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Effectiveness of tele-monitoring by patient severity and intervention type in chronic obstructive pulmonary disease patients: A systematic review and meta-analysis

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ABSTRACT

Background: Chronic obstructive pulmonary disease is a major burden on healthcare systems worldwide. Tele-monitoring has recently been used for management of chronic obstructive pulmonary disease patients.
Objectives: We analyzed the effect of tele-monitoring on chronic obstructive pulmonary disease patients and performed subgroup analysis by patient severity and intervention type.
Design: Systematic review.
Data source: Electronic databases including Ovid-Medline, Ovid-Embase, and the Cochrane Library.
Review methods: We conducted a meta-analysis of randomized controlled trials published up to April 2017. Three databases were searched, two investigators independently extracted data and assessed study quality using risk of bias.
Results: Out of 1,185 studies, 27articles were identified to be relevant for this study. The included studies were divided by intervention: 15studies used tele-monitoring only, 4studies used integrated tele-monitoring (pure control), and 8studies used integrated tele-monitoring (not pure control). We also divided the studies by patient severity: 16studies included severely ill patients, 8studies included moderately ill patients, and 3studies did not discuss the severity of the patients' illness. Meta-analysis showed that tele-monitoring reduced the emergency room visits (risk ratio 0.63, 95% confidence interval 0.55-0.72) and hospitalizations (risk ratio 0.88, 95% confidence interval 0.80–0.97). The subgroup analysis of patient severity showed that tele-monitoring more effectively reduced emergency room visits in patients with severe vs. moderate disease (risk ratio 0.48, 95% confidence interval 0.31–0.74; risk ratio 1.28, 95% confidence interval 0.61–2.69, retrospectively) and hospitalizations (risk ratio 0.92, 95% confidence interval 0.82–1.02; risk ratio 1.24, 95% confidence interval 0.57–2.70, retrospectively). The mental health quality of life score (mean difference 3.06, 95% confidence interval 2.15–3.98) showed more improved quality of life than the physical health quality of life score (mean difference -0.11, 95% confidence interval -0.83–0.61).
Conclusions: Tele-monitoring reduced rates of emergency room visits and hospitalizations and improved the mental health quality of life score. Integrated tele-monitoring including the delivery of coping skills or education by online methods including pulmonary rehabilitation is recommended to produce significant improvement. This application of integrated tele-monitoring (the delivery of education, exercise etc. in addition to tele-monitoring) is more useful for patients with (very) severe chronic obstructive pulmonary disease than those with moderate disease. Tele-monitoring might be a useful application of information and communication technologies, if the intervention includes the appropriate intervention components for eligible patients. Further studies such as large size randomized controlled trials with sub-group by patient severity and intervention type is needed to confirm these finding.

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What is already known about the topic?

- Tele-monitoring has recently been used for management of chronic obstructive pulmonary disease patients.
- It can promote interactions between patients and medical teams by monitoring the patient's symptoms, and may assist with unexpected patient hospitalizations or emergency room visits.
- The conflicting outcomes of systematic reviews are that while some studies require more research to reach definite conclusions, others show a positive effect of tele-monitoring.

What this paper adds

- Our results showed that tele-monitoring reduced emergency room visits, hospitalizations, and the mental health quality of life, while there were no differences in mortality, outpatient visits, or length of stay.
- Tele-monitoring has proved to be more useful in reducing the number of emergency room visits and hospitalization of patients with (very) severe chronic obstructive pulmonary disease than those with moderate diseases.
- Active integrated tele-monitoring, which includes the act of delivering skills and education to cope with disease and online pulmonary rehabilitation, produced more improvement than tele-monitoring only intervention when it comes to emergency room visits and hospitalization.

1. Introduction

Chronic obstructive pulmonary disease is a major burden on healthcare systems worldwide (Rabe et al., 2007). Exacerbations of chronic obstructive pulmonary disease are related to increased hospital admission, costs and anxiety, in addition to reduced social contact and quality of life. Chronic obstructive pulmonary disease is a comprehensive disorder and patients often suffer from further comorbidities, including anxiety and depression, cardiovascular disease and osteoporosis, which significantly increase their healthcare requirements. Therefore, chronic obstructive pulmonary disease has emerged as a public health issue with worldwide attention in medical systems (Nici et al., 2006).

The management of patients with chronic obstructive pulmonary disease covers established intervention such as pulmonary rehabilitation, inhaled therapies and smoking cessation, which can decrease exacerbation rates and improve health related quality of life. Tele-monitoring has recently been used for management of chronic obstructive pulmonary disease patients. Definition of tele-monitoring is the use of technology for timely information transmission from home to health service center (Jaana et al., 2009). Tele-monitoring involves digital wireless transmission of physiological and other non-invasive data, such as a patient's health symptoms. Tele-monitoring was able to evaluate several parameters such as peripheral oxygen saturation, body weight, temperature by using different devices (telephone, computer, or wearable and non-wearable devices) that are connected to a transmitting device (e.g. a cellular telephone). The information transmitted by transmitting devices is usually evaluated by healthcare professionals such as doctors or nurses. When readings are outside a specified range of normality, tele-monitoring systems can generate alerts to warn the personnel or put in action to respond to the situation (Pedone and Lelli, 2015). The systems can promote interactions between patients and medical teams by monitoring patients' symptoms and making it possible to manage an unexpected hospitalization or emergency room (ER) visits (McKinstry, 2013; Paget et al., 2010).

Many systematic reviews on chronic obstructive pulmonary disease patients with tele-monitoring have conflicting outcomes. While some researchers have stated that there was insufficient evidence in establishing its effectiveness definitively (Pedone and Lelli, 2015; Sanchez-Morillo et al., 2016; Hwang et al., 2015; Al Rajeh and Hurst, 2016), others have shown a positive effect of tele-monitoring (Lundell et al., 2015; Kamei et al., 2013). To ensure the effectiveness of tele-monitoring, a comprehensive systematic review including recently published literature needs to be performed again.

Lundell et al. stated that it was difficult to determine the effectiveness of tele-monitoring because the tele-monitoring intervention was combined with different variations of education and exercise training. Gregersen et al. also asserted that the interventions should be analyzed in two groups: the one that provided services similar to those of the control group; the other that provided additional services such as education, self-management etc. compared to the services provided to the control group. And, the author suggested that further studies are needed by classifying patients according to disease severity because he hypothesized that severe chronic obstructive pulmonary disease patients will benefit more from active tele-monitoring intervention. So, the subgroup analysis should be conducted by including patient's severity and intervention types.

The purpose of our study was to analyze the effect of tele-monitoring on chronic obstructive pulmonary disease patients and to perform subgroup analysis by patient severity and intervention type

2. Methods

2.1. Search strategy

We performed a systemic review to identify relevant articles that compared the tele-monitoring group with a control group that didn't receive tele-monitoring for chronic obstructive pulmonary disease using three English databases Ovid-Medline (1946 – May 2017), Ovid-EMBASE(1974-May 2017), and the Cochrane Central Register of controlled Trials (Central). We designed strategies that included Medical Subject Headings (MeSH), keywords such as "Pulmonary Disease, Chronic Obstructive", "tele monitoring", "telecare", "telehomecare", "telehealth", "telephone monitoring", "telemedicine", "telepathology", "telecommunication" and combinations of search terms (Supplementary 1).

2.2. Inclusion and exclusion criteria

To exclude irrelevant studies, two reviewers (HYA and LSH) independently screened the articles' titles and abstracts, and full-text review was subsequently conducted for potentially relevant articles. The inclusion criteria were as follows: (a) randomized trials; (b) patient with chronic obstructive pulmonary disease; (c) a tele-monitoring intervention; (d) outcome measures including quality of life, hospitalization, emergency room visits, mortality, length of stay, readmission, chronic obstructive pulmonary disease exacerbations, and outpatient visits. We defined the outcomes of interest in advance before the conduct of the systematic review. Non-randomized trials, review articles, abstracts, conference posters, and unpublished gray literature were excluded.

