Performance-based outcome measures for assessing physical capacity in patients with pulmonary embolism: A scoping review

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Review Article

Performance-based outcome measures for assessing physical capacity in patients with pulmonary embolism: A scoping review

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ABSTRACT

Introduction: Up to 50 % of patients surviving a pulmonary embolism (PE) report persisting shortness of breath, reduced physical capacity and psychological distress. As the PE population is heterogeneous compared to other cardiovascular patient groups, outcome measures for assessing physical capacity traditionally used in cardiac populations may not be reliable for the PE population as a whole. This scoping review aims to 1) map performance-based outcome measures (PBOMs) used for assessing physical capacity in PE research, and 2) to report the psychometric properties of the identified PBOMs in a PE population.

Methods: The review was conducted according to the Joanna Briggs Institute framework for scoping reviews and reported according to the PRISMA-Extension for Scoping Reviews guideline.

Results: The systematic search of five databases identified 4585 studies, of which 243 studies met the inclusion criteria. Of these, 185 studies focused on a subgroup of patients with chronic thromboembolic pulmonary hypertension. Ten different PBOMs were identified in the included studies. The 6-minute walk test (6MWT) and cardiopulmonary exercise test (CPET) were the most commonly used, followed by the (Modified) Bruce protocol and Incremental Shuttle Walk test. No studies reported psychometric properties of any of the identified PBOMs in a PE population.

Conclusions: Publication of studies measuring physical capacity within PE populations has increased significantly over the past 5–10 years. Still, not one study was identified, reporting the validity, reliability, or responsiveness for any of the identified PBOMs in a PE population. This should be a priority for future research in the field.

1. Introduction

Pulmonary embolism (PE) is the most serious manifestation of venous thromboembolism (VTE), a chronic illness affecting nearly 10 million people every year worldwide [1]. The total annual health-care costs associated with VTE are estimated to range between €1.5–3.3 billion in Europe [2]. With regard to PE, both the post-thrombotic syndrome and the post-PE syndrome are important long-term VTE complications that reduce physical function, mental well-being and quality of life and result in a substantial economic burden [3,4]. Time trend analyses, including population-based studies, suggest that the incidence of PE is increasing, while mortality is decreasing [5]. Combined with ageing populations, this points to an increasing prevalence of PE survivors in the years to come.

Guideline-based anticoagulation reduces morbidity and mortality, yet up to 50 % of patients report persisting symptoms with shortness of

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breath, pain, reduced physical performance and psychological distress, leading to inactivity, disability and poor quality of life [6–14]. This may add significantly to the risk of recurrent VTE, re-hospitalization and increased health-care use, as particularly reduced physical capacity entails a higher risk of cardiovascular morbidity and mortality [15]. Such long-term negative outcomes have also been reported in patients with other cardiovascular diseases; but in contrast to patients with e.g. acute coronary syndrome, valve surgery, or heart failure, patients with PE are not offered systematic follow-up and rehabilitation addressing these challenges [16,17]. Therefore, the European Society of Cardiology (ESC) guidelines on management of PE recommend the provision of rehabilitation for patients who do not recover from their PE event [17,18]. Importantly, to be able to identify at-risk patients, valid and reliable outcome measurement instruments are required. Equally important, such instruments are also essential for monitoring and evaluating improvements achieved through treatment and rehabilitation interventions and thereby increase the efficiency of patient care.

The PE population is more heterogeneous compared to other cardiovascular patient groups, and the risk of a PE increases with age and co-morbidity similar to other cardiovascular patient groups. However, risk factors also include immobilization following trauma or surgery, use of contraceptive pills, genetic dispositions, and many patients have no obvious risk factors [19]. This means that the patient population includes subgroups of young and active as well as old and inactive patients, and therefore, outcome measures for physical capacity traditionally used in cardiac rehabilitation may not be reliable. A cardiopulmonary exercise test (CPET) is considered the gold standard for assessment of physical (aerobic) capacity [20]. However, CPET have inherent limitations due to the specialized and expensive equipment and trained personnel required to perform the test [21]. For this reason, a variety of submaximal tests have been employed to estimate physical capacity in research and clinical practice, including the 6-minute walk test (6MWT), watt-max test, 1-minute sit-to-stand test and more [6,22–24]. This scoping review aims to map the research literature using performance-based outcome measures (PBOMs) for assessment of physical capacity in a PE population, and to describe the psychometric properties of the identified PBOMs in this population. This will provide an overview of PBOMs used in research and delineate whether there is a knowledge gap in relation to valid and reliable instruments for measuring physical capacity in the PE population, thus guiding further research and clinical practice in the field.

Review questions:

1. Which PBOMs are used in the research literature to assess physical capacity among patients recovering from a PE?
2. What are the psychometric properties of the identified PBOMs in a PE-population?

2. Methods

2.1. Design

A scoping review design was chosen, as this type of review can map out and provide insight into the scope and quantity of available research literature in the given field [25]. The methodology of the review process was guided by the Joanna Briggs Institute (JBI) framework for scoping reviews [26] and reporting followed the PRISMA (Extension for Scoping Reviews) guidelines [27]. The review was registered in Open Science Framework (OSF) registries prior to data extraction (https://osf.io/8tywj). The review was carried out in two steps in line with the two review questions. Thus, in the first step an identification and mapping of the PBOMs used across the research literature was conducted. In the second step a search was carried out investigating the psychometric properties of the identified PBOMs in a PE population.

2.2. Search strategy and selection process

Review question 1: A systematic literature search was performed in the databases PubMed, Embase, Cochrane Library, Cinahl, and PEDro (see Appendix 1 for keywords and search terms used). Prior to the final searches, an initial search was performed in PubMed to identify relevant keywords and search terms (e.g. MeSH words). This was followed by a second search using the identified keywords and search terms identified in collaboration with a research librarian in order to qualify the keywords, search strings, filters, and search databases used, leading to the development of the final search string. Keywords and examples of search words used for review question 1 is shown in Table 1. The literature search was repeated twice; at inception (September 6th 2022) and prior to the final management of results (April 25th 2023). The reference lists of included studies and a trial register (clinicaltrials.gov) were also checked for eligible studies. Results from the searches in the various databases were exported to Covidence, a web-based software platform that supports the production of literature reviews (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). Following removal of duplicates, studies were independently screened on title and abstract by two reviewers (CKC and SIM) and selected for further assessment based on the predetermined inclusion and exclusion criteria described below. Full-text screening of selected studies was conducted by CKC and NR to determine if the studies were eligible. Disagreements among reviewers in the inclusion or exclusion of studies were settled by consulting the author group to reach an agreement.

