



REVIEW

Virtual reality for COPD rehabilitation: a technological perspective



V. Colombo^{a,b,*}, A. Aliverti^b, M. Sacco^a

^a Institute of Intelligent Industrial Technologies and Systems for Advanced Manufacturing – National Research Council, via Previati 1/E, 23900, Lecco, Italy

^b Department of Electronics, Information and Bioengineering – Politecnico di Milano, via Ponzio 34, 20133, Milano, Italy

Received 18 August 2020; accepted 30 November 2020

KEYWORDS

COPD;
Virtual reality;
Rehabilitation;
eHealth

Abstract Virtual Reality (VR) is a promising technology for implementing personalized, motivating and controlled rehabilitation scenarios. Although its clear potential benefits, VR has been poorly investigated in pulmonary rehabilitation. This review analyses the state of the art, by searching the scientific and grey literature, regarding the use of VR for the rehabilitation of patients with chronic obstructive pulmonary disease, providing a technological perspective. First, the main characteristics of the included systems are presented in terms of visualization devices, way of interaction and type of feedback they provide. Then, results of the selected studies are reported considering feasibility, safety, usability and user experience as outcomes. Finally, the main findings are discussed and future directions for research are outlined.

© 2020 Sociedade Portuguesa de Pneumologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Chronic obstructive pulmonary disease (COPD) is a widespread chronic disease considered a leading cause of mortality and morbidity worldwide.¹ It represents a

substantial health and economic burden for both developed and low-income countries, with financial impact on national health care systems.² Due to an impaired respiratory function, COPD leads to an umbrella of comorbidities: physical impairment, cognitive decline, social isolation and lower quality of life. Pulmonary Rehabilitation (PR) is an evidence-based non-pharmacological treatment, consisting of a comprehensive intervention performed by a multi-disciplinary team³; it includes physical training, learning breathing techniques, psychological support and nutritional advice. Since the advent of new technologies, researchers have been working on different solutions to improve the rehabilitation process both from the clinical and the eco-

Abbreviations: AVGs, Active Video Games; COPD, chronic obstructive pulmonary disease; FOV, Field of View; HMD, Head Mounted Display; PR, Pulmonary Rehabilitation; SUS, System Usability Scale; VR, Virtual Reality; VE, Virtual Environment.

* Corresponding author.

E-mail address: vera.colombo@stiima.cnr.it (V. Colombo).

<https://doi.org/10.1016/j.pulmoe.2020.11.010>

2531-0437/© 2020 Sociedade Portuguesa de Pneumologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



Figure 1 An example of a Virtual Reality-based system for physical endurance training.

nomie point of view.⁴ These include, for example, mobile applications for the self-management of COPD,⁵ tele-monitoring systems exploiting multiple sensors⁶ and digital environments for exercise training. Within these solutions, Virtual Reality (VR) represents a powerful tool for improving exercise training allowing personalized treatments, performance monitoring and quantitative measurement—also integrating sensors and external devices.^{7,8} Virtual Reality, by creating engaging scenarios may enable the “attentional shift”, distracting the patient from negative sensations (e.g. fatigue, breathlessness) during physical activity⁹; VR can be also effective in increasing motivation, by turning repetitive exercises—typical of the sometimes-boring conventional protocols—in engaging and enjoyable tasks.¹⁰ Moreover, VR helps to simulate realistic scenarios that would be otherwise challenging or impossible to reproduce in the real world, in a safe and controlled way. The possibility of providing contextualized tasks which stimulate the cognitive functions of the patients, fosters the transfer of skills acquired during the rehabilitation sessions to activities of daily living.¹¹ In the context of COPD, VR is especially suitable for physical and breathing training. Physical training mainly includes endurance training, aimed to condition the muscles of ambulation and improve cardiorespiratory fitness, and strength training, in which local muscle groups are trained by repetitive movements performed with relatively heavy loads³; breathing training consists of different techniques (e.g. diaphragmatic breathing, pursed-lip breathing, inspiratory sighs) aimed at altering respiratory muscles recruitment and improving their performance thus decreasing breathlessness.¹² Hereafter we will consider these components of the intervention when referring to PR. Although it has been extensively used successfully in the treatment of different groups of patients e.g. post-stroke,¹³ patients with Mild Cognitive Impairment,¹⁴ frail elderly,¹⁵ children with neuromotor deficits,¹⁶ the application of VR to rehabilitation of COPD is still not fully explored. An example of a VR system for physical training is shown in Fig. 1. The aim of this work is to analyse the current state of the art in this topic, focusing on technical aspects and on the user’s perception of technology.

With respect to the analysis of the technical aspects, we need to clarify the term “Virtual Reality”, which

researchers often use when referring to any computer-based device that provides visual and audio stimuli, e.g. videogames, on a monitor.¹⁷ However, in VR, the user, surrounded by a 3D computer-generated representation, is “transported” into the virtual environment (VE), should be able to move in it and to interact with the virtual objects in a natural way as he/she is part of the scene.¹⁸ In fact, two key factors that characterize a VR system are *immersion* and *interaction*. These elements, as described in Table 1, influence the *sense of presence*, which in turn affects the effectiveness of the VR experience, e.g. the training.¹⁹

All these technical aspects contribute to the realism of the experience, the satisfaction of the user and, consequently, to the effectiveness of the rehabilitation intervention. In addition, when considering a system for rehabilitation two essential requirements are feasibility and safety, which should be evaluated in the context of use. A third factor that should be considered is usability, which should always be high for any kind of technology. Moreover, the overall user experience should be positive and engaging and, therefore, investigating different aspects such as enjoyment, interest, and acceptability is crucial for creating solutions that are well perceived by the patients. Digital solutions, including VR, should induce a positive user experience in patients because “if the users feel like the technology does not match their needs and preferences, or cannot be embedded in their routines, it will not be used”.²⁶ For all these reasons, it is important to consider these aspects both when designing and when evaluating a VR system for rehabilitation.

To the best of our knowledge, this work represents the first analysis providing a technological perspective on VR for PR. However, the increasing interest in understanding whether and how such technology could be effectively applied in this field is demonstrated by four reviews published between February 2019 and May 2020.^{27–30} All the four reviews focus mainly on the clinical effectiveness of videogames for patients with respiratory diseases. Three of them analyse exergames (i.e. exercise + videogame) for physical training, while Sanchez and colleagues include also studies providing educational intervention.²⁹ We will include in our analysis only the systems for physical and breathing training since these are the elements of PR that may benefit the most from an interactive multi-stimuli training environment, like the one provided by VR. Simmich and colleagues examine the effectiveness of game-based interventions vs. traditional protocols on physiological outcome measures, adherence and enjoyment in subjects with chronic respiratory diseases.²⁸ All respiratory conditions are admitted including asthma, thus widening the target population to children. Since age is a key factor in the perception and adoption of technology, our review will focus only on elderly patients. Similarly, Wang and colleagues published a systematic review including controlled trials but limiting the analysis to COPD patients.³⁰ Based on the seven papers they have analysed, the authors conclude that exergames, in particular active video games (AVGs), are useful and enjoyable as an adjunct to PR. The review by Butler et al. presents controlled studies involving different chronic diseases and considers exercise capacity as the primary outcome; secondary outcomes are dyspnoea, fatigue, energy expenditure as well as enjoyment and user preference.²⁷ The analysis by

Table 1 Definitions.