2.3. Quality assessment

A quality assessment was also independently performed by two reviewers (HYA and LSH) using the Cochrane risk of bias (RoB) for randomized controlled trials. Cochrane risk of bias for randomized control trials (RCTs) assessed selection bias, allocation bias,

performance and detection bias, attrition bias and reporting bias by scoring low, high and unclear risk. All discrepancies were resolved by discussion with a third reviewer. Two reviewers (HYA and LSH) extracted the following variables onto a data extraction form and double-checked them: baseline demographic and clinical characteristics of the study participants (i.e., age, sex ratio,).

2.4. Statistical analysis

The dichotomous variables included emergency room visits, hospitalization, mortality, and outpatient visits. And the continuous variables included range of hospitalization, quality of life, and length of stay. The risk ratios (RRs) and weighted mean differences (WMDs) were calculated and reported with 95% confidence intervals (CIs). If studies only reported the median, standard error, or p-value, then the median was substituted for the mean, and standard deviations were calculated using the algorithms proposed by Hozo et al. (2005). The chi square test with significance set at $p < 0.05$ was used to assess statistical heterogeneity among studies, including meta-analysis, and I^2 statistics quantified heterogeneity. If I^2 were greater than 50%, we used the random effect model; otherwise, we used the fixed effect model. Publication bias was tested by using a funnel plot analysis. We conducted all meta-analysis with Review Manager, Version 5.3 (RevMan, Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2013), and used a two-tailed test of significance ($p < 0.05$).

3. Results

After a full-text review, 24 articles were identified to be relevant for this study. Three additional articles were found by manually searching relevant bibliographies, and 27 publications were finally selected for inclusion in the meta-analysis. (Fig. 1)

3.1. Characteristic of included studies

Table 1 shows the characteristics of the 27 included studies. All these RCTs included patients who underwent tele-monitoring and a control group. The selected studies were published from July 2006 through July 2017. Twenty-one studies were conducted in Europe, 4 were conducted in Asia including Australia, and 2 were conducted in North America. The included studies were divided by intervention: 15 studies used tele-monitoring only, 4 studies used integrated tele-monitoring (pure control), and 8 studies used integrated tele-monitoring (not pure control). 'Usual care' means the clinical care from primary physicians in the outpatient setting regularly after discharge. 'Integrated tele-monitoring with pure control' described in this systematic review was delivering home-based intervention with exercise, education and so on. However, this exercise or education was not applied to control group. 'Integrated tele-monitoring with not pure control' in this systematic review cannot have the pure control group which received only standard care. The control group received some degree of chronic obstructive pulmonary disease education or exercise additionally.

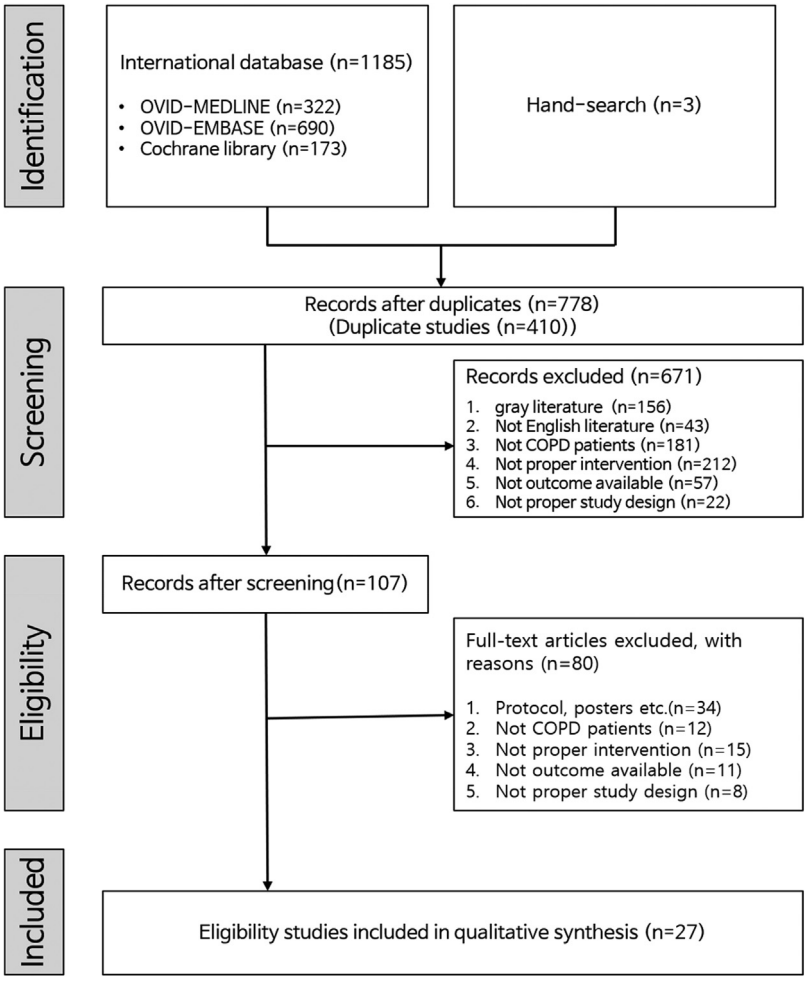

Fig. 1. Study flow chart.

Table 1
Characteristics of included studies.

Author Year Country	Patient No Mean age (intervention group/control group)	severity	Technology	Index	Intervention	Control	Outcomes
Rixon et al. (2015) UK	281 / 212 71.60/72.24	unknown	Tele-monitoring	Blood pressure Oxygen saturation Symptom Weight	• Data were transmitted by participants to a monitoring center • Home monitoring response (nothing, repeat reading, home visit, refer)	• Regular outpatient visits at baseline and after 6months by the pulmonologist • Interim outpatient visits at 2 and 4 months with a pulmonary nurse practitioner	• Emergency room visits • Hospitalization • Quality of life • Mortality
Ho et al.(2016) Taiwan	53/53 81.4 ± 7.8/ 79.0 ± 9.6	Severe	Tele-monitoring	Blood pressure chronic obstructive pulmonary disease exacerbation Oxygen saturation Symptom (Breathless, sputum), Spirometry, Temperature, Weight	• Phone line from 8 am-6 pm • electronic diary: report symptoms (each day for two months after discharge) • warning response (pulmonologist contact and evaluating the patient by phone)	• Usual care • Phone line from 8-18	• Emergency room visits • Hospitalization
Lavesen et al. (2016) Denmark	84 / 84 69.72 ± 10.3/ 70.90 ± 9.79	Severe	Tele-monitoring	Medication Symptom	• Usual care: final medical round • Telephone call • Day 2: ask for experience, provide knowledge, disease management • Day 30: last follow-up call	• Usual care: final medical round • Day 30: answer questionnaire	• Hospitalization • Mortality
Vianello et al. (2017) Italy	230 / 104 75.96 ± 6.54/ 76.48 ± 6.16	Severe	Tele-monitoring	Heart rate Oxygen saturation	• Self-managed education • Heart rate, Oxygen Saturation -> every other day and/or in the event of subjective clinical worsening • Daily review (Mon - Fri from 8 am-6 pm) of abnormal symptoms • Acute exacerbation of chronic obstructive pulmonary disease: undertook action	• No tele-monitoring service	• Emergency room visits • Hospitalization • Quality of life • Mortality • Outpatient visits • Length of stay
Berkhof et al. (2015) Netherland	52 / 49 68 ± 9/68 ± 9	Severe	Tele-monitoring	chronic obstructive pulmonary disease exacerbation Health status Symptom	• Pulmonologist visit at baseline and after 6months • Phone call by nurse every 2weeks • clinical chronic obstructive pulmonary disease questionnaire • If the clinical chronic obstructive pulmonary disease questionnaire total score exceeded the minimal clinical important difference assess patient • Choose treatment or visits to outpatient clinic or general practitioner	◦ Pulmonologist visit at baseline and after 6months ◦ Interim outpatient visits at 2 and 4months by pulmonary nurse	◦ Hospitalization ◦ Quality of life ◦ Length of stay
McDowell et al. (2015) UK	55 / 55 69.8 ± 7.1/ 70.2 ± 7.4	moderate	Integrated tele-monitoring (not pure)	Blood pressure Heart rate Oxygen saturation Symptom (breathing, cough, sputum)	• Standardized home-based program • Clinical observations daily, questions related to symptoms • >=2 home visits: community respiratory team physiotherapist and nurse • Rehabilitation or access to weekly maintenance exercise class. • Daily data reviewed within 10 minutes for signs of deterioration; ◦ -alert: contact to patient / no alert: contact every week	• Standardized home-based program	◦ Emergency room visits ◦ Hospitalization ◦ Quality of life ◦ Length of stay