Review question 2: To identify studies reporting on psychometric properties (in a PE population) of the PBOMs identified in review question 1, a search in PubMed, Cinahl and Embase was conducted (see Appendix 1 for keywords and search terms). The searches were conducted using validated COSMIN search filters (https://www.cosmin.nl/tools/pubmed-search-filters/). Keywords and examples of search words used for review question 2 are shown in Table 1. The selection process with inclusion/exclusion of studies was handled by two reviewers as described for review question 1.

2.3. Inclusion criteria

Review question 1: Using the Participant, Concept and Context approach suggested by JBI [26], studies were included in this review if they addressed:

- Participants: adult patients (≥18 years) with non-cancer-related PE
- Concept: a minimum of one PBOM to assess physical capacity and/or functional ability
- Context: any clinical setting (both primary, secondary and tertiary care settings)

Studies published in English, Danish, Swedish, Dutch, or Norwegian were included. Qualitative studies, editorials, letters to the editor, animal studies, conference posters/abstract and abstracts with no full-text were excluded. Studies with multiple patient populations were excluded if they did not report results from PBOMs separately for the PE population.

In addition, ClinicalTrials.gov and systematic reviews were checked for eligible studies that were not discovered in the initial search.

Review question 2: Again using the Participant, Concept and Context approach suggested by JBI [26], studies were screened for inclusion in this review if they addressed:

- Participants: adult patients (≥18 years) with non-cancer-related PE
- Concept: at least one psychometric property described for the given PBOM (e.g. validity, reliability, responsiveness, floor-ceiling effect)
- Context: any clinical setting (both primary, secondary and tertiary care settings)

Table 1
Keywords and example of synonyms used for literature search. Complete list of search words is shown in Appendix 1.

	Participant: patients with pulmonary embolism	Concept: physical performance measures	Context
Review question 1	Venous thromboembolism Pulmonary embolism Lung embolism Post-PE syndrome	Examples: functional status, walk test, physical capacity, endurance, VO2 max, cycle test, chair rise test	Any clinical setting
Review question 2	Venous thromboembolism Pulmonary embolism Lung embolism Post-PE syndrome CTEPH Chronic thromboembolic pulmonary hypertension	PBOM identified in research question 1	Psychometrics (COSMIN-search filters)

Post-PE syndrome = post pulmonary embolism syndrome; CTEPH = chronic thromboembolic pulmonary hypertension; VO2 max = maximal oxygen consumption; PBOM = performance based outcome measure; COSMIN = COnsensus-based Standards for the selection of health status Measurement INstruments.

Studies published in English, Danish, Swedish, Dutch or Norwegian were included. Qualitative studies, editorials, letters to the editor, animal studies, conference posters/abstract and abstracts with no full-text were excluded. Furthermore, if the purpose of the study was not to investigate validity, reliability, responsiveness etc., and/or the study design was not suited for psychometrics, the study was excluded. Studies with multiple patient populations were excluded if they did not report results from PBOMs separately for the PE population.

2.4. Risk of bias and quality assessment

Review question 1: Studies included in review question 1 did not undergo quality assessment, as an assessment of the risk of bias across studies is not required for scoping reviews [26]. Furthermore, the aim of this review was to map out *which* performance-based outcome measures are used in the research literature, and not to assess the quality of the studies using the outcomes.

Review question 2: Studies investigating the psychometric properties of the identified PBOMs were quality-assessed using relevant risk-of-bias assessment tools, e.g.;

- Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) [28]
- The ROBINS-I tool to assess risk of bias in non-randomized studies [29]
- CASP checklist for assessing quality of observational studies (cohort, case-control and cross-sectional studies) [30]

The quality assessment was conducted independently by two reviewers, CKC and SIM. Disagreements were settled by consulting the review group to reach agreement.

2.5. Data extraction

The main reviewer, CKC, was responsible for the data extraction for both review questions. A second reviewer, NR, performed data extraction on a random sample of 60 articles (25 %), to check if there was consensus on the process of extracting data. Data were extracted into one table for each review question with characteristics of the study and participants.

2.6. Deviations from protocol

After the registration of the protocol in OSF, the following changes were made; Studies were excluded if they were: editorials, letters to the editor, conference posters/abstract, animal studies and abstracts with no full-text. Regarding extraction of data, some variables described in the protocol were removed as the reviewers agreed that they did not serve any purpose according to the study aim and review questions (gender, time since PE, PE-severity score, other co-morbidities, setting, intervention).

During the selection and data extraction process it became clear that a substantial amount of research is focused on patients with chronic thromboembolic hypertension (CTPH), which is a rare but more serious condition seen in a subgroup of patients (1–2 %) following a symptomatic or asymptomatic PE [19]. CTEPH has an estimated incidence and prevalence of 2–6 and 26–38 cases/million adults, respectively [19,31,32], and is a progressive condition resulting in limited exercise capacity, dyspnea, functional limitations, and has a poor prognosis if left untreated [31–35]. This finding resulted in a rather large inclusion of studies through references in reviews on the CTEPH population. Also, to accommodate this finding, the keywords 'CTEPH' and 'chronic thromboembolic pulmonary hypertension' were included in search 2. The results will be presented with quantities for each of the PE subgroups to provide insight into the scope of research in the different groups.

Another identified subgroup of PE identified in a very small number of studies, was chronic thromboembolic vascular disease (CTED). CTED patients experience functional impairment due to chronic thromboembolic remains in the pulmonary artery tree, but without pulmonary hypertension in difference to CTEPH patients [19].

3. Results

3.1. Review question 1

We identified a total of 4585 potentially relevant studies of which 1559 were duplicates. The remaining 3026 studies were screened on title/abstract, and 364 studies were found eligible for full-text screening. Of these, 173 studies met the inclusion criteria, and an additional 59 studies were identified through reviews. In total 232 studies were included from the primary search 1. Search 1 was re-run before final reporting of results, to enable inclusion of studies published since the initial search. From this final search 11 new studies were found eligible for inclusion. This resulted in 243 included studies in the final analysis.