Virtual Reality	a three-dimension computer-generated representation of a reality that can be similar or completely different from the real world where the participant is able to move in a natural way while receiving multisensory stimulation
Immersion	a quality of the system's technology, an objective measure of the extent to which the system presents a virtual environment capable of delivering an inclusive (i.e. shutting out physical reality), extensive (i.e. depending on the sensory modalities accommodated), surrounding (i.e. the extent to which the virtual environment is panoramic rather than limited to a narrow field of view) and vivid (indicating the resolution, the fidelity of the virtual representation) illusion of reality. ²⁰ Depending on the level of immersion it provides a VR system can be: semi-immersive (e.g. a large projected screen) or immersive (e.g. a head mounted display).
Interaction	the combination of hand gestures, natural echo on the screen and manipulation of virtual objects that allow the user to navigate within the scene, to identify objects and to modify them. ²¹
Sense of presence	a subjective measure of a state of consciousness, the psychological sense of being in the virtual environment. ^{20,22}
Feasibility	a feasibility study is an iterative, formative and adaptive study that focuses on conducting research to examine whether the study can be done. ²³
Usability	the extent to which a specific user achieves a definite goal by effectively, efficiently and satisfactorily using a system within a specified context. ²⁴
User experience	encompasses user perceptions and responses resulting from the use or the anticipated use of a product, system, or service ISO. ²⁵

Sanchez et al. also covers not only COPD but also chronic bronchitis, emphysema, asbestosis, asthma, cystic fibrosis and bronchiectasis.²⁹ Like the other reviews, the analysis is focused on clinical outcomes (e.g. respiratory function, exercise capacity, symptoms, quality of life); knowledge of the disease is also considered with respect to educational interventions.

All the reviews mentioned share a clinical perspective, focusing on the comparison of physiological response and clinical outcomes with a control group. Instead, the present work provides a technological point of view through the analysis of the characteristics of the proposed systems in terms of technology and user experience. The aim of our work is thus to analyse the state-of-the-art-technology and to identify gaps in the existing literature regarding the application of VR to respiratory rehabilitation—and in particular training exercise (physical and breathing).

Methods

Since our analysis focuses on the technological aspects rather than on clinical effectiveness, a scoping review has been preferred. Such a methodology allows inclusion of not only the scientific but also the grey literature, which in this case may present preliminary works not yet eligible for full publication process. We observed the recommendations on scoping studies by Arskey & O'Malley³¹ to guarantee the application of a rigorous protocol.

Literature search and study selection

A literature search was carried out between September 2019 and November 2019; an update was carried out on October 31st 2020 in the following scientific databases: MEDLINE, IEEExplore, Scopus (EMBASE). Grey literature was analysed through Google Scholar. The search was restricted to year

2000 in the past because VR technology—in terms of both hardware and software—has significantly improved starting from 1999.³²

The authors searched the databases and selected the systems that met the following inclusion criteria.

- The system is designed for pre-elderly (between 50–65 y. old) or elderly (>over 65 y. old); main target users are COPD patients;
- It provides physical or breathing training;
- It is a digital solution, VR application or exergame/active videogame providing a virtual scenario and (at least) visual and/or audio stimuli, active interaction and feedback.

Mobile apps for self-management and apps for rehabilitation—e.g. based on written or video instructions—not providing an interactive virtual scenario were excluded as considered out of the scope of our analysis.

Data extraction and analysis

The following information was retrieved for each of the articles: year and type of publication, type of training, technology used, interaction device, visualization device, the presence and the type of physiological sensors integrated in the system.

Results

The study selection process and keywords are reported in Fig. 2. As a result, 21 articles, published between 2011 and 2020, were included in the analysis. As a scoping review, all types of publications have been admitted: 10 journal papers,

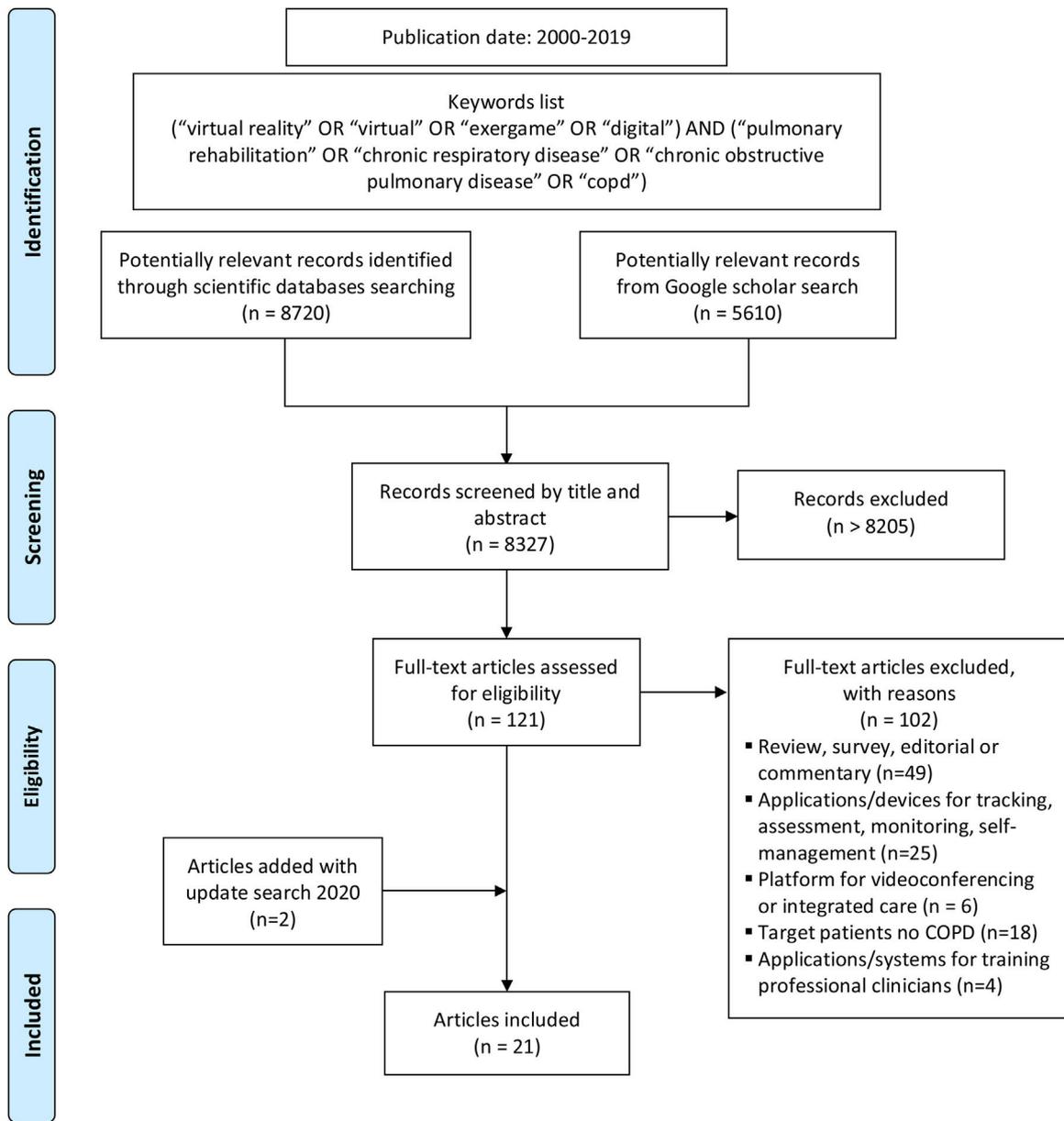


Figure 2 Flow diagram of study selection.

