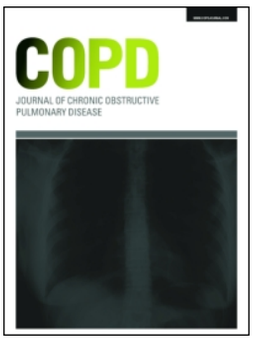

COPD: Journal of Chronic Obstructive Pulmonary Disease

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icop20

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To cite this article: Miguel T. Barbosa , Cláudia S. Sousa , Mário Morais-Almeida , Maria J. Simões & Pedro Mendes (2020): Telemedicine in COPD: An Overview by Topics, COPD: Journal of Chronic Obstructive Pulmonary Disease, DOI: 10.1080/15412555.2020.1815182

To link to this article: https://doi.org/10.1080/15412555.2020.1815182

Published online: 07 Sep 2020.

COPD: JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE
https://doi.org/10.1080/15412555.2020.1815182

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REVIEW

Telemedicine in COPD: An Overview by Topics

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ABSTRACT

COPD is a major cause of morbidity and mortality worldwide and carries a huge and growing economic and social burden. Telemedicine might allow the care of patients with limited access to health services and improve their self-management. During the COVID-19 pandemic, patient's safety represents one of the main reasons why we might use these tools to manage our patients. The authors conducted a literature search in MEDLINE database. The retrieval form of the Medical Subject Headings (Mesh) was ((Telemedicine OR Tele-rehabilitation OR Telemonitoring OR mHealth OR Ehealth OR Telehealth) AND COPD). We only included systematic reviews, reviews, meta-analysis, clinical trials and randomized-control trials, in the English language, with the selected search items in title or abstract, and published from January 1st 2015 to 31st May 2020 ($n = 56$). There was a positive tendency toward benefits in tele-rehabilitation, health-education and self-management, early detection of COPD exacerbations, psychosocial support and smoking cessation, but the heterogeneity of clinical trials and reviews limits the extent to which this value can be understood. Telemonitoring interventions and cost-effectiveness had contradictory results. The literature on teleconsultation was scarce during this period. The non-inferiority tendency of telemedicine programmes comparing to conventional COPD management seems an opportunity to deliver quality healthcare to COPD patients, with a guarantee of patient's safety, especially during the COVID-19 outbreak.

ARTICLE HISTORY
Received 2 July 2020
Accepted 19 August 2020

KEYWORDS
Telemedicine; ehealth; self-management; COPD; telemonitoring; COVID-19

Introduction

Chronic obstructive pulmonary disease (COPD) is a complex chronic respiratory condition, usually caused by exposure to toxic gases or particles [1]. Worldwide, COPD is a major cause of morbidity and mortality and carries a huge and growing economic and social burden [2,3]. Through the global digital transformation and using the data from the recently characterized COPD phenotypes, several studies focusing on the effects of different telemedicine programs for patients with COPD have been published.

Telemedicine is defined as the use of electronic information and communication technology by medical personnel to provide and support health care to patients when they are far away from the health care institutions [4,5]. It encompasses a wide range of technologies such as videoconferencing, wearable devices, internet platforms, mobile applications, store-and-forward devices, streaming media, and terrestrial and wireless communication.

Telemedicine can be used for a wide range of purposes, such as to decrease the demand on existing hospital and healthcare services, to promote health education, to reduce the cost of care, to measure and endorse treatment adherence, to quickly identify disease worsening, and to extend the accessibility of services to patients living in remote locations. Telemedicine is therefore a broad concept that involves diagnosis, treatment, monitoring, education and prevention [6].

The global market of telemedicine, particularly during this time of the COVID-19 pandemic, has been emerging as a safer alternative to usual clinical management in chronic respiratory diseases. In addition, the development of new technologies, easy to use and inexpensive, will increase the number of patients requesting telemedicine services.

Nevertheless, details of the implementation of telemedicine interventions in COPD have not been described, and the effectiveness of telemedicine interventions is still unclear. Therefore, with this organized review by topics of recent literature, we attempt to clarify which areas of interest of telemedicine in COPD care have been well appraised, which outcomes we can except from different interventions, and the possible future programs' changes to achieve better outcomes in COPD home-based care.

Material and methods

A literature search was carried out in MEDLINE database, for peer-reviewed articles published in English language between January 2015 and June 2020. The retrieval form of the Medical Subject Headings (Mesh) was: ((Telemedicine OR Tele-rehabilitation OR Telemonitoring OR mHealth OR

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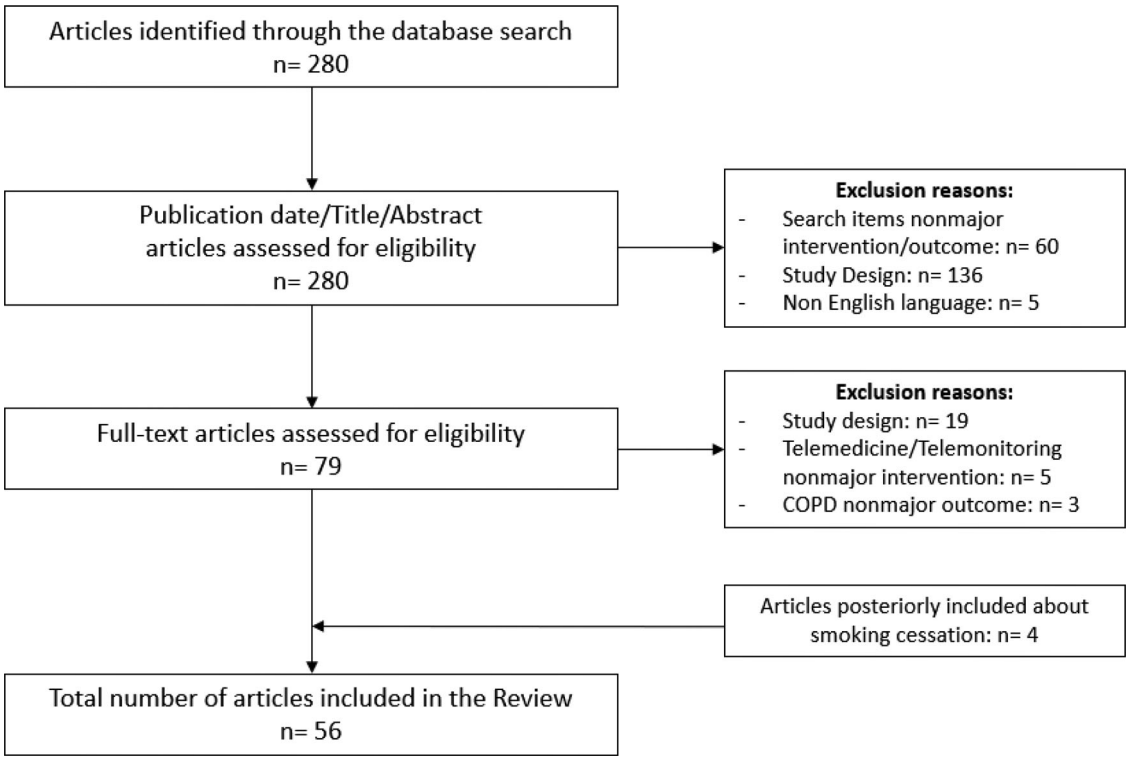

Figure 1. Flow chart showing the process of selection of the articles included in our review.

