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Virtual reality in adults with respiratory diseases experiencing dyspnoea: a systematic review and meta-analysis

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ABSTRACT

Objectives Our aim was to evaluate virtual reality's effects in dyspnoea's management.

Methods Information sources: Trials were identified through a systematic search carried out on MEDLINE. Web of Science, Scopus and CINAHL until 17 March 2025. Eligibility criteria: Eligible studies were controlled trials including adults with dyspnoea associated with respiratory diseases, for whom virtual reality was implemented and compared with another intervention. Risk of bias: Risk of bias (ROB) was assessed using the ROB 2 tool. Synthesis of results: The primary outcome was dyspnoea. Secondary outcomes included exercise capacity, healthrelated quality of life (HRQOL) and muscle function. Effect size was expressed using standardised mean difference (SMD) or MD for primary and secondary outcomes, respectively (random-effects model). We used the Grading of Recommendations Assessment, Development and Evaluation approach to judge the certainty of evidence. Results Included studies: 13 studies were selected, including 483 adults and using non-immersive tools (n=7) or immersive tools (n=6). Risk of bias in these studies was low (n=1), some concerns (n=8) and high risk (n=4). Synthesis of results: No difference was found in dyspnoea (8 studies, 224 participants; SMD 0.02, 95% CI −0.82 to 0.86, I^2 =88.2%), exercise capacity (5 studies, 183 participants; MD 3.62, 95% CI -19.39 to 26.63, $I^2=39.8\%$) and in HRQOL (4 studies, 127 participants; MD -11.81, 95% CI -42.95 to 19.33, $I^2=98.9\%$). The data available were insufficient to conduct a pooled analysis for muscle

Conclusions Limitations of evidence: The evidence is very uncertain about virtual reality's effects on dyspnoea due to risk of bias, imprecision and heterogeneity. Interpretation: Further studies are needed and should explore various aspects of the application of immersive virtual reality. PROSPERO registration number CRD42023443280.

INTRODUCTION

Dyspnoea is defined as a subjective experience of breathing discomfort that may occur during exertion, even at low intensities or at rest. Respiratory diseases represent the main comorbidities associated with this multidimensional symptom.²

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Respiratory diseases represent the main comorbidities associated with dyspnoea, a significant source of discomfort. Therefore, it appears imperative to offer treatments aimed at alleviating dyspnoea, An increasing number of studies are focusing on the use of virtual reality (VR) in respiratory diseases. A systematic review with meta-analysis was needed to evaluate the effects of VR on perceived dyspnoea.

WHAT THIS STUDY ADDS

⇒ Screening across four databases identified 6624 reports. A total of 13 studies were included in this systematic review. No difference was found in dyspnoea (8 studies, 224 participants), exercise capacity (5 studies, 183 participants) and in health-related quality of life (4 studies, 127 participants).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our confidence in effect estimates prevents us from drawing recommendations for the use of VR in clinical practice. This meta-analysis highlights the need to address several gaps in the use of VR: (1) more studies are needed, (2) multidimensional assessment tools for dyspnoea should be used and (3) multiple applications should be explored.

As a chronic manifestation, dyspnoea is a high-burden symptom. Chronic dyspnoea is defined as a persistent experience of breathing discomfort despite receiving the optimal treatment, leading to disability and deconditioning.³ People suffering with chronic dyspnoea have been shown to have a significant increase in mortality, greater exercise limitation, impaired muscle function and a severe decline in activities of daily living and health-related quality of life (HRQOL).4 Chronic dyspnoea is highly prevalent among individuals with chronic obstructive pulmonary disease (COPD), occurring in over 80% of cases, thereby making COPD the main cause of chronic dyspnoea.²⁵ In this context,



the severity of dyspnoea generally increases with disease progression and during acute exacerbations.⁶

Dyspnoea may also be acute and is a frequent reason for hospital admission. The may occur de novo (eg, pneumoniae, pulmonary embolism, pneumothorax) with, for instance, dyspnoea reported in 40%-90% of hospitalised patients with COVID-19 infection.⁸ Alternatively, it may also manifest in the context of chronic dyspnoea (ie, acute-on-chronic). In this context, prevalence of dyspnoea exceeds 90% for people with acute exacerbation of COPD.² Finally, individuals experiencing severe dyspnoea at the onset of an acute respiratory condition may face challenges in recovering from this symptom. ^{9 10}