5 conference proceedings papers, 5 abstracts and a book chapter.

Training systems characteristics

The literature search focused on systems designed for physical and/or breathing training. Most of the systems (73%) are designed for physical exercise; around 16% provides breathing exercises only and 21% allows for both training modalities.

Most of the studies (68%) use active video games (AVGs) as a training tool for both physical and breathing exercises. Active video games, usually experienced through a PC/TV monitor or a *mobile* device screen, fall into the *exergames* category. Exergames, coupling physical activity and videogames, show some of the features of VR, e.g. *gami-*

fication, even if they are characterized by lower naturalistic sensory-motor interaction, limited ecological validity and lower degree of immersion. Regarding the reviewed studies, AVGs are based on consumer devices and, in particular, on Microsoft Kinect for XBOX, Nintendo Wii fit—either with or without the Balance Board. Six systems out of 21 are considered VR systems (see Introduction). Two studies provide training feedback and guidance through *mobile* applications. The main characteristics of the identified systems are summarised in Table 2.

Visualization

Different types of devices were used (see Fig. 3—Panel a) to display virtual contents to the user, each characterized by specific field of view (FOV), dimension and providing a given level of immersion. Most of the systems identified used a

Table 2 Main characteristics of the training systems (AVG = Active Video Game, VR = Virtual Reality, Y = yes, N = no, Semi = semi-immersive, Full = immersive, N* = not specified but likely not).

Authors	Article	Training	Type	Virtual scenario	Interaction	Immersion
Albores et al. 2011 ³³	Abstract	Physical (aerobic + upper body + lower body + balance)	AVG	3D mini-games cartoon-like: run in outdoor scenario, flapping arms to fly, free step on a stage, obstacle course (Wii fit plus)	Y	N
Albores et al. 2013 ³⁴	Journal	Physical (aerobic + upper body + lower body) + Breathing	AVG	3D mini-games cartoon-like: run in outdoor scenario, flapping arms to fly, free step on a stage, obstacle course (Wii fit plus)	Y	N
Colombo et al. 2019 ³⁵	Conference paper	Physical (aerobic + lower body)	VR	3D VE: bicycle ride in a park	Y	Semi
Dikken et al. 2015 ³⁶	Conference paper	Physical (aerobic + lower body)	VR	3D VE: bicycle ride on a roadway in a forest	Y	N
Jung et al. 2020 ³⁷	Journal	Physical	VR	3D virtual coach avatar showing how to perform exercises	N	Full
LeGear et al. 2014 ³⁸	Journal	Physical (aerobic + upper arm + lower body)	AVG	3D mini-game sports realistic scenarios: marching, dancing, air punching (EA SportsActive)	Y	N*
Makhabah et al. 2015 ³⁹	Abstract	Physical (upper body + lower body + aerobic) + Breathing	AVG	3D realistic scenario virtual coach on a mat: yoga, strength training, aerobic (Wii fit)	Y	N*
Marqueste et al. 2011 ⁴⁰	Abstract	Physical (lower body)	AVG	3D scenario with 2D representation of the board to guide the user on the next step (Wii fit)	Y	N*
Mazzoleni et al. 2014 ⁴¹	Journal	Physical (upper body + lower body + aerobic) + Breathing	AVG	3D game realistic scenario avatar on a mat either controlled by the patient or as virtual coach (Wii fit plus)	Y	N
Moorhouse et al. 2019 ⁴²	Book chapter	Physical (also educational contents)	VR	3D virtual coach avatar showing how to perform exercises	N	Full
Parent et al. 2017 ⁴³	Conference paper	Physical (upper body + lower body)	AVG	3D mini-games realistic avatar in a gaming scenario: squat movements; punch targets appearing; twist the core to navigate avoid bombs stopping (Shape Up XBOX fitness)	Y	N

Table 2 (Continued)

Authors	Article	Training	Type	Virtual scenario	Interaction	Immersion
Parent et al. 2018 ⁴⁴	Journal	Physical (aerobic + upper body + lower body)	AVG	3D mini-game realistic avatar in a gaming scenario: running on a railway with obstacles; punch targets appearing; twist the core to navigate avoid bombs stopping; (Shape Up XBOX fitness)	Y	N
Qin et al. 2014 ⁴⁵	Abstract	Breathing	VR	2D mini-games: filling a balloon inhaling to lift a bucket from a well to hydrate flowers; feeding the character rhythmically; inhale to stretch a slingshot exhale to get the best launch angle and cough to shoot the penguin	Y	N
Rutkowski et al. 2019 ⁴⁶	Journal	Physical (balance + aerobic + upper body + lower body)	AVG	3D mini-games in realistic scenarios: underwater scenario; cross-country running on a railway avoiding obstacles; rafting; hitting balls in a sports hall (Kinect Adventures)	Y	Semi
Rutkowski et al. 2020 ⁴⁷	Journal	Physical (balance + aerobic + upper body + lower body)	AVG	3D mini-games in realistic scenarios: underwater scenario; cross-country running on a railway avoiding obstacles; rafting; hitting balls in a sports hall (Kinect Adventures)	Y	Semi
Stafford et al. 2016 ⁴⁸	Conference paper	Breathing	<i>mobile</i>	2D mini-game: avoiding obstacles with a ball moved according to breathing (inhaling - go up; exhaling; go down)	Y	N
Sutanto et al. 2019 ⁴⁹	Journal	Physical (aerobic + upper body + lower body) + Breathing	AVG	3D mini-games free run in realistic scenarios + yoga deep breathing/half-moon; torso twist with a virtual coach on a mat (Wii fit plus)	Y	N
Tabak et al. 2012 ⁵⁰	Journal	Physical (lower body)	AVG	2D mini-games: catching balls with a submarine	Y	N
Tekerlek et al. 2017 ⁵¹	Abstract	Physical (aerobic + lower body)	VR	Not specified	(Not enough information)	Full
Wardini et al. 2013 ⁵²	Journal	Physical (aerobic + upper body + lower body)	AVG	3D mini-games cartoon-like: run/cycling in outdoor scenario, free step on a stage, obstacle course, stepping in a rhythm parade, boxing, canoeing (Wii fit plus + Wii sports + Wii resorts)	Y	N
Xu et al. 2013 ⁵³	Conference paper	Breathing	<i>mobile</i>	2D game: moving a ball through a pathway with obstacles	Y	N

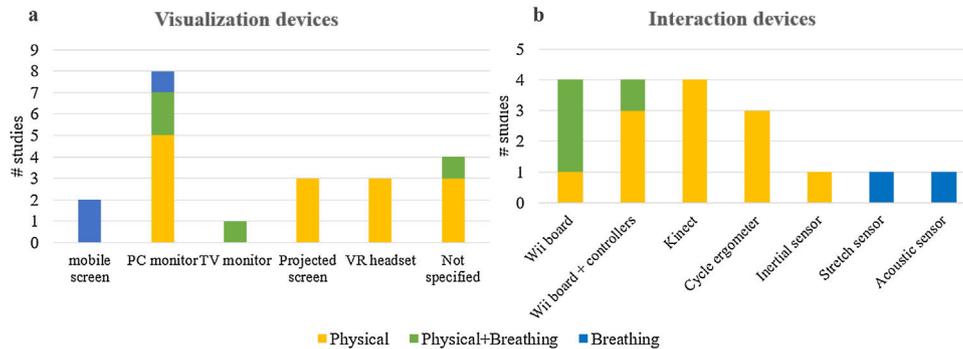


Figure 3 The visualization (a) and interaction (b) devices grouped according to the type of training (In panel a: Not specified are likely to be either PC monitor or TV monitor).