Ehealth OR Telehealth) AND COPD). Two researchers (CSS and MTB) independently extracted data from the abstract of the included studies, being exclusively: systematic reviews, reviews, meta-analysis, clinical trials and randomized-control trials, with the search items in title or abstract. A second assess to eligibility was carried by full-text articles analysis. Any disagreements during the process were resolved by discussion with a third researcher (MMA). An additional search was conducted for relevant recent studies regarding telemedicine assets on smoking cessation. Ultimately, 56 reports were included in this review (detailed information about the search methods is illustrated in the flow chart below—Figure 1).

Literature review

A significant number of reports have been published, evaluating the benefits and limitations of these technologies in managing and monitoring COPD patients in multiple ways. This review is organized by four main topics of telemedicine use in COPD: Tele-rehabilitation, Tele-health education and self-management, Telemonitoring, and other Mobile applications and websites. In addition, we reviewed four major outcomes: exacerbations of COPD and mortality rates; cost-effectiveness; psychosocial support and smoking cessation.

Tele-rehabilitation

The literature about tele-rehabilitation is plentiful when applied to COPD patients (Table 1). The majority of the studies obtained in our search showed either potential or positive results in augmenting rehabilitation adherence [7,13] and reduction of healthcare consumption (due to a decrease in number of COPD exacerbations, emergency department visits and hospitalizations) [10,16]. Also, it seems established a gain in quality of life (HRQoL and QoL) and in exercise tolerance (Six minute walk test) [8,13,15,16]. Likewise, it is noted an improvement in reduction of symptoms, increase in exercise capacity or tolerance and sense of social support [8,13,15]. It seems to be established that rehabilitation through telemedicine, especially by video platform, is safe [8,15], and well accepted by the patients that were satisfied with this type of programme [13,15]. A recent review also stated that it is feasible to deliver teleconsultations prior the initiation of pulmonary rehabilitation for rural or remote patients [14].

Tele-health education and self-management interventions

Tele-health education and self-management is characterized by certain interventions that empower patients, giving them the ability to manage by themselves their diseases with confidence [16]. The complexity of the digital health for self-management of COPD has escalated with recent advancement in technology [17]. Many reports attempted to show the short and long-term benefits of these interventions in chronic respiratory diseases (Table 2). The majority of studies determined that telemedicine and e-health interventions have a positive impact in self-management, adherence to treatment [22,23], quality of life improvement [16,19] and symptom management ability [22], though a trial by Rixon, L., et al. [19] specified that telehealth only significantly improved quality of life in long term follow-ups (compared

Table 1. Summary of the studies selected on the topic Tele-rehabilitation applied to patients with COPD.

Author	Study design	Publishing date/Country of Trial	Included patients/literature	Intervention & Conclusions
Broadbent, E., et al. [7]	Pilot, non-blinded RCT TR n = 30 vs UC n = 30 Follow-up: 4months	February, 2018 New Zealand	• Not specified in detail • COPD patients • 2 physiotherapists recruited participants in hospital	• An iRrobot measured pulse oximetry, forced expiration volume, heart rate, symptoms, mental state, and functional status weekly or as-needed, provided education about COPD and inhalation technique, and reminded patients when to take medication, inhalers and rehabilitation exercises. • This pilot trial suggested that a robot delivering telehealth care may be useful for augment adhesion to rehabilitation exercises in COPD, although hospitalizations may not be reduced.
Bernocchi P., et al. [8]	RCT TR n = 56 vs UC n = 56 Follow-up: 6months	Jan, 2018 Italy	• Patients with combined COPD and CHF undergoing in-hospital rehabilitation • Confirmed diagnosis of CHF (NYHA class II-IV) by echocardiogram and COPD (B, C and D GOLD class) documented by a spirometry performed within the previous 12 months	• Tele-rehabilitation programme 4-months long included remote monitoring of cardiorespiratory parameters, weekly phone-calls by a nurse, and exercise programme, monitored weekly by a physiotherapist. • Tele-rehabilitation in patients with COPD and CHF was feasible, safe, effective and was able to maintain the results for 6 months with no major side effects recorded and with a significant improvement in exercise tolerance (6MWT), QoL, dyspnea, physical activity profile, disability and time-to-event.
Bourne S, et al. [9]	Single-blinded RCT TR n = 64 vs OR n = 26 Follow-up: 7 weeks	Nov, 2017 UK	• $\geq$ 40 years-old • COPD diagnosis as defined by the NICE COPD guidelines • COPD patients referred to pulmonary rehabilitation • mMRC $\geq$ 2 • Access to the internet and ability to operate a web platform	• A 6-week programme of online-supported PR was non-inferior to a conventional model delivered in face-to-face sessions in terms of effects on 6MWT distance, symptom scores and it was safe and well tolerated.
Vasilopoulou, M., et al. [10]	RCT TR n = 50 vs OR n = 50 vs UC n = 50 Follow-up: 12months	May, 2017 Greece	• $\geq$ 40 years-old • COPD diagnosis as defined in GOLD with moderate to very severe airflow obstruction (post-bronchodilator FEV1 $<$ 80%) • Optimal medical treatment according to GOLD without regular use of systemic corticosteroids • History of acute exacerbations of COPD within the previous 12 months	• Home-based maintenance tele-rehabilitation was as effective as hospital-based, outpatient, maintenance PR and superior to usual care in terms of reducing the risk for acute exacerbation of COPD and hospitalizations, while preserving the functional and HRQoL benefits of a primary PR programme over a period of 12 months. • Moreover, only home-based maintenance tele-rehabilitation and not hospital-based, outpatient, maintenance PR was an independent predictor of reduced risk for ER visits.
Tsai, L. L., et al. [11]	Blinded RCT TR n = 19 vs UC n = 17 Follow-up: 8weeks	May, 2017 Australia	• Patients who were referred to a tertiary hospital PR programme with a primary medical diagnosis of stable COPD • Can operate a computer independently (following training) • Can use a stationary lower limb cycle ergometer and a walking	• Telerehabilitation was conducted as supervised group exercise training only, three times a week for 8 weeks. All participants performed lower limb cycle ergometry, walking training and strengthening exercises. • Telerehabilitation using real-time videoconferencing showed significant increase in

(*continued*)

Table 1. Continued.

