adherence, two studies found non-significant effects, whereas one study found a significant effect, and one study found mixed results depending on how adherence was operationalized. With respect to exercise adherence, three out of five studies reported no significant effects, whereas one study found significant effects, and one study found mixed results depending on the operationalization and time point of assessment. Besides effects of e-health intervention on medication or exercise adherence, all studies investigated the effect on clinical outcomes such as dyspnea, exacerbations or quality of life as well. Overall, the results were inconclusive due to several reasons.

No firm conclusions on the effect of e-health adherence intervention be drawn due to the heterogeneity of the studies. More specifically, in the studies on medication adherence, there were differences in the operationalization of adherence (e.g. questionnaires vs. pill counts) and differences in the types of intervention that consequently resulted in differences in the amount of guidance (e.g. online monitoring and as-needed telephone contact vs. telephone-based counseling and education). Not all studies that found a positive effect on medication adherence reported a positive effect on clinical outcomes, which could have resulted from differences in clinical outcomes (dyspnea vs. quality of life) and differences in assessing a particular clinical outcome.

With respect to the studies on exercise adherence, the results were also ambiguous. There were differences in the operationalization of exercise adherence (e.g. step-count vs. minutes of exercise) and differences in the type of e-health intervention under investigation. The only study that reported a positive effect of e-health interventions on exercise adherence, used personalized videotapes as compared to the internet-based platforms or portals used in all other studies. In addition, this study also reported positive effects on clinical outcomes as operationalized as Health Related Quality of Life.

In conclusion, the use of e-health adherence interventions in COPD might improve medication and exercise adherence, but it is unclear under which circumstances it would do so. Its efficacy seems to be influenced by many factors such as the operationalization of outcome measures and type of intervention.

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Appendix 1: Seach string

Search conducted on March 20th, 2018

PsycINFO (EBSCO)

(DE "Compliance" OR DE "Treatment Compliance" OR DE “Treatment dropouts” OR TX(“fidelity” OR "complian*" OR "non-complian*" OR "noncomplian*" OR "adheren*" OR "non-adheren*" OR "nonadheren*" OR “dropout*” OR “drop-out*” OR “no-show*” OR “noshow*” OR “attend*” OR “non-attend*” OR “nonattend*” OR “absence*” OR “absent*” OR “non-appear*” OR “nonappear*”))AND (DE "Computer Assisted Therapy" OR DE "Telecommunications Media" OR DE "Electronic Communication" OR DE "Online Social Networks" OR DE "Online Therapy" OR DE "Social Media" OR DE "Telemedicine" OR DE "Text Messaging" OR DE “Computer Mediated Communication” OR DE “Teleconferencing” OR DE “mobile devices” OR DE “communications media” OR DE “cellular phones” OR DE “Internet” OR DE “technology” OR DE “information technology” OR DE “virtual reality” OR DE “computer applications” OR TI(“Internet*” OR “Web*” OR “Online*” OR “tele*” OR “electronic*” OR “video*” OR “device*” OR “digital*” OR “software*” OR “mobile*” OR “technolog*” OR “e-health” OR “ehealth” OR “computer*” OR “e-treat*” OR “e-therap*” OR “mhealth” OR “m-health” OR “distance counsel*” OR “cybercounsel*” OR “cyber-counsel*” OR “cyber-treat*” OR “text-messag*” OR “textmessag*” OR “text messag*” OR “SMS*” OR “texting*” OR “short message service*” OR “smartphone*” OR “cell-phone*” OR “cellphone*” OR “cellular phone*” OR “blended*” OR “handheld device*” OR “hand held device*” OR “iPad*” OR “iPhone*” OR “email*” OR “e-mail*” OR “sensor*” OR “wearable*” OR “social media*” OR “social network*” OR “e-counsel*” OR “ecounsel*” OR “palmtop*” OR “telephone*” OR “WhatsApp” OR “Twitter” OR “Facebook” OR “Instagram” OR “forum” OR “chat*” OR “virtual reality*” OR “virtual-reality*” OR “avatar*” OR “Conversational agent*” OR “virtual coach” OR “virtual agent*” OR “embodied agent*” OR “avatar*” OR “relational agent*” OR “interactive agent*” OR “virtual character*” OR “virtual human*” OR “virtual assistant*”) OR AB(“Internet*” OR “Web*” OR “Online*” OR “tele*” OR “electronic*” OR “video*” OR “device*” OR “digital*” OR “software*” OR “mobile*” OR “technolog*” OR “e-health” OR “ehealth” OR “computer*” OR “e-treat*” OR “e-therap*” OR “mhealth” OR “m-health” OR “distance counsel*” OR “cybercounsel*” OR “cyber-counsel*” OR “cyber-treat*” OR “text-messag*” OR “textmessag*” OR “text messag*” OR “SMS*” OR “texting*” OR “short message service*” OR “smartphone*” OR “cell-phone*” OR “cellphone*” OR “cellular phone*” OR “blended*” OR “handheld device*” OR “hand held device*” OR “iPad*” OR “iPhone*” OR “email*” OR “e-mail*” OR “sensor*” OR “wearable*” OR “social media*” OR “social network*” OR “e-counsel*” OR “ecounsel*” OR “palmtop*” OR OR “telephone*” OR “WhatsApp” OR “Twitter” OR “Facebook” OR “Instagram” OR “forum” OR “chat*” OR “virtual reality*” OR “virtual-reality*” OR “avatar*” OR “Conversational agent*” OR “virtual coach” OR “virtual agent*” OR “embodied agent*” OR “avatar*” OR “relational agent*” OR “interactive agent*” OR “virtual character*” OR “virtual human*” OR “virtual assistant*”)) AND (DE “Asthma” OR DE “sleep apnea” OR DE “Chronic obstructive pulmonary disease” OR DE “Pulmonary Emphysema” OR TX(“Asthma*” OR “sleep apn*” OR “OSA*” OR **“**hypopnea*” OR “hypopnea*” OR “sleep disordered breath*” OR “COPD” OR “COAD” OR “chronic obstructive*” OR “chronic airflow obstruct*” OR “emphysema*” OR “chronic bronchitis” OR “chronic airway obstruct*” OR “obstructive pulmonary disease*” OR “obstructive respiratory disease*” OR “obstructive respiratory tract disease”))

Filters:

- Publication Year: 2000-2018
- Language: English

Pubmed

("Treatment Adherence and Compliance"[Mesh:NoExp] OR "Patient Compliance"[Mesh] OR “Patient Dropouts”[Mesh] OR (fidelity[tiab] OR complian*[tiab] OR non-complian*[tiab] OR noncomplian*[tiab] OR adheren*[tiab] OR non-adheren*[tiab] OR nonadheren*[tiab] OR dropout*[tiab] OR drop-out*[tiab] OR no-show*[tiab] OR noshow*[tiab] OR attend*[tiab] OR non-attend*[tiab] OR nonattend*[tiab] OR absence*[tiab] OR absent*[tiab] OR non-appear*[tiab] OR nonappear*[tiab]))AND ("Telemedicine"[Mesh] OR "Mobile Applications"[Mesh] OR "Social Media"[Mesh] OR "Therapy, Computer-Assisted"[Mesh:NoExp] OR "Drug Therapy, Computer-Assisted"[Mesh:NoExp] OR "Telecommunications"[Mesh:NoExp] OR "Electronic Mail"[Mesh] OR "Videoconferencing"[Mesh] OR "Cell Phone"[Mesh] OR "Distance Counseling"[Mesh] OR “Wearable Electronic Devices”[Mesh] OR “virtual reality”[Mesh] OR (internet*[tiab] OR web*[tiab] OR online*[tiab] OR computer*[tiab] OR electronic*[tiab] OR digital*[tiab] OR ehealth[tiab] OR e-health[tiab] OR e-treat*[tiab] OR e-therap*[tiab] OR mhealth[tiab] OR m-health[tiab] OR distance counsel*[tiab] OR cybercounsel*[tiab] OR cyber-counsel*[tiab] OR text-messag*[tiab] OR textmessag*[tiab] OR text messag*[tiab] OR SMS*[tiab] OR texting*[tiab] OR short message service*[tiab] OR mobile*[tiab] OR smartphone*[tiab] OR cell-phone*[tiab] OR cellphone*[tiab] OR cellular phone*[tiab] OR blended*[tiab] OR software app*[tiab] OR handheld device*[tiab] OR hand held device*[tiab] OR iPad*[tiab] OR iPhone*[tiab] OR email*[tiab] OR e-mail*[tiab] OR sensor*[tiab] OR wearable*[tiab] OR monitoring[tiab] OR social media*[tiab] OR social network*[tiab] OR e-counsel*[tiab] OR ecounsel*[tiab] OR palmtop*[tiab] OR telephone*[tiab] OR WhatsApp[tiab] OR Twitter[tiab] OR Facebook[tiab] OR Instagram[tiab] OR forum[tiab] OR chat*[tiab] OR virtual reality*[tiab] OR virtual-reality*[tiab] OR avatar*[tiab] OR Conversational agent*[tiab] OR virtual coach[tiab] OR virtual agent*[tiab] OR embodied agent*[tiab] OR avatar*[tiab] OR relational agent*[tiab] OR interactive agent*[tiab] OR virtual character*[tiab] OR virtual human*[tiab] OR virtual assistant*[tiab] OR tele-health [tiab] OR telehealth[tiab] OR tele-medicine[tiab] OR telemedicine[tiab] OR tele-care[tiab] OR telecare[tiab] OR tele-psychiatry[tiab] OR telepsychiatry[tiab] OR tele-guid*[tiab] OR teleguid*[tiab] OR tele-based[tiab] OR tele-deliver*[tiab] OR teledeliver*[tiab] OR tele-treat*[tiab] OR teletreat*[tiab] OR tele-therap*[tiab] OR telethera*[tiab] OR tele-intervention*[tiab] OR tele-counsel*[tiab] OR telecounsel*[tiab] OR tele-assist*[tiab] OR teleprevent*[tiab] OR tele-conferenc*[tiab] OR teleconferenc*[tiab] OR tele-monit*[tiab] OR telemonit*[tiab] OR tele-communicat*[tiab] OR telecommunicat*[tiab] OR tele-application*[tiab] OR tele-consult*[tiab] OR teleconsult*[tiab] OR video-guid*[tiab] OR videoguid*[tiab] OR video-mediated[tiab] OR video-based[tiab] OR videobased[tiab] OR video-deliver*[tiab] OR video-treat*[tiab] OR video-therap*[tiab] OR videothera*[tiab] OR video-intervention*[tiab] OR video-counsel*[tiab] OR video-assist*[tiab] OR video-conferenc*[tiab] OR videoconferenc*[tiab] OR video-monit*[tiab] OR videomonit*[tiab] OR video-communicat*[tiab] OR videocommunicat*[tiab] OR video-remind*[tiab] OR video-administered*[tiab] OR video-aided[tiab] OR video-application*[tiab] OR video-consult*[tiab] OR videoconsult*[tiab] OR video-enabled[tiab])) AND (“Asthma”[Mesh] OR “Sleep Apnea, Obstructive”[Mesh:NoExp] OR “Pulmonary Disease, Chronic Obstructive"[Mesh] OR “sleep apnea syndromes”[Mesh:NoExp] OR (Asthma*[tiab] OR sleep apn*[tiab] OR OSA*[tiab] OR hypopnea*[tiab] OR hypopnea*[tiab] OR sleep disordered breath*[tiab] OR sleep-disordered breath*[tiab] OR COPD[tiab] OR COAD[tiab] OR chronic obstructive*[tiab] OR chronic airflow obstruct*[tiab] OR emphysema*[tiab] OR chronic bronchitis[tiab] OR chronic airway obstruct*[tiab] OR obstructive pulmonary disease*[tiab] OR obstructive respiratory disease*[tiab] OR obstructive respiratory tract disease*[tiab]))

Filters:

- Publication Year: 2000-2018
- Language: English or Dutch
- Availability of full-text article
- Species: human

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('patient compliance'/exp OR 'adherence'/exp OR 'dropouts'/exp OR 'patient dropout'/exp OR 'patient attendance'/exp OR ('fidelity':ab,ti,kw OR 'complian*':ab,ti,kw OR 'non-complian*':ab,ti,kw OR 'noncomplian*':ab,ti,kw OR 'adheren*':ab,ti,kw OR 'non-adheren*':ab,ti,kw OR 'nonadheren*':ab,ti,kw OR 'dropout*':ab,ti,kw OR 'drop-out*':ab,ti,kw OR 'no-show*':ab,ti,kw OR 'noshow*':ab,ti,kw OR 'attend*':ab,ti,kw OR 'non-attend*':ab,ti,kw OR 'nonattend*':ab,ti,kw OR 'absence*':ab,ti,kw OR 'absent*':ab,ti,kw OR 'non-appear*':ab,ti,kw OR 'nonappear*':ab,ti,kw)) AND ('telemedicine'/exp OR 'telehealth'/exp OR 'e-mail'/exp OR 'mobile phone'/exp OR 'social media'/exp OR 'teleconference'/exp OR 'text messaging'/exp OR 'videoconferencing'/exp OR 'mobile application'/exp OR 'e-counseling'/exp OR 'digital technology'/exp OR 'mobile device'/exp OR 'iphone'/exp OR 'ipad'/exp OR 'computer assisted therapy'/de OR 'monitoring'/exp OR 'personal digital assistant'/exp OR 'wearable sensor'/exp OR 'wearable device'/exp OR 'wearable technology'/exp OR 'virtual reality'/exp OR 'facebook'/exp OR 'twitter'/exp **OR** ('internet*':ab,ti,kw OR 'web*':ab,ti,kw OR 'online*':ab,ti,kw OR 'tele*':ab,ti,kw OR 'video*':ab,ti,kw OR 'computer*':ab,ti,kw OR 'electronic*':ab,ti,kw OR 'digital*':ab,ti,kw OR 'ehealth':ab,ti,kw OR 'e-health':ab,ti,kw OR 'e-treat*':ab,ti,kw OR 'e-therap*':ab,ti,kw OR 'mhealth':ab,ti,kw OR 'm-health':ab,ti,kw OR 'distance counsel*':ab,ti,kw OR 'cybercounsel*':ab,ti,kw OR 'cyber-counsel*':ab,ti,kw OR 'cyber-treat*':ab,ti,kw OR 'text-messag*':ab,ti,kw OR 'textmessag*':ab,ti,kw OR 'text messag*':ab,ti,kw OR 'SMS*':ab,ti,kw OR 'texting*':ab,ti,kw OR 'short message service*':ab,ti,kw OR 'mobile*':ab,ti,kw OR 'smartphone*':ab,ti,kw OR 'cell-phone*':ab,ti,kw OR 'cellphone*':ab,ti,kw OR 'cellular phone*':ab,ti,kw OR 'blended*':ab,ti,kw OR 'software app*':ab,ti,kw OR 'handheld device*':ab,ti,kw OR 'hand held device*':ab,ti,kw OR 'iPad*':ab,ti,kw OR 'iPhone*':ab,ti,kw OR 'email*':ab,ti,kw OR 'e-mail*':ab,ti,kw OR 'sensor*':ab,ti,kw OR 'wearable*':ab,ti,kw OR 'monitoring':ab,ti,kw OR 'social media*':ab,ti,kw OR 'social network*':ab,ti,kw OR 'e-counsel*':ab,ti,kw OR 'ecounsel*':ab,ti,kw OR 'palmtop*':ab,ti,kw OR 'telephone*':ab,ti,kw OR 'WhatsApp':ab,ti,kw OR 'Twitter':ab,ti,kw OR 'Facebook':ab,ti,kw OR 'Instagram':ab,ti,kw OR 'forum':ab,ti,kw OR 'chat*':ab,ti,kw OR 'virtual reality*':ab,ti,kw OR 'virtual-reality*':ab,ti,kw OR 'avatar*':ab,ti,kw OR 'Conversational agent*':ab,ti,kw OR 'virtual coach':ab,ti,kw OR 'virtual agent*':ab,ti,kw OR 'embodied agent*':ab,ti,kw OR 'avatar*':ab,ti,kw OR 'relational agent*':ab,ti,kw OR 'interactive agent*':ab,ti,kw OR 'virtual character*':ab,ti,kw OR 'virtual human*':ab,ti,kw OR 'virtual assistant*':ab,ti,kw)) AND ('Asthma'/exp OR 'chronic bronchitis'/exp OR 'chronic obstructive lung disease'/exp OR 'sleep disordered breathing'/de OR 'sleep apnea syndrome'/exp OR ('Asthma*':ab,ti,kw OR 'sleep apn*':ab,ti,kw OR 'hypopnea*':ab,ti,kw OR 'hypopnoea*':ab,ti,kw OR 'sleep disordered breath*':ab,ti,kw OR 'sleep-disordered breath*':ab,ti,kw OR 'OSA*':ab,ti,kw OR 'COPD':ab,ti,kw OR 'COAD':ab,ti,kw OR 'chronic obstructive*':ab,ti,kw OR 'chronic airflow obstruct*':ab,ti,kw OR 'emphysema*':ab,ti,kw OR 'chronic bronchitis':ab,ti,kw OR 'chronic airway obstruct*':ab,ti,kw OR 'obstructive pulmonary disease*':ab,ti,kw OR 'obstructive respiratory disease*':ab,ti,kw OR 'obstructive respiratory tract disease*':ab,ti,kw)) AND ([article]/lim OR [article in press]/lim OR [editorial]/lim OR [letter]/lim OR [review]/lim) AND ([dutch]/lim OR [english]/lim) AND [humans]/lim AND [embase]/lim AND [2000-2018]/py AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)

Filters:

- Publication Year: 2000-2018
- EMBASE only
- Species: humans
- Language: English or Dutch
- Article type: article in press, article, editorial, review

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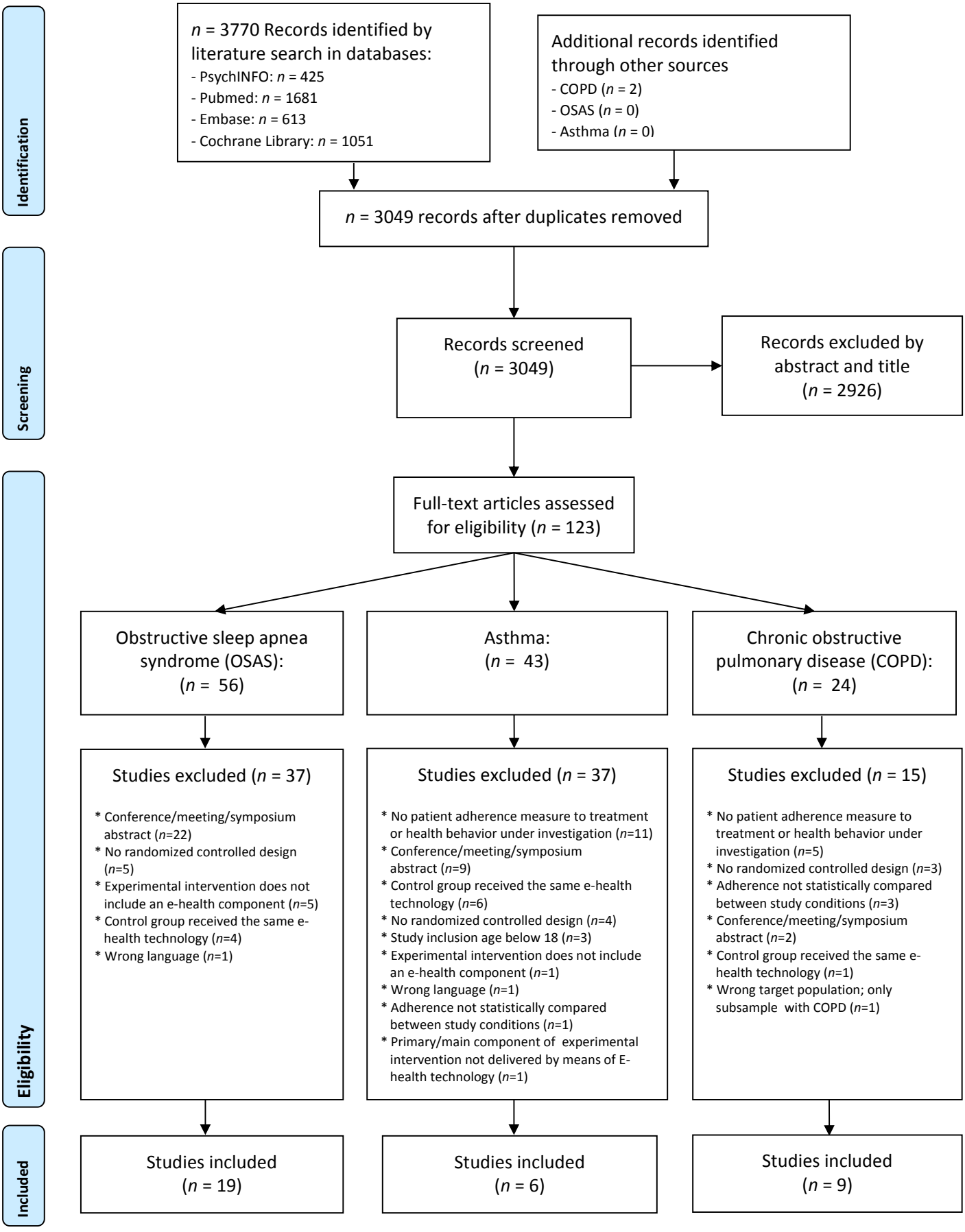
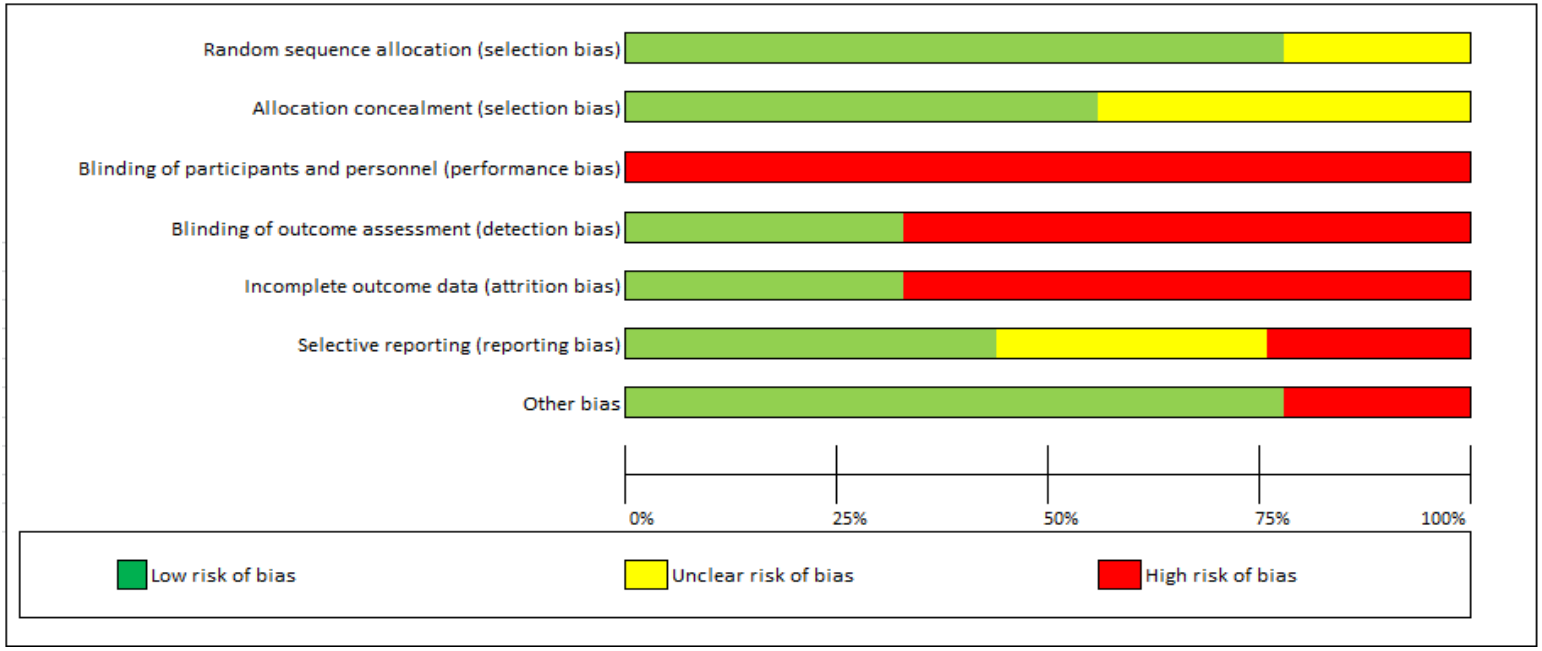
([mh “patient compliance”] OR [mh^“treatment adherence and compliance”] OR [mh “Patient dropouts”] OR (‘fidelity’:ab,ti,kw OR ‘complian*’:ab,ti,kw OR ‘non-complian*’:ab,ti,kw OR ‘noncomplian*’:ab,ti,kw OR ‘adheren*’:ab,ti,kw OR ‘non-adheren*’:ab,ti,kw OR ‘nonadheren*’:ab,ti,kw OR ‘dropout*’:ab,ti,kw OR ‘drop-out*’:ab,ti,kw OR ‘no-show*’:ab,ti,kw OR ‘noshow*’:ab,ti,kw OR ‘attend*’:ab,ti,kw OR ‘non-attend*’:ab,ti,kw OR ‘nonattend*’:ab,ti,kw OR ‘absence*’:ab,ti,kw OR ‘absent*’:ab,ti,kw OR ‘non-appear*’:ab,ti,kw OR ‘nonappear*’:ab,ti,kw)) AND ([mh “Telemedicine"] OR [mh "Mobile Applications"] OR [mh "Social Media"] OR [mh^"Therapy, Computer-Assisted"] OR [mh"Drug Therapy, Computer-Assisted"] OR [mh "Telecommunications"] OR [mh "Electronic Mail"] OR [mh "Videoconferencing"] OR [mh "Cell Phone"] OR [mh "Distance Counseling"] OR [mh “Wearable Electronic Devices”] OR [mh “virtual reality”] **OR** (‘internet*’:ab,ti,kw OR ‘web*’:ab,ti,kw OR ‘online*’:ab,ti,kw OR ‘tele*’:ab,ti,kw OR ‘video*’:ab,ti,kw OR ‘computer*’:ab,ti,kw OR ‘electronic*’:ab,ti,kw OR ‘digital*’:ab,ti,kw OR ‘ehealth’:ab,ti,kw OR ‘e-health’:ab,ti,kw OR ‘e-treat*’:ab,ti,kw OR ‘e-therap*’:ab,ti,kw OR ‘mhealth’:ab,ti,kw OR ‘m-health’:ab,ti,kw OR ‘distance counsel*’:ab,ti,kw OR ‘cybercounsel*’:ab,ti,kw OR ‘cyber-counsel*’:ab,ti,kw OR ‘cyber-treat*’:ab,ti,kw OR ‘text-messag*’:ab,ti,kw OR ‘textmessag*’:ab,ti,kw OR ‘text messag*’:ab,ti,kw OR ‘SMS*’:ab,ti,kw OR ‘texting*’:ab,ti,kw OR ‘short message service*’:ab,ti,kw OR ‘mobile*’:ab,ti,kw OR ‘smartphone*’:ab,ti,kw OR ‘cell-phone*’:ab,ti,kw OR ‘cellphone*’:ab,ti,kw OR ‘cellular phone*’:ab,ti,kw OR ‘blended*’:ab,ti,kw OR ‘software app*’:ab,ti,kw OR ‘handheld device*’:ab,ti,kw OR ‘hand held device*’:ab,ti,kw OR ‘iPad*’:ab,ti,kw OR ‘iPhone*’:ab,ti,kw OR ‘email*’:ab,ti,kw OR ‘e-mail*’:ab,ti,kw OR ‘sensor*’:ab,ti,kw OR ‘wearable*’:ab,ti,kw OR ‘monitoring’:ab,ti,kw OR ‘social media*’:ab,ti,kw OR ‘social network*’:ab,ti,kw OR ‘e-counsel*’:ab,ti,kw OR ‘ecounsel*’:ab,ti,kw OR ‘palmtop*’:ab,ti,kw OR ‘telephone*’:ab,ti,kw OR ‘WhatsApp’:ab,ti,kw OR ‘Twitter’:ab,ti,kw OR ‘Facebook’:ab,ti,kw OR ‘Instagram’:ab,ti,kw OR ‘forum’:ab,ti,kw OR ‘chat*’:ab,ti,kw OR ‘virtual reality*’:ab,ti,kw OR ‘virtual-reality*’:ab,ti,kw OR ‘avatar*’:ab,ti,kw OR ‘Conversational agent*’:ab,ti,kw OR ‘virtual coach’:ab,ti,kw OR ‘virtual agent*’:ab,ti,kw OR ‘embodied agent*’:ab,ti,kw OR ‘avatar*’:ab,ti,kw OR ‘relational agent*’:ab,ti,kw OR ‘interactive agent*’:ab,ti,kw OR ‘virtual character*’:ab,ti,kw OR ‘virtual human*’:ab,ti,kw OR ‘virtual assistant*’:ab,ti,kw)) AND ([mh“Asthma”] OR [mh^“obstructive sleep apnea”] OR [mh“Chronic obstructive pulmonary disease”] OR [mh^“sleep apnea syndromes”] OR (‘Asthma*’:ab,ti,kw OR ‘sleep apn*’:ab,ti,kw OR ‘hypopnea*’:ab,ti,kw OR ‘hypopnoea*’:ab,ti,kw OR ‘sleep disordered breath*’:ab,ti,kw OR ‘sleep-disordered breath*’:ab,ti,kw OR ‘OSA*’:ab,ti,kw OR ‘COPD’:ab,ti,kw OR ‘COAD’:ab,ti,kw OR ‘chronic obstructive*’:ab,ti,kw OR ‘chronic airflow obstruct*’:ab,ti,kw OR ‘emphysema*’:ab,ti,kw OR ‘chronic bronchitis’:ab,ti,kw OR ‘chronic airway obstruct*’:ab,ti,kw OR ‘obstructive pulmonary disease*’:ab,ti,kw OR ‘obstructive respiratory disease*’:ab,ti,kw OR ‘obstructive respiratory tract disease*’:ab,ti,kw))

Filters:

- Publication year 2000-2018
- Word variations have been searched
- Limited to trials only

Figure 1: PRISMA flowchart describing study identification and selection process




Random sequence allocation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias

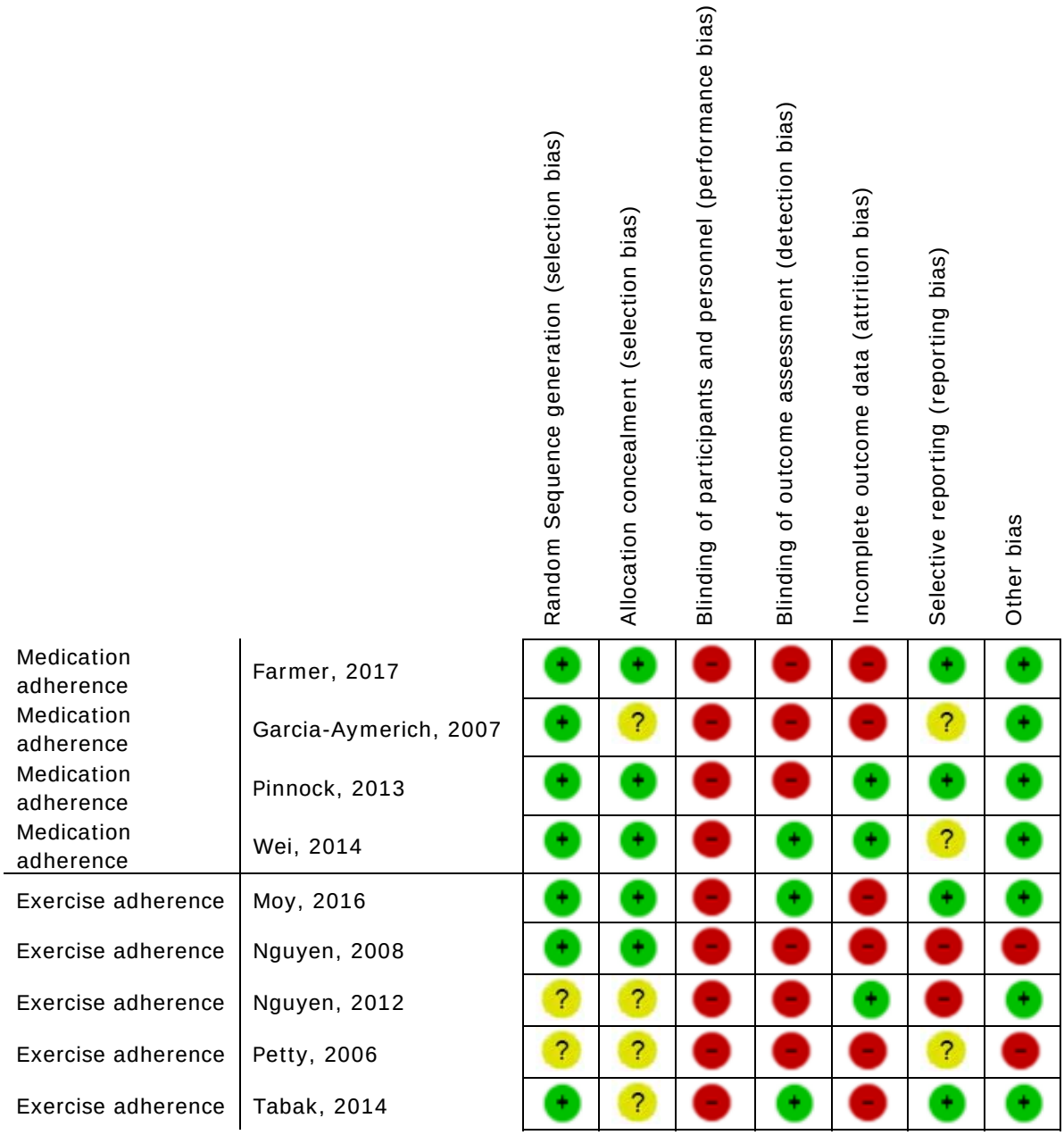

Random Sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Medication adherence
Farmer, 2017
Medication adherence
Garcia-Aymerich, 2007
Medication adherence
Pinnock, 2013
Medication adherence
Wei, 2014
Exercise adherence
Moy, 2016
Exercise adherence
Nguyen, 2008
Exercise adherence
Nguyen, 2012
Exercise adherence
Petty, 2006
Exercise adherence
Tabak, 2014

Table 1: An overview of the relevant characteristics of the included studies on treatment adherence (*n* = 4).

Study reference #1	
Authors	Farmer et al.
Year of publication	2014
Country	UK
Study design	
Study conditions (*N*)	- UC (56) - Fully automated internet-linked, tablet computer-based system of monitoring and self-management support (EDGE) (110)
Measurements	- Baseline - 3 Months - 6 months - 12 months
Study population	
Age (*M, SD*)	- 69.8 ± 10.6 - 69.8 ± 9.1
Gender (% female)	- 39.3 - 38.2
Target population and recruitment strategy	Adults with moderate to very severe COPD, as recruited from a variety of settings encompassing primary and secondary care as well as community services.
Eligibility criteria	*Inclusion criteria:* - aged ≥ 40 years - diagnosis of COPD - smoking-pack history >10 pack-years - medical research council dyspnea score ≥ 2 - In case of inability to provide a spirometry reading at baseline: a clinical decision of trial suitability and prior clinical evidence of COPD - Registered with a GP and having had an exacerbation of COPD requiring home treatment or hospital admission in the previous year or have been referred for pulmonary rehabilitation *Exclusion criteria:* - Having other significant lung disease or chronic heart failure, i.e. New York Heart Association classification system as severe (grade IV)) or a life expectancy of <3 months - cognitive impairment - Living in areas without access to an Internet-enabled mobile phone network, hence unable to transmit and receive data.
Diagnostic procedure	Confirmed diagnosis of COPD defined as a FEV1, post-bronchodilation of <70%, and a predicted ratio of FEV1 to forced vital capacity of <0.70.
Interventions	
E-health condition	
Type technology	Internet-linked, tablet computer-based system, Bluetooth-enabled pulse oximeter, telephone or SMS (if needed, see 'type intervention'), software modules including personalized videos
Type intervention	Participants were provided an Android tablet computer and a Bluetooth-enabled pulse oximeter, by which they received a fully automated Internet-linked, tablet computer-based system of monitoring and self-management support (EDGE). EDGE was designed to help patients identify exacerbations and to monitor their condition, to help support good compliance with inhaled medication, and to support psychological well-being. Patients were instructed that EDGE was not a replacement for usual clinical care, and that in the event of deterioration in their health they should contact their GP or community respiratory nurse as usual. 1) Monitoring: Patients completed the symptom diary and recorded oxygen saturation and heart rate with the pulse oximeter on a daily basis. Also, every 4 weeks, the platform presented mood screening questionnaires. Data of an initial 6-week run-in period were used to calculate individual safety threshold regarding patients' oxygen saturation, heart rate, and symptom scores. One of 3 respiratory clinicians reviewed this data twice weekly, and dealt with safety alerts in case there were any. Also, if data appeared to reflect any clinically important change in the data, the patient was contacted either via message or telephone. 2) Self-management support modules.

	- Videos tailored to the patient's entries in the symptom diary or answers to the mood-screening questionnaires. These videos provide additional self-management support, and included inhaler techniques, pulmonary rehabilitation exercises, educational advice on managing COPD, smoking cessation, diet, and self-management techniques for breathlessness. - Personalized plans for self-management and treating an exacerbation of their condition. - Facility to receive a brief message from their respiratory nurse.
Duration & frequency	12-month intervention with: - daily monitoring of symptoms, oxygen saturation, and heart rate, as well as monthly mood monitoring. - contact (message or telephone) with clinician in case of meeting safety thresholds on any of the above - self-management support modules (variable frequency and duration).
Control condition	Participants were provided with all the information given to those allocated to EDGE (see 'type intervention'), but without the use of a tablet computer or the facility for daily monitoring of symptoms and physiological variables. Participants were provided with leaflets based on those produced by the Oxfordshire Community Respiratory service. Personalized information intended to help patients understand their condition, including how and when to use their medications, and a self-management plan with written guidelines on what to do and whom to contact if they experience an exacerbation and dietary advice is provided.
Outcome(s)	
Assessment adherence	Self-reported medication adherence as measured with the Medication Adherence Report Schedule.
Operationalization adherence	Not specified
Results	
Effects (*M, SD*) on adherence, incl. significance (*p*-values)	12-month results: Non-sign. (p=.77): 0.33 ± 3.65 VS 0.17 ± 2.47
Dropout (%)	15.07
Other	
Source of funding and competing interest	The publication presented independent research supported from the Department of Health and Wellcome Trust through the Health Innovation Challenge (HIC) Fund commissioned by the Health Innovation Challenge Fund (HICF-1010-032), a parallel funding partnership between the Wellcome Trust and the Department of Health. The views expressed in this publication are those of the authors and not necessarily those of the Department of Health or Wellcome Trust. The trial was sponsored by the University of Oxford. First and last author received funding from the Oxford National Institute for Health Research (NIHR) Biomedical Research Centre (BRC). Also, first author was an NIHR Senior Investigator.
Study limitations and other comments	-

Study reference #2	
Authors	Garcia-Aymerich et al.
Year of publication	2007
Country	Spain
Study design	
Study conditions (*N*)	- UC (n=69) - UC + Integrated care (n=44) Analyses conducted on subsample: - n=41 - n=21
Measurements	- Baseline - 6 Months - 12 Months
Study population	
Age (*M, SD*)	73.0 ± 0.8
Gender (% female)	14.0
Target population and recruitment strategy	Patients with COPD, as recruited in tertiary hospital immediately after hospital discharge for an episode of exacerbation.
Eligibility criteria	*Inclusion criteria:* - An episode of exacerbation requiring hospitalization for more than 48 hours *Exclusion criteria:* - Not living in the healthcare area or living in a nursing home - Lung cancer or other advanced malignancies - Logistic limitations due to extremely poor social condition, illiteracy, or no phone access at home - Extremely severe neurological or cardiovascular co-morbidities
Diagnostic procedure	COPD patients discharged at tertiary hospital after admission because of an episode of exacerbation, diagnostic not further specified. FEV 1 and FEV1% predicted measures available at baseline.
Interventions	
E-health condition	
Type technology	Telephone, Information and Communication Technologies (ICT) platform including a web-based call center.
Type intervention	Usual care (see 'control condition') plus integrated care comprising 4 elements: 1) Comprehensive assessment of patient at discharge 2) A 2-hour educational session on self-management of the disease administered by a specialized nurse. Patients were taught to make a phone call to the call center in case of clinical deterioration. Accordingly, specialized nurse (i.e. case manager) either solved the problem by phone or triggered a home visit. 3) Individually tailored care plan following international guidelines. Weekly phone calls during the first month after discharge, as well as 3- and 9-month phone call in order to reinforce self-management strategies. 4) Access to the specialized nurse at the hospital, caregivers and primary care professionals during the follow-up period through an Information and Communication Technologies (ICT) platform including a web-based call center.
Duration & frequency	12-months with weekly phone calls in the first month, phone call at month 3 and 9, and additional calls if needed
Control condition	Pharmacological prescriptions at discharge and in-hospital treatment followed the standard protocols of the center.
Outcome(s)	
Assessment adherence	1) Medication Adherence Scale (MAS) 2) Inhaler Adherence Scale (IAS) 3) Observed skills for administration of inhaled drugs according to Spanish guidelines for the use of inhaled drugs
Operationalization adherence	1) % of adherers to oral treatment (MAS adherence defined by having all correct answers in the scale). 2) % of adherers to inhaled treatment (IAS adherence defined by having all correct answers in the scale). 3) Correct inhaler maneuver (%)
Results	
Effects (*M, SD*) on adherence, incl.	12-Month results: 1) Non-sign. (p=.57): 85.0% VS 90.0%

significance (*p*-values)	2) Sign. (p=.009): 37.0% VS 71.0% 3) Sign. (p<.001): 24.0% VS 86.0%
Dropouts (%)	45.14
Other	
Source of funding and competing interest	Supported in part by Linkcare eTEN C517435 from the European Union; Marato de TV3; Comissionat per a S4 i Recerca de la Generalitat de Catalunya (SGR-00386) and Red Respira—ISCIII —RTIC-03/11 and Red Telemedicina ISCIII—RTIC —03/117. Also, main author had researcher contract from the Instituto de Salud Carlos III (CP05/00118), Ministry of Health, Spain. Finally, fourth author was research fellow supported by CHRONIC (IST-1999/12158) from the European Union.R3
Study limitations and other comments	Small sample size and high proportion of patients lost to follow-up in both study conditions (47% and 40%).

Study reference #3	
Authors	Pinnock et al.
Year of publication	2013
Country	UK
Study design	
Study conditions (*N*)	- UC (n=69) - UC + Integrated care (n=44) Analyses conducted on subsample: - n=41 - n=21
Measurements	-Baseline - 3 months - 6 months - 9 months - 12 months
Study population	
Age (*M*, *SD*)	- 68.4 ± 8.4 - 69.4 ± 8.8
Gender (% female)	- 51.0 - 59.0
Target population and recruitment strategy	Adults with ≥ admission for COPD in the last year, as recruited through community respiratory and nursing teams, databases of respiratory consultants at hospitals, and primary care practitioners.
Eligibility criteria	Inclusion criteria: - Adults who had been admitted to hospital with an exacerbation of COPD in previous year Exclusion criteria: - Other significant lung diseases - Unable to use the technology or complete the questionnaires - Advised exclusion participant's GP for other significant social or clinical problems
Diagnostic procedure	Diagnosis confirmed by the presence of chronic airflow limitation on spirometry normally performed at the baseline assessment by the research nurse trained in spirometry. COPD was confirmed if the post-bronchodilator FEV1 divided by the forced vital capacity was less than 0.7. Recordings undertaken by a specialist respiratory service within the previous 3 months were accepted if spirometry at the baseline assessment was not possible or declined.
Interventions	
E-health condition	
Type technology	Telemonitoring, telephone
Type intervention	Usual care (see 'Control condition') plus telemonitoring. Telemonitoring comprised using touch screen telemonitoring equipment that was installed in patient's homes. Patients recorded and transmitted a daily questionnaire about symptoms and use of treatment, and monitored oxygen saturation using linked validated instruments. Supporting clinical team monitored the daily online data. Algorithms, based on the symptom score, alerted the clinical monitoring team if daily readings had not been submitted or if a score of 4 or 5 had been recorded. The action taken was the responsibility of the monitoring clinician who normally knew the patient and was able to interpret the monitoring data in the light of the patient's history. Typically, this involved contacting the patient by telephone (although the system could support a video link) and undertaking a further clinical assessment to enable a decision about further management.
Duration & frequency	1 year of telemonitoring, telephone contact as-needed (see 'type intervention')
Control condition	Clinical care based on national and international guideline recommendations: 1) Education on self-management of exacerbations, reinforced by a copy of the British Lung Foundation's booklet about living with COPD, which includes a written management plan, and an emergency supply of antibiotics and steroids were made available. 2) Care in accordance to service models in the corresponding region of Lothian, either being 2.1) dedicated respiratory physiotherapy service being available 7 days a week, 2.2) weekday service of nurse specialist, or 2.3) care as provided by GP.
Outcome(s)	
Assessment adherence	Self-report by means of Medication Adherence Report Scale (MARS).
Operationalization	Treatment adherence score as calculated as the MARS total score (range 5-25).

adherence	
Results	
Effects (*M, SD*) on adherence, incl. significance (*p*-values)	12-Month results: Non-sign. (p-value not reported): 23.7 ± 1.9 VS 24.0 ± 1.7
Dropouts (%)	19.9
Other	
Source of funding and competing interest	Support from the Chief Scientist Office of the Scottish government and NHS Lothian for the submitted work. First author was supported by a primary care research career award from the Chief Scientist's Office of the Scottish government. Second and last author were supported via NHS Lothian through the Edinburgh Health Services Research Unit. Seventh author was supported by the Commonwealth Fund, a private independent foundation based in New York City.
Study limitations and other comments	The clinical services into which the telemonitoring was integrated varied between the different Lothian regions, which may have influenced the effect of the intervention (although randomization was stratified by different Lothian regions). For example, outcomes might have been different in rural areas where telemonitoring might have had a greater effect.