Ringbæk et al. (2015) Denmark	141 / 140 69.8 ± 9.0/ 69.4 ± 10.1	Severe	Integrated tele-monitoring (pure)	chronic obstructive pulmonary disease exacerbation Oxygen saturation, Weight Spirometry, Symptom (dyspnea, sputum, volume, purulence)	• Call center(9am-3 pm) with red, yellow, green codes • Measurement without video consultation • Video consultation • Unscheduled video consultation occurred if necessary	• Managed by nurses at home or at the outpatient visit • Scheduled visits at the out-patient clinics once or twice a year • Contact outpatient clinic weekdays (9am −3 pm)	• ○ Emergency room visits ○ Hospitalization ○ Length of stay
Stoddart et al. (2016) UK	128 / 128 69.4 ± 8.8/ 68.4 ± 8.4	moderate	Integrated tele-monitoring (not pure)	Heart rate Medication Oxygen saturation Symptom	• Education (self -management of exacerbations) + booklet 'Living With chronic obstructive pul-monary disease ' • Questionnaire about symptom and medication via touch screen, broadband link. ○ transmitted to clinical team and call patients	• ○ usual care: ○ clinical care, education on self-management of exacerbations ○ emergency supply of antibiotics and steroids	• ○ Quality of life
Bentley et al. (2014) UK	19 / 19 67.22 ± 11.6/ 65.88 ± 9.39	Severe	Tele-monitoring	Blood pressure, Heart rate Oxygen saturation Respirator rate, Temperature	• ○ 3 home visits (1, 3, 5days after hospital discharge) ○ Daily vital signs monitoring ○ Discharge home visit, remove equipment at 8weeks ○ Assess SGRQ, EQ-5D, general practitioner recorded diaries on device	• Home visit; nurse • Assess quality of life and general practitioner record diaries	• Emergency room visits • Hospitalization • Quality of life • Mortality • Outpatient visits
Segrelles Calvo et al. (2014) Spain	29 / 30 75.0 ± 9.7/ 72.7 ± 9.	Severe	Tele-monitoring	Blood pressure, Heart rate Oxygen saturation, PEF(3 T/week) Respirator rate, Temperature	• ○ Daily follow-up ○ Measurements -> once a day in the morning, 20 min after medication ○ Clinical Monitoring Center monitored and assessed from 9 am-5 pm ○ During weekends data were directly analyzed	• Usual care	• ○ Emergency room visits ○ Mortality
Tabak et al. (2014) Netherlands	12 / 12 64.1 ± 9.0/ 62.8 ± 7.4	moderate	Integrated tele-monitoring (pure)	Major symptom (breathlessness, sputum, production, sputum color), Minor symptom (wheeze, running nose, sore, throat, fever, cough)	• ○ Activity coach for monitoring and real-time coaching ○ Web-based exercise program ○ Self-management of chronic obstructive pul-monary disease exacerbations ○ Teleconsultation	• Usual care	• ○ Emergency room visits ○ Hospitalization ○ Quality of life
Jódar-Sánchez et al. (2013) Spain	24 / 21 74 ± 8/ 71 ± 10	Severe	Tele-monitoring	Blood pressure chronic obstructive pulmonary disease exacerbation Heart rate, Temperature Oxygen saturation Respirator rate, Spirometry	• ○ Vital signs from Monday to Friday, 20 min after taking prescribed inhaled therapy, seated, rested, while on oxygen therapy ○ Perform spirometry 2days a week	• Usual care	• ○ Emergency room visits ○ Hospitalization ○ Quality of life ○ Outpatient visits ○ Length of stay
Pare et al. (2013) Canada	60 / 60	Severe	Integrated tele-monitoring (pure)	Medication Symptom	• ○ Complete a data entry table about symptoms and medication ○ Patient read specific learning capsules on chronic obstructive pulmonary disease adapted from the self-management program called "Living well with chronic obstructive pulmonary disease " ○ Consult the data every day	• Usual care	• ○ Emergency room visits ○ Hospitalization ○ Length of stay
Pedone et al. (2013) Italy	50 / 49 74.1 ± 6.4/ 75.4 ± 6.7	Severe	Tele-monitoring	Blood pressure, Heart rate, galvanic skin response, Oxygen saturation, Respirator rate, Temperature	• Wristband contained sensors and pulse oximeter connected to bluetooth transmitter • Commercial cellular telephone coupled with the wristband to send the data • Physician received data every day	• Usual care	• ○ Hospitalization

Table 1 (*Continued*)