Author	Study design	Publishing date/Country of Trial	Included patients/literature	Intervention & Conclusions
			course independently at home • Home walking course of at least 8 meters long • Can mobilize independently without a walking frame	endurance shuttle walk test time and self-efficacy, and a trend toward improvement in HRQoL when compared with usual medical care.
Franke, K., et al. [12]	Prospective crossover randomized study 44 patients Follow-up: 6months	Nov, 2016 Germany	• Patients with moderate to very severe COPD were eligible in a stable phase of their disease	• 6-months domiciliary bicycle ergometer training with telemonitoring in stable COPD. • Daily training time during the intervention phase was significantly superior. • Telemonitoring of home exercise cycle training is a simple method to enhance physical activity, improving health-related quality of life of patients with COPD.
Marquis, N., et al. [13]	Pre-experimental 26 patients one-group pretest–posttest	Nov, 2015 Canada	• $\geq$ 40 years-old • COPD diagnosis as defined in GOLD • FEV1 $<$ 70% • mMRC dyspnea score $\geq$ 2 • Smoker or smoking history $\geq$ 10 pack-years • No respiratory infection or exacerbation in the 4 weeks prior • Not having done PR in the previous 12 months • Access to a high speed Internet connection	• 8-week in-home pulmonary telerehabilitation via videoconference. • The study showed positive relevant changes after telerehabilitation for exercise tolerance and quality of life. Users (with moderate or severe COPD) were very satisfied with the programme, and adherence was high.
Selzler, A. M., et al. [14]	Review and example	Feb, 2018	• Literature review focused on telehealth in pulmonary rehabilitation	• Teleconsultations have been shown to be an effective means to assess patients' disease prior to the initiation of PR, and tele-rehabilitation has been shown to be as effective as institution-based PR at improving functional exercise capacity and health-related quality of life. • There is potential of virtual programs and telemonitoring to effectively delivery pulmonary rehabilitation to the rural and remote patients who are unable to access a specialized institution.
Almojaibel, A. A., et al. [15]	Review	Sep, 2016	• Literature review focused on real-time telerehabilitation for COPD patients at home	• Telerehabilitation seems feasible, accepted, and safe, besides that it was associated with positive clinical outcomes in quality of life, exercise capacity, dyspnea level, and the sense of social support. • Further research with a high level of evidence investigating the use of telehealth in pulmonary rehabilitation is still needed.

RCT: randomized control trial, TR: Tele-rehabilitation; UC: Usual care; GOLD: Global initiative for chronic obstructive lung disease; NYHA: New York Heart Association; OR: Outpatient-rehabilitation; 6MWT: Six minute walk test; QoL: quality of life; HRQoL: Health-related quality of life; mMRC: modified Medical Research Council dyspnea scale; CHF: Chronic heart failure; PR: Pulmonary rehabilitation; FEV1: Forced expiratory volume in 1 s.

to short term follow-ups). These interventions were well accepted by patients and facilitated doctor-patient relationship [23,25] and transition from inpatient to home-based care after an exacerbation [21]. Despite the overall positive outcomes, two studies have shown contradictory results. One RCT did not manage to find a positive effect on global health status even though suggesting there may be benefits in reduced hospital admissions and primary care visits [20] and another RCT found no significant reduction in unplanned all-cause hospitalization days, but showed that

Table 2. Studies selected on the topic Tele-health education and self-management in COPD.

Author	Study design	Publishing date/Country of Trial	Included patients/studies	Intervention & Conclusions
Kessler, R., et al. [18]	RCT (COMET) TH n = 157 vs UC n = 162 Follow-up: 12months	Jan, 2018 France (12 centres), Germany (8), Italy (6), Spain (7)	• ≥ 35 years-old • COPD diagnosis as defined in GOLD • FEV1 < 50% • Smoking history >10 pack-years • ≥ 1 severe exacerbation in the previous year • Patients could receive all relevant COPD treatments, including long-term oxygen therapy and home mechanical ventilation	• Multicomponent home-based disease management intervention (self-management, home monitoring and e-health telephone/web platform for reporting frequent health status updates, rapid intervention when necessary, and oxygen therapy monitoring). • High adherence to the intervention. • The COMET disease management intervention did not significantly reduce unplanned all-cause hospitalization days, but reduced acute care hospitalization days and mortality in severe COPD patients.
Rixon, L., et al. [19]	RCT TH n = 766 vs UC n = 811 Follow-up: 12months	Jul, 2017 United Kingdom	• COPD diagnosis in a GP care facility • Telephone, internet connection, and digital television at home • Sufficient cognitive capacity and English language skills to complete a self-reported questionnaire	• There was a trend of improved QoL and mood in the telehealth group at longer-term follow-up (12months), but not short-term follow-up (6 months). • Telehealth showed minimal benefit to QoL in COPD patients who were not preselected to be at increased risk of acute exacerbations.
Farmer, A., et al. [20]	RCT (EDGE) TH n = 110 vs UC n = 56 Follow-up: 12months	May, 2017 UK	• ≥40 years-old • Diagnosis of COPD as defined in GOLD • Smoking history >10 pack-years • mMRC dyspnea score ≥2	• Self-management support using a Digital Health System (daily measurement of pulse rate, SpO2 and symptom scores). • Tablet computer-based system of monitoring and self-management support does not impact, either positively or negatively on COPD-specific health status (SGRQ-C) over a period of 12 months in severe COPD patients. • However, there may be an overall benefit to patients through better overall health status (reduced hospital admissions and primary care visits).
Ritchie, C. S., et al. [21]	Non-blind RCT TH n = 223 vs UC n = 111 Follow-up: 1month	Sep, 2016 USA	• Patients admitted to the hospital from home with CHF or COPD • Estimated prognosis of greater than 6 months • Telephone • Expected to be discharged to their home.	• E-Coach technology-assisted transition from inpatient to home-based care (CHF and COPD) after an exacerbation. • Reduction in 30-day re-hospitalization rates in COPD patients when using an interactive voice response enhanced care transition. • No meaningful reduction in CHF patients.
Niznik J.D., et al. [22]	Systematic Review	Aug, 2018	• Literature review focused on pharmacist services delivered via telemedicine in chronic diseases management, such as asthma and COPD	• Clinical pharmacy telemedicine interventions in the outpatient or ambulatory setting, have an overall positive impact on outcomes related to clinical disease management, patient self-management, and adherence in the management of chronic diseases, such as asthma and COPD.
Morrison D., et al. [23]	Review	Nov, 2017	• Literature review focused on technology to support self-management in asthma and COPD	• New technologies as smartphone apps, web and telehealth can facilitate and promote self-management in

(*continued*)

Table 2. Continued.

Author	Study design	Publishing date/Country of Trial	Included patients/studies	Intervention & Conclusions
				both asthma and COPD patients and facilitate health professionals to meet their patient's treatment goals.
Murphy, L., et al. [16]	Overview of Reviews	Aug, 2017	• Literature review focused on clinical-effectiveness of self-management interventions in COPD	• Self-management supported by telehealth confers significant reductions in healthcare utilization, including hospitalization and emergency department visits. • Through education or as a component of pulmonary rehabilitation, self-management confers significant gain in health-related quality of life.
Hanlon, P., et al. [24]	Review	May, 2017	• Literature review focused on telehealth to support self-management of diabetes (types 1 and 2), heart failure, asthma, COPD and cancer	• Telehealth-mediated self-management was not consistently superior to usual care. None of the reviews assessing mortality in COPD showed any significant improvement with telehealth. No single component was consistently effective in any disease area, although none were associated with harm. • Larger-scale trials of telehealth-supported self-management, are needed before the extent to which telehealth technologies may be used to support self-management can be established.

TH: Tele-health; QoL: quality of life; UK: United Kingdom; SGRQ-C: St. George's Respiratory Questionnaire; CHF: Congestive heart failure; UC: Usual care; RCT: Randomized control trial; GOLD: Global initiative for chronic obstructive lung disease.

the implemented intervention reduced mortality in severe COPD patients [18]. Although, there were no reported main negative effects, further studies are needed to consolidate the possible impact of these technologies in self-management and health education in COPD patients [24,26,27].

Telemonitoring

The definition of this concept implies the transmission of physiologic and other noninvasive data [4]. The literature obtained by our search was extensive on this topic and the monitoring assessment and data alerts differed from study to study as it was already identified [28]. Telemonitoring is not generally accepted yet because of a lack of compelling evidence of its beneficial long-term effects and, once again, the results obtained were mixed (Table 3). Studies report improvements in some outcomes assessed: quality of life [12,31], hospital readmissions at three months after discharge [41], and time to readmissions and all cause emergency department or hospital admissions [29,34]. Vianello, A., et al. contradicts this information, with negative results in quality of life and a RCT with 578 patients intervened by Lilholt PH, et al. exposed a non-superior health-related quality of life in a 12-months follow-up [32,33]. Other data suggests it might not have impact in reducing mortality and exacerbation-related outcomes in COPD [35], with others showing reticence regarding the application of these interventions in a generalized way (34), stating that the benefits might come from the fact that patients submitted to clinical trials have more attention and support with the disease than otherwise they would receive. Few reports also established positive results and possibilities for the successful application of telemonitoring interventions: with regard to noninvasive ventilation [38] forced expiratory volume [39], peripheral oxygen saturation [28,29,42] and physical activity [12]. There are also investigations into new technologies and telemonitoring methods with encouraging outcomes, such as, respiratory oscillometry [30,36,43], exhaled breath temperature [37] or telemonitoring machine learning that will enable treatments to be personalized and early detect COPD exacerbations [6,38,40].

Mobile applications and websites

Some recent reviews advocate that mobile applications and websites might have positive outcomes (Table 4), promoting self-management, health-education and facilitating the way healthcare providers meet their patient's needs [23,48]. However more research is encouraged so that conclusions can be drawn in the future [47,48] considering that current information about mobile applications and websites in COPD health-education, self-management, and physical activity maintenance after a pulmonary rehabilitation program seems limited [44,45].

Table 3. Studies selected on the topic telemonitoring in COPD.

Author	Study design	Publishing date/Country of Trial	Included patients/studies	Intervention & Conclusions
Soriano J. B., et al. [29]	Non-blind RCT (PROMETE II) TH n = 115 vs UC n = 114 Follow-up: 12months	Nov, 2018 Spain (multicentre)	• 50-90 years-old • COPD GOLD diagnosis • Severe airflow obstruction defined as FEV1 < 50% • Treated with chronic home oxygen therapy • ≥2 moderate or severe exacerbations in the previous year (with or without hospitalization), but currently clinically stable	• Daily telemonitoring of blood pressure, SpO2, heart rate, respiratory rate and spirometry with remote patient management by a specialized nurse did not reduce COPD-related ER visits or hospital admissions compared to routine clinical practice. • A marked but non-significant trend toward a shorter duration of hospitalization and days in ICU. • The number of all-cause or respiratory-related deaths was comparable between groups, as was total resource utilization cost. • There were no differences by group in anxiety, depression, daily activity, EQ5D or COPD symptoms. • Telehealth was evaluated highly positively by patients and doctors.
Walker, P. P., et al. [30]	Non-blind RCT TM n = 154 vs UC n = 158 Follow-up: 9months	Sep, 2018 Spain UK Slovenia Estonia Sweden	• ≥ 60 years-old • COPD GOLD ≥ II • Acute exacerbation with/without hospitalization in the previous 12 months • Smoking history ≥ 10 pack-years • ≥1 Nonpulmonary chronic conditions	• In older patients with COPD and comorbidities, daily telemonitoring by forced oscillation technique and cardiac parameters was practical, well tolerated, and acceptable. • However, did not affect the time to first hospitalization, antibiotic prescriptions, hospitalization rate, or CAT, EQ5D and PHQ9 questionnaire scores. • There was no statistically significant change in QALYs but a potentially significant reduction in the mean cost per patient. • In an exploratory analysis, telemedicine was associated with fewer repeat hospitalizations and less total days hospitalized.
Tupper, O. D., et al. [31]	RCT TM n = 141 vs UC n = 140 Follow-up: 6months	Aug, 2018 Denmark	• COPD GOLD diagnosis and judged by the study staff as the leading cause of disability. • FEV1 < 60% • Hospital admission due to COPD exacerbation within the previous 36 months and/or prescribed long-term oxygen therapy due to chronic respiratory failure for at least 3 months. • Regularly scheduled visits to the respiratory outpatient clinics.	• Telemonitoring with close contact between the patient and the health care providers at the hospital had a positive impact on QoL in patients with more severe COPD. • Telemonitoring as an add-on to usual care over a 6-month period in severe COPD had a positive impact on QoL questionnaire, whereas no significant difference in CAT score. • Future studies should aim at determining the optimal cutoff point for health-related QoL assessment scores to select good telemonitoring candidates.
Lilholt PH, et al. [32]	RCT + Economic analysis (TeleCare North) TM n = 578 vs UC n = 647 Follow-up: 12months	May, 2017 Denmark	• COPD as primary disease, diagnosis by spirometry, in treatment according to GOLD • ≥ 2 exacerbations within the past 12 months • Motivated for treatment	• In addition to usual care, patients in the intervention group received a set of self-telehealth care equipment (tablet, sphygmomanometer, oximeter, scale) and were

(*continued*)

Table 3. Continued.