Study reference #4	
Authors	Wei et al.
Year of publication	2014
Country	China
Study design	
Study conditions (*N*)	* UC (n=59) * Pharmaceutical care program (n=58) 1-month analyses based on: * n=57 * n=57 6-month analyses based on: * n=53 * n=51 1-year analyses based on: * n=45 * n=42
Measurements	* Baseline * 1 Month * 6 Months * 12 Months
Age (*M, SD*)	* 63.9 ± 6.2 * 65.2 ± 8.1
Gender (% female)	* 32.2 * 34.5
Target population and recruitment strategy	Patients with COPD, as recruited through a university medical hospital.
Eligibility criteria	Inclusion criteria: * Stable COPD (respiratory symptoms and medication unchanged for ≥4 weeks before enrollment * Post-bronchodilator FEV1 to forced vital capacity (FVC) ratio of less than 0.70 and FEV1 between 25% and 79% of predicted value * ≥ 2 consecutive visits to study hospital for the treatment of COPD * No participation in a respiratory rehabilitation in the past year * No previous diagnosis of asthma, dementia, uncontrolled psychiatric disease and severe heart, liver, and kidney disease Exclusion criteria: * Medication adherent: taking > 80% of the daily dose prescribed
Diagnostic procedure	Post-bronchodilator FEV1 to forced vital capacity (FVC) ratio of less than 0.70 and an FEV1 between 25% and 79% of predicted value.
E-health condition	
Type technology	Telephone
Type intervention	Individualized face-to-face education (5-6 sessions of 20-30 minutes) and a series of telephone counseling (maximum 12 sessions of +-10 minutes) provided by clinical pharmacists. * Education was provided individually in a structured step-by-step fashion during the clinic visit, including effective use of respiratory devices, pathophysiology of the disease, interpretation of medical testing and rationale for medication. Afterwards, medication management records for patients were established evaluating participant preferences and possible barriers to medication adherence. * The frequency of a 10-minute telephone call was based on the results of last interview (maximum reach 12 sessions, weekly call at first month in 25% patients), but generally telephone call (4-5 sessions) at the midpoint between two clinic visits. During telephone counseling, the pharmacist asked about the patient's treatment effects, clarified any misconceptions, explained the nature of any side effects and reminded patients of their next clinical appointment.
Duration & frequency	5-6 Face-to-face education sessions and additional telephone calls of approximately 10 minutes (max. 12, generally 4-5) over period of 6 months.

Control condition	General counseling (i.e. no individualized education and follow-up telephone counseling).
Assessment adherence	Pill counts plus direct interview: pharmacist asked patients to describe their regimen prescribed at their last visit by drug dosages (nr of pills) and frequency. Also, they were asked whether they had missed any medication, or changed their regimens in terms of dose and frequency. This information was checked against the dispensing information.
Operationalization adherence	% medication adherence: the number of prescribed drugs a patient took divided by the total number of prescribed drugs.
Results	
Effects (*M*, *SD*) on adherence, incl. significance (*p*-values)	1-Month results: Non-sign. (p=.14): 56.8 ± 10.6 VS 62.1 ± 9.7 6-Month results: Sign. (p=.02): 52.7 ± 21.9 VS 73.4 ± 11.1 1-Year results: Sign. (p=.04): 54.4 ± 12.5 VS 66.5 ± 8.6
Dropouts (%)	25,7
Other	
Source of funding and competing interest	-
Study limitations and other comments	-

COPD = Chronic Obstructive Pulmonary Disease; FEV1 = forced expiratory volume in 1s; GP = General Practitioner UC = Usual care

Table 2: An overview of the relevant characteristics of the included studies on exercise adherence (*n* = 5).

Study reference #1	
Authors	Moy et al.
Year of publication	2016
Country	US & Puerto Rico
Study design	
Study conditions (*N*)	* WLC (n=84) * Internet-mediated, pedometer-based walking program (n=155) Analyses conducted on subsample: * n=84 * n=154
Measurements	* Baseline * 4 Months * 12 Months
Study population	
Age (*M, SD*)	66.8 ± 8.8
Gender (% female)	6.3
Target population and recruitment strategy	Adult patients with COPD, as recruited from national patient care databases of US veterans.
Eligibility criteria	*Inclusion criteria:* * Veteran * Aged□≥□40 years * Diagnosis of COPD, emphysema, or chronic bronchitis based on administrative ICD-9 codes * Able to walk a minimum of one block * Sedentary: <□150 minutes of self-reported physical activity per week * Have a doctor or primary care provider who can give medical clearance * Regular email user (checking weekly) * Having access to a computer with an Internet connection, a USB port, and Windows XP, Vista, Windows 7, or Windows 8 * Not involved in another pedometer-based walking program. *Exclusion criteria:* * Failure to submit medical clearance form * Veterans from Veterans Integrated Service Networks-1, where another COPD study using the Taking Healthy Steps platform was actively recruiting participants * No baseline data regarding step-count * No baseline data regarding health-related quality of life
Diagnostic procedure	COPD diagnosis according to the International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code of 491.x, chronic bronchitis; 492.x, emphysema; or 496.x, chronic airway obstruction NEC). Spirometric confirmation of the COPD diagnosis was not made at study entry.
Interventions	
E-health condition	
Type technology	Internet-based platform for education, goal setting, self-monitoring and feedback, an online community forum, and a pedometer
Type intervention	4-month intervention phase: Internet-mediated pedometer-based program "*Taking Healthy Steps*": Instructions to wear the pedometer every day, weekly reminders to log into website to upload step-count data at least weekly, and access to the website. The latter has 4 key components: 1) individualized goal setting based on uploaded step counts 2) iterative feedback allowing self-monitoring of step counts 3) motivational content providing new educational tip every other day and a new motivational message each week 4) online community forum enhancing social support. 8-month maintenance phase: Instructions to continue to wear the pedometer, upload daily step counts, receiving weekly step-count goals and feedback, and access to online community forum. Participants were

	able to view the educational content and motivational messages that were provided during the intervention phase, but no longer received new content.
Duration & frequency	4-month intervention period and 8-month maintenance phase
Control condition	Instructions to wear pedometer every day, monthly reminders to log into website to upload step-count data, and asked to report all adverse events.
Outcome(s)	
Assessment adherence	Step-count data of Omron HJ-720 ITC pedometer as uploaded by means JAVA software.
Operationalization adherence	1) Mean daily step count: calculated using at least 5 days of valid data (having at least 100 steps and 8 hours of step counts recorded on a wear-day) within a period of 7 consecutive days. It was calculated within a window of +/-14 days around day 121 for 4-month values, and +/-14 days around day 366 for 12-month values. 2) Mean monthly daily step calculated by examining the data in 30-day increments. Values were used from the last valid week (at least 5 days of valid data within a period of 7 consecutive days) in each of those months.
Results	
Effects (*M*, *SD*) on adherence, incl. significance (*p*-values)	1) 12-Month results: Non-sign. (p=.73): 163 VS 270 2) 4-Month results: Sign. (p<.001) 8-Month-data: Non-sign. (p=.28) 12-Month data: Non-sign. (p=.82)
Dropouts (%)	0.4%
Other	
Source of funding and competing interest	Funding: Department of Veterans Affairs, Health Services Research and Development Service (Grant IIR 09-366, Richardson); Department of Veterans Affairs, Rehabilitation Research and Development Service (Career Development Award, F6847W, Moy); and NIH National Heart, Lung and Blood Institute (Grant T32 HL007749-20, Martinez).
Study limitations and other comments	Spirometric confirmation of the COPD diagnosis was not made at study entry.

Study reference #2	
Authors	Nguyen et al.
Year of publication	2008
Country	US
Study design	
Study conditions (*N*)	* Face to face dyspnea self-management program (n=26) * Internet-based dyspnea self-management program (n=24) Analyses conducted on subsample: * n=20 * n=19
Measurements	* Baseline * 3 Months * 6 Months
Study population	
Age (*M, SD*)	69.5 ± 8.5
Gender (% female)	43.6
Target population and recruitment strategy	Patients with moderate to severe COPD, as recruited through a combination of Web-based (i.e. email distribution lists and online support groups for patients with COPD and older adults) and non-Web-based sources (i.e. chest clinic referrals, letter mailings to university clinic patients with a COPD-related diagnosis, announcements at Better Breathers support groups and pulmonary rehabilitation programs, and newspaper advertisements.
Eligibility criteria	*Inclusion criteria:* * Diagnosis of COPD and being clinically stable for at least 1 month * Spirometry results showing at least mild obstructive disease defined as post-bronchodilator FEV1 to forced vital capacity (FVC) ratio < 0.70 with FEV1 < 80% predicted, or FEV1/FVC < 0.60 with FEV1 > 80% predicted * Activities of daily living limited by dyspnea * Use of the Internet and/or checking email ≥ per week with a Windows operating system * Oxygen saturation > 85% on room air or ≤ 6 L/min of nasal oxygen at the end of a 6-minute walk test *Exclusion criteria:* * Any active symptomatic illness * Participated in other pulmonary rehabilitation program in the last 12 months * Current participation in > 2 days of supervised maintenance exercise.
Diagnostic procedure	A diagnosis of COPD (not further specified), spirometry results showing at least mild obstructive disease defined as post-bronchodilator FEV1 to forced vital capacity (FVC) ratio < 0.70 with FEV1 < 80% predicted, or FEV1/FVC < 0.60 with FEV1 > 80% predicted.
Interventions	
E-health condition	
Type technology	Web-based portal (training and self-monitoring, interactive modules), PDA (self-monitoring), e-mails (feedback and reinforcement), live group chat sessions and bulletin board.
Type intervention	Internet-based dyspnea self-management program: 1) Dyspnea and exercise consultation (1-1.5 hours) provided in individual face-to-face session, and by means of training on website and PDA. 2) Unsupervised independent exercise: endurance (4 times/week, 30 min/session) and arm strengthening (3 times/week) exercise program. 3) Collaborative self-monitoring of exercise and respiratory symptoms (i.e. PDA and web diary) and reinforcement of dyspnea management strategies by e-mails, weekly in month 1; biweekly in months 2-6). Specifically, nurses reviewed data to provide individualized feedback & reinforcement by e-mail. Furthermore, participants were encouraged to communicate exercise goals and progress to the nurse by using a Web-based goal-setting tool. Also, automated e-mail alerts were sent to nurses based on real-time symptom (worsening symptoms) and exercise (reports of not performing exercise for ≥ 3 consecutive days).

	4) Structured education of dyspnea management strategies, skills training, and peer interactions (6 1-hour sessions, by means of interactive web modules, live chat sessions by study nurses, and a bulletin board.
Duration & frequency	6 months: 1) 1-1.5 hours consultation 2) Endurance (4 times/ week, 30 min./ session) and arm strengthening (3 times/week) exercise program 3) self-monitoring and reinforcement: weekly in month 1, biweekly in months 2-6. 4) Education, skills training, and peer interactions: six 1-hour sessions
Control condition	Face-to-face dyspnea self-management program: 1) Dyspnea and exercise consultation (1-1.5 hours) as provided in individual face-to-face session 2) Unsupervised independent exercise: endurance (4 times/week, 30 min/session) and arm strengthening (3 times/week) exercise program. 3) Collaborative self-monitoring of exercise and respiratory symptoms (i.e. paper diaries) and reinforcement of dyspnea management strategies by telephone calls (5-10 minutes, weekly in month 1; biweekly in months 2-6) 4) Structured education of dyspnea management strategies, skills training, and peer interactions (6 1-hour sessions, by means of paper modules and face-to-face group sessions)
Outcome(s)	
Assessment adherence	Self-reported frequency and duration (5-,10-, 20-, 30-, 40-, 60-minute increments) of endurance, strengthening, and stretching exercises for a typical week during the last 4 weeks.
Operationalization adherence	Exercise adherence: Total minutes per week of exercise for 3 types of exercise: 1) Endurance 2) Strengthening 3) Stretching These were calculated by multiplying the total minutes per week with each type of exercise by session time in minutes.
Results	
Effects (*M, SD*) on adherence, incl. significance (*p*-values)	3-Month results: 1) 141 ± 100 VS 173 ± 130 2) 56 ± 66 VS 53 ± 70 6-Month results: 1) 121 ± 81 VS 128 ± 111 2) 53 ± 59 VS 34 ± 37 Between-group results: 1) Non-sign. (p=.22) 2) Non-sign. (p=.54) *Note: repeated measures ANOVA only allowed for testing the main effect of time (3 levels), treatment group (2 levels), and the interaction of these.*
Dropouts (%)	24%
Other	
Source of funding and competing interest	Study was supported in part by Robert Wood Johnson Health e-Technologies Initiative grant RWJ49153 to Dr. Carrieri-Kohlman, General Clinical Research Centers at the University of Washington (MO1-RR-000037) and UC San Francisco (MO1-RR-00079) and Grant Number 1KL2RR025015-01 from the National Center for Research Resources (NCRR).
Study limitations and other comments	Due to the technical and usability challenges with the Web and PDA application and differential participant attrition, study was terminated before reaching our sample target. Study participants were primarily Caucasian and generally well educated, reflecting demographics of early Internet adopters. These characteristics make the findings less generalizable to the broader population of COPD patients.

Study reference #3	
Authors	Nguyen et al.
Year of publication	2013
Country	US
Study design	
Study conditions (*N*)	* General health education attention control (n=41) * Face to face dyspnea self-management program (n=41) * Internet-based dyspnea self-management program (n=43)
Measurements	* Baseline * 3 Months * 6 Months * 12 Months
Study population	
Age (*M, SD*)	68.7 ± 9.7
Gender (% female)	46.0%
Target population and recruitment strategy	Adults with COPD, as recruited through a combination of online and off-line sources.
Eligibility criteria	*Inclusion criteria:* * Aged > 40 years * Diagnosis of COPD which is clinically stable (including medications) for ≥1 month * Spirometry results showing at least mild obstructive disease: post bronchodilator EV1/forced vital capacity (FVC) ratio <0.70 with FEV1<80% predicted or post-bronchodilator FEV1/FVC ratio <0.60 with FEV1>80% predicted * Activities of daily living limited by dyspnea * Ability to speak English * Actively using a computer and the Internet * Receiving supplemental oxygen acceptable if O2 saturation can be maintained at >80% on <6L/min of nasal oxygen; * Understands how to and is able to rate their shortness of breath during exercise; *Exclusion criteria:* • Active symptomatic illness (e.g., cancer, left heart failure, ischemic heart disease with known coronary artery or valvular heart disease, psychiatric illness, and neuro-muscular disease). * Participation in pulmonary rehabilitation training in last 6 months * Currently participating in >2 days a week of supervised exercise.
Diagnostic procedure	Baseline assessments included spirometry, which had to show at least mild obstructive disease defined as post bronchodilator FEV1/forced vital capacity (FVC) ratio <0.70 with FEV1<80% predicted or post-bronchodilator FEV1/FVC ratio <0.60 with FEV1>80% predicted.
Interventions	
E-health condition	
Type technology	Web-based portal (training and self-monitoring, interactive modules), smartphone (self-monitoring), e-mails (feedback and reinforcement), live group chat sessions and bulletin board.
Type intervention	Internet-based dyspnea self-management program: similar content to face-to-face program (see 'control condition'), but incorporated technological enhancements to support earlier recognition of worsening symptoms through real-time monitoring, prompt feedback, and convenient access to information and support: 1) Dyspnea and exercise consultation (1-2 hours) provided in individual face-to-face session, and by means of training on website and smartphone. 2) Unsupervised independent exercise: endurance (4 times/week, 30 min/session) and arm strengthening (3 times/week) exercise program. 3) Collaborative self-monitoring of exercise and respiratory symptoms (i.e. smartphone and web diary) and reinforcement of dyspnea management strategies by e-mails, weekly in month 1; biweekly in months 2-12). Specifically, nurses reviewed data to provide individualized feedback & reinforcement by e-mail. Furthermore, participants were

	encouraged to communicate exercise goals and progress to the nurse by using a Web-based goal-setting tool. Also, automated e-mail alerts were sent to nurses based on real-time symptom (worsening symptoms) and exercise (reports of not performing exercise for ≥ 3 consecutive days). 4) Structured education of dyspnea management strategies, skills training, and peer interactions (6 1-hour sessions, by means of interactive web modules, live group chat sessions by study nurse and access to chat transcripts, and a bulletin board.
Duration & frequency	12 months: 1) 1-2 hours consultation 2) Endurance (4 times/ week, 30 min./ session) and arm strengthening (3 times/week) exercise program 3) self-monitoring and reinforcement: weekly in month 1, biweekly in months 2-12. 4) Education, skills training, and peer interactions: six 1-hour sessions
Control condition	General health education control: Home visit from study staff and participation in monthly face-to-face education classes that focused on health topics of interest to middle-and older-aged adults and unrelated to lung disease (e.g., nutrition and general safety with medications). Participants were mailed the educational materials if they did not attend the sessions. They also received biweekly phone calls that provided general health information, and were offered to participate in the dyspnea self-management programs at the end of the control period. Face to face dyspnea self-management: 1) Dyspnea and exercise consultation (1-1.5 hours) as provided in individual face-to-face session. 2) Unsupervised independent exercise: endurance (4 times/week, 30 min/session) and arm strengthening (3 times/week) exercise program. 3) Collaborative self-monitoring of exercise and respiratory symptoms (i.e. paper diaries) and reinforcement of dyspnea management strategies by telephone calls (5-10 minutes, weekly in month 1; biweekly in months 2-12). 4) Structured education of dyspnea management strategies, skills training, and peer interactions (6 1-hour sessions, by means of paper modules and face-to-face group sessions).
Outcome(s)	
Assessment adherence	Self-reported frequency and duration (5-, 10-, 20-, 30-, 40-, 60-minute increments) of endurance and strengthening exercises for a typical week during the last 4 weeks.
Operationalization adherence	1) Endurance duration (minutes/week) 2) Endurance frequency (number of times a week) 3) Strengthening frequency (number of times a week)
Results	
Effects (*M, SD*) on adherence, incl. significance (*p*-values)	12-Month results: 1) 115 (58-172) VS 208 (150-267) VS 221 (166-276) 2) 4.5 (3.7-5.3) VS 4.8 (4.0-5.6) VS 5.1 (4.4-5.9) 3) 1.1 (0.4-1.9) VS 2.6 (1.8-3.3) VS 2.5 (1.8-3.2) *Note: values presented as means (95% CI)* Between-group results: 1) Non-sign. p=.24 2) Non-sign. p=.97 3) Non-sign. p=.22 *Note: repeated measures ANOVA only allowed for testing the main effect of time (4 levels), treatment group (3 levels), and the interaction of these.*
Dropouts (%)	12%
Other	
Source of funding and competing interest	This work was supported in part by UCSF (R01 NR008938), UW GCRCs (MO1-RR- 000037 and MO1 RR-00079), and National Institutes of Health grants 1KL2RR025015 and 1 UL1

	RR025014. The third author has funding through the Oncology Nursing Society and the Department of Veterans Affairs. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs.
Study limitations and other comments	The dyspnea self-management program to which the patients were randomized was not always concordant with their preferences. Authors note that participants often desired a combination of the Internet-based and face-to-face features. Authors note the effort to maintain fidelity to the respective programs as being difficult at times, especially when patients chose not to participate in the in-person group sessions and/or only responded to phone calls instead of communicating via secure messaging.