Regardless of the condition, dyspnoea is a significant source of discomfort, and it therefore appears imperative to offer treatments aimed at alleviating dyspnoea. Among the most efficient rehabilitation treatments, exercise training is a key intervention and arguably the most fundamental one.11 Exercise training has been demonstrated to alleviate dyspnoea and maintain HRQOL, while simultaneously enhancing exercise capacity. In addition, as is well documented, deconditioning and sarcopenia have been shown to have a significant impact on dyspnoea intensity. Conversely, exercise training has been demonstrated to result in substantial increases in muscle strength and mass.¹¹ However, the management of dyspnoea is challenging. Indeed, the expectation of dyspnoea may unfortunately be one of the primary barriers to participation in physical activity, thereby compromising the potential benefits of exercise. 12

Virtual reality (VR) is a technology that allows users to be immersed in a computer-generated environment, which can be fully immersive (via head-mounted displays) or non-immersive (delivered through standard screens). Immersive VR creates an illusory visual environment at the expense of the real physical world. ¹³ In contrast, nonimmersive VR is typically two-dimensional and delivered through a computer or screen.¹³

An increasing number of studies are focusing on the use of VR in respiratory diseases. 14 15 The hypotheses underlying the effects of VR on dyspnoea are numerous, with some manifesting from a single exposure and others requiring repeated exposure. For instance, Betka et al showed that participants with COVID-19 infection improved their persistent dyspnoea with a single VR exposure. 14 In this study, participants received VR at rest during which they observed an avatar in addition to synchronous feedback of their own breathing. This 5 min exposure suggested short-term effects, underpinned by multisensory integration. Distraction and emotional modulation are other short-term mechanisms which have been described after a single exposure. 14 16 Finally, with repeated exposure, the long-term effectiveness of VR in modulating dyspnoea may be linked to the sustained effects previously mentioned or, in the context of rehabilitation, to its ability to enhance self-efficacy, motivation and the enjoyment of physical activity, thereby promoting adherence to exercise.1

Recent meta-analyses demonstrated that VR effectively improves both functional capacity and pulmonary function in people with COPD. However, these studies do not focus on dyspnoea, ¹⁸¹⁹ neither acute nor chronic, ^{18–20} nor on quality of life. ^{18–20} Moreover, authors do not consider the potential impact of immersion levels or number of exposures on dyspnoea perception and management. Finally, while COPD is the primary respiratory disease associated with dyspnoea, other conditions, such as COVID-19, may also be impacted.

Our objective was to evaluate the effects of VR on dyspnoea in adults with respiratory diseases. The secondary objectives were to evaluate the effect of VR on exercise capacity, muscle function and HRQOL in a population of individuals suffering from chronic breathlessness.

METHODS

Protocol and registration

This systematic review and meta-analysis followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines,²¹ was registered in PROSPERO (CRD42023443280) and commenced on 13 July 2023.

Eligibility criteria

Studies including adults with acute or chronic respiratory conditions causing dyspnoea were eligible. To be considered, participants had to experience dyspnoea; in this context, studies had to assess dyspnoea, whether as an inclusion criterion, an outcome or a baseline measurement. All controlled interventional trials were included when VR (immersive and non-immersive) was implemented and compared with another intervention. The intervention settings, durations and frequencies were not restricted. We excluded studies that were (1) lacking sufficient detail on outcomes or the VR intervention, (2) not clearly measuring dyspnoea and (3) using a no-intervention control group. Full details of our eligibility criteria are available in online supplemental material 1.

Information sources

Databases screened were MEDLINE, Web of Science, Scopus and CINAHL. We conducted a systematic search in databases from their creation to 17 March 2025.

Search strategy

Our search equation was built around Cochrane's recommendations²² specifying: (1) the population (eg, "Respiratory disease"), (2) the intervention (eg, "Virtual Reality") and (3) the study design. These three components were constructed using Medical Subject Headings (MeSH) terms (or their equivalent) and free-text keywords and combined using the corresponding boolean operators. The full search strategy was detailed in online supplemental material 2.



Selection process

Two reviewers (JW and CR) independently searched and extracted citations from each database. All duplicates were removed manually. The same reviewers conducted the selection process independently following title and abstract. Next, selected studies were retrieved and independently assessed based on their full text by the two reviewers to make the final inclusion. Any discrepancies were resolved by discussion between the two assessors. If no agreement was reached, another reviewer (FP) determined whether the article met inclusion criteria or not. We also searched the reference lists at the end of the included studies to identify additional relevant articles.

Data collection process

Two reviewers (JW and CR) independently extracted information in an excel form regarding: authors, year of publication, study design, number and characteristics of participants, inclusion and exclusion criteria, details of the intervention (immersive or non-immersive) and comparator, outcomes, follow-up times, dropouts and withdrawals. Any disagreements were resolved by a third assessor (FP).

The primary outcome was dyspnoea. Secondary outcomes were exercise capacity, muscle function and HRQOL. Data were reported in standardised data recording forms as means±SD. In case of missing data, authors were contacted for clarification.

Risk-of-bias appraisal

Two assessors (JW and CR) independently evaluated the risk of bias (ROB). For this purpose, the Cochrane risk of bias tool (ROB2) was used. ²³ Disagreements between the assessors were resolved by discussion with the methodologist (GC) if consensus was not reached.

Statistical analysis

As dyspnoea was measured on different scales, standardised mean differences (SMDs) were calculated.²⁴ For secondary outcomes, MDs were calculated. As we assumed heterogeneity across studies, we used the random-effects model to obtain the summary estimate. Data are presented using a forest plot (point estimates with 95% CIs). Heterogeneity was investigated using forest plot inspection and I2 statistic (with I2 strictly over 50% considered as substantial). Subgroup analyses were conducted to explore heterogeneity according to: (1) immersive or non-immersive VR, (2) single session or multiple sessions, (3) population (COVID-19, COPD, others) and (4) acute or chronic conditions. A funnel plot was used to assess publication bias and influence analysis was performed by calculating pooled estimates omitting one study at a time. This analysis was performed in the R language environment (V.4.2.2). Full details of statistical analysis are provided in online supplemental material 3.

Two independent reviewers (JW and CR) also assessed for each outcome the certainty of evidence following the Grading of Recommendations Assessment, Development and Evaluation approach.²⁵

Patient and public involvement

There was no patient or public involvement in the design and conduct of the present study.

RESULTS

Study selection

A total of 6624 records were identified until 17 March 2025. 2914 duplicates were removed before the screening. The remaining 3710 reports were screened for eligibility criteria and 3657 did not meet the inclusion criteria during title and abstract analysis. Handsearching identified seven reports. Next, 60 studies were assessed for eligibility and 45 reports were excluded during this full-text analysis, with the main reason for exclusion being unpublished (n=16) or not being a VR intervention (n=11) (Full details of exclusion in online supplemental material 4).

Following The Cochrane Handbook, ²² four reports were considered as two studies, with common register numbers NCT05244135²⁶ and ACTRN12617000275369. ²⁸ ²⁹ Finally, 15 reports ²⁶⁻⁴⁰ were included with a total of 13

Finally, 15 reports^{26–40} were included with a total of 13 studies. ²⁶ ²⁸ ^{30–40} Full details of the study selection process are available in figure 1.

Study characteristics

Nine of the included studies were classified as randomised controlled trial (RCT). $^{26\ 28\ 30\ 33\ 35-37\ 39\ 40}$ Four studies were classified as cross-over controlled studies. $^{31\ 32\ 34\ 38}$ Only one study was multicentre. 35

Total sample size was 483 participants. Most of them had COPD (n=325), 28 30 $^{32-34}$ 36 37 39 acute COVID-19 (n=44) 35 or post-COVID-19 syndrome (n=52). 26 38 Participants' ages ranged between 28 and 71 years. As only two studies included participants in acute settings (n=44), 30 35 most of the total size was in stable conditions (n=389). 26 28 $^{31-34}$ $^{36-40}$ The characteristics of the included studies are synthesised in table 1 (online supplemental material 5 and table S1).

Interventions are synthesised in table 1 (online supplemental material 5 and table S2). Seven studies focused on a non-immersive VR tool. 28 31-34 39 40 Six studies used an immersive VR tool through VR head-mounted display goggles. 26 30 35-38 Five studies focused on the immediate impact of the treatment, 31 32 34 35 38 while eight studies investigated a longer-term effect by incorporating the treatment into a rehabilitation programme. 26 28 30 33 36 37 39 40 Only three studies used a relaxation-based rest therapy 35 36 or breathing exercises, 37 while the remaining studies applied an exercise therapy 28 30-34 38-40 or a combination of both components. 26 Finally, four studies use VR alone compared with usual care (cycling or exercise training), 31 32 34 38

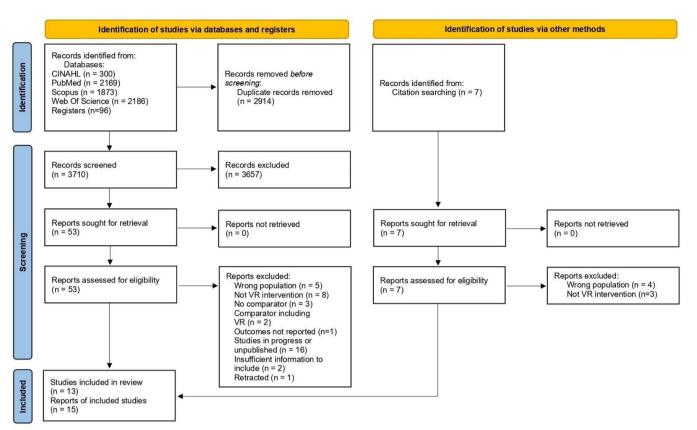


Figure 1 PRISMA flow diagram of the study selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; VR, virtual reality.

while the rest of the studies incorporate VR in addition to usual care. $^{26\,28\,30\,33\,35-37\,39\,40}$

Risk of bias

For dyspnoea, only one study had an overall low ROB, ⁴⁰ while the others were considered to have some concerns (n=4) ²⁶ ³⁰ ³⁵ ³⁷ or high ROB (n=3). ³³ ³⁸ ³⁹ Details of bias assessment are available in figure 2 and online supplemental figure S1.

RESULTS

Dyspnoea

Seven RCTs²⁶ 30 33 35 37 39 40 and four cross-over trials³¹ 32 34 38 compared dyspnoea between VR and standard treatment. Three studies³¹ 32 34 were not included in the quantitative analysis for several reasons described in the discussion. Finally, eight studies were pooled in the meta-analysis. ²⁶ 30 33 35 37-40 These studies enrolled 273 participants (138 in the control group and 135 in the VR group). Quantitative synthesis showed no difference between groups on dyspnoea (SMD 0.02, 95% CI (-0.82 to 0.86), I²=88.2%) with a substantial heterogeneity (figure 3 and online supplemental figure S2a). Our certainty was very low because of serious concerns about a high ROB, heterogeneity and imprecision (online supplemental table S3).

In subgroup analyses, the number of studies is insufficient in some subgroups and substantial heterogeneity remains in all subgroups (figure 3 and online supplemental figures S2b, S2c and S2d).

Secondary outcomes: exercise capacity, quality of life and muscle function

Seven RCTs compared exercise capacity between VR and standard treatment. 26 28 30 33 36 39 40 Five of these were pooled, ^{26 28 33 39 40} as they each measured 6 min walk test (6MWT) distance. For the two remaining studies, as the 1 min sit-to-stand³⁰ and the metabolic equivalent of task³⁶ have distinct constructs, it prevented us from metaanalysing it with 6MWT. These 5 studies enrolled 183 participants (88 participants in the control group and 95 participants in the VR group). 26 28 33 39 40 Random-effects meta-analysis showed no difference between groups on exercise capacity (MD 3.62, 95% CI (-19.39 to 26.63), $I^2=39.8\%$) with a moderate heterogeneity (figure 4A). The two remaining studies reported little to no difference in favour of VR on exercise capacity. 30 36 Our certainty was low because of serious concerns about imprecision (online supplemental table S3).

Five RCTs compared HRQOL between VR and standard treatment. ^{27 33 37 39 40} Four RCTs were pooled, as they each measured HRQOL using St George's Respiratory Questionnaire (SGRQ). ^{33 37 39 40} The remaining study reported