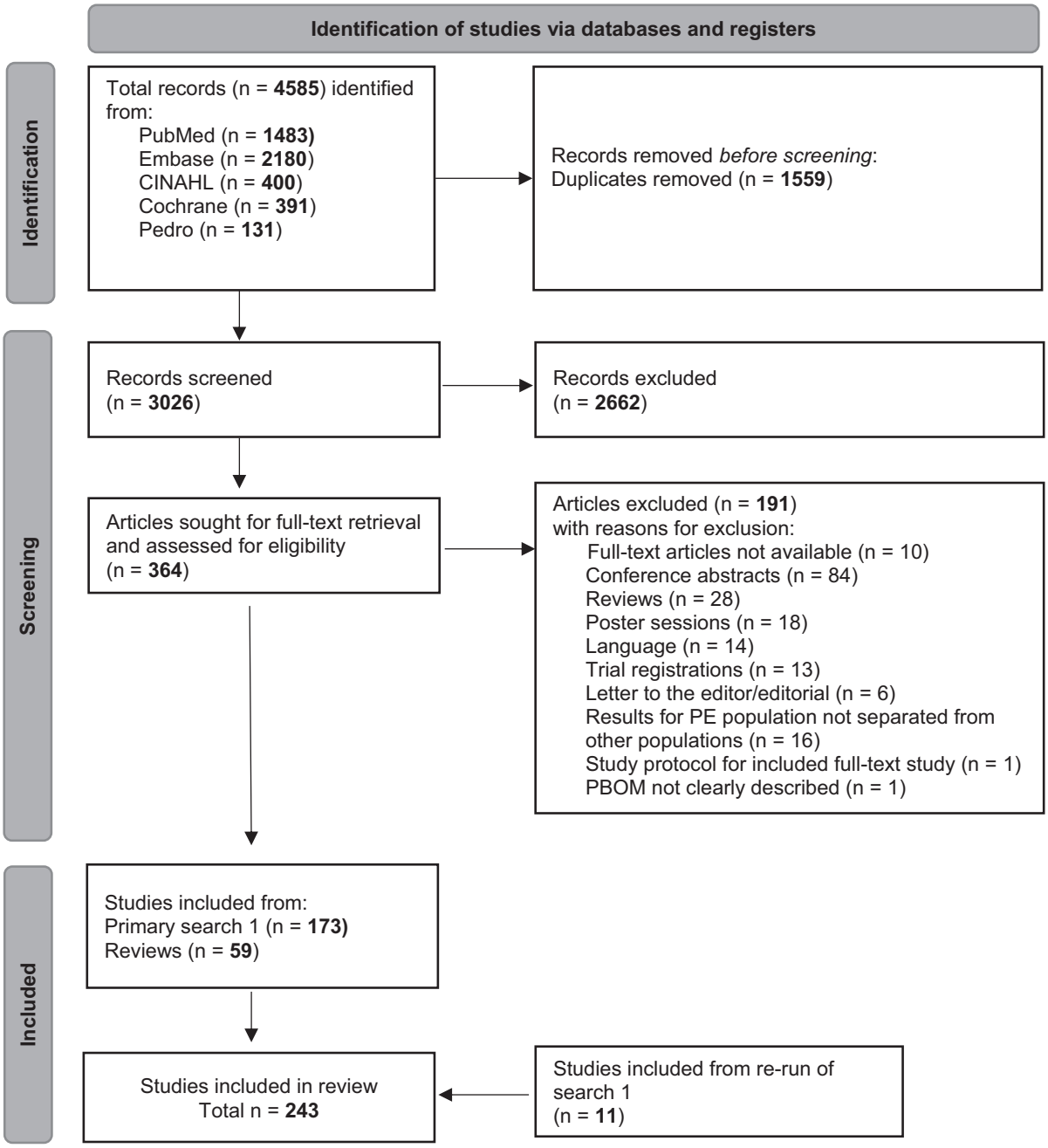

Fig. 1. PRISMA flow diagram showing the selection process for review question 1.

Fig. 1 illustrates the flow of the selection process, including the most common reasons for exclusion.

3.2. Map of the research area

A complete list of the characteristics of the 243 included studies, i.e. country of origin, publication year, study design, number of participants and the PBOMs used, are summarized in Appendix 2. Fig. 2 illustrates the distribution of included studies according to their continent of origin. Fifty-one percent of the studies originated from Europe, with the five largest contributors being Germany (32 studies), the Netherlands (17 studies), United Kingdom (11 studies), Italy (10 studies) and Turkey (9 studies). Studies from Asia constituted 36 %, with 51 studies originating from Japan and 13 from China. Eighteen studies were from North America, while <5 originated from South America and Oceania.

With regard to the frequency of publications per year, the included studies were published between 2001 and 2023, with the majority of studies published between 2010 and 2022 ($n = 205$), as shown in Fig. 3. An increase in publication rate was particularly seen from around year 2014.

The study designs used in the included studies were primarily randomized controlled studies or observational cohort studies using prospective data collection methods, which was reported by 134 studies (55 %), while 80 studies (33 %) used a retrospective design. Fourteen studies were cross-sectional studies, five were case studies, four were study protocols, while six studies did not report the design clearly.

The included studies used PBOMs at different time-points in the course of disease or treatment, in some studies for diagnostic/predictive

purposes or to monitor a disease trajectory, but mostly PBOMs were used to demonstrate effect of a medical intervention.

3.3. Studies on subpopulations

Of the 243 included studies, 185 studies (76 %) included patients with CTEPH, 47 (19 %) studies included patients with PE, 6 studies included patients with CTED (2.5 %), four studies included both CTEPH and CTED (2 %), and one study included both PE and CTEPH. The studies mainly aimed to investigate different diagnostic procedures or prediction of clinical outcomes (e.g. recurrence), the effect of medication or surgical interventions, or describe the nature of the disease at given time-points. Few studies focused on effects of a rehabilitation interventions including physical exercise and patient education.