Author Year Country	Patient No Mean age (intervention group/control group)	severity	Technology	Index	Intervention	Control	Outcomes
Pinnock et al. (2013) UK	128 / 128 69.4 ± 8.8/ 68.4 ± 8.4	moderate	Tele-monitoring	chronic obstructive pulmonary disease exacerbation Oxygen saturation, Temperature, Symptom (dyspnea, fever, respiratory tract infection, cough, sputum purulence & volume, wheeze)	• Touch screen tele-monitoring equipment -> recorded and transmitted a daily questionnaire about symptoms, monitored oxygen saturation • Information sent to UK's health service, accessible to the supporting clinical team-> monitoring • Involve contacting the patient by telephone	• Usual clinical care (including self- management advice)	• ○ Hospitalization ○ Mortality ○ Quality of life ○ Length of stay
San Miguel et al. (2013) Australia	36 / 35 71 / 74	severe	Integrated tele-monitoring (not pure)	Blood pressure, Health status Heart rate, Oxygen saturation Respirator rate, Temperature Weight	• ○ Visited home and provided educational book about chronic obstructive pulmonary disease & telehealth instruction manual ○ Measured vital signs and answered questions relating to general state of health on daily basis ○ Phone to discuss about measurements and provide advice/support or make an appointment to visit the general practitioner	• Usual care + visited by the telehealth nurse to provide them with the same chronic obstructive pulmonary disease book	• ○ Emergency room visits ○ Hospitalization ○ Length of stay
Sorknaes et al. (2013) Denmark	132 / 134 71 ± 10/ 72 ± 9	Severe	Integrated tele-monitoring (not pure)	Heart rate Oxygen saturation Spirometry	• ○ Conducted in home visit between 8am-3 pm 7days/week (59days) ○ Telephone follow-up call was made ○ Patient received advice and treatment was discussed with nurse ○ Patient could take readings of the measurements ○ Nurse could organize rapid treatment, teleconsultation	• Conventional treatment	• ○ Hospitalization ○ Length of stay
Antoniades et al. (2012) Australia	22 / 22 70 ± 10/ 68 ± 9	moderate	Tele-monitoring	Blood pressure, Heart rate chronic obstructive pulmonary disease exacerbation, Medication Oxygen Saturation, Respirator rate, Temperature, Spirometry Symptom (Health status dyspnea, sputum color & volume, respiratory tract infection)	• ○ Remote in-home monitoring system-> data uploaded daily to central server ○ Access to nurse outreach via telephone if they felt unwell	• Standard best practice care • Access to nurse outreach via telephone if they felt unwell	• ○ Hospitalization ○ Quality of life ○ Length of stay
Chau et al. (2012) Hong kong	22 / 18 73.5 ± 6.05/ 72.22 ± 6.13	moderate	Integrated tele-monitoring (not pure)	Heart rate Oxygen saturation Respirator rate	• ○ Education: self-care, symptom management including medication, purse-lip breathing, modification of lifestyle, and exercise by community nurse ○ Give device kit -> monitor 3 times a day	• Education self-care: self-care, symptom management • no extra care or intervention	• ○ Emergency room visits ○ Hospitalization ○ Quality of life ○ Length of stay
Dinesen et al. (2012) Denmark	57 / 48 68 / 68	Severe	Integrated tele-monitoring (not pure)	Blood pressure Oxygen saturation Spirometry Weight	• Provide standardized information on exercises • Telehealth -> sent to web-based portal • Once a month tele-rehabilitation team consisting of healthcare professionals held a video meeting	• Provide standardized information on exercises	• Hospitalization
Haesum et al. (2012) Denmark	57 / 48 67.9 /68.1	unknown	Integrated tele-monitoring (not pure)	Blood pressure Heart rate Lung function Oxygen saturation Weight	• ○ Instructed how to take clinical measurements, how to use a step counter, received general advice on how to exercise ○ Once a month, tele-rehabilitation team consisting of healthcare professionals would meet online to discuss	• Instructions on performing home exercises	• ○ Quality of life

Halpin et al. (2011) UK	40 / 29 68.5 ± 1.5/ 70.2 ± 1.6	Severe	Tele-monitoring	Symptom (symptoms of cold flu, color of phlegm, breathing problems)	• ○ Alert call: automated system if an elevated risk of exacerbations was forecast ○ The Exacerbations of Chronic Pulmonary Disease Tool patient-reported outcome: complete a daily diary ○ Comprising the Exacerbations of Chronic Pulmonary Disease Tool questionnaire and ask if whether they wanted the study team to contact them	• Usual care	• ○ Hospitalization
Lewis et al. (2010a) UK	20 / 20 67 ± 9/ 70 ± 10	moderate	Tele-monitoring	Oxygen saturation Temperature Symptom Physical observations	• ○ Standard care + Docobo Health Hub monitor for 26 weeks ○ Symptoms and physical observations recorded twice daily which were stored and then uploaded at 2am through a free-phone landline ○ Nurse could access the data through a secured web site and received alert e-mails if certain combinations of data occurred.	• Standard care for 52 weeks	• ○ Emergency room visits ○ Quality of life
Lewis et al. (2010b) UK	20 / 20 61.73/ 63.79	moderate	Tele-monitoring	Oxygen saturation Temperature Symptom	• ○ Home monitors -> provided answers to questions, twice a day for 26 weeks ○ Data transferred to central server daily ○ Community-based chronic disease management team for 26 weeks	• Usual Care + Community-based chronic disease management team 52weeks	• ○ Quality of life
Koff et al. (2009) USA	19 / 19 66.6 ± 9.1/ 65.0 ± 8.2	Severe	Integrated tele-monitoring (pure)	Oxygen saturation FEV1 Symptom 6MW	• ○ Patients transmitted self-reported symptoms oximetry and spirometry readings to a central record system. ○ Daily completion of illness education and disease management module. ○ Contact with coordinator via mobile phone	• Usual care	• ○ Quality of life
Vitacca et al. (2009) Italy	118 / 102 61.2 ± 17.6/ 61.1 ± 17.4	Severe	Tele-monitoring	Oxygen saturation	• ○ Regular telephone appointments with a nurse where patients reported their oximetry readings and symptoms ○ Access to call center	• Usual care	• ○ Hospitalization ○ Mortality
de Toledo et al. (2006) Sapin	67 / 90 71 ± 8/ 72 ± 8	unknown	Integrated tele-monitoring (not pure)	Heart rate Pulse oximetry Blood pressure Spirometry Symptom	• ○ Patients received an educational session and home visit (24-72 hours post discharge) and had telephone access to a call center. The care team had access to a central patient management module from any location.	• Patients received an educational session and home visits as needed, but did not have access to the call center.	• ○ Emergency room visits ○ Hospitalization ○ Mortality

In our review, the definition of the severe patients was forced expiratory volume in 1 (FEV1) sec/forced vital capacity (FVC) <0.70 or forced expiratory volume in 1 s<50% (FEV1/FVC < 0.70 or FEV1 < 50%). The studies were divided by patient severity as follows: 16 studies had patients with severe chronic obstructive pulmonary disease, 8 studies had patients with moderate chronic obstructive pulmonary disease, and 3 studies did not discuss illness severity (Table 1).

The quality assessment of the included studies showed the following results. Four studies had a high risk of selection bias, and almost all studies reported an unclear allocation concealment. Only 2 studies reported blindness, and most did not (Fig. 2). The funnel plot representing potential publication bias among the studies was fairly symmetric.

3.2. Emergency room visits

Eleven studies included emergency room visits, and we conducted sub-group analysis of the type of intervention and patient' severity. The first subgroup analysis was carried out