Table 1 Characteristics of the included studies

				Intervention				
Authors, year, country	Design	Number of participants	Respiratory disorders	Duration	Number of sessions	Intervention group	Control group	Outcomes
Kizmaz <i>et al</i> , 2024, Turkey ³⁰	RCT	50	Acute exacerbation of COPD (hospitalised)	N/S	3	Standard rehabilitation+immersive VR	Standard rehabilitation	► MRC ► 1STS
Kuys <i>et al</i> , 2011, Australia ³¹	Cross over	19	Cystic fibrosis	2 days	1	Non-immersive VR	Moderate interval training	Borg
LeGear et al, 2016, Canada ³²	Cross over	10	COPD	1 day	1	Non-immersive VR	Continuous moderate training	Borg
Mazzoleni <i>et al</i> , 2014, Italy ³³	RCT	40	Chronic respiratory disease	21 days	21	Standard rehabilitation Non-immersive VR	Standard rehabilitation	MRC-6MWT- SGRQ
Nicolas <i>et al</i> , 2021, France ³⁴	Cross over	20	Chronic respiratory disease	1 day	1	Non-immersive VR	Endurance training	Borg
Rodrigues et al, 2022, Brazil ³⁵	RCT	44	Acute COVID-19 (hospitalised)	1 day	1	Usual therapy+immersive VR	Usual therapy+sham immersive VR	Numeric Scale
Rutkowski <i>et al</i> , 2020, Poland ²⁸	RCT	110	COPD	2 weeks	10	Standard rehabilitation+non immersive VR	Standard rehabilitation	6MWT
Rutkowski <i>et al</i> , 2021, Poland ³⁶	RCT	50	COPD	2 weeks	10	Standard rehabilitation+immersive VR	Standard rehabilitation	6MWT
Rutkowski <i>et al</i> , 2023, Poland ²⁶	RCT	32	Post-COVID-19 Syndrome	3 weeks	15	Standard rehabilitation+immersive VR	Standard rehabilitation	Borg-6MWT- WHOQOL-BREF
Simsekli <i>et al</i> , 2025, Turkey ³⁷	RCT	48	COPD	8 weeks	24	Usual care+immersive VR	Usual care	► MRC ► SGRQ
Stavrou et al, 2023, Greece ³⁸	Cross over	20	Post-COVID-19 Syndrome	1 day	1	Cycling with immersive VR	Continuous endurance training	Borg
Sutanto et al, 2019, Indonesia ³⁹	RCT	20	COPD	6 weeks	18	Cycle endurance training+non-immersive VR	Cycle endurance training	MRC-6MWT- SGRQ
Yuen <i>et al</i> , 2019, USA ⁴⁰	RCT	20	Idiopathic pulmonary fibrosis	12 weeks	36	Non-immersive VR	Sham non- immersive VR	▶ Borg-6MWT▶ SGRQ

COPD, chronic obstructive pulmonary disease; MRC, Medical Research Council; 6MWT, 6 min walk test; N/S, not specified; RCT, randomised controlled trial; SGRQ, St George's Respiratory Questionnaire; 1STS, 1 min sit to stand; VR, virtual reality; WHOQOL, WHO Quality of Life.

HRQOL using the WHO Quality of Life-BREF questionnaire, 27 which has the distinctive characteristic of not having a total score; it prevented us from meta-analysing it with SGRQ. These studies enrolled 127 participants (64 participants in the standard group and 63 participants in the VR group). The pooled results showed no difference between groups on HRQOL (MD –11.81, 95% CI (–42.95 to 19.33), 12=98.9%) with a substantial heterogeneity (figure 4B). Rutkowski *et al* reported no difference between groups on HRQOL. 27 Our certainty was very low because of serious concerns about a high ROB, heterogeneity and imprecision (online supplemental table S3).

Two RCTs^{28 33} and two cross-over trials^{34 38} reported outcomes concerning muscle function. This includes quantitative measures such as maximal inspiratory pressure³³ and leg strength,²⁸ or qualitative measures such as self-reported muscle fatigue³⁸ or hardship.³⁴ Lack of data and outcomes' heterogeneity prevented us from conducting a pooled analysis. Finally, only one study reported adverse effects and indicated that no adverse events were associated with VR.⁴⁰

Influence analysis and publication bias assessment are provided in online supplemental material 6 and figures S3a, S3b, S3c.

DISCUSSION

Summary of main results

Thirteen studies were identified in this meta-analysis. ²⁶ ²⁸ ^{30–40} Only two studies were conducted in acute settings. ³⁰ ³⁵ The data available were insufficient for the drawing of definitive conclusions regarding muscle function ²⁸ ³³ ³⁴ ³⁸ and adverse effects, as only one study reported this latter outcome. ⁴⁰ Available evidence is very uncertain regarding the impact of VR on dyspnoea and HRQOL on individuals with respiratory disorders suffering from dyspnoea. Furthermore, evidence is unclear as to the effect on exercise capacity, as the CI includes both a clinically important benefit and a potential negative effect.

Our results are consistent with two recent metaanalyses, in which no effect of VR on dyspnoea has been

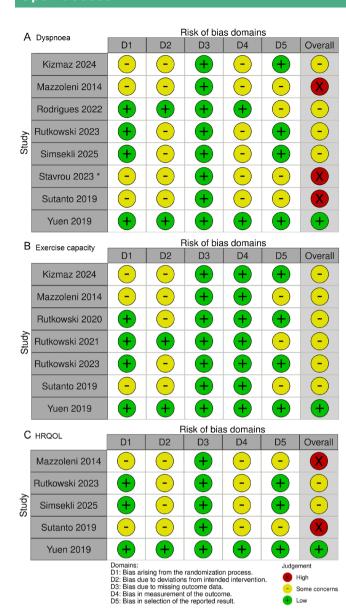


Figure 2 Summary of risk of bias 2. (A) Outcomes on dyspnoea. (B) Outcomes on exercise capacity. (C) Outcomes on HRQOL. *For Stavrou 2023: In bias arising from domain S (Bias arising from period and carryover effects), some concerns were identified. Risk-of-bias plots were created using the Robvis tool (McGuinness, LA, Higgins, JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Syn Meth. 2020; 1–7. https://doi.org/10.1002/jrsm.1411). HRQOL, Health-related quality of life.