flat screen of small to medium dimensions and limited FOV providing no immersion: a PC monitor ($n=8$), a TV ($n=1$), a tablet/smartphone display ($n=2$). In 4 cases, the authors did not explicitly specify the type of visualization device, however, based on the described systems, it is very likely that a PC/TV monitor was used.^{38–40,52} Wider screens with a greater FOV were used in 3 studies in the form of a large projected screen.^{35,46,47} In this case, the VE covers a large part of the FOV thus allowing the viewer to be partly immersed in the virtual scenario (semi-immersive). Only 3 studies used a head mounted display (HMD), characterized by higher FOV providing a fully immersive experience.^{37,42,51}

Interaction and exercise feedback

To allow the user interact with the virtual contents, the analysed systems use different devices as shown in Fig. 3—Panel b. Most systems ($n=8$) are based on the Nintendo Wii fit consisting of the Balance Board—a board embedded with weight sensors placed at the four corners detecting the weight displacement over it—and one or two controllers—usually held in the hands and measuring the hands’ displacement through an accelerometer. The user interacts with the VE either moving on the Balance Board (e.g. stepping or swinging) or through the movements of the arms detected by controllers. Four of the included studies used the Microsoft XBOX Kinect, which features an RGB camera, a depth sensor and a microphone array.^{43,44,46,47} It can track the whole body and compute position and orientation of each joint of the skeleton. The user’s body movement is usually mapped to the human-like body skeleton of a virtual avatar. Those systems providing cycling training ($n=3$) used a cycle-ergometer with sensors for measuring the cycling speed, which controls the navigation in the VE.^{35,36,51} The solution presented by Tabak et al. consists of an accelerometer attached to the patient’s hip detecting the vertical displacement during the squat movement.⁵⁰ The systems for breathing training employed either acoustic sensors^{48,53} (i.e. a microphone placed at the mouth of the user) or a stretch sensor^{45,48} (i.e. a chest elastic band) to measure the respiratory signal, through which the user controls specific virtual objects.

In most cases ($n=10$), feedback on the performance is provided to the patient through a human-like virtual avatar, controlled by the user’s movement, in third-person perspective. In two of the cycling systems, the user navigates the environment in first-person perspective, as if he/she is rid-

ing a virtual bicycle.^{35,36} In all systems for physical training, the patient receives visual and audio feedback on correct movements and remaining time/time passing. In the studies using commercial AVGs, correct movements are often represented by the increase of the total score. When an aerobic task is foreseen—e.g. cycling or jogging in place—also real-time physical parameters, such as cycling speed or distance travelled, are shown to the patient. Few systems include physiological parameters as feedback during the exercise: three of them show heart rate and oxygen saturation level to either the patient or the physiotherapist only^{35,42,50}; one of the AVGs reports energy expenditure.³⁸

Study results

Seventeen papers—the characteristics of which are summarised in Table 3—present a clinical study involving COPD patients. Among these, 5 randomized controlled trials compared the outcomes of a group of patients training in VR with those assessed in patients undergoing traditional rehabilitation. Assessments were performed before and after the rehabilitation period, which lasted from 2 to 8 weeks, corresponding to the typical duration of PR. Five pilot studies and one longitudinal descriptive study present results of a VR-based physical training program on COPD patients. Three qualitative studies focused on the user experience investigating patients’ attitude towards the use of technology for rehabilitation. Participants of all studies are adults, most of them are elderly: average age is over 65 for 10 out of 17 studies; two studies do not provide details on participants’ age.^{39,40}

The study results are presented hereinafter focusing on the aspects of interest of our analysis: feasibility, safety, usability and user experience.

Feasibility and safety

The included studies demonstrate that using VR solutions for training is feasible for patients with COPD. Albores and colleagues designed an intervention based on 6 Nintendo Wii exergames involving upper and lower limbs.³³ Results in a small group of patients demonstrated the feasibility of such intervention, which elicits a level of exercise intensity similar to that recommended by standard protocols. The Nintendo Wii system has also been proven safe and feasible as an additional tool to traditional protocols with

Table 3 Characteristics of the included studies (M = male, F = female, CG = control group, EG = experimental group, HR = heart rate, VO₂ max = maximum rate of oxygen consumption, SpO₂ = oxygen saturation, RPE = rate of perceived exertion, FETCO₂ = end-tidal fractional concentrations of CO₂, HRQL = health-related quality of life, SUS = system usability scale).

Authors	Study type	Duration	Sample size	Target users	Outcomes
Albores et al. ³³	Pilot study	Single session	5	COPD (n = 5); age 68 ± 6; 1 M/4 F	1) exercise capacity 2) HR 3) max VO ₂ 4) minute ventilation 5) inspiratory capacity
Albores et al. ³⁴	Longitudinal descriptive	18 weeks (6 of usual care + 12 home exercise training)	20	COPD (n = 20); age 68 ± 10; 6 M/14 F	1) exercise capacity 2) health status 3) dyspnea 4) sit-to-stand in 30 test 5) arm lift repetitions
Colombo et al. ³⁵	Qualitative study	Single session	9	COPD, bronchial asthma (n = 9); age 69 ± 8; 4 M/5 F	1) SUS 2) Acceptability (Technology Acceptance Model)
Jung et al. ³⁷	Pilot study	8 weeks	10	COPD (n = 10); age: 68.9 ± 5; 6 M/ 4 F	1) focus groups and interviews (also see Moorhouse); 2) dyspnea 3) fatigue 4) emotional function 5) mastery 6) depression, anxiety 7) patient activation 8) strength, mobility, flexibility (self-reported)
LeGear et al. ³⁸	Cross-over	Single session (2 conditions)	10	COPD (n = 10); age: 65; 5 M/5 F	1) energy expenditure 2) SpO ₂ , HR 3) RPE 4) Dyspnea (Borg scale) 5) Blood pressure 6) Enjoyment 7) Perceived safety
Makhabah et al. ³⁹	Randomized controlled trial	6 weeks	20	COPD (n = 20); age/gender: not specified;	1) exercise capacity

Table 3 (Continued)

Authors	Study type	Duration	Sample size	Target users	Outcomes
Marqueste et al. ⁴⁰	Cross-over	Single session (2 conditions)	16	COPD (n = 16); age: 68.9 ± 11 (EG)/73.5 ± 9.2 (CG); gender: not specified;	2) dyspnea 3) baseline and transitional dyspnea 4) quality of life 1) ventilatory th
Mazzoleni et al. ⁴¹	Randomized controlled trial	3 weeks	40	COPD, ILD, Asthma, Bronchiectasis, RCD (n = 40); age: 68.9 ± 11 (EG)/ 73.5 ± 9.2 (CG); gender	2) HR 3) max oxygen uptake 4) respiratory exchange ratio and timing 1) lung and respiratory muscle function
Moorhouse et al. ⁴²	Qualitative study	8 weeks	10	COPD (n = 10); age: 68.9 ± 5; 6 M/ 4 F	2) arterial blood gases 3) exercise capacity 4) dyspnea 5) health status 6) HRQL 7) Emotional response focus groups and interviews area of improvements, satisfactions, perceptions, immersive learning, usability, intention to use
Parent et al. ⁴³	Pilot study	Single session	14	COPD (n = 14); age: 69.6 ± 5 (M); 74 ± 6 (F); 8 M/6 F	1) HR 2) ventilation and breathing rate 3) oxygen uptake 4) % quadricep saturation
Parent et al. ⁴⁴	Pilot study	Single session	14	COPD (n = 14); age: 69.6 ± 5 (M); 74 ± 6 (F); 8 M/6 F	physiological response 1) oxygen uptake 2) minute ventilation 3) tidal volume 4) FETCO ₂ at peak exercise

Table 3 (Continued)

Authors	Study type	Duration	Sample size	Target users	Outcomes
Rutkowski et al. ⁴⁶	Randomized controlled trial	2 weeks	68	COPD (n = 68); age: 60.5 ± 4.3 (EG)/ 62.1 ± 2.9 (CG); 35 M/33 F	5) effort perception 6) dyspnea 7) number of repetitions subjective responses 8) enjoyment 9) satisfaction 1) physical fitness
Rutkowski et al. ⁴⁷	Randomized controlled trial	2 weeks	106	COPD (n = 106); age: 60.5 ± 4.3 (EG)/ 62.1 ± 2.9 (CG); 47 M/63 F	1) strength upper lower body 2) flexibility upper and lower body 3) agility and dynamic balance 4) exercise capacity
Sutanto et al. ⁴⁹	Randomized controlled trial	6 weeks	20	COPD (n = 20); age: 65.1 ± 7.5 (EG)/ 65.6 ± 4.7 (CG); 19 M/1 F	1) exercise capacity/tolerance 2) dyspnea 3) quality of life
Tabak et al. ⁵⁰	Qualitative study	Single session	19	COPD (n = 19); age: 47–72; gender not specified	1) SUS 2) SpO ₂ , HR
Tekerlek et al. ⁵¹	Cross-over	3 single sessions	7	Chronic respiratory diseases (n = 7); age 53 ± 17; 2 M/5 F	1) exercise capacity 2) HR 3) SpO ₂ 4) dyspnea 5) affective responses 6) satisfaction
Wardini et al. ⁵²	Pilot study	3–4 weeks	32	COPD (n = 32); age: 66 ± 9; gender not specified	1) adherence 2) attendance rate 3) dyspnea 4) SpO ₂ 5) HR 6) enjoyment

a group of 32 elderly training for 3–4 weeks.⁵² In a more recent study by Albores and colleagues, the same intervention proved safe and feasible in an unsupervised scenario with patients training independently at home for 12 weeks with no adverse effects.³⁴ The same system was also used by LeGear and colleagues in a cross-over trial with 10 patients performing a single session of training including marching, dancing and two air punching exercises.³⁸ An education session with therapists explaining and demonstrating the exergames was performed prior to the training. All participants found the intervention enjoyable and safe; they all felt comfortable with the possibility of performing the exercises at home without supervision. Relatives and colleagues evaluated the feasibility of a training program based on high intensity AVGs by Microsoft Kinect XBOX.⁴⁴ In this study, the original descriptions of some tasks, provided by the manufacturer, have been adapted to match the patients' requirements better, e.g. "Squat as much as you can" has been modified to "Sit and stand on chair". Although most participants enjoyed the intervention and expressed their willingness to have the system at home, not all of them felt sufficiently confident about using it by themselves. More clear instructions and reminders (e.g. using pictures) should be added to ease the interaction especially for those patients who have little experience with technology. Moreover, monitoring the physiological response is considered crucial for both clinicians and patients to ensure safety in home-based setting. In most of the cases, safety was assured by the presence of a therapist, monitoring the vital signs and symptoms (e.g. heart rate, SpO₂, fatigue) during the whole exercise session using external devices, as used in the standard practice. These include pulse oximeters,^{38,41} respiratory monitor,⁴¹ heart rate sensors,⁴⁷ activity monitor to measure energy expenditure³⁸ and a portable metabolic analyzer.⁴⁴ In a few cases, these measurements were integrated in the application receiving data from a heart rate band and a pulse-oximeter,³⁶ a finger clip⁵⁰ and a wrist worn pulse-oximeter.^{35,37}

Usability and user experience

Three studies evaluated the usability, either through a standard tool (i.e. the System Usability Scale – SUS) or through one-to-one interviews. For both the cases in which the SUS was used, the usability was excellent.^{35,50} In both cases, however, the interaction between the user and the virtual contents was quite simple, representing a limitation to the positive results. In the system by Colombo et al. the user navigates the VE by simply cycling on the real ergometer³⁵; in Tabak et al., the user controls the exercise—i.e. moving a submarine to collect bubbles—through his/her movements acquired by an accelerometer attached to the hip.⁵⁰ When a higher level of interaction was required, i.e. using a VR headset for performing exercises, the patients found the system fairly easy to use even if some technical aspects could be improved (e.g. "adding the possibility to pause the system easily") to make the interaction easier.^{37,42}

Two studies explicitly include the evaluation of acceptability, assessed through ad-hoc questionnaires and spontaneous comments by the users. Colombo et al. focused attention on four variables: intention to use, perceived ease of use, perceived usefulness and subjective norm, which

represents the perceived social pressure to engage or not to engage in a specific behaviour (here adhering to the treatment).³⁵ Mazzoleni et al. evaluate the acceptability of a Nintendo Wii program in a group of patients undergoing 3-week rehabilitation addressing the following items: "comfort", "absence of pain", "fatigue", "enjoyment", "advantages", "desire to continue" and "suggest to anyone". In both studies, the acceptability was high.⁴¹ Even if a direct comparison cannot be made due to different methodology, both results suggest that patients show positive attitudes towards the use of technology for performing physical exercise. It is worth mentioning that both protocols foresaw the presence of a physiotherapist supervising the situation.

Tekerlek compared cycling on a stationary bike in three conditions: no feedback, music and VR. Patients reported low satisfaction—assessed through a 10-cm Visual Analog Scale—when in the VR condition mainly due to characteristics of the headset (weight, induced over sweating); they found the virtual content (video) repetitive and boring.⁵¹ A little discomfort with the use of an HMD has been reported in the study presented by Moorhouse et al. and Jung et al.^{37,42} Even if patients found the interaction quite easy to use, some of them complained about the weight of the device. The authors also performed focus groups and one-to-one interviews with participants to investigate all aspects of the VR training, which was divided into modules of increasing difficulty. A few patients found some modules too easy; a more personalized solution would make the VR experience more challenging and attractive. Nevertheless, all participants were satisfied with the training program; they reported a sense of satisfaction and increased motivation when successfully achieving a new training goal, e.g. completing a level of difficulty. Moreover, knowing that their usage and data were being tracked by health practitioners represented a strong motivator to adhere to the treatment. These qualitative results were supported by quantitative self-reported data presented in Jung et al. demonstrating improvements also in anxiety disorders, self-confidence and perceived physical strength and mobility.³⁷

In general, all studies reported that patients enjoy training with technology finding the virtual contents fun and motivating either at home or as part of the rehabilitation program in the hospital.^{35,44,50,52}

Discussion

Although the application of VR to PR is still developing, our review supports its feasibility, and its potential effectiveness to improve patients' motivation and engagement thus maintaining the benefits of rehabilitation over a longer period of time.

The papers included in our analysis are mainly focused on physical training; some are about teaching breathing techniques while few others combine breathing and physical exercise. This is in line with the standard practice for PR, which foresees physical training as cornerstone. The effects of breathing exercises on dyspnoea and overall patient's health condition is, instead, variable so that their role in the comprehensive management of COPD is not as widespread as physical activity.¹² Even if physical activity seems to also

improv cognitive functions and the use of VR itself is able to stimulate cognitive functions even without specific tasks, more research should focus on investigating the effect of integrating specific cognitive training in PR programs.^{14,54} In fact, no studies providing cognitive training have been identified even if the literature suggests that, also due to the typical age of COPD patients, cognitive decline impacts on their quality of life.⁵⁵

Most of the available studies employed AVGs, based on consumer devices, adapting the level of difficulty to the patients' needs. As a result, most of the proposed solutions did not follow a user-centred design approach; AVGs have a wider and more heterogeneous audience. Patients with COPD have specific needs and are in a vulnerable condition so that additional safety concerns should be considered (e.g. assuring that the intensity of the exercise is adequate through real-time monitoring). However, commercial exergames, which undergo product testing based on standards for quality, guarantee functional safety and reliability. Moreover, they provide attractive graphics and audio feedback. On the other hand, for prototypes, only basic functional testing is performed while no functional safety standards are applicable because the development efforts would exceed the scope of a prototype build-up. Among the included studies, 7 prototypes have been specifically designed for elderly patients.

Strengths of these systems are that they are based on standard PR protocols following the guidelines provided by the American Thoracic Society and the European Respiratory Society: cycling on a stationary bike for those referring to physical training; "pursed-lip breathing" and "holding breath and coughing" for those pertaining breathing training.

The most common visualization modality is the flat screen (either PC or TV monitors), which is cheap and simple to use both for clinicians and for patients. This is in line with most of the rehabilitation systems for the elderly, even if, in recent years, more complex and immersive systems are successfully spreading in other fields, e.g. in neuro-motor rehabilitation.¹³

As explained in §1, the level of *immersion*, which is defined by the number and range of motor and sensory channels involved, influences the *sense of presence* and, as a consequence, may positively alter the effectiveness of the VR-based training. The importance of presence makes VR different to exergaming, which uses video feedback or distraction techniques (e.g., watching a video) where presence is not required. Our analysis demonstrates the first attempts to introduce more immersive solutions in PR too. Projected screens represent a valuable solution for providing a wider FOV, which should make the user feel more present in the VE, even if they require a proper set up and a dedicated room. This may be the reason why only three studies have preferred such a solution. Head Mounted Displays provide a higher level of immersion—and consequently sense of presence—and are more portable, while there are still concerns about using such devices for this group of patients. Regarding technical aspects of HMDs and their acceptability, the few available studies show different results. In one situation, most participants tolerated wearing the helmet well, but even though they found the experience acceptable, some of them would have appreciated a lighter weight

device. In the second case, most patients complained about the weight of the device and the over sweating induced. The differing results are likely to be related to the different headsets used.

The other factor influencing presence is the *interaction*, which depends on the device through which the interaction is made possible and the feedback provided to the user (see Table 1). The more realistic the interaction—i.e. the user reacts as if he/she were actually there—the higher the level of ecological validity, which represents an important advantage of VR.⁵⁶ Interaction with the virtual contents was simple and natural in most of the analysed systems thanks to specific embedded sensors (e.g. accelerometers, encoders, acoustic sensors) able to measure the physical performance, e.g. in terms of hand's position and rotation, cycling speed and breathing rate. In most studies, physiological parameters were assessed using external devices both to assure safety and to assess primary outcomes (e.g. heart rate, energy expenditure). Embedding monitoring functionality in the applications may represent a step towards more efficient and more complete solutions, able both to provide a comprehensive overview to the clinicians and to be used by the patients at home with low supervision.

Given these characteristics, studies showed that VR-based training (aerobic, strength and breathing exercises) is feasible and safe for patients. A technological solution for health should be feasible—from technical, organisational and economic points of view—and safe, especially when dealing with vulnerable people, e.g. elderly, children, patients.²⁶ Regarding the studies analysed, the feasibility has been proven both as an alternative solution to standard protocols and as integrative one. Although few studies demonstrated that home-based training is feasible, most of them preferred a supervised scenario with an expert clinician constantly monitoring and guiding the patient. Further research should focus on evaluating feasibility in unsupervised situations. Continuity of care at home is indeed one of the main challenges in improving PR and the treatment of chronic conditions in general. Furthermore, promoting effective home-based rehabilitation is becoming more and more crucial, also given the recent COVID-19 pandemic, which has highlighted the need for more effective interventions that do not require patients, who are at higher risk of a more severe infection, to physically go to hospitals or clinical care facilities. Regardless of the level of supervision, we found that a familiarization session and step-by-step instructions are needed in order to make the patients—even the less confident—feel comfortable with technology.

As most of the studies are based on commercial exergames—which undergo product testing before being launched into market—only few studies evaluated the usability. Despite the scarcity of information, our analysis suggests that further research is needed to understand if more complex systems—such as HMDs—with a high level of interaction and immersion can be effectively used with COPD patients. In particular, the most advanced HMDs should be evaluated in order to guarantee the most comfortable experience thus avoiding weight and over sweating issues. Usability is a crucial requirement, especially for those users, such as the elderly, who may be less confident with technology; however, there are other factors influencing the

individual adoption of a technological solution which are worth investigating.

Only two studies presented results on acceptability; both showed that VR-based systems are considered useful and are well accepted by patients, who would like to have them at home. All patients were satisfied with this innovative way of training and enjoyed the virtual contents. They all found the proposed intervention highly motivating both because it distracts them from negative sensations (e.g. fatigue and breathlessness) and because it generates a report that the therapist can access thus inducing a sense of responsibility. Despite some evidence, the impact of these “human” factors on the motivation, engagement and, therefore, on the clinical outcomes is still under investigated.

Conclusions

In this paper, we investigate the use of Virtual Reality as a promising solution to improve both at home and in-hospital PR, providing a technological perspective and focusing on subjective experience of patients. Despite an increasing number of studies showing encouraging results demonstrating feasibility, acceptability and safety of VR for physical and breathing training of COPD, further research is needed. In particular, most of the systems identified are commercial exergames and are characterized by low levels of immersion and interaction. Further research should investigate whether higher immersion (e.g. using head mounted displays) and a more natural interaction (e.g. integrating physiological and motion sensors) enhances the rehabilitation outcomes, e.g., by inducing attentional shift from negative sensations.