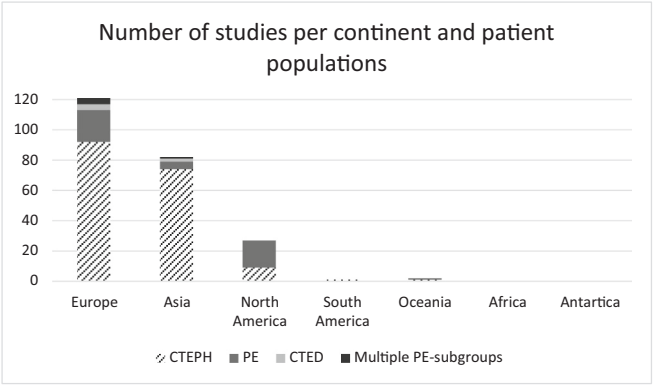

Fig. 2. Distribution of included studies (n = 233) according to continent of origin.
Multinational studies (n = 10) are not shown.
CTEPH = chronic thromboembolic pulmonary hypertension; PE = pulmonary embolism; CTED = chronic thromboembolic disease.

3.4. Performance-based outcome measures

In total, ten different PBOMs were identified for measuring physical capacity (Table 2). The two most commonly used PBOMs by far, were the 6-minute walk test (6MWT), reported in 200 studies (82 %), and the CPET, reported in 73 studies (30 %). Other identified PBOMs were (modified) Bruce protocol (n = 5), Incremental Shuttle Walk test (ISWT) (n = 4), 3-minute walk test (3MWT) (n = 1), Long-Distance Corridor Walk test (LDCW) (n = 1), Endurance Shuttle Walk test (ESWT) (n = 1), Watt max test (Wmax) (n = 1), Constant work rate test (CWR) (n = 1), and 1-minute sit-to-stand test (1MSTST) (n = 1).

3.5. Description of identified PBOMs

6MWT is a sub-maximal walking test of functional ability, requiring the patient to walk back and forth on a walking track of ideally 30 m, although conducting the test on a 20-m track is also considered valid and reliable [269]. The test has a standardized protocol which describes setup, verbal instructions, equipment needed, scoring etc. The outcome measured is the longest distance (in meters) a patient is able to walk in 6 min. Reference values have been published for a healthy population [270].

CPET is considered the gold standard for assessment of physical capacity [20]. The test is a maximal exercise test with concomitant gas exchange analysis and is typically performed using a cycle ergometer or treadmill. The test provides data on e.g. oxygen uptake, exhaled carbon dioxide and is often combined with measurements such as heart rate, blood pressure and work rate. Specialized equipment and trained personnel is required to perform the test [21].

Bruce protocol/Modified Bruce protocol is a treadmill exercise test, where the patient walks on an inclined treadmill, which increases in speed and incline every 3 min following a standardized protocol (in the modified protocol the test is started at a lower workload) [271]. The patient continues until exhaustion, and the distance walked in meters or time in minutes is registered. The oxygen consumption is then estimated through a standardized equation, unless specialized equipment has been applied, which can measure for example oxygen consumption.

ISWT is a walking test with gradually increasing speed that focuses

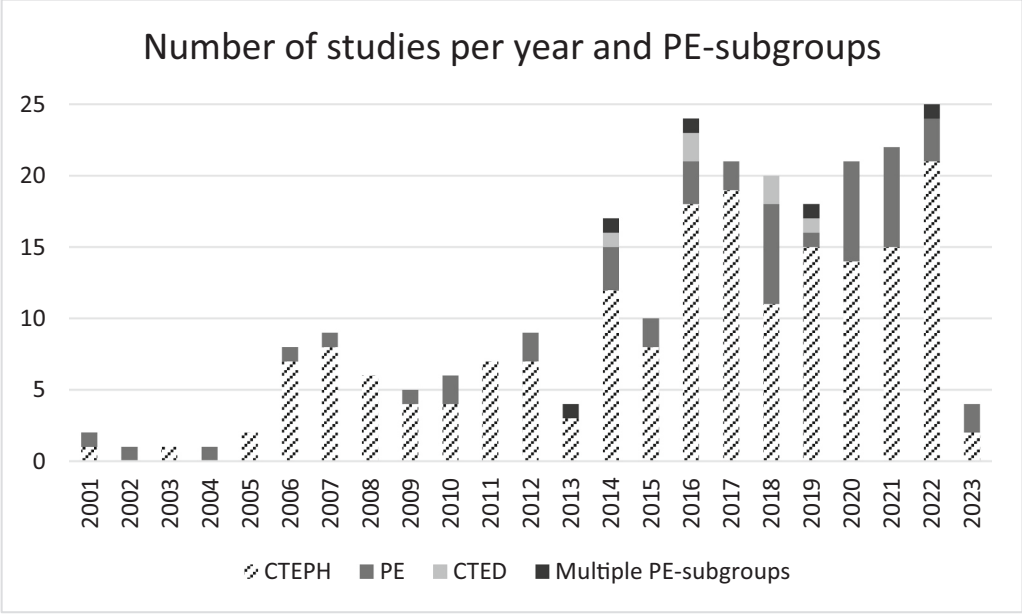

Fig. 3. Number of published studies (n = 243) per year divided into PE-subgroups.
CTEPH = chronic thromboembolic pulmonary hypertension; PE = pulmonary embolism; CTED = chronic thromboembolic disease.

Table 2
List of identified PBOMs, studies using the PBOMs, and the number of studies reporting on various PE-subpopulations.

PBOM	References	Total (n)
6MWT	Abozeed et al. 2022 [36], Akaslan et al. 2022 [37], Akizuki et al. 2017 [38], Akizuki et al., 2020 [39], Amoury et al. 2018 [40], Aoki et al. 2016 [41], Aoki et al. 2017 [42], Avgerinos et al. 2018 [43], Badesch et al. 2012 [44], Balki et al. 2022 [45], Bartenstein et al. 2018 [46], Bazmpani et al. 2018 [47], Bhosle et al. 2022 [48], Blanquez-Nadal et al. 2022 [49], Bonderman et al. 2005 [50], Bonderman et al. 2011 [51], Brenot et al. 2019 [52], Cabrol et al. 2007 [53], Calabrese et al. 2021 [54], Calé et al. 2021 [55], Cannon et al. 2016 [56], Charalampopoulos et al. 2016 [57], Chen et al. 2018 [58], Chen et al. 2021 [59], Chow et al. 2014 [60], Ciurzyński et al. 2004 [61], Claessen et al2. 2015 [62], Claeys et al. 2019 [63], Condliffe et al. 2008 [64], Daigo et al. 2023 [65], Danielsbacka et al. 2020 [66], Danielsbacka et al. 2018 [22], D'Armini et al. 2014 [67], Darocha et al. 2017 [68], de Perrot et al. 2011 [69], de Perrot et al. 2015, Delcroix et al. 2016 [70], Escribano-Subias et al. 2019 [71], Ewert et al. 2022 [72], Feinstein et al. 2001 [73], Freed et al. 2011 [74], Freed et al. 2008 [75], Fujii et al. 2021 [76], Fukui et al. 2014 [77], Fukui et al. 2016 [78], Ghofrani et al. 2003 [79], Ghofrani et al. 2010 [80], Ghofrani et al. 2013 [81], Ghofrani et al. 2017 [82], Grazioli et al. 2021 [83], Grünig et al. 2012 [84], Gu et al. 2010 [85], Guth et al. 2018 [86], Halank et al. 2017 [87], Hayato et al. 2022 [88], Hoeper et al. 2005 [89], Hoole et al. 2020 [90], Hughes et al. 2006 [91], Imtiaz et al. 2021 [92], Inagaki et al. 2014 [93], Inagaki et al. 2018 [94], Inami et al. 2014 [95], Inami et al. 2019 [96], Jais et al. 2008 [97], Jin et al. 2019 [98], Kahn et al. 2017 [7], Kahn et al2. 2017 [6], Kamimura et al. 2018 [99], Kanar et al. 2019 [100], Kawakami et al. 2016 [101], Kearney et al. 2021 [102], Kenichi et al. 2018 [103], Kepez et al. 2014 [104], Kim et al. 2017 [105], Kimura et al. 2017 [106], Kline et al. 2006 [107], Kline et al. 2014 [108], Kline et al. 2009 [109], Klok et al. 2010 [110], Klok et al. 2022 [111], Koike et al. 2016 [112], Koike et al. 2021 [113], Korsholm et al. 2017 [33], Kurzyna et al. 2017 [114], Kwon et al. 2018 [115], Küçükoğlu et al. 2020 [116], La Rovere et al. 2019 [117], Lang et al. 2006 [118], Li et al. 2021 [119], Lindner et al. 2009 [120], Liu, Hao-Yun et al. 2022 [121], Martínez-Santos et al. 2021 [122], Matsuda et al. 2006 [123], Matsuoka et al. 2021 [124], Matthews et al. 2016 [125], Mayer et al. 2011 [126], McCabe et al. 2013 [127], McGettrick et al. 2022 [128], McLaughlin et al. 2017 [129], Meinel et al. 2014 [130], Minatsuki et al. 2020 [131], Mizoguchi et al. 2012 [132], Moriyama et al. 2018 [133], Nagel et al. 2020 [134], Nagel et al. 2012 [135], Nakano et al. 2022 [136], Nishikawa-Takahashi et al. 2014 [137], Nopp et al. 2020 [24], Ogawa et al. 2017 [138], Ogo et al. 2017 [139], Ogo et al. 2022 [140], Oka et al. 2022 [141], Olgun Yıldızeli et al. 2018 [142], Olsson et al. 2017 [143], Pepke-Zaba et al. 2011 [144], Pereira et al. 2022 [145], Petrucci et al. 2007 [146], Piazza et al. 2020 [147], Plácido et al. 2021 [148], Post et al. 2009 [149], Ramos et al. 2016 [150], Reesink et al. 2006 [151], Reesink et al. 2010 [152], Reichenberger et al. 2007 [153], Reichenberger et al2. 2007 [154], Richter et al. 2015 [155], Richter et al. 2016 [156], Richter et al. 2017 [157], Roik et al. 2016 [158], Roik et al. 2017 [159], Romanov et al. 2020 [160], Rossi et al. 2008 [161], Ruaro et al. 2022 [162], Ruigrok et al. 2020 [163], Ruigrok et al2. 2020 [164], Sablinskis et al. 2019 [165], Sadushi-Kolici et al. 2019 [166], Sanchez et al. 2010 [167], Saouti et al. 2009 [168], Sato et al. 2016 [169], Scholzel et al. 2012 [170], Schweikert et al. 2014 [171], Segel et al. 2019 [172], Segel et al. 2020 [173], Semaan et al. 2023 [174], Seyfarth et al. 2007 [175], Shetty et al. 2022 [176], Shi et al. 2016 [177], Simonneau et al. 2015 [178], Simonneau et al. 2016 [179], Skoro-Sajer et al. 2007 [180], Smukowska-Gorynia et al. 2018 [181], Stevinson et al. 2007 [182], Sugimura et al. 2012 [183], Sunbul et al. 2014 [184], Sunbul et al. 2015 [185], Suntharalingam et al. 2007 [186], Suntharalingam et al. 2008 [187], Surie et al. 2013 [188], Surie et al. 2014 [189], Taboada et al. 2014 [190], Tajima et al. 2019 [191], Takei et al. 2019 [192], Tanabe et al. 2006 [193], Tanabe et al. 2020 [194], Taniguchi et al. 2019 [195], Taş et al. 2022 [196], Tatebe et al. 2016 [197], Tavoly et al. 2016 [198], Tavoly et al. 2018 [199], Tiede et al. 2015 [200], Tobita et al. 2021 [201], Tsuboi et al. 2017 [202], Tsugu et al. 2020 [203], Tsugu et al. 2016 [204], Türer Cabbar et al. 2022 [205], Ulrich et al. 2007 [206], Umemoto et al. 2022 [207], Urushibara et al. 2015 [208], van der Plas et al. 2010 [209], van der Plas et al. 2011 [210], van Kan et al. 2016 [211], Valerio et al. 2022 [212], van Thor et al. 2019 [213], van Thor et al. 2020 [214], Vassallo et al. 2009 [215], Velázquez et al. 2019 [216], Vinke et al. 2021 [217], Vizza et al. 2006 [218], Wang et al. 2022 [219], Waziri et al. 2020 [220], Wiedenroth et al. 2018 [221], Wiedenroth et al. 2022 [222], Xi et al. 2014 [223], Yamagata et al. 2018 [224], Yamamoto et al. 2017 [225], Yamasaki et al. 2017 [226], Yan et al. 2012 [227], Zhai et al. 2011 [228]	200 studies in total, of which PE were included in 26 studies, CTEPH in 170 studies and CTED in 8 studies.
CPET	Akizuki et al. 2017 [38], Albaghdadi et al. 2018 [229], Andreassen et al. 2013 [230], Bhagat et al. 2002 [231], Blanquez-Nadal et al. 2022 [49], Blanquez-Nadal et al2. 2022 [232], Bonderman et al. 2011 [51], Boon et al. 2021 [233], Broch et al. 2016 [234], Charalampopoulos et al. 2016 [57], Chen et al. 2018 [58], Claessen et al. 2015 [235], Claessen et al2. 2015 [62], Claeys et al. 2019 [63], Dumitrescu et al. 2016 [236], Ewert et al. 2022 [72], Fernandes et al. 2020 [237], Fukui et al. 2016 [78], Godinas et al. 2017 [238], Grünig et al. 2012 [84], Guo et al. 2016 [239], Guth et al. 2018 [86], Habedank et al. 2018 [240], Held et al. 2014 [241], Held et al2. 2014 [242], Held et al. 2016 [243], Hirashiki et al. 2014 [244], Hoeper et al. 2005 [89], Hoole et al. 2020 [90], Huang et al. 2020 [245], Inami et al. 2019 [96], Jin et al. 2022 [246], Jin et al. 2019 [98], Kahn et al. 2017 [7], Kahn et al2. 2017 [6], Kamimura et al. 2018 [99], Kenichi et al. 2018 [103], Kikuchi et al. 2020 [247], Knox et al. 2019 [248], Leung Wai Sang et al. 2016 [249], Li et al. 2021 [119], Ma et al. 2018 [250], Matsuda et al. 2006 [123], Matsuoka et al. 2021 [124], McCabe et al. 2013 [127], McGettrick et al. 2022 [128], Milne et al. 2023 [251], Miura et al. 2021 [252], Nagaya et al. 2022 [253], Nagel et al. 2020 [134], Nagel et al. 2012 [135], Ogo et al. 2017 [139], Ramos et al. 2016 [150], Ravnestad et al. 2023 [254], Richter et al. 2015 [155], Richter et al. 2016 [156], Richter et al. 2017 [157], Ruigrok et al. 2020 [163], Ruigrok et al2. 2020 [164], Scheidl et al. 2012 [255], Shi et al. 2016 [177], Smukowska-Gorynia et al. 2018 [181], Stadlbauer et al. 2021 [256], Stavrou et al. 2021 [257], Surie et al. 2014	73 studies, of which PE was included in 19 studies, CTEPH in 55 studies, and CTED in 8 studies