demonstrated. 41 42 Compared with the first one, we included more studies and focused on an adult population. 41 Similarly, Patsaki *et al* pooled two studies to estimate effect on dyspnoea. 42 The authors focused on a specific population (COPD) rather than the symptom, whereas we included all adults with respiratory disease experiencing dyspnoea. Conversely, a recent meta-analysis showed a positive effect on dyspnoea which is inconsistent with our results. In this meta-analysis, the authors combined the COPD Assessment Test (CAT) with

mMRC.²⁰ As mMRC captures activity-related dyspnoea, the CAT measures multiple symptoms such as cough or sleeping. In contrast, our results were obtained by pooling scales that only measured dyspnoea. Moreover, included studies in this meta-analysis are different, which may be attributable to the selection of COPD alone and the use of Chinese databases and studies.

Prespecified subgroup analyses were conducted to explore the high heterogeneity of our results, considering several aspects: (1) immersive and non-immersive modalities, (2) single and multiple exposures, (3) the population of interest and (4) acute or chronic.

Immersive and non-immersive modalities

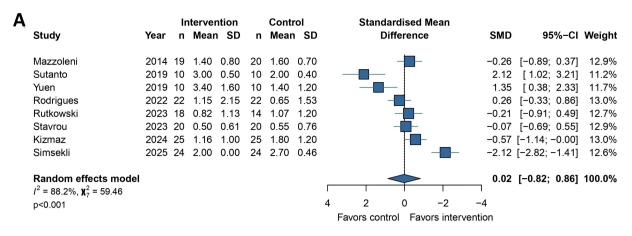
Subgroup analysis comparing immersive and non-immersive VR shows considerable imprecision and a high heterogeneity within groups, preventing us from drawing any conclusion.

However, the degree of immersion and modalities of VR is a key aspect to be considered. Indeed, the sense of presence grows with the level of immersion, fostering greater user engagement. Consequently, the use of an immersive VR device may be more effective than a non-immersive one in distracting participants, modulating emotional responses and enhancing self-efficacy and motivation. Moreover, a greater level of immersion and engagement may be linked to a greater motivation and satisfaction, thus increasing adherence. A suitable design to address these differences would be to compare levels of immersion.

Short-term effect (single exposure)

Five studies used VR after a single exposure. 31 32 34 35 38 Nonetheless, we included only two studies to assess shortterm effects. The remaining three studies were not pooled in the meta-analysis for several reasons.^{31 32 34} First, participants had to exercise for a defined period at a fixed target dyspnoea that induced sufficient symptoms, either in the intervention or control groups. 31 32 34 Second, having the same exertional dyspnoea target value in both groups prevents clear interpretation of dyspnoea evolution. Moreover, doing exercises with the aim of reaching a certain level of dyspnoea requires focusing on this symptom, which makes distraction difficult to achieve. Nevertheless, distraction is not the only explanation for how VR works. In studies on pain, full immersion has shown positive results when participants were asked to focus on their pain in order to control it, suggesting a different mechanism from that of simple distraction. 44 A similar effect may be produced by focusing on dyspnoea in specific conditions. However, the use of non-immersive exercise modalities by Kuys et al, 31 LeGear et al, 22 and Nicolas et al^{64} makes it difficult to draw conclusions, as it is not directly transposable to immersive VR.