Author	Study design	Publishing date/Country of Trial	Included patients/studies	Intervention & Conclusions
			• Fixed residence in North Denmark Region • mMRC ≥2 or mMRC ≥ 3 and CAT ≥ 10	monitored by a community-based healthcare team. • There was an indication of some positive effects on HRQoL within certain subgroups, but no statistically significant differences in HRQoL between telehealth care and usual practice.
Vianello, A., et al. [33]	Non-blind RCT TM n = 223 vs UC n = 111 Follow-up: 12months	Nov, 2016 Italy	• Adult patients diagnosed with Class III-IV COPD • Life expectancy > 12 months • Capability of using, alone or assisted, the TM equipment	• Telemonitoring over a 1-year period had no significant effect on HRQoL, in preventing exacerbations or other cause-related hospitalizations. • Telemonitoring facilitate continuity of care during the hospital-to-home transition, improving outcomes in patients discharged after an exacerbation.
Ho, T., et al. [34]	RCT TM n = 53 vs UC n = 53 Follow-up: 6months	Mar, 2016 Taiwan	• ≥ 20 years-old • COPD exacerbation as the main diagnosis discharge to home • Spirometry-confirmed airflow limitation • Current or former smokers • Accessibility to the internet and phone at home	• Telemonitoring after patients discharged for COPD exacerbation • Telemonitoring improved outcomes in terms of time to COPD-related re-admission, and average number of all-cause re-admissions and emergency room visits in the six-month follow-up.
Li, X., el al [35]	Overview of Systematic Reviews	Jan, 2020	• Literature review focused on telemonitoring interventions in COPD patients	• Telemonitoring might not reduce mortality, improve QoL, exercise capacity, or exacerbation-related outcomes in COPD patients. Currently insufficient clinical evidence to support the effectiveness of telemonitoring for COPD.
Kruse, C., et al. [27]	Systematic Review	Mar, 2019	• Literature review focused on effectiveness of telemonitoring for COPD	• High variability between the articles and the telemonitoring services created conflicting results: 45% (13/29) stated that patient outcomes were improved, while 38% (11/29) indicated no improvement. • Authors identified the following facilitators to the adoption of telemedicine: reduced need for in-person visits, better disease management, and strengthened patient-provider relationship. • Important barriers included: low-quality data, increased workload for providers, and cost.
Zimmermann, S. C., et al. [36]	Review	Mar, 2019	• Literature review focused on the use of new pulmonary function indices in asthma and COPD	• Forced oscillation technique given its effort-independent nature and ease of performance, lends itself well for telemonitoring. Several studies demonstrated its feasibility in home telemonitoring of asthma and COPD. • FOT telemonitoring may enable early detection of exacerbations, early treatment and reduction of health and economic burden of acute exacerbations.
Popov, T. A., et al. [37]	Review	Aug, 2017	• Literature review focused on exhaled breath	• Exhaled breath temperature, is a simple, cheap and noninvasive tool to assess and

(*continued*)

Table 3. Continued.

Author	Study design	Publishing date/Country of Trial	Included patients/studies	Intervention & Conclusions
			temperature in respiratory medicine	monitor the state of the airways. • Ongoing systematic research will determine its place as a tool in home monitoring in line with the modern trends of personalized and telemedicine.
Arnal, J. M., et al. [38]	Review	Aug, 2017	• Literature review focused on monitoring of home noninvasive ventilation	• Telemonitoring might reinforce and change the organization of home NIV for COPD patients, improving daily use and reducing the number of treatment discontinuation by early detection of issues and problem solving.
Baroi S, et al. [39]	Systematic Review	Jun, 2018	• Literature review focused on remote respiratory assessments in COPD	• Forced expiratory volume assessed daily by using a spirometer is the most common modality of remote respiratory assessment. • Remote respiratory assessments are feasible and when combined with sufficient organizational backup can improve health-related outcomes, especially in high-risk people for acute exacerbations and who have limited access to the best care.
Tomasic, I., et al. [40]	Review	Apr, 2018	• Literature review focused on the available devices and technologies for the remote monitoring of COPD patients	• Remote monitoring systems for COPD might become integrated into the personalized medicine, which will reduce costs and improve care. • This will enable the treatments and care to be tailored to each patient's needs based on their predicted response and individual risks.
Yang, F., et al. [41]	Systematic Review and Meta-Analysis	Apr, 2017	• Literature review focused on continuity of care to prevent readmissions for COPD patients	• Health education reduced all-cause readmission at 3 months. The meta-analysis showed that comprehensive nursing intervention and telemonitoring interventions currently have the best evidence for reducing all-cause readmissions up to 6 months for patients with COPD. • However, telemonitoring, action plan and home visit interventions did not reduce mortality.

RCT: randomized control trial, TM: Tele-monitoring; UC: Usual care; GOLD: Global initiative for chronic obstructive lung disease; ICU: intensive care unit; CAT: COPD Assessment Test; EQ5D: EuroQoL 5 Dimensions; PHQ9: Patient Health Questionnaire-9; HRQoL: Health related quality of life; QoL: quality of life; NIV: non-invasive ventilation; mMRC: modified Medical Research Council dyspnea scale; SpO2: peripheral oxygen saturation; FOT: Forced oscillation technique; QALY: Quality-adjusted life year; FEV1: Forced expiratory volume in 1 s.

Exacerbations of COPD and mortality rates

Smartphones, artificial intelligence and wearable devices are emerging (Table 5) and their role for early prediction and prevention of COPD exacerbations has been rising [17]. The studies in our review reported contradictory outcomes regarding exacerbation and mortality rates. Hospitalization and readmissions decreased after implementation of a personalized care delivered through a web-based call center [26]. Acute exacerbations of COPD, emergency department visits and hospital admissions reduced after a tele-rehabilitation programme [10,49] and two other telemonitoring interventions [21,34]. Ding, L., et al. [17] suggested in a recent review a favorable decrease in exacerbation rate but with limited or inconsistent evidence. Other recent report also outlined positive outcomes. Walker, P., et al. [30] stated that telemonitoring by respiratory oscillometry and cardiac parameters reduced hospital readmissions and hospitalization length. Intermediate conclusions were obtained by two systematic reviews: smartphone mediated interventions, when combined with other strategies, might reduce COPD exacerbations [48] and home monitoring by daily spot check SpO2 measurements might be used as a

Table 4. Studies selected on the topic mobile applications and websites in COPD.

Author	Study design	Publishing date/Country of Trial	Included patients / studies	Intervention & Conclusions
Vorrink SN, et al. [44]	Investigator-blinded RCT TH n = 102 vs UC n= 81 Follow-up: 12months	Oct, 2016 The Netherlands	• ≥ 40 years-old • COPD patients GOLD stage 2 or 3 from 32 physiotherapy practices in the Netherlands • Who had completed a pulmonary rehabilitation programme of 3 months within the past 6 months and lived independently	• mHealth intervention to stimulate physical activity in COPD patients after pulmonary rehabilitation. The intervention consisted of a smartphone application for the patients and a monitoring website for the physiotherapists. • Although functional exercise capacity did not deteriorate, our mHealth intervention did not improve or maintain physical activity in patients with COPD after a period of pulmonary rehabilitation.
Ahern DK, et al. [45]	Report from a RCT 17 patients screened	Jul, 2016 USA	• In a general medical clinic, patients were approached by study staff while waiting in the examination room • Patients were not selected on the basis of having a diagnosis of COPD	• Evaluation of an iPad software application to assess patient's risk of developing COPD and to provide COPD and spirometry education information via video. • Tablet computers and mHealth apps for identification of COPD in primary care can be used to deploy acceptable and useable electronic risk assessments. • Future research focused on the impact and outcomes of patient-centered, mHealth apps is warranted.
Marcolino, M., et al. [46]	Review	Jan, 2018	• Literature review focused on the impact of mHealth interventions	• Evidence for mHealth efficacy is still limited. There is moderate quality evidence of improvement in asthma patients and increased smoking abstinence rates. • Most studies were performed in high-income countries, implying that mHealth is still at an early stage of development in low-income countries.
Hallensleben C., et al. [47]	Review	Jul, 2019	• Literature review focused on 47 eHealth applications for COPD in the Netherlands	• In the Netherlands 47 eHealth applications were found that focused on COPD care, medication adherence, smoking cessation, and information about COPD-related topics. More research into the effectiveness is needed. • Recommendation to develop a nationwide open source platform where well evaluated eHealth applications can be showcased for patients and health care providers to improve COPD care.
Alwashmi, M., et al. [48]	Systematic review	Sep, 2016	• Literature review focused on smartphone Interventions in COPD	• Smartphone interventions with synergistic strategies may reduce COPD exacerbations across a wide variety of contexts. • There is still need for more studies.

RCT: randomized control trial, TH: Tele-health; UC: Usual care; GOLD: Global initiative for chronic obstructive lung disease.

Table 5. Summary of the studies selected on the topic exacerbations of COPD.

Author	Study design	Publishing date/ Country of Trial	Included patients/studies	Intervention & Conclusions
Shah, S. A., et al. [42]	Analysis from the RCT (EDGE) EDGE patients (n = 110)	Mar, 2017 United Kingdom	• Data from 110 patients from 1-year long EDGE clinical trial, with a combined monitoring period of more than 35.000 days (average of 5.3 times per week).	• Pulse oximeter measurements are predictive of COPD exacerbations. • SpO_2 was the most predictive vital sign, followed by respiratory rate and pulse rate.
Liu, F., et al. [49]	Systematic Review	Feb, 2020	• Literature review focused on telemedicine in COPD in China	• Telemedicine in China can improve the quality of life (CAT score) and reduce the rates of hospitalization in COPD.
Ding, H., et al. [17]	Review	Oct, 2019	• Literature review focused on digital health approaches for COPD care: hospital, post-discharge and public health	• Digital-technology-enabled care programs to reduce hospitalizations and mortality have been demonstrated in many studies, but the clinical evidence often is limited and/or inconsistent.
Buekers, J., et al. [28]	Systematic review	Feb, 2018	• Literature review focused on oxygen saturation measurements in telemonitoring of COPD	• In many studies, deviating SpO2 values were used to raise alerts that led to immediate action from healthcare professionals (e.g. patient visits or hospital admissions). • Long-term follow-up of COPD patients using daily spot check SpO2 measurements is practically feasible, and could be valuable for exacerbation detections or predictions.
Al Rajeh, A., et al. [50]	Systematic Review	Nov, 2016	• Literature review focused on monitoring of physiological parameters to predict COPD exacerbation	• Currently insufficient information on how physiological parameters (vital signs and lung function) vary prior to exacerbation to support routine domiciliary monitoring.
Ko, F. W., et al. [26]	Review	Oct, 2016	• Literature review focused on acute exacerbations management in COPD	• Individually tailored care plan upon discharge through a web-based call center suggested a lower rate of hospitalization and readmissions, but no difference in mortality at 12-month follow-up. Minimal effects were found on self-efficacy, anxiety and health-promoting behavior.

RCT: randomized control trial, TH: Tele-health; TM: Tele-monitoring; UC: Usual care; GOLD: Global initiative for chronic obstructive lung disease; ICU: intensive care unit; CAT: COPD Assessment Test; EQ5D: EuroQoL 5 Dimensions; ER: Emergency room; SpO2: peripheral oxygen saturation; HRQoL: Health related quality of life; CHF: Congestive heart failure; FEV1: Forced expiratory volume in 1 s.

predictor of exacerbation [28]. Nonetheless, more studies are needed to consolidate these suppositions. More self-assured was the conclusion of the paper by Shah, S. et al. that determined pulse oximeter measurements are predictive of COPD exacerbations. Other studies advocated currently insufficient information on how physiological parameters (vital signs and lung function) vary prior to exacerbation to support routine domiciliary monitoring [50]. In severe COPD patients a remote patient management did not reduce emergency room visits or hospital admissions [33] despite reducing the duration of both hospital and ICU stays [29].

Concerning mortality rates, a recent 12-months RCT by Kessler, R., et al. [18] revealed a reduced acute care hospitalization days and mortality rate in severe COPD patients. Nevertheless, four reviews stated that telemonitoring and tele-health programs failed to significantly reduce mortality [24,26,35,41].

Table 6. Summary of the studies selected on the topic cost-effectiveness of telemedicine in COPD.

Author	Study design	Publishing date/ Country of Trial	Included patients/studies	Intervention & Conclusions
Mudiyanselage SB, et al. [51]	Single-blinded RCT + Economic analysis TH n = 83 vs UC n = 80 Follow-up: 12months	Jul, 2019 Australia	• Patients with Diabetes and/or COPD • High likelihood of hospital readmission over the next 12 months according to PRaDA model • Able to enter and submit their own data via a computer or similar device • English speaking • Lived in their own house • Willing and able to take their own vital signs and biometric readings via an appropriate device.	• Home-based personalized telemonitoring program exposed a significant saving in the cost of hospitalization over 12 months, due to a mean saving of 3.9 bed days, which offset the increased cost of telemonitoring. • Telemonitoring intervention improved patient's health outcomes and quality of life with no additional cost.
Witt Udsen F, et al. [52]	RCT + Economic analysis (TeleCare North) TH n = 578 vs UC n = 647 Follow-up: 12months	May, 2017 Denmark	• COPD as primary disease, diagnosis by spirometry, in treatment according to GOLD • $\geq$ 2 exacerbations within the past 12 months • Motivated for treatment • Fixed residence in North Denmark Region • mMRC $\geq$2 or mMRC $\geq$ 3 and CAT $\geq$ 10	• In addition to usual care, patients in the intervention group received a set of telehealth care equipment and were monitored by a community-based healthcare team. • Telehealth care is unlikely to be a cost-effective addition to usual COPD patients care (non-significant QALY-gain and higher costs).
Michaud, T. L., et al. [53]	Systematic review	Jan, 2018	• Literature on the costs of home-based telemedicine programs in chronic diseases management	• The costs of home-based telemedicine programs varied substantially by program components, disease type, equipment used, and services provided. • Telemedicine programs in general (COPD, Diabetes, CHF) reduced costs, although detailed costs data were either incomplete or not presented in detail.

RCT: randomized control trial, TH: Tele-health; UC: Usual care; GOLD: Global initiative for chronic obstructive lung disease; mMRC: modified Medical Research Council dyspnea scale; CAT: COPD Assessment Test; QALY: Quality-adjusted life year; FEV1: Forced expiratory volume in 1 s.

Table 7. Summary of the studies selected on the topic telemedicine psychosocial support in COPD.

Author	Study design	Publishing date / Country of Trial	Included patients/studies	Intervention & Conclusions
Barken TL, et al. [54]	Meta-ethnography	Dec, 2019	• Literature review focused on telemedicine in COPD	• Severe COPD patients are more likely to benefit by telemedicine, when it involves emotional, social, and clinical support, including regular contact with healthcare professionals.
Rzadkiewicz M, et al. [55]	Review	Sep, 2019	• Literature review focused on psychosocial interventions in COPD	• Self-management and exercise programs, enriched with digital monitoring, seem able to reach most affected patients with severe COPD (also those with respiratory failure), improving their psychosomatic condition. • Psychosocial interventions by telehealth with contradictory results, further studies needed.
Brunton L, et al. [56]	Qualitative Meta-synthesis	Oct, 2015	• Literature review focused on telehealth user experience in COPD	• Notable difference between patients' and health professionals' views and experiences of telehealth, with patients being generally more positive about tele-health use than health professionals.

RCT: randomized control trial, TH: Tele-health; UC: Usual care; GOLD: Global initiative for chronic obstructive lung disease; EQ5D: EuroQoL 5 Dimensions; SpO2: peripheral oxygen saturation; FEV1: Forced expiratory volume in 1 s.

Table 8. Summary of the studies selected on the topic telemedicine in smoking cessation.

Author	Study design	Publishing date/ Country of Trial	Included patients/studies	Intervention & Conclusions
Carrasco-Hernandez L., et al. [57]	RCT TH n = 120 Vs UC n = 120 Follow-up: 12months	Dec, 2019 Spain	• ≥ 18 years-old • Smokers with desire to stop • Owning an android smartphone • Ability to interact with smartphones	• The study aimed to analyze the long-term efficacy of a mobile app supporting psychopharmacological therapy for smoking cessation and complementarily assess the involved innovative technology. • A mHealth solution/mobile app, when complementing psychopharmacological therapy showed greater efficacy for achieving 52 weeks tobacco abstinence when compared with psychopharmacological therapy alone
Richter K., et al. [58]	RCT ITM n = 283 Vs Phone n = 283 Follow-up: 12months	May, 2015 USA	• ≥ 18 years-old • Recruited offline from 20 primary care and safety net clinics across Kansas • Smoke ≥5 cigarettes/day for at least 1 year • Smoke 25 out of the past 30 days • Speak English or Spanish • Have a telephone	• 4 sessions of ITM or 4 sessions of Phone counseling. Patients in ITM received real-time video counseling, similar to Skype, delivered by computer/ webcams in clinic exam rooms. • There was no superiority of telemedicine over telephone counseling for helping rural patients quit smoking. • Telemedicine increased utilization of cessation pharmacotherapy and increased participant satisfaction, but telephone counseling was significantly less expensive.
Cupertino, A., et al. [59]	Prospective study 40 patients Follow-up: 12weeks	Apr, 2019 Mexico	• ≥ 18 years-old • Mexican smokers interested in quitting within the next 30 days • Had smoked for at least 6 months • Smoked at least 3 days per week • had a cell phone with text messaging capacity • Willing to complete baseline and 12-week follow-up surveys	• Smoking cessation program that used a tablet-based decision support software to drive a 12-week text messaging smoking cessation program and pharmacotherapy support. • Integration of e-Health tools in primary healthcare settings has the potential to improve knowledge about cessation treatments among smokers and integrate smoking cessation into routine of care.
Whittaker R., et al. [60]	Cochrane Systematic review	Apr, 2016	• Literature review focused on mobile phone-based smoking cessation interventions	• There is moderate-certainty evidence that automated text message-based smoking cessation interventions can result in superior quit rates than minimal smoking cessation support.

RCT: randomized control trial, TH: Tele-health; ITM: Integrated Telemedicine; UC: Usual care; GOLD: Global initiative for chronic obstructive lung disease.

Cost-effectiveness

Although there are numerous studies about telehealth monitoring interventions, there is still limited evidence about its economic evaluation (Table 6). Michaud, T. L., et al. [53] recent systematic review showed a general reduction in costs using telemedicine programs in various chronic diseases management, besides incomplete detailed costs. The existing recent economic analyses from RCTs showed disparity results in cost-effectiveness of telemedicine in COPD care [29,51,52].

Psychosocial support

In recent studies, the focus on self-management, telehealth and pulmonary rehabilitation in both physical and mental health preservation is noticeable (Table 7). In advanced stages of COPD, chronic respiratory failure often develops, which might undermine mental health and reduce physical activity [55]. Recent outcomes of reviews about psychosocial support and interventions in COPD patients using telemedicine seem contradictory [26,55]. Nonetheless, Mudiyanselage et al., stated an improvement in anxiety and depression and health literacy with telemedicine [51] and another study reported that when a programme of telemedicine in severe COPD involves regular contact with healthcare professionals, patients are more likely to benefit from it [54]. A positive effect on well-being, emotional problems and sense of social support is also described in tele-rehabilitation programmes [15,55].