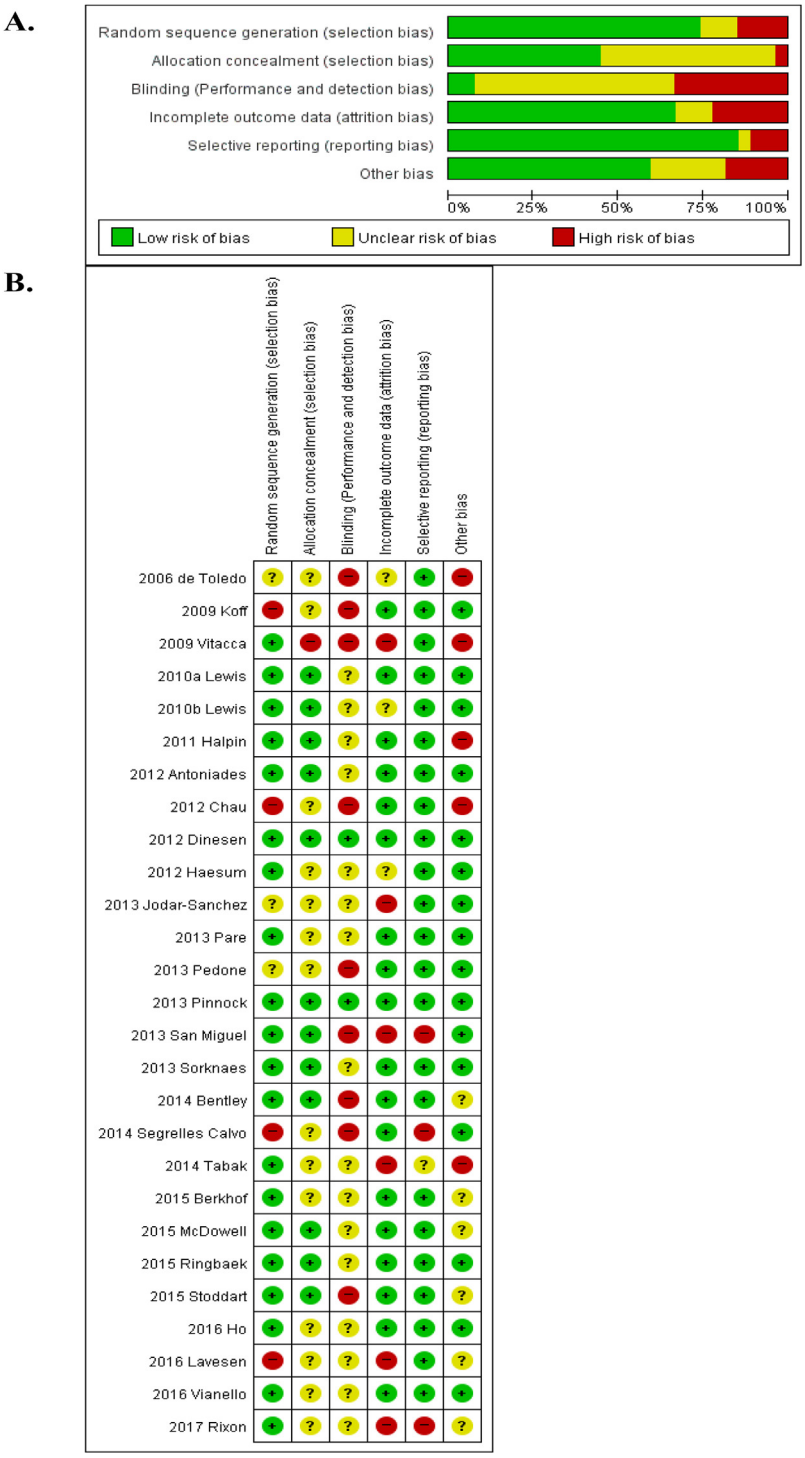

Fig. 2. Quality assessment A. Risk of bias graph B. Risk of bias summary.

according to the type of intervention: tele-monitoring only, integrated tele-monitoring (pure control), or integrated tele-monitoring (not pure control). Tele-monitoring only ($p < 0.01$, RR = 0.65, 95% CI 0.55– 0.76, $I^2 = 72\%$) and integrated tele-monitoring monitoring ($p < 0.01$, RR = 0.42, 95% CI 0.28–0.62, $I^2 = 65\%$) significantly reduced emergency room visits. However, the group with tele-monitoring (not pure control) did not show a significant decrease in emergency room visits ($p = 0.11$, RR = 0.75, 95% CI 0.53–1.07, $I^2 = 64\%$). Analysis without subgroups showed a significant reduction in emergency room visits in the tele-monitoring group ($p < 0.01$, RR = 0.63, 95% CI 0.55– 0.72, $I^2 = 69\%$).

When we reviewed the included studies again because of high heterogeneity, we found two studies (Vianello et al., 2017; Tabak et al., 2014) which measured only heart rate and oxygen saturation, while the others measured comprehensive index as well as heart rate and oxygen saturation. When we performed sensitivity analysis by removing those two studies from analysis, the heterogeneity was reduced from $I^2 = 72\%$, 65% to $I^2 = 0\%$, 33% respectively. Analysis of the total population showed significantly reduced emergency room visits in the tele-monitoring group ($p < 0.01$, RR = 0.51, 95% CI 0.43– 0.61, $I^2 = 40\%$).

A second sub-group analysis was conducted to study disease severity: severe, moderate, or not stated. Tele-monitoring significantly reduced emergency room visits in patients with severe or undefined chronic obstructive pulmonary disease severity ($p < 0.01$, RR = 0.48, 95% CI 0.31 to 0.74, $I^2 = 78\%$; $p < 0.01$, RR = 0.63, 95% CI 0.47 to 0.83, $I^2 = 0\%$, retrospectively). However, there was no significant difference in emergency room visits in patients with moderate chronic obstructive pulmonary disease ($p = 0.51$, RR = 1,28, 95% CI 0.61 to 2.69, $I^2 = 0\%$). The meta-analysis of emergency room visits is shown in Fig. 3, and the data excluded from the meta-analysis are shown in Table 2 .

3.3. Hospitalization

When the hospitalization was analyzed, some studies used dichotomous variables and others used continuous variables; hence, we conducted the meta-analysis including both dichotomous variables and continuous variables.

Twelve studies were included for hospitalization, and we conducted sub-group analysis for the type of intervention and disease severity. The first sub-group analysis compared tele-monitoring only with integrated tele-monitoring. Tele-monitoring reduced hospitalizations but this was not statistically significant ($p = 0.13$, RR = 0.92, 95% CI 0.82–1.03, $I^2 = 36\%$). On the other hand, integrated tele-monitoring did significantly reduce hospitalizations ($p = 0.03$, RR = 0.79, 95% CI 0.64 to 0.98, $I^2 = 26\%$). Analysis without subgroups showed a significant reduction ($p = 0.01$, RR = 0.88, 95% CI 0.80 to 0.97, $I^2 = 31\%$).

The second sub-group analysis was conducted to examine patient severity: severe, moderate, or not stated. Tele-monitoring decreased slightly in the severe and not stated groups, but there was no statistically significant difference ($p = 0.12$, RR = 0.92, 95% CI 0.83 to 1.02, $I^2 = 13\%$; $p = 0.16$, RR = 0.85, 95% CI 0.67 to 1.07, $I^2 = 55\%$, retrospectively). Hospitalization were not decreased in patients with moderate chronic obstructive pulmonary disease ($p = 0.59$, RR = 1.24, 95% CI 0.57 to 2.70, $I^2 = 15\%$) However, analysis without subgroups showed a significant difference ($p = 0.05$, RR = 0.91, 95% CI 0.83 to 1.00). The data excluded from the meta-analysis are shown in Table 2 .

We conducted a meta-analysis for the continuous variable, it was a range of hospitalization. Four studies were included, with no statistically significant difference ($p = 0.49$, MD=-0.08, 95% CI -0.31 to 0.15). No heterogeneity was found ($I^2 = 0\%$, $p = 0.78$). The meta-analysis of hospitalization is shown in Fig. 4.

3.4. Quality of life

The measurement tools for quality of life for analysis included the St George's Respiratory Questionnaire (SGRQ), the Short Form-36 (SF-36), and the EuroQol five dimension scale (EQ-5D). Four studies used the SGRQ, which did not show a significant difference between the tele-monitoring group and the control group ($p = 0.89$, MD=-0.21, 95% CI -3.29 to 2.86), and heterogeneity was not found ($p = 0.16$, $I^2 = 42\%$). In the SF-36 physical component summary, which was only used by 2 studies, there was no significant difference between the groups ($p = 0.77$, MD=-0.11, 95% CI -0.83 to 0.61) and heterogeneity was not found ($p = 0.45$, $I^2 = 0\%$). On the other hand, the SF-36 mental component summary, which was used in two studies, showed a significant improvement in quality of life ($p < 0.01$, MD = 3.06, 95% CI 2.15–3.98), and heterogeneity was not found ($p = 0.20$, $I^2 = 40\%$). Three studies used the EQ-5D, but we did not carry out a meta-analysis because the heterogeneity was too high ($I^2 = 99\%$) (Fig. 5).

3.5. Mortality

Eight studies were included for mortality. There was a slight reduction in mortality between the tele-monitoring group and the control group, but it was not statistically significant ($p = 0.25$, RR = 0.85, 95% CI 0.64–1.13). No heterogeneity was found ($p = 0.66$, $I^2 = 0\%$) (Fig. 5).