Study reference #4	
Authors	Petty et al.
Year of publication	2006
Country	US
Study design	
Study conditions (*N*)	* UC (n=73) * Standard video (n=69) * Customized video (n=72) Analyses conducted on subsample: * n=61 * n=62 * n=51
Measurements	* Baseline * 4 Weeks * 8 Weeks * 4 Months * 9 Months *Note: response rate for 9 months was low, data not presented*
Study population	
Age (*M*, *SD*)	* 66.8 ± 9.9 * 68.4 ± 9.0 * 68.8 ± 9.2
Gender (% female)	*45.2 *40.6 *45.8
Target population and recruitment strategy	Patients with COPD, as recruited through physician referrals from private offices, a medical office, and a veterans' affairs medical center. Additional recruitment through newspaper advertisements, health fair screenings, COPD support groups, and retirement communities.
Eligibility criteria	*Inclusion criteria:* * Medically stable patients with diagnoses of COPD, emphysema, or chronic bronchitis * Predicted FEV1 of less than 50% * Predicted ratio of FEV1 to forced vital capacity of less than 70% *Exclusion criteria:* * Terminal conditions such as late-stage lung cancer * Actively involved in a formal pulmonary rehabilitation program
Diagnostic procedure	Physician referrals. Medically stable patients with diagnoses of COPD, emphysema, or chronic bronchitis who also had a predicted FEV1 <50% and a predicted ratio of FEV1 to forced vital capacity of less than 70%.
Interventions	
E-health condition	
Type technology	Videotapes, with or without customization by means of a library of segments.
Type intervention	* Standard video: Participants received 2 videotapes on pulmonary rehabilitation exercises and educational information. * Customized video: Participants were mailed customized videotapes appropriate for their disease level (severe or moderate according to performance on a 6-minute walking test: < 3 L of oxygen and able to walk more than 600 ft were categorized as moderate) and psychological state as indicated by their responses on the Stages of Change questionnaires. Patients received a series of educational segments chosen by their physician or a VA pulmonologist. Physicians selected from a library of 49 exercise segments and chose an intervention time (baseline, 4 weeks, and 8 weeks) or elected an education routine encompassing all the segments.

	For patients referred from private practice, the physician appeared at the beginning of the tape. A library of 29 exercise segments was produced and available for inclusion in customized videotapes by the physicians in the study. Physicians were given 2 exercise customization options: (1) select both exercises and number of repetitions/number of seconds from all 29 exercise segments or (2) select the number of repetitions/number of seconds and exercise frequency for a 16-exercise routine. In both cases, patient's feedback on prescription tolerance was used to modify the exercise prescription during the study.
Duration & frequency	16 weeks
Control condition	UC delivered by physician, which may have included verbal or written information.
Outcome(s)	
Assessment adherence	Self-reported exercise rates.
Operationalization adherence	Exercising habits defined as: - Sedentary: no regular exercise in the last 6 months or last month and not having thought of starting an exercise program - Non-exercising: not having exercised in the month prior to baseline - Moderately (≥20 minutes most days of the week) 1) % of participants with self-reported maintenance of moderate exercise habits 2) % of participants who shifted from sedentary to exercising habit 3) % of participants who shifted from non-exercising to exercising habit.
Results	
Effects (*M, SD*) on adherence, incl. significance (*p*-values)	1) Sign. (p<.01): 40% (UC) VS 'more than 80%' (video groups, not further specified). 2) Sign. (p<. 05): 21% (UC) VS 38% (video groups, not further specified). 3) Sign. (p=.004): 50 VS 68 VS 84
Dropouts (%)	18.7
Other	
Source of funding and competing interest	This project was supported by NIH Grant No. R43 HL5587701: Rvision Corporation ''Multimedia Education for COPD Patient Education.''
Study limitations and other comments	Differential dropout rate (p=.013) with a disproportionate number of dropouts in the customized videotape: 29% customized videotape, 10% standard tape, 18% control Also, note that outcomes and specification of self-reported exercise poorly defined.

Study reference #5	
Authors	Tabak et al
Year of publication	2014
Country	The Netherlands
Study design	
Study conditions (*N*)	* UC (n=16) * UC + Telerehabilitation application (n=18) Analyses conducted on subsample: * n=16 * n=13
Measurements	* Baseline * 4 Weeks
Study population	
Age (*M, SD*)	* 67.9 ± 5.7 * 65.2 ± 9.0
Gender (% female)	* 31.3 * 42.9
Target population and recruitment strategy	Patients with a clinical diagnosis of COPD, as recruited by a chest physician or nurse practitioner.
Eligibility criteria	Inclusion criteria: * A clinical diagnosis of stable COPD defined by GOLD criteria (note: this criterium is reported in the Netherlands Clinical Trial Register) * GOLD classification II-III (note: this criterium is reported in the Netherlands Clinical Trial Register) * No infection or exacerbation in 4 weeks prior to measurement * Current or former smoker * Able to read and speak Dutch * Internet access at home Exclusion criteria: * Impaired hand function causing inability to use the application * Disorders or progressive disease seriously influencing daily activities (e.g. amputation) * Other diseases influencing bronchial symptoms and/or lung function (e.g. sarcoidosis) * Need for regular oxygen therapy (>16 hours per day or pO2 < 7.2 kPa) * History of asthma * <6 weeks ago started training with a physiotherapist
Diagnostic procedure	Not specified in paper, but the following is specified in trial registration in the Netherlands Clinical Trial Register (no. NTR2440): A clinical diagnosis of stable COPD defined by GOLD criteria. Meeting GOLD classification II or III: II: moderate: 50% ≤FEV1 <80% predicted III: severe: 30% ≤FEV1 <50% predicted Thus, FEV1% predicted measures available at baseline.
Interventions	
E-health condition	
Type technology	Web-based portal (symptom diary), smartphone application (activity data and automated feedback messages), and activity sensor/pedometer.
Type intervention	Usual care (see 'Control condition') plus tele application, consisting of 2 modules: 1) Activity coach: For ambulant activity registration and feedback. This coach consisted of a 3-dimensional-accelerometer and smartphone. Both the activity sensor and smartphone were worn on the subject's belt. The smartphone showed the measured activity cumulatively in a graph, together with the cumulative activity the users should aim for: the reference activity line. Users also automatically received feedback text messages, for awareness and extra motivation. These messages were based on the difference between the measured activity

	and the reference line and always consist of a) short summary of activity behavior and b) advice on how to improve or maintain the activity behavior. 2) Web-based portal: Included a symptom diary for self-treatment of exacerbations and an overview of the measured activity levels. Every day, participants were asked to fill in the diary on the web portal. A decision-support system automatically forms an advice to start medication in case of an exacerbation. Before using the web-based portal, participants had to attend two 90-minute self-management sessions given by a nurse practitioner, to learn how to complete the daily diary, how to recognize symptoms of an impending exacerbation, and how to deal with the exacerbation.
Duration & frequency	Participants used activity coach for 4 weeks from waking till 22.00 hours, for a minimum of 4 days per week. Week 1 was a baseline measurement to establish the reference line, followed by 3 weeks in which participant received feedback to change activity behavior.
Control condition	Usual care could consist for example of medication and physiotherapy. The latter mostly included weekly (group) training sessions at the local physiotherapy practices. In case of an exacerbation, the participants had to contact their medical doctor.
Outcome(s)	
Assessment adherence	Pedometer (Yamax Digiwalker 200).
Operationalization adherence	Adherence to physical exercise, defined as daily activity level as measured in steps per day
Results	
Effects (*M, SD*) on adherence, incl. significance (*p*-values)	Non-sign. (p=.38): 4617 ± 865 VS 5603 ± 964
Dropouts (%)	5.9%
Other	
Source of funding and competing interest	Study was supported by a research grant from The Netherlands Organization Development (ZonMW).
Study limitations and other comments	A very high compliance was found using the activity coach, and a higher usage of the system appeared to be significantly associated with an improvement in activity levels.

UC = Usual care; CG = Control group; WLC = Waiting list control; COPD = chronic obstructive pulmonary disease; GP = general practitioner; GOLD = Global Initiative for Chronic Obstructive Lung Disease; PDA = Personal Digital Assistant; FEV = forced expiratory volume; FEV1 = forced expiratory volume; in 1 second

Table 1: Specification of reasons for exclusion regarding COPD studies (*n*=15).

- N =3 No randomized controlled design
- N = 2 Conference/meeting/symposium abstract
- N =1 Control group received the same e-health technology
- N = 3 Adherence not statistically compared between study conditions
- N = 5 No patient adherence measure to treatment or health behavior under investigation
- N = 1 Wrong target population

Study	**Reason exclusion**
Akrom et al. 2015	No randomized controlled design
Franke et al. 2016	No randomized controlled design
Margolis et al. 2013	Adherence not statistically compared between study conditions
Moore et al. 2009	No patient adherence measure to treatment or health behavior under investigation
Nguyen et al. 2009	Control group received the same e-health technology *Note: Control group participants also used the mobile self-monitoring that was provided in experimental condition.*
Poureslami et al. 2016	No patient adherence measure to treatment or health behavior under investigation
Ries et al. 2003	No patient adherence measure to treatment or health behavior under investigation
Ringbaek et al. 2015	No patient adherence measure to treatment or health behavior under investigation
Scalvini et al. 2016	Conference/meeting/symposium abstract
Steele et al. 2008	Wrong target population Note: Only subsample of total study population had COPD: (85 out of 106) as inclusion criteria were self-reported diminished physical functioning related to a pulmonary problem and pulmonary function impairment.
Stickland et al. 2011	No randomized controlled design
Tabak et al. 2014 ***(Int J Chron Obstruct Pulmon Dis)***	Adherence not statistically compared between study conditions
Velardo et al. 2007	No patient adherence measure to treatment or health behavior under investigation
Wrong et al. 2012	Conference/meeting/symposium abstract
Wootton et al. 2018	Adherence not statistically compared between study conditions