(*continued on next page*)

Table 2 (*continued*)

PBOM	References	Total (n)
	[189], Tobita et al. 2021 [201], Topilsky et al. 2012 [258], Tsuboi et al. 2017 [202], van Kan et al. 2016 [211], Xi et al. 2014 [223], Yan et al. 2012 [227], Zhai et al. 2011 [228], Zhu et al. 2021 [259]	
3 minute walk test	Amin et al. 2015 [260]	1 study on PE
Long-Distance Corridor Walk test	Cires-Drouet et al. 2020 [261]	1 study on PE
ISWT	Condliffe et al. 2008 [64], Haukeland-Parker et al. 2021 [262], Jervan et al. 2021 [263], Rolving et al. 2020 [23]	4 studies of which PE was included in 3 studies and CTEPH in 1 study
ESWT	Haukeland-Parker et al. 2021 [262]	1 study on PE
Watt max test	Nopp et al. 2020 [24]	1 study on PE
Constant work rate test	Nopp et al. 2020 [24]	1 study on PE
1-min sit-to-stand test (1-MSTST)	Nopp et al. 2020 [24]	1 study on PE
Bruce protocol/ modified Bruce protocol	Corsico et al. 2008 [264], Ghram et al. 2021 [265], Larsen et al. 2015 [266], Lewczuk et al. 2001 [267], Romaszkiewicz et al. 2006 [268]	5 studies of which PE was included in 3 studies and CTEPH in 2 studies

on maximal exercise (walking) capacity [272]. The patient walks back and forth on a 10-m shuttle course with an audio signal to control the increasing walking speed. The test stops when the patient cannot manage to reach the end of the 10-m course before the audio sound, or if the patient chooses to stop. The total distance walked is measured and maximal oxygen consumption (VO2max) can be estimated using a standardized equation model.

ESWT is a walking test performed at the same speed throughout the test, focusing on endurance capacity. The patient walks back and forth on a 10-meter shuttle course with an audio signal to ensure that the same walking speed is kept throughout the test. The walking speed should be at 85 % of the VO2max [273] (typically estimated with the ISWT). The test stops when the patient cannot manage to reach the end of the 10-meter course before the audio signal, if the patient chooses to stop, or if the patient completes the full duration of the test (20 min). The result of the test is the amount of time the patient can walk at the given speed.

3MWT is a submaximal walking test for assessing functional capacity and predicting VO2max using a standardized equation model [274,275]. The protocol is not as well-described as the 6MWT but it is suggested to use the same setup. Patients walk back and forth a walking course for 3 min, and the total distance walked is noted.

LDCW is a walking-based test of exercise tolerance and level of fitness [276] It consists of two stages; first a 2-minute walk where the patient should walk as far as they can in 2 min on a 20-meter walking course, and following that, a 400 m walk where the patients should walk as fast as they can on the same 20-m walking course. A standardized protocol for the LDCW test is available with setup, verbal instructions, equipment etc. [277].

Watt-max is a cycle ergometer test, estimating VO2max. The maximal workload (Watt max measured in watt) is converted into VO2max using a standardized equation model [278,279]. Increase in the resistance follows a standardized protocol, with the aim to keep the person pedaling at 58–70 rounds-per-minute (RPM) during the test. The test stops when the person can no longer keep the cadence (>58 RPM). Maximal resistance (watt) and time pedaling at maximal resistance are noted and converted into VO2max.

CWR seeks to quantify endurance capacity by having the participant walk on a treadmill or cycle on a cycle ergometer at a constant speed until exhaustion [280]. The tests are often performed at a high intensity, i.e. typically 75–85 % of peak exercise capacity. Knowledge of the participants' peak exercise capacity is therefore required prior to conduction of the test.

1MSTST is a test developed for quantifying exercise capacity [281]. The patient is seated on an armless chair of standard height (45–48 cm) and asked to repeatedly stand up and sit down as fast as they can, with an aim to complete as many sit-to-stand cycles as possible in 1 min. The score is the number of fully completed sit-to-stand cycles in 1 min.

3.6. Review question 2

Search 2 was conducted on February 15th 2023, and identified 651 potentially relevant studies, of which 180 were duplicates. After title/abstract screening, 23 studies were found eligible for full-text screening. None of the studies were found eligible for inclusion in the review, primarily due to the study aims or methods not being within psychometrics (e.g. not validation or reliability studies). Please see Fig. 4 for flow of the selection process and reasons for exclusion.

4. Discussion

With this scoping review, we aimed to identify and present the the research literature regarding PBOMs employed to measure physical capacity in a PE population. Moreover, we mapped the nature of research, showing a large increase in the number of publications over the past decade, with two of the major contributors to the research literature being Germany and Japan. Interestingly, around half of the published studies focus on CTEPH, although only approximately 3 % of patients will experience this condition. We found that of the ten different PBOMs identified in the literature, none were well-described nor well-assessed regarding psychometric properties for use in a PE population.

The far most commonly used PBOM was the 6MWT, which is a well-described standardized instrument that has been validated for many different patient populations, including cardiac and COPD populations [282,283]. The test is not without limitations, though, as the results can be affected by a variety of factors unrelated to cardiopulmonary status, including age, sex, height, and weight, as well as the self-paced nature of the test (as opposed to the ISWT). One may consider whether similar validity, reliability and responsiveness might also be assumed in a PE population, considering that these psychometric properties have been found satisfactory in other populations. However, although this may be the case, separate studies in a PE population are warranted to establish, e.g., threshold values for a poor expected prognosis or the minimal clinical important change. As can be seen in studies by Wicks et al. and Rasekaba et al., the minimal clinical important difference (MCID) differ between cardiac and COPD populations [284,285], and thus, to validly assess the effect of treatment and rehabilitation interventions, a MCID in the PE population – including the CTEPH subpopulation – should be robustly examined. This is supported by a study by Robertson et al., investigating associations of a modified version of the 6MWT (where bodyweight is taken into account, 6MWW) and peak VO2 measured with CPET [286]. The authors conclude that although the test is associated with peak VO2, and may thus be a good indirect indicator of maximal oxygen consumption in a CTEPH population, "the validation of the predictive equations showed a variable level of agreement and therefore may have limited clinical applicability". They further recommend that

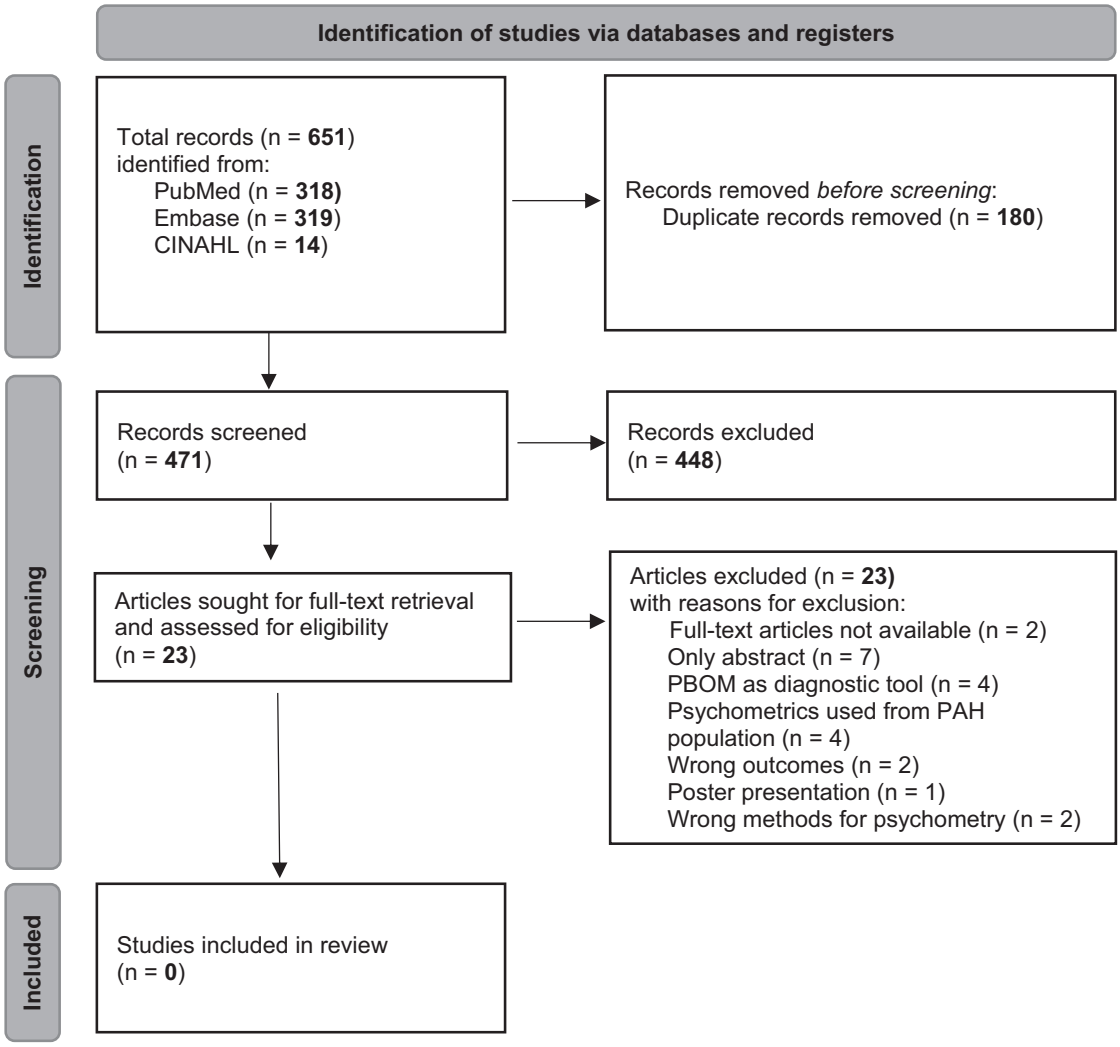

Fig. 4. PRISMA flow diagram showing the selection process for review question 2.

the clinical value of the test and its sensitivity in detecting clinically relevant change should be the focus of future research [286,287]. However, until the psychometric properties, including MCID and prognostic threshold values, have been established for a PE population, the best basis for comparison must be psychometric properties from validation of the 6MWD in cardiac populations, COPD and pulmonary arterial hypertension for CTEPH, which several studies also do when they use cutoff values on 6MWD measures [22,66,288].