3.6. Outpatient visits

Three studies were included for outpatient visits. There was a slight reduction in outpatient visits between the tele-monitoring group and the control group, but it was not statistically significant ($p = 0.09$, RR = 0.84, 95% CI 0.69 to 1.03). No heterogeneity was found ($p = 0.39$, $I^2 = 0\%$). The data excluded from the meta-analysis are shown in Table 2 (Fig. 5).

3.7. Length of stay

Nine studies were included for length of stay. There was no reduction in the length of stay between the tele-monitoring group and the control group ($p = 0.55$, RR=-0.33, 95% CI -1.42 to 0.75). No heterogeneity was found ($p = 0.23$, $I^2 = 24\%$) (Fig. 5).

4. Discussion

We included 27 studies related to tele-monitoring for chronic obstructive pulmonary disease at home in our systematic review. Our study is the most updated and comprehensive systematic review, and the only one that analyzed subgroups by patient severity and intervention type. The principal finding of this systematic review is that tele-monitoring reduced emergency room visits, hospitalizations, and the mental health quality of life, but did not make a difference in mortality, outpatient visits, or length of stay, though the result was in favor of tele-monitoring. Tele-monitoring was more effective at preventing emergency room visits and hospitalizations in patients with severe respiratory failure with FEV1/FVC < 0.70 and FEV1 < 50% or those who required home oxygen therapy and/or mechanical ventilation.

4.1. Appropriate intervention components

The interventions analyzed here could be divided into those that provided only tele-monitoring service and those represented integrated tele-monitoring, such as the delivery of self-management education or teleconsultation by phone in addition to tele-monitoring of vital sign and systems. Two types of interventions

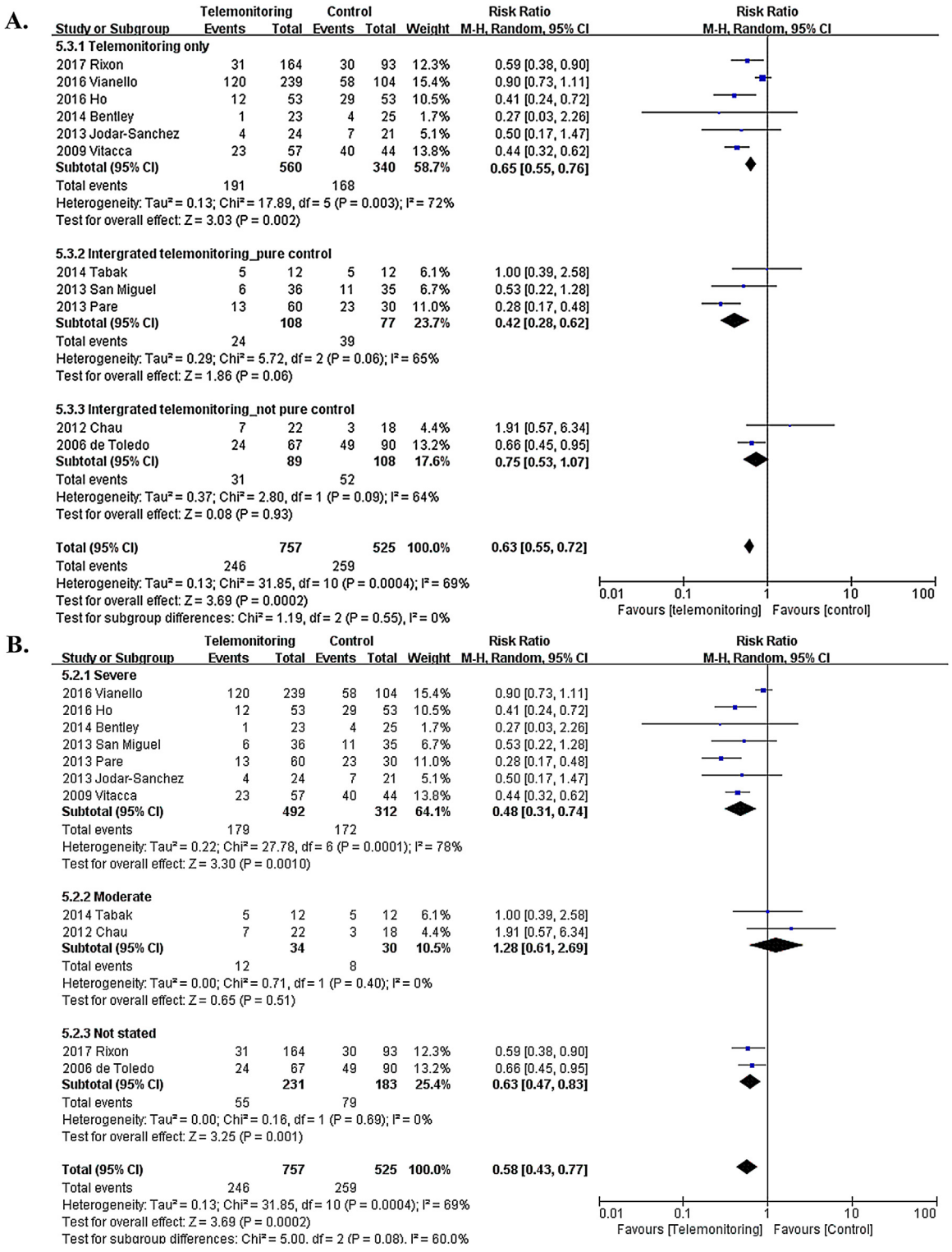

Fig. 3. Meta-analysis A. emergency room (ER) visits (subgroup analysis with intervention); B. Emergency room visits (subgroup analysis with severity).

reduced emergency room visits significantly. However, integrated tele-monitoring reduced emergency room visits more effectively than tele-monitoring only. In case of the hospitalization, while integrated tele-monitoring reduced hospitalization, tele-monitoring only group didn't reduced hospitalization statistically significantly. Our analysis, similar to those of previous studies, showed that integrated interventions, including the delivery of coping skills or education online produced more significant improvement. McDowell et al. (2015) and Blumenthal et al. (2014) reported that the quality of life for chronic obstructive pulmonary disease patients improved by integrated tele-monitoring interventions offering some form of coping of self-management skills training. Koff et al. (2009) showed similar results that integrated tele-monitoring, including specific coping skills training, were more effective than control group. Gregersen et al. (2016), the systematic review study, said that different types of tele-monitoring

Table 2
Data that were not included the meta-analysis.

Author Year	f/u (mon)	IG (N)	CG (N)	Intervention	Control	p
◆ Emergency room visits						
McDowell et al. (2015)	6	55	55	0.60(0.9)	0.79(1.3)	0.40
Ringbæk et al. (2015)	6	141	140	0.55(0-5)	0.54(0-4)	0.74
Segrelles Calvo et al. (2014)	7	29	30	20 visits	57 visits	0.001
Lewis et al. (2010a)	6	50	50	0(0, 0.8)	0(0, 1.0)	0.24
◆ Hospitalization						
Ho et al. (2016)	6	53	53	0.23(0.47)	0.68(0.94)	0.002
Berkhof et al. (2015)	6	52	49	1(0-3)	0(0-3)	NA
McDowell et al. (2015)	6	55	55	2.35(1.8)	2.81(1.9)	0.22
Soaknaes (2013)	6.5	121	121	1.22(1.92)	1.28(2.10)	0.82
◆ Out-patient visit						
Berkhof et al. (2015)	6	52	49	2(0-12)	2(0-12)	0.81
McDowell et al. (2015)	6	55	55	1.94(2.22)	2.84(2.2)	0.079
Ringbæk et al. (2015)	6	141	140	0.26(0-3)	0.99(0-7)	<0.001
San Miguel et al. (2013)	6	36	35	0.97(1.3)	0.94(1.3)	NA

◆ Segrelles Calvo et al., 2014: total number of visits.
◆ Lewis 2010a: median (IQR).

intervention have affected the outcomes in chronic obstructive pulmonary disease and assumed that integrated tele-monitoring intervention including education or coping skills offers better outcomes. Based on this result, we recommend integrated tele-monitoring which is more active than passive monitoring. And, additional study is needed to analyze the effect size of each type of intervention.