Conversely, Stavrou *et al* reported slightly different exercise procedures.³⁸ Participants were cycling with an immersive VR headset at a constant and defined speed



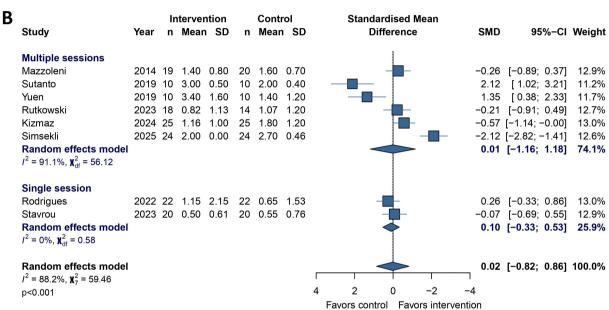


Figure 3 Meta-analysis of comparative effects between VR and control group on dyspnoea. (A) All studies, (B) Forest plots of subgroup analyses: single session versus multiple sessions. SMD, standardised mean difference; VR, virtual reality.

without any consideration about dyspnoea.³⁸ Unfortunately, despite full immersion, participants experienced mild dyspnoea during the intervention, which did not demonstrate a potential difference in dyspnoea intensity associated with VR use. Greater effort may be necessary to induce sufficient dyspnoea as it is done during pulmonary rehabilitation.⁴⁵ Moreover, the duration of exertion may appear to have been insufficient, with a constant exertion period of only 10 min, as supported by the perceived difficulty reported by the participants in this study. Consequently, in order to test the distraction hypothesis, an objective physical exertion target (eg, heart rate, oxygen consumption or work rate) should be set, with the patient being either exposed to VR or not.

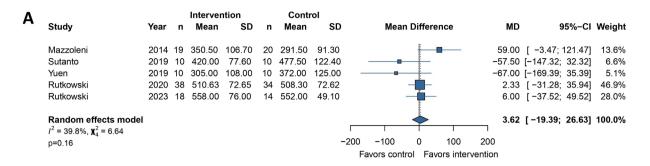
Long-term effect (repetitive exposure)

On the other hand, six studies using VR in repetitive exposure were pooled in our meta-analysis. ²⁶ ³⁰ ³³ ³⁷ ³⁹ ⁴⁰ Interestingly, whereas 6 weeks of rehabilitation are usually recommended as the optimal duration whether in case of

stable chronic diseases (COPD) or postacute conditions such as COVID-19,¹¹ only two studies had an intervention period and a follow-up superior to 3 weeks.^{39 40} Unexpectedly, these two RCTs revealed an effect on dyspnoea favouring control groups.^{39 40} However, in the study from Yuen *et al*,⁴⁰ while having the lowest ROB, the adherence rate to VR treatment remains a major issue as only 20% of the participants eventually underwent the intervention. Another confounding factor is the severity at baseline with more severe disease and impairment in VR groups, which has been known as a predictor for a lesser response to rehabilitation.⁴⁶ In the study from Sutanto *et al*,³⁹ with high ROB, dyspnoea was evaluated by the mMRC score, a tool unable to measure exertional dyspnoea precisely.⁴⁷

Dysphoea assessment

Studies included in this systematic review measure dyspnoea with different tools such as mMRC, ^{30 33 37 39} Baseline Dyspnoea Index (BDI) ^{33 39} and Borg dyspnoea. ^{26 31 32 34 38 40} Although these measures are correlated and have enabled



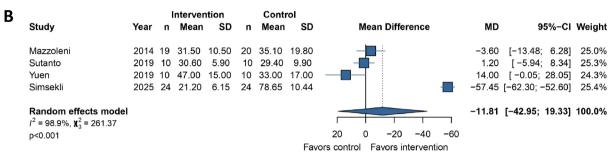


Figure 4 Meta-analysis of comparative effects between VR and control group on exercise capacity and HRQOL (A) Exercise capacity, (B) HRQOL, HRQOL, health-related quality of life; MD, mean difference; VR, virtual reality.

us to pool them in our meta-analysis, they capture different dimensions of dyspnoea. The mMRC, which categorises the level of activity-related dyspnoea, reflects the level of exertion at which dyspnoea limits the activity. 48 One limitation of this scale is that it may underestimate dyspnoea in people who actually avoid certain activities to prevent dyspnoea.47

On the other hand, the Borg dyspnoea scale only captured the intensity-related to a 6MWT. An important limitation of this scale is that it does not assess dyspnoea in relation to a standardised level of exertion (such as a constant workload cycling test). For instance, while the 6MWT is a valid test of exercise capacity, distance may increase with treatment but the level of dyspnoea is likely to be unchanged. 48 Determining a fixed level of exertion thus seems necessary in this context.

Finally, mMRC and Borg dyspnoea scales are unidimensional and show clear limitations in measuring changes during interventions for complex dyspnoeaspecific phenomena. 47 48 Multidimensional dyspnoea scales may allow for a more accurate analysis. 49 BDI and Transition Dyspnoea Index are of peculiar interest in this context. 33 39 However, despite a better sensitivity to changes, their characteristics did not allow a metaanalysis with other scales.

Implications for practice and research

Our confidence in effect estimates prevents us from drawing recommendations on the use of VR in clinical practice. Nevertheless, numerous applications of VR are described in this systematic review, providing a comprehensive overview of the current literature in this field. Studies mainly focused on breathing exercises,

endurance training, exergaming or promoting relaxation through techniques similar to hypnosis.

In pulmonary rehabilitation, VR may promote engagement during cycle endurance training and, in this context, enable a higher level or a higher volume of effort, thus maximising the effectiveness of rehabilitation.¹⁷ Besides distraction, dyspnoea expectation is another important aspect to consider.⁵⁰ For instance, Finnegan et al focused on the 'manipulation of the brain' through immersive VR: they demonstrated that during a pedalling exercise, immersion in a simulation of varying uphill gradients influenced the perception of dyspnoea independently of the workload. 16 This is an interesting finding that could be applied in respiratory rehabilitation, where participants may experience anxious anticipation or fear of dyspnoea.⁵⁰ Moreover, through safe, repeated and graded exposure to dyspnoea, VR could have positive effects on the fear of dyspnoea, similar to its impact on kinesiophobia in chronic pain⁴⁴

None of the included studies considered breathing patterns during physical activities. However, people with COPD may experience dynamic hyperinflation during exercise.⁵¹ Managing respiratory rate and hyperinflation during exertion is thus crucial as it could increase exercise tolerance.⁵² Interestingly, in passive conditions without exercises, participants receiving VR in addition to synchronous feedback of their breathing, embodied via a virtual body, improved their dyspnoea in comparison to those receiving asynchronous feedback under VR.14

Finally, traditional rehabilitation conducted at a centre has several limits which hinder the completion of sessions. Şimşekli and Tan have focused on performing

home-based breathing exercises with immersive VR, such as pursed lips and diaphragmatic breathing.³⁷ Interestingly, this study demonstrated the most positive effects with a great satisfaction according to the participants and a high adherence. Conversely, Yuen et al reported a poor adherence in their home-based rehabilitation. 40 Participants in this study were instructed to 'play' with a non-immersive VR without supervision. The supervision approach used by Şimşekli and Tan could explain the positive result.³⁷ Beyond the potential impact of varying degrees of immersion, this is an innovative and unfamiliar tool for some people. Monitoring seems essential in this context to ensure proper use and safety. This is particularly relevant as one of the major advantages of VR is its potential for adaptation on a tailored basis.

Limitations and strengths

This study has some limitations. First, participants included in this meta-analysis mostly suffered from COPD and COVID-19, limiting the external validity in other chronic respiratory diseases. Nonetheless, this strengthens the level of evidence for these two pathologies. Second, despite heterogeneity in intervention, duration of session and follow-up, number of sessions and exercise intensity, these broad treatment modalities suggest numerous applications of VR. Third, the inability to conduct a meta-analysis on changes from baseline may potentially reduce the power of the analysis by failing to account for baseline imbalances for small-sample trials. However, this highlights the importance of ensuring that new studies report their findings adequately or in sharing individual-level data in repositories. Fourth, beyond a seemingly modest sample size, it appears important to note that VR is a recent therapy, and several RCTs have been identified as actively recruiting and not yet published.

Our study has some strengths. The broad database screening allowed us to explore a large number of studies. Moreover, the inclusion of recent studies provides an update of pre-existing systematic reviews. Finally, this meta-analysis highlights the need to address several gaps in studies using VR: (1) few studies were conducted in acute settings, (2) data are scarce regarding muscle function, (3) proper designs are required to assess effects in single exposure and short-term effects, (4) many applications are possible in regard to the different objectives: distraction, treating dyspnoea expectation or fear of dyspnoea, being more engaging and enjoyable, (5) more appropriate dyspnoea tools, such as multidimensional scales, are highly relevant in this context and (6) adverse events are not systematically reported. Future studies should exercise the utmost vigilance on this particular matter and ensure that adverse events, such as cybersickness,⁵³ are reported in a clear and unambiguous manner.

CONCLUSIONS

This meta-analysis found that available evidence is very uncertain regarding the impact of VR on dyspnoea and HROOL in adults with respiratory diseases. Furthermore, evidence is unclear as to the effect on exercise capacity. VR opens new perspectives and further studies with proper methodological designs and more appropriate dyspnoea assessments are needed to demonstrate the potential effects of VR on individuals with respiratory disorders suffering from dyspnoea. Moreover, few studies have investigated the impact of such interventions on muscle function, despite its major role in rehabilitation.

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