Given the variety of factors affecting the successful implementation of technological solutions for health, cooperation between developers and clinicians is fundamental in order to maximize the benefits of VR for COPD rehabilitation. Only in this way can ad-hoc VR systems be built which exploit the most advanced technologies and which, at the same time, follow rigorous clinical protocols, with a real impact on patients’ quality of life.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. WHO. WHO | Projections of mortality and causes of death, 2016 to 2060 http://www.who.int/healthinfo/global_burden_disease/projections/en/ 2016 [Accessed 2020 Jul 22].
2. WHO. Global status report on noncommunicable diseases 2014: attaining the nine global noncommunicable diseases targets; a shared responsibility. <https://www.who.int/nmh/publications/ncd-status-report-2014/en/> 2014 [Accessed 2020 Jul 22].
3. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nicl L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key

- concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med.* 2013;188:e13–64, <http://dx.doi.org/10.1164/rccm.201309-1634ST>.
4. Riva G, Villani D, Cipresso P, Gaggioli A. Positive technology: the use of technology for improving and sustaining personal change. *IGI Global.* 2016, <http://dx.doi.org/10.4018/978-1-4666-9986-1.ch001>.
5. Yang F, Wang Y, Yang C, Hu H, Xiong Z. Mobile health applications in self-management of patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis of their efficacy. *BMC Pulm Med.* 2018;18:147, <http://dx.doi.org/10.1186/s12890-018-0671-z>.
6. Angelucci A, Aliverti A. Telemonitoring systems for respiratory patients: technological aspects. *Pulmonology.* 2020;26:221–32, <http://dx.doi.org/10.1016/j.pulmoe.2019.11.006>.
7. Rizzo A. “Skip”, Kim GJ. A SWOT analysis of the field of virtual reality rehabilitation and therapy. *Presence Teleoperators Virtual Environ.* 2005;14:119–46, <http://dx.doi.org/10.1162/1054746053967094>.
8. Lange B, Flynn SM, Rizzo AA. Game-based telerehabilitation. *Eur J Phys Rehabil Med.* 2009;45:143–51.
9. Matsangidou M, Ang CS, Mauger AR, Intarasirisawat J, Otkhmezuri B, Avraamides MN. Is your virtual self as sensational as your real? Virtual reality: the effect of body consciousness on the experience of exercise sensations. *Psychol Sport Exerc.* 2019;41:218–24, <http://dx.doi.org/10.1016/j.psychsport.2018.07.004>.
10. Palazzo C, Klinger E, Dorner V, Kadri A, Thierry O, Boumenir Y, et al. Barriers to home-based exercise program adherence with chronic low back pain: Patient expectations regarding new technologies. *Ann Phys Rehabil Med.* 2016;59:107–13, <http://dx.doi.org/10.1016/j.rehab.2016.01.009>.
11. Koenig ST, Krch D, Lange BS, Rizzo A. Virtual reality and rehabilitation. In: *Handbook of rehabilitation psychology.* 3rd ed Washington, DC, US: American Psychological Association; 2019. p. 521–39, <http://dx.doi.org/10.1037/0000129-032>.
12. Holland AE, Hill CJ, Jones AY, McDonald CF. Breathing exercises for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2012, <http://dx.doi.org/10.1002/14651858.CD008250.pub2>.
13. Laver KE, George S, Thomas S, Deutsch JE, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database Syst Rev.* 2015:CD008349, <http://dx.doi.org/10.1002/14651858.CD008349.pub3>.
14. Mrakic-Spota S, Di Santo SG, Franchini F, Arlati S, Zangiacomi A, Greci L, et al. Effects of combined physical and cognitive virtual reality-based training on cognitive impairment and oxidative stress in MCI patients: a pilot study. *Front Aging Neurosci.* 2018;10, <http://dx.doi.org/10.3389/fnagi.2018.00282>.
15. Pedroli E, Cipresso P, Greci L, Arlati S, Boilini L, Stefanelli L, et al. An immersive motor protocol for frailty rehabilitation. *Front Neurol.* 2019;10, <http://dx.doi.org/10.3389/fneur.2019.01078>.
16. Ravi DK, Kumar N, Singhi P. Effectiveness of virtual reality rehabilitation for children and adolescents with cerebral palsy: an updated evidence-based systematic review. *Physiotherapy.* 2017;103:245–58, <http://dx.doi.org/10.1016/j.physio.2016.08.004>.
17. Tieri G, Morone G, Paolucci S, Iosa M. Virtual reality in cognitive and motor rehabilitation: facts, fiction and fallacies. *Expert Rev Med Devices.* 2018;15:107–17, <http://dx.doi.org/10.1080/17434440.2018.1425613>.
18. Keshner EA. Virtual reality and physical rehabilitation: a new toy or a new research and rehabilitation tool? *J Neuroengine Rehabil.* 2004;1:8, <http://dx.doi.org/10.1186/1743-0003-1-8>.
19. Slater M, Usoh M, Steed A. Depth of presence in virtual environments. *Presence Teleoperators*