We also studied integrated tele-monitoring without pure controls. In our meta-analysis, while integrated tele-monitoring reduced emergency room visits [RR 0.42, CI 0.28-0.62], integrated tele-monitoring without pure controls didn't reduced emergency room visits statistically significantly [RR 0.75, CI 0.53–1.07]. These studies delivered some form of home–based respiratory monitoring without leaving the control group out; that is, the control group received some degree of education, so there was no pure control group who received only standard care. This may have weakened the statistical power of the study outcomes. One trial (Koff et al., 2009) reported that proactive integrated tele-monitoring increased the SGRQ score compared to control group. However, in out meta-analysis which includes four trials, integrated tele-monitoring (nor pure control) failed to improve the SGRQ score. It is predicted that the small number of studies included in our meta-analysis of the SGRQ score brought such result. Because in emergency room visits which include 11 sufficient studies integrated pure control reduces emergency room visits compared to not pure control. Therefore, further meta-analysis results through additional SGRQ-related researches are needed.

Tele-monitoring encompasses various measurements of both physiologic indicators and symptoms. The most common approach monitored a combination of symptoms and physiological measurements. However, some studies including those by Lavesen et al. (2016); Berkhof et al. (2015), and Halpin et al. (2011) measured only symptoms without physiological measurements. These studies showed that tele-monitoring did not reduce hospitalization. Thus, tele-monitoring that measured physiologic parameters including oxygen saturation, blood pressure, and heart rate as well as symptoms such as dyspnea, sputum, and cough could be more effective.

Studies in which both the intervention group and control group received pulmonary rehabilitation did not differ in reduction of hospitalization rates. Two studies (Lewis et al., 2010; Antoniades et al., 2012) suggested that the main reason that there was no difference in hospitalization reduction may be because the patients were already optimized, as they were included directly after pulmonary rehabilitation. This negative result may hint that pulmonary rehabilitation is the most important intervention component that affects health status.

4.2. Eligible patients

Our meta-analysis results also showed that tele-monitoring significantly decreased emergency room visits in patients with severe chronic obstructive pulmonary disease [RR 0.48, CI 0.31-0.74]. However, there was no difference in the moderate patients [RR 1.28, CI 0.61–2.69]. It comes to the hospitalization rate, our study showed similar result. Tele-monitoring of the severe chronic obstructive pulmonary disease patient group tend to decrease hospitalization rate [RR 0.92, CI 0.31–1.02], while there was no difference in patients with moderate chronic obstructive pulmonary disease [RR 1.24, CI 0.57–2.70]. These outcomes are consistent with other studies. Vitacca et al. (2009) previously showed that tele-monitoring effectively prevented hospital admissions in severe and frail patients with chronic respiratory failure requiring home oxygen therapy and/or mechanical ventilation. In addition, there was a trend toward reduced hospitalization rates in 2 small studies comprising a high proportion of patients on long-term oxygen therapy (Jódar-Sánchez et al., 2013; Maiolo et al., 2003). Lundell et al. (2015) said that tele-monitoring interventions must be considered across disease severity in order to generalize the results for chronic obstructive pulmonary disease patients and to assess differences according to disease severity. Additionally, Gregersen et al. (2016) said that patients with severe chronic obstructive pulmonary disease will have more effect on tele-monitoring than other groups of chronic obstructive pulmonary disease patients'. This is consistent with the recommendation of the Danish health authorities. The Danish health authorities recommend that patients with severe and very severe chronic obstructive pulmonary disease have outpatient follow-up twice yearly and are seen for unscheduled visits as needed, whereas patients with mild-to-moderate chronic obstructive pulmonary disease are expected to be managed by their general practitioner, including regular follow-up (Sundhedskoordinationsudvalget, 2009). Therefore, the application of tele-monitoring is recommended for patients with severe and very severe chronic obstructive pulmonary disease. Based on these results, additional study related to patient's severity is needed to analyze the effect size.

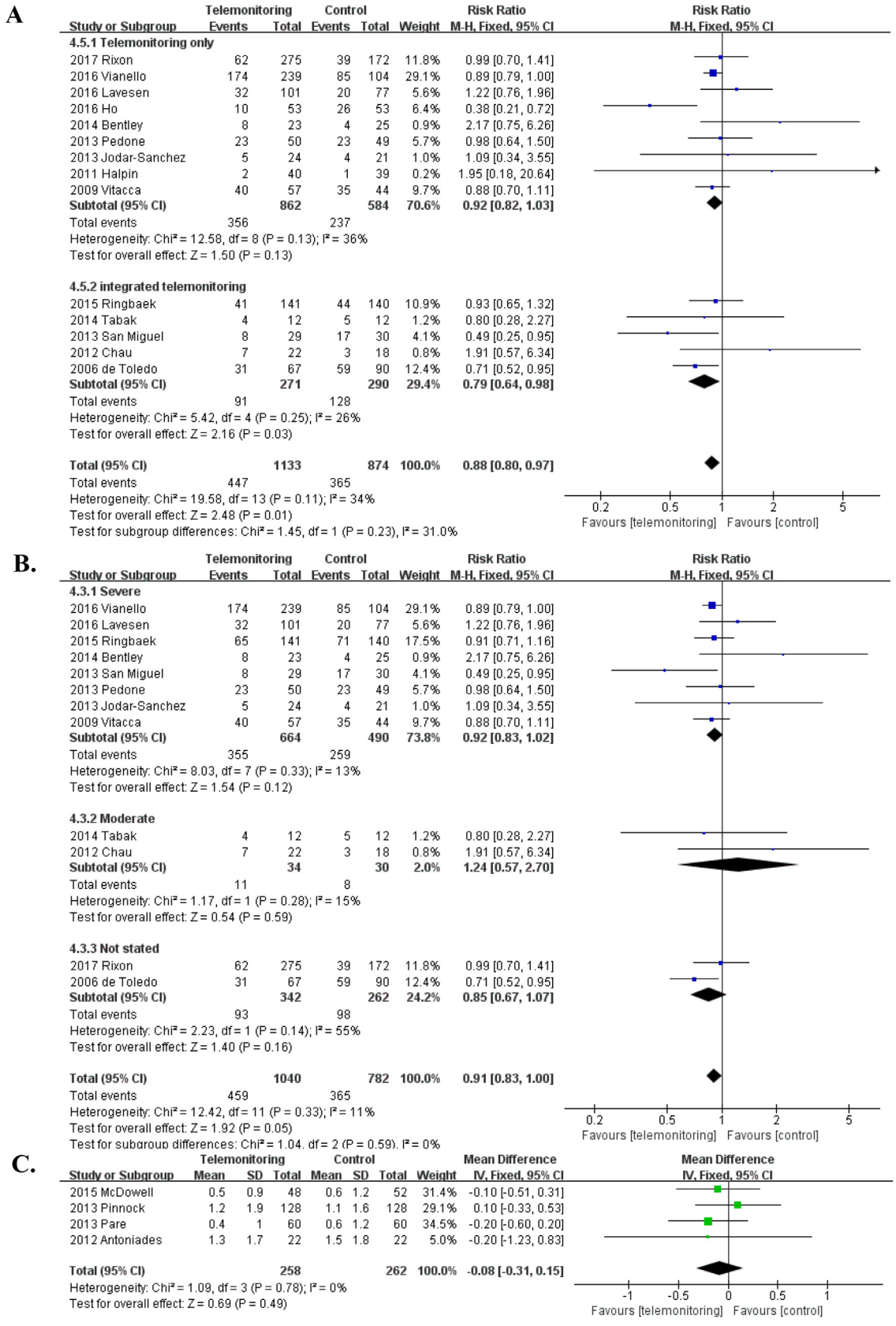

Fig. 4. Meta-analysis A. Hospitalization (subgroup analysis with intervention); B. Hospitalization (subgroup analysis with severity); C. Range of hospitalization.