Table 9. Summary of other recent literature reviews about Telemedicine in COPD management.

Author	Study design	Publishing date	Main conclusions
Gaveikaite, V., et al. [61]	Review	Sep, 2019	• Positive tendency of European telehealth interventions to positive outcomes, but the heterogeneity of clinical trials and systematic reviews limits the extent to which this value can be understood. • Need for more standardized methods and updated systematic reviews.
Vitacca, M., et al. [6]	Review	Jan, 2018	• The overall extent and significance of benefits to patients and economic organizational expectations are not always consistent, however telemedicine will provide a framework for patient care, changing the future clinical practice and implementing flexible systems that can be customized to individual COPD patients' requirements.
Ambrosino, N., et al. [62]	Review	Nov, 2017	• Telemedicine might allow the care of patients with limited access to health services, and improve their self-management. • Controlled trials have investigated the feasibility, cost-effectiveness, security, and perspectives of tele-medicine; nevertheless, current literature is inconclusive on the real clinical benefits.
Ambrosino, N., et al. [63]	Review	Apr, 2017	• Telemedicine can improve the care of patients with difficult access to services, particularly those in rural/remote areas. However, this approach might be an alibi to reduce standard services in more developed health systems. • Despite the hopes in telemedicine as a means of patients' care, we need much more evidence before this modality can be considered as a real improvement in the management of patients. • The legal problems are still to be solved. Regulators must indicate ethical, legal, regulatory, technical, and administrative standards. • Much more research is needed before considering telemedicine a standard management of these patients.

Smoking cessation

Our first literature search did not find results regarding telemedicine assets on smoking cessation. However, a more global search showed some interesting outcomes about mHealth/mobile applications when complementing psychopharmacological therapy (Table 8), although with some extra costs [57–59]. In addition, a recent systematic review states that there is a moderate-certainty evidence that automated text message-based smoking cessation interventions can result in superior quit rates than minimal smoking cessation support [60].

Literature reviews of telemedicine in COPD

Recent literature reviews regarding a general sight of telemedicine approaches in COPD care (Table 9) also reported a positive tendency to telehealth interventions, yet inconclusive clinical enhancements and the need for more standardized trials and systematic reviews [6,61–63].

Discussion

The escalation in complexity and recent advancement in technology and the need for a safe and efficacious follow-up put telemedicine in the spotlight. Therefore, in the past five years, some fallouts have been pointed out regarding telemedicine use in COPD management.

Concerning tele-rehabilitation, our review supports that it seems a feasible and safe alternative to face-to-face pulmonary rehabilitation with an established non-inferiority of major clinical outcomes, such as exercise tolerance, dyspnea level and quality of life [14,15].

Digital health solutions regarding telemonitoring of COPD patients obtained contradictory outcomes, partly because of technical difficulties and low patient compliance. To address these matters, an integrative approach, possibly with continuous improvement and monitoring, seems essential [47]. Another important feature that optimizes the use of telemonitoring is to implement flexible systems that can be customized to individual patients' requirements, adapted to our diverse healthcare contexts and to correctly identify who the ideal candidates are, at what time they need it, and for how long [6]. Additionally, COPD patients are a very heterogeneous population with different phenotypes, with an overall decline in health status and a variable baseline physiological parameters [40]. Therefore, future research could optimize self-management by using individualized, time-dependent thresholds or predictive algorithms to account for individual differences, diminishing false-alerts, anxiety and lack of compliance [28]. Moreover, artificial intelligence and wearable devices are emerging and finding their way into the health sector and may provide new opportunities for early prediction and prevention of COPD exacerbation, diminishing hospitalizations, emergency room visits and hospital services burden, which would be especially useful during the current pandemic [17,55]. Unexpectedly, none of the reviews assessing mortality in COPD showed a statistically significant improvement within telemedicine programs [24].

COPD is often accompanied by anxiety disturbance, depression, lack of social support, and feeling of isolation. The majority of the reports about psychosocial support interventions or that considered the patients quality of life and general satisfaction about the telemedicine intervention got favorable outcomes, especially with regular contact with healthcare professionals [55,61].

Future clinical trials should include a cost analysis in their reporting to provide financial insights related to the implementation of the intervention [61]. The lack of detailed data on program costs and health-care service savings make it tricky for home-based telemedicine programs to make a solid economic case when considering reimbursement or investment in these programs [53].

Patients' age, education, experience in technological devices, cognitive, motor and visual abilities or deficits, their families and home environment play an important role in the use of technologies [62]. Therefore, technology-based interventions may not be as effective in some populations, what might limit the wider diffusion of telemedicine programs [64]. In this review the majority of the trials were grounded on high income countries which may not reflect the outcomes in less developed countries/areas. Nevertheless, the tendency for low cost technology, its wide spread throughout the world in different social/age groups and additional training in communication technology of the population, might balance this matter in a near future.

In this COVID-19 pandemic time, we are currently limited in our abilities to diagnose, monitor and manage chronic airway diseases in face-to-face consultations [36]. Surprisingly, none of the included studies intentionally analyzed COPD teleconsultations *via* telephone or videoconference as first doctor-patient, follow-up or second opinion medical consultations [14]. We consider it is a gap which necessarily should be complemented to the evolution of telemedicine in COPD as a cost-effective and safer health care alternative [65,66].

In conclusion, there was a positive tendency toward benefits in tele-rehabilitation, health-education and self-management, early detection of COPD exacerbations, psychosocial support and smoking cessation. Telemonitoring interventions and cost-effectiveness had contradictory results. The extent and significance of benefits to patients and healthcare organizations were not always consistent.

An important limitation of this study is that it only included articles written in English. Other important limitations are the short follow-up period, the small sized population studies and the different inclusion criteria of the majority of the RCTs/reviews included in this report which restrict conclusions and clinical recommendations.

Telemedicine itself seems to be not sufficient to yield a significantly better outcome, but it could be a key add-on in COPD care, especially in the COVID-19 pandemic, reducing both inpatient and outpatient health care burden.

In this time of major health services demand and very unique infection control concerns with the COVID-19 pandemic, a non-inferiority in the main outcomes of telemedicine programs presented in this review seems significant. It is quite likely that from now on telemedicine will allow significant changes in our clinical practice.

Support

No funding was received in the publication of this review.

Declaration of interest

The authors report no conflicts of interest.

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