- Virtual Environ. 1994;3(2):130–44, <http://dx.doi.org/10.1162/pres.1994.3.2.130>.
20. Slater M, Wilbur S. A Framework for Immersive Virtual Environments (FIVE): Speculations on the Role of Presence in Virtual Environments. *Presence Teleoperators Virtual Environ.* 1997;6:603–16, <http://dx.doi.org/10.1162/pres.1997.6.6.603>.
 21. Figueiredo M, Böhm K, Teixeira J. Advanced interaction techniques in virtual environments. *Comput Graph.* 1993;17:655–61, [http://dx.doi.org/10.1016/0097-8493\(93\)90114-O](http://dx.doi.org/10.1016/0097-8493(93)90114-O).
 22. Witmer BG, Singer MJ. Measuring presence in virtual environments: a presence questionnaire. *Presence Teleoperators Virtual Environ.* 1998;7:225–40, <http://dx.doi.org/10.1162/105474698565686>.
 23. Orsmond GI, Cohn ES. The distinctive features of a feasibility study: objectives and guiding questions. *OTJR Occup Particip Health.* 2015;35:169–77, <http://dx.doi.org/10.1177/1539449215578649>.
 24. ISO 9241-11:1998 Ergonomic requirements for office work with visual display terminals (VDTs) - Part 11: Guidance on usability <https://www.iso.org/standard/16883.html> 1998 [Accessed 2020 Jul 31].
 25. ISO 9241-9304:2008 - Ergonomics of human-system interaction. - Part 304: User performance test methods for electronic visual displays <https://www.iso.org/standard/40099.html> 2008 [Accessed 2020 Nov 21].
 26. Van Gemert-Pijnen L, Kelders SM, Kip H, Sanderman R. *eHealth Research, Theory and Development : A Multi-Disciplinary Approach.* Routledge; 2018.
 27. Butler SJ, Lee AL, Goldstein RS, Brooks D. Active video games as a training tool for individuals with chronic respiratory diseases: a systematic review. *J Cardiopulm Rehabil Prev.* 2019;39:85, <http://dx.doi.org/10.1097/HCR.0000000000000320>.
 28. Simmich J, Deacon AJ, Russell TG. Active video games for rehabilitation in respiratory conditions: systematic review and meta-analysis. *JMIR Serious Games.* 2019;7:e10116, <http://dx.doi.org/10.2196/10116>.
 29. Torres Sánchez I, Megías Salmerón Y, et al. Videogames in the treatment of obstructive respiratory diseases: a systematic review. *Games Health J.* 2019;8:237–49, <http://dx.doi.org/10.1089/g4h.2018.0062>.
 30. Wang Y-Q, Liu X, Ma R-C, Yin Y-Y, Yang Z, Cao H-P, et al. Active video games as an adjunct to pulmonary rehabilitation of patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Am J Phys Med Rehabil.* 2020;99:372–80, <http://dx.doi.org/10.1097/PHM.0000000000001341>.
 31. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol.* 2005;8:19–32, <http://dx.doi.org/10.1080/1364557032000119616>.
 32. Slater M. Grand challenges in virtual environments. *Front Robot AI.* 2014;1, <http://dx.doi.org/10.3389/frobt.2014.00003>.
 33. Albores J, Normandin E, Marolda C, ZuWallack R, Lahiri B. *Physiologic Variables Observed In COPD Patients While Exercising With An Interactive Activity-Promoting Video Game.* In: B109. **PHYSICAL ACTIVITY, WALKING AND PULMONARY REHABILITATION FOR COPD.** *American Thoracic Society;* 2011. A3969–A3969.
 34. Albores J, Marolda C, Haggerty M, Gerstenhaber B, Zuwallack R. The use of a home exercise program based on a computer system in patients with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil Prev.* 2013;33:47–52, <http://dx.doi.org/10.1097/HCR.0b013e3182724091>.
 35. Colombo V, Mondellini M, Gandolfo A, Fumagalli A, Sacco M. Usability and acceptability of a virtual reality-based system for endurance training in elderly with chronic respiratory diseases. In: Bourdot P, Interrante V, Nedel L, Magnenat-Thalmann N, Zachmann G, editors. *Virtual Real Augment Real. Cham: Springer International Publishing;* 2019. p. 87–96, http://dx.doi.org/10.1007/978-3-030-31908-3_6.
 36. Dikken JBJ, van Beijnum B-JF, Hofs DHW, Botman MPL, Vollenbroek-Hutten MM, Hermens HJ. An integrated virtual group training system for COPD patients at home. In: Plantier G, Schultz T, Fred A, Gamboa H, editors. *Biomed Eng Syst Technol. Cham: Springer International Publishing;* 2015. p. 346–59, http://dx.doi.org/10.1007/978-3-319-26129-4_23.
 37. Jung T, Moorhouse N, Shi X, Amin MF. A virtual reality-supported intervention for pulmonary rehabilitation of patients with chronic obstructive pulmonary disease: mixed methods study. *J Med Internet Res.* 2020;22:e14178, <http://dx.doi.org/10.2196/14178>.
 38. LeGear T, LeGear M, Preradovic D, Wilson G, Kirkham A, Camp PG. Does a Nintendo Wii exercise program provide similar exercise demands as a traditional pulmonary rehabilitation program in adults with COPD? *Clin Respir J.* 2016;10:303–10, <http://dx.doi.org/10.1111/crj.12216>.
 39. Makhbah D, Suradi S, Doewes M. The role of interactive game-based system in pulmonary rehabilitation of patients with COPD. *Eur Respir J.* 2015;46, <http://dx.doi.org/10.1183/13993003.congress-2015.PA549>.
 40. Marqueste T, Lassus F, Castagna O, D'Amore D, Escarguel B, Marqueste L. Late-breaking abstract: Wii Fit™-step is a suitable exercise in rehabilitation programs in patients with COPD: a feasibility study. *Eur Respir J.* 2011;38.
 41. Mazzoleni S, Montagnani G, Vagheggin G, Buono L, Moretti F, Dario P, et al. Interactive videogame as rehabilitation tool of patients with chronic respiratory diseases: preliminary results of a feasibility study. *Respir Med.* 2014;108:1516–24, <http://dx.doi.org/10.1016/j.rmed.2014.07.004>.
 42. Moorhouse N, Jung T, Shi X, Amin F, Newsham J, McCall S. Pulmonary rehabilitation in virtual reality for COPD patients. In: tom Dieck MC, Jung T, editors. *Augmented Reality and Virtual Reality: The Power of AR and VR for Business.* Cham: Springer International Publishing; 2019. p. 277–90, http://dx.doi.org/10.1007/978-3-030-06246-0_20.
 43. Parent A-A, Comtois A-S. Pilot project: feasibility of high-intensity active video game with COPD patients. Tools for home rehabilitation. 2017 International Conference on Virtual Rehabilitation (ICVR) IEEE. 2017:1–2, <http://dx.doi.org/10.1109/ICVR.2017.8007476>.
 44. Parent A-A, Gosselin-Boucher V, Houle-Peloquin M, Poirier C, Comtois A-S. Pilot project: physiologic responses to a high-intensity active video game with COPD patients-tools for home rehabilitation. *Clin Respir J.* 2018, <http://dx.doi.org/10.1111/crj.12760>.
 45. Qin Y, Vincent C, Bianchi-Berthouze N, Shi Y. AirFlow: Designing immersive breathing training games for COPD; 2014. p. 2419–24, <http://dx.doi.org/10.1145/2559206.2581309>.
 46. Rutkowski S, Rutkowska A, Jastrzębski D, Racheniuik H, Pawelczyk W, Szczegieliński J. Effect of virtual reality-based rehabilitation on physical fitness in patients with chronic obstructive pulmonary disease. *J Hum Kinet.* 2019;69:149–57, <http://dx.doi.org/10.2478/hukin-2019-0022>.
 47. Rutkowski S, Rutkowska A, Kiper P, Jastrzębski D, Racheniuik H, Turola A, et al. Virtual reality rehabilitation in patients with chronic obstructive pulmonary disease: a randomized controlled trial. *Int J Chron Obstruct Pulmon Dis.* 2020;15:117–24, <http://dx.doi.org/10.2147/COPD.S223592>.
 48. Xu W. Flappy Breath: A Smartphone-Based Breath Exergame. 2016 IEEE First Int Conf Connect Health Appl Syst Eng Technol CHASE. 2016:332–3, <http://dx.doi.org/10.1109/CHASE.2016.70>.
 49. Sutanto YS, Makhbah DN, Aphridasari J, Doewes M, Suradi, Ambrosino N. Videogame assisted exercise training in patients with chronic obstructive pulmonary dis-

- ease: a preliminary study. *Pulmonology*. 2019;25:275–82, <http://dx.doi.org/10.1016/j.pulmoe.2019.03.007>.
50. Tabak M, Perianu RM, Hermens HJ. A serious game for COPD patients to perform physiotherapeutic exercises. *Natl Longdagen*. 2012;2012:56–7.
 51. Tekerlek H, Yagli NV, Saglam M, Cakmak A, Ozel CB, Ulu HS, et al. Short-term effects of virtual reality and music with exercise training on affective responses and satisfaction level in patients with chronic respiratory disease. *Eur Respir J*. 2017;50:PA2537, <http://dx.doi.org/10.1183/1393003.congress-2017.PA2537>.
 52. Wardini R, Dajczman E, Yang N, Baltzan M, Préfontaine D, Stathatos M, et al. Using a virtual game system to innovate pulmonary rehabilitation: safety, adherence and enjoyment in severe chronic obstructive pulmonary disease. *Can Respir J Can Thorac Soc*. 2013;20:357–61.
 53. Xu W, Huang M-C, Liu JJ, Ren F, Shen X, Liu X, et al. mCOPD: Mobile phone based lung function diagnosis and exercise system for COPD. Proceedings of the 6th International Conference on Pervasive Technologies Related to Assistive Environments. 2013:1–8, <http://dx.doi.org/10.1145/2504335.2504383>.
 54. Bherer L. Cognitive plasticity in older adults: effects of cognitive training and physical exercise. *Ann N Y Acad Sci*. 2015;1337:1–6, <http://dx.doi.org/10.1111/nyas.12682>.
 55. Cleutjens FAHM, Spruit MA, Ponds RWHM, Vanfleteren LEGW, Franssen FME, Gijzen C, et al. Cognitive impairment and clinical characteristics in patients with chronic obstructive pulmonary disease. *Chron Respir Dis*. 2018;15:91–102, <http://dx.doi.org/10.1177/1479972317709651>.
 56. Parsons TD. Virtual reality for enhanced ecological validity and experimental control in the clinical, affective and social neurosciences. *Front Hum Neurosci*. 2015;9, <http://dx.doi.org/10.3389/fnhum.2015.00660>.