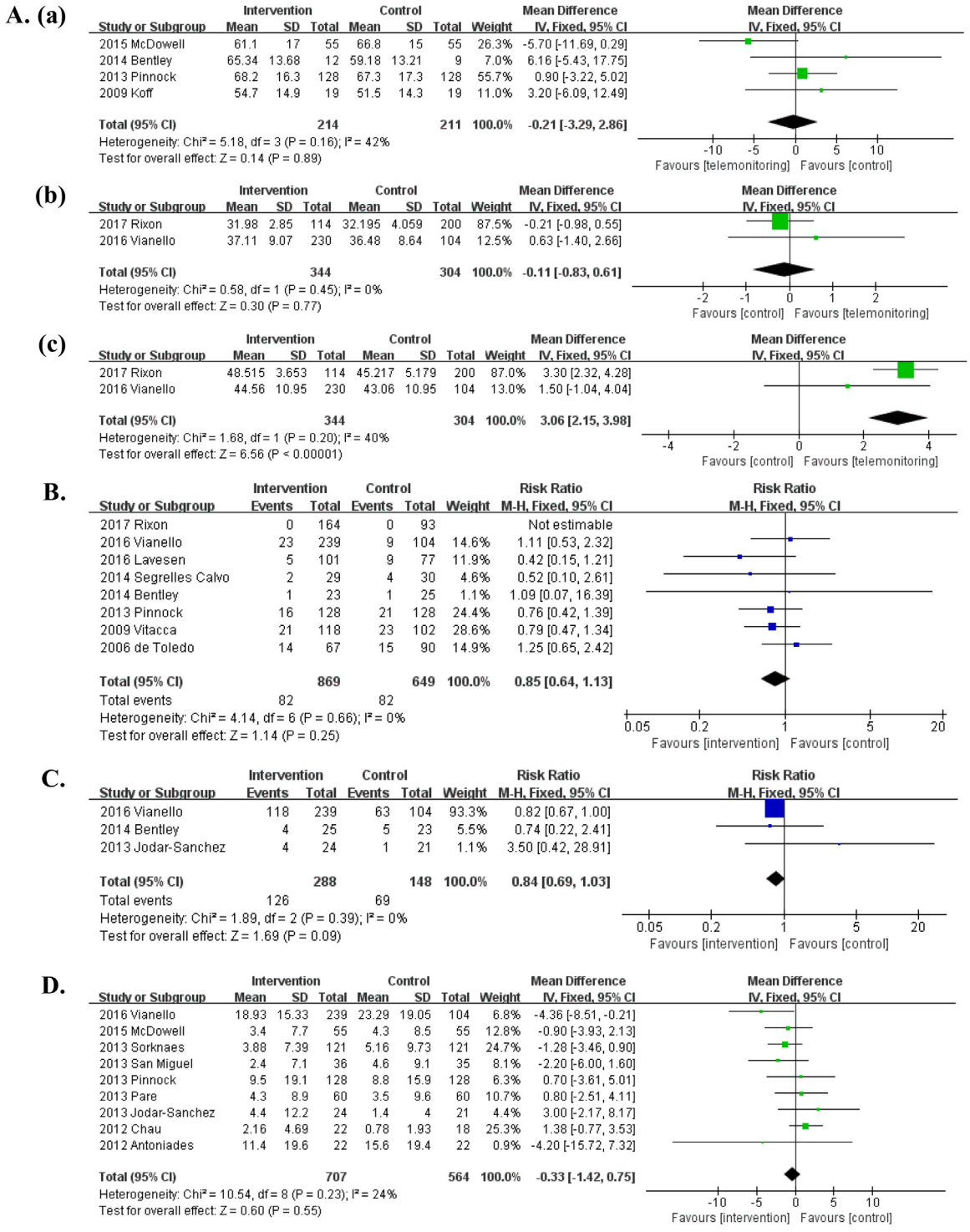

Fig. 5. Meta-analysis A. Quality of life (a) SGRQ; (b) SF-36 Physical Component Summery; (c)SF-36 Mental Component Summery; B. Mortality; C. Outpatient visits; D. Length of stay.

4.3. The impact on QOL

This systematic review examined the use of tele-monitoring in addition to standard care and found that tele-monitoring failed at improving quality of life in the intervention group compared to the control group. But, when we analyzed the physical health quality of life and the mental health quality of life separately, the mental health quality of life did improve significantly [RR 3.06, CI 2.15–3.98], while the physical health quality of life still did not improve. So, in case of the quality of life, it is necessary to analyze physical and mental quality of life separately thereby making it clear to where each quality of life exerts influence on.

In Gregersen et al. (2016) study, the tele-monitoring intervention did not make a strong case in the quality of life because only few studies showed statistically significant improvements relative to control groups. This is consistent with our study. Nonetheless, it is important to note that while the physical health quality of life did not improve, the mental health quality of life did improve

significantly. Blumenthal et al. (2014) reported similar results that the tele-monitoring group had greater improvement in psychological quality of life, including overall mental health, compared to control group. This suggests tele-monitoring makes patients become more aware of their illness and facilitates their natural coping and acceptance of their disease, which may improve the mental component of quality of life.

4.4. Strengths and limitations

Our systematic review is the most updated and comprehensive quantitative synthesis of the data on tele-monitoring to date. We explored the appropriate intervention components and the criteria for eligible patients in detail. One limitation of this study is that some studies were small and had methodological weaknesses. The blinding of participants was lacking, but treatment for participants cannot be blinded because of intervention characteristic. In the Cochrane Handbook, it is stated that 'assessments of risk of bias resulting from lack of blinding may need to be made separately for different outcomes. The outcomes including emergency room visits, hospitalization, mortality, and length of stay in our study were so objective that those were not affected by the lack of blinding of participants. Second, the heterogeneous interventions make comparisons difficult, and it can be challenging to draw conclusions. Third, there was a lack of information about the assessment of outcomes, such as exacerbations. Finally, outcome measurements, such as, quality of life and admission rates, were often reported in different ways, which makes meta-analysis of all the available studies impossible.

5. Conclusion

The cost of care assistance in chronic obstructive pulmonary disease patients is dramatically increasing. Based on this systematic review, tele-monitoring reduced rates of emergency room visits, hospitalization, and the SF-36 mental component summery. Active integrated tele-monitoring including the delivery of coping skills or education online, including pulmonary rehabilitation, is recommended in order to produce significant improvement. This application of integrated tele-monitoring is more useful to patients with severe and very severe chronic obstructive pulmonary disease than to mild patients. Tele-monitoring might be a useful application of information and communication technologies if it includes the appropriate intervention components for eligible patients. More evidence is needed before tele-monitoring can be considered as a useful management fool for chronic obstructive pulmonary disease patients. Further studies such as large size RCTs with sub-group by patient severity and intervention type is needed to confirm these findings.

Author contributions

S.H.L. contributed to the design of the study. All authors undertook the searches and screened studies for eligibility, assessed the quality of papers and performed statistical analyses. S.H.L. drafted the manuscript. All authors critically revised the manuscript for important intellectual content and the manuscript and approved the final version.

Competing interests

The authors declare that no competing interests exist.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijnurstu.2018.12.006.

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