CPET was used in 73 studies, often alongside another PBOM, and is considered the gold standard for measuring physical capacity. Considering that it is direct measurement of VO2 max, it must therefore be considered the most valid and reliable tool for measuring physical capacity in patients with PE, until further validation studies of other PBOMS have been conducted. However, CPET is a measurement tool that is not readily available in many clinical settings and is probably most often used in specialized hospital settings and in research. CPET requires specialist knowledge from e.g. a trained physiotherapist, and the equipment is expensive and testing is time consuming compared to simpler and submaximal tests like a walk test [21]. Furthermore, patient preferences may play an important role, as the CPET is a more strenuous test compared to submaximal tests. At the same time, some patients find the mask unpleasant to wear, which all together may limit the acceptability of the test for some patients. The extensive use of CPETs found in the studies included in the present review thus probably reflects the research setting of the studies, and not usual clinical practice, where patients are seen in different in- and out-hospital practices, rehabilitation facilities in municipalities or at their GP, where such testing facilities are not available.

Compared to the 6MWT and the CPET, the remaining eight PBOMs identified were rarely used in the literature, ranging between one to five studies using the various outcomes. Seven of these were also PBOMs aiming to assess aspects of physical capacity using submaximal tests, and the challenges related to these tests are similar to those described for the 6MWT. The 1MSTS differs, however, seeing that it is more a measure of lower limb strength, rather than cardiovascular performance or endurance. Still, being a test of physical performance, the 1MSTS may be considered relevant in research where an easily applicable assessment of leg muscle strength is the outcome of interest. More research is needed for clarification of these issues.

The review process revealed at large amount of research on the small CTEPH subgroup. CTEPH represents the most severe presentation of PE sequelae [199], and has therefore naturally gained a lot of attention in order to improve the symptom burden and save lives. Exercise capacity in particular seems to have an important influence on quality of life in this subgroup [14]. However, the literature search did not reveal any validation or reliability studies of the PBOMs used in either PE or CTEPH populations. Therefore, future research should assess the psychometric properties and calculate a MCID of this subpopulation as well as patients

with CTEPH specifically, is a much more severely disabled patient population compared to patients with post-PE syndrome.

Only 24 % of the identified studies included the overall PE population, despite the fact that approximately 50 % of all patients affected by a PE will develop long term negative consequences, including exercise intolerance, reduced functional ability and poorer quality of life [6–14]. This underlines that research on long-term consequences after PE has been an under-prioritized area for years, as also indicated by our findings. Within the past decade, however, the number of studies published in the field has increased, as shown in Fig. 3, a fact highlighting the need for valid and reliable outcome measurements of physical capacity. This will ensure more valid descriptions and investigations on the nature of PE, diagnostic methods and effects of treatment and rehabilitation interventions in both research and clinical practice.

In the mapping process of the included literature, it became clear that none of the identified studies originated from, or included patients from, the African continent, nor from South American continent (except one study). We therefore chose to look closer into the included studies' reporting on ethnicity, to be able to report for whom the findings may apply (data not shown). However, we found that this was rarely explicitly described, and of the 243 included studies, only 17 studies clearly reported the ethnicity of the included individuals in the study population [6,7,44,80–82,87,105,107–109,118,126,144,174,182,214]. As ethnicity may play a role in the nature, development and treatment effects of PE [289,290], researchers should therefore start reporting the ethnicity of the study population.

4.1. Strengths and limitations

We followed the JBI recommendations for scoping reviews to increase the quality and transparency of the review process. Thus, the scoping review is based on a comprehensive and broad literature search, conducted with the assistance of a research librarian. Moreover, two reviewers conducted both the title/abstract screening and the full-text screening, and the data extraction process was quality ensured by the author group, all in all adding to the quality of the review.

The primary limitation of the study is related to the lack of inclusion of CTEPH in search 1. As described under "Deviations from protocol" the inclusion of CTEPH as a specific search term in search 2 was decided as a result of the findings during search 1. The author group collectively decided not to re-run search one with the inclusion of CTEPH in the "P" (population) search string, as it was believed that the overall findings would not change, seeing that so many studies with a CTEPH population was identified looking through reviews and references of included studies, which lead to only few limited additional studies to include. We therefore believe that we have retrieved all relevant literature.

5. Conclusions, clinical implications and perspectives for future research

A mapping of the past 20 years of research literature, using the strengths of a JBI scoping review methodology, showed an increase in studies using PBOMs for assessing physical capacity in PE and in particular CTEPH populations. Studies were primarily European or Asian (Japanese) in origin. Ten PBOMs were identified, with the most common by far being the 6MWT. However, no studies were identified reporting on validity, reliability, responsiveness or similar psychometric properties of any PBOMs in a PE population. This should be considered a major challenge, as a lack of well-established psychometric properties of PBOMs may result in untrustworthy results in both research and clinical practice. As mentioned in several of the included studies, future research in the field should therefore aim to establish validity, reliability, MCID and other psychometric properties of the most commonly used PBOMs in PE populations. This is essential to make valid assessments of intervention effects, enable identification of at-risk populations (e.g. establishing prognostic threshold values), and make trustworthy interpretations of test results of PBOMs performed in both research and clinical practice.

Supplementary data to this article can be found online at .

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CRediT authorship contribution statement

Christina Krogner Caspersen: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Writing – original draft. **Stian Ingemann-Molden:** Formal analysis, Investigation, Validation, Writing – review & editing. **Erik Lerkevang Grove:** Funding acquisition, Supervision, Writing – review & editing, Conceptualization. **Anette Arbjerg Højen:** Supervision, Writing – review & editing. **Jane Andreasen:** Methodology, Supervision, Writing – review & editing, Conceptualization. **Frederikus A. Klok:** Writing – review & editing, Supervision. **Nanna Rolving:** Conceptualization, Funding acquisition, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Appendix A. Supplementary data

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