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EXTENDED ABSTRACT

A13 Establishing a minimal clinically important difference in pulmonary rehabilitation: Digging in the methods

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Introduction

Interpretation of pulmonary rehabilitation (PR) benefits [1] in people with chronic obstructive pulmonary disease (COPD) is often challenging and can be enriched using minimal clinically important differences (MCIDs)[2-4]– the smallest change in each measure that will be perceived as relevant by patients.[5] Establishing MCIDs for outcome measures used in PR will aid to guide and personalise interventions, enhance judgement about the clinical relevance and magnitude of PR effect, define endpoints in clinical trials and sample sizes.[6-8] A wide variety of statistical methods to estimate MCIDs has been reported but two have been distinguished: anchor-based - use an external criterion (e.g., self-reported opinion or clinicians' judgements) to provide clinical meaning;[9,10] and distribution-based - add statistical significance by expressing change scores according to the sample variability and measurement precision.[9,11] Currently, no clear consensus exists regarding which methods are most suitable or on how to combine them. Thus, we aimed to explore the variability in the MCIDs using different methods.

Methods

This was a retrospective analysis of data obtained from four studies that established MCIDs in people with COPD after PR.[12-15] All studies consisted of a secondary analysis of data from a real-world non-randomised controlled trial (NCT03799666) to assess the effects of a 12-week community-based PR programme.[16] Details have been published elsewhere.[16] For each study, we gathered data about: characteristics of the study and population, primary outcome measure(s), MCID statistical estimation methods, results according to each estimation method (anchor and distribution-based) and the MCID pooled value.

Results

Table 1 presents the characteristics of studies and population and the methods used to estimate MCIDs. The four studies established the MCID for eleven outcome measures. Anchor- and distribution-based methods were used for computing the MCID for all outcome measures,[12-15] except one (hand-held dynamometry), where only distribution-based methods were used.[12] Of those combining both methods, MCIDs were weighted on a ratio of 2/3 and 1/3, respectively.[12-15] Studies calculated the anchor-based methods of the MCIDs using three different methods: mean change, receiver operating characteristic (ROC) curves and linear regression analysis.[12-15] Suitability of the respective anchors were confirmed when the Pearson correlation coefficients were ≥0.3.[12-15] Distribution-based methods were calculated using: 0.5*standard deviation, standard error of measurement (SEM), 1.96*SEM, minimal detectable change (MDC), and effect size.[12-15] The final MCIDs were calculated through the arithmetic weighted mean.[12-15]

Table 2 shows the wide variety of MCID according to the different statistical methods used for each outcome measure across studies.

Keywords:
anchor-based methods; distribution-based methods; minimal clinically important difference.

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Table 1 – Characteristics of studies and population, and statistical methods used for estimating the minimal clinically important differences (anchor- and distribution-based methods) for each outcome measure of community-based pulmonary rehabilitation in people with chronic obstructive pulmonary disease.[12-15]

Study	Population	Primary outcome measure(s)	MCID estimation statistical methods				
			Anchor-based			Distribution-based	
			$n_{anchor(s)\ used}$	Anchor(s)	Statistical method(s)	$n_{methods\ used}$	Statistical methods
1. Rebelo *et al* 2020	N_{total}=49 participants with COPD Male=40 (82%) 70±7years $FEV_{1\%pred}$=50±19	LCQ	1	Patients' GRC	Mean change, Linear regression	5	0.5SD, SEM, 1.96SEM, MDC, ES
		CASA-Q Cough symptoms	3	SGRQ total score, CAT, Patients' GRC	Mean change, ROC, Linear regression	5	0.5SD, SEM, 1.96SEM, MDC, ES
		Cough impact	1	Patients' GRC	Mean change, ROC	5	0.5SD, SEM, 1.96SEM, MDC, ES
		Sputum symptoms	1	SGRQ total score	Mean change, ROC	5	0.5SD, SEM, 1.96SEM, MDC, ES
		Sputum impact	1	SGRQ total score	Mean change, Linear regression	5	0.5SD, SEM, 1.96SEM, MDC, ES
2. Rebelo *et al* 2020	N_{total}=53 participants with COPD Male=42 (79%) 68±8years $FEV_{1\%pred}$=48±17	FACIT-FS	3	SGRQ impact score, SGRQ total score, AECOPD	Mean change, Linear regression	5	0.5SD, SEM, 1.96SEM, MDC, ES
		Modified FACIT-FS	3	SGRQ impact domain, SGRQ total score, AECOPD	Mean change, Linear regression	5	0.5SD, SEM, 1.96SEM, MDC, ES
		CIS-FS	1	AECOPD	Mean change	5	0.5SD, SEM, 1.96SEM, MDC, ES
3. Oliveira *et al* 2021	N_{total}=89 participants with COPD Male=75 (84%) 70±8years $FEV_{1\%pred}$=50±19	1RM	1	6MWD	Mean change, Linear regression	5	0.5SD, SEM, 1.96SEM, MDC, ES
		HHD	0	-	-	5	0.5SD, SEM, 1.96SEM, MDC, ES
4. Paixão *et al* 2021	N_{total}=71 participants with COPD Male=54 (76%) 69±8years $FEV_{1\%pred}$=50±18	Brief-BESTest	2	mMRC, 6MWD	Mean change, Linear regression	5	0.5SD, SEM, 1.96SEM, MDC, ES

1RM, 1-repetition maximum; 6MWT, 6-minute walk distance; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; Brief-BESTest, Brief-Balance Evaluation Systems Test; CASA-Q, Cough and sputum assessment questionnaire; CAT, COPD assessment test; CIS-FS, checklist of individual strength-fatigue subscale; COPD, chronic obstructive pulmonary disease; ES, effect size; FACIT-FS, Functional Assessment of Chronic Illness Therapy-Fatigue subscale; FEV1%pred, forced expiratory volume in one second, percentage of the predicted value; GRC, global rating of change; HHD, hand-held dynamometry; LCQ, Leicester Cough Questionnaire; MCID, minimal clinically important difference; MDC, minimal detectable change; mMRC, modified British Medical Research Council; n, number; ROC, receiver operating characteristic; SD, standard deviation; SEM, standard error of measurement; SGRQ, St. George's Respiratory Questionnaire.

Table 2 – Results obtained with anchor- and distribution-based methods used to calculate the minimal clinically important differences for each outcome measure of community-based pulmonary rehabilitation in people with chronic obstructive pulmonary disease.

Study	Primary outcome measure(s)	MCID estimation statistical methods								Pooled MCID
		Anchor-based			Distribution-based					
		Mean change	Linear regression	ROC	0.5SD	SEM	1.96SEM	MDC	ES	
1. Rebelo *et al* 2020	LCQ	1.4 (Patients' GRC)	0.7 (Patients' GRC)	-	1.7	1.0	1.9	2.6	0.21	1.3
	CASA-Q Cough symptoms	9.3 (SGRQ total score) 9.1 (CAT) 9.9 (Patients' GRC)	1.6 (SGRQ total score)	4.2 (SGRQ total score) 4.2 (CAT)	11.5	11.0	21.6	30.5	0.23	10.6
	Cough impact	11.8 (Patients' GRC)	-	4.7 (Patients' GRC)	11.2	7.8	15.2	21.5	0.19	10.1
	Sputum symptoms	7.7 (SGRQ total score)	-	4.2 (SGRQ total score)	11.4	10.2	20.0	28.2	0.09	9.5
	Sputum impact	6.0 (SGRQ total score)	2.2 (SGRQ total score)	-	10.3	8,7	17.1	24.2	0.12	7.8
2. Rebelo *et al* 2020	FACIT-FS	5.7 (SGRQ- impact score) 4.9 (SGRQ total score) 6.4 (AECOPD)	3.4 (SGRQ-impact score) 3.2 (SGRQ total score)	-	4.3	2.6	5.1	7.2	0.42	4.7
	Modified FACIT-FS	4.4 (SGRQ- impact score) 3.9 (SGRQ total score) 4.7 (AECOPD)	2.3 (SGRQ-impact score) 1.9 (SGRQ total score)	-	3.7	2.2	4.4	6.2	0.38	3.8
	CIS-FS	9.6 (AECOPD)	-	-	6.4	5.0	9.7	13.8	0.44	9.3
3. Oliveira *et al* 2021	1RM	6.4 (6MWD)	5.9 (6MWD)	-	6.6	2.6	5.2	7.3	0.5	5.7
	HHD	-	-	-	4.1	2.9	5.7	8.1	0.2	5.2
4. Paixão *et al* 2021	Brief-BESTest	3.6 (mMRC) 3.4 (6MWD)	3.3 (mMRC) 2.6 (6MWD)	-	2.35	1.99	3.91	5.53	0.66	3.3

1RM, 1-repetition maximum; 6MWT, 6-minute walk distance; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; Brief-BESTest, Brief-Balance evaluation systems test; CASA-Q, Cough and sputum assessment questionnaire; CAT, COPD assessment test; CIS-FS, checklist of individual strength-fatigue subscale; ES, effect size; FACITFS, Functional Assessment of Chronic Illness Therapy-Fatigue subscale; HHD, hand-held dynamometry; LCQ, Leicester Cough Questionnaire; GRC, global rating of change; MCID, minimal clinically important difference; MDC, minimal detectable change; mMRC, modified British Medical Research Council; ROC, receiver operating characteristic; SD, standard deviation; SEM, standard error of measurement; SGRQ, St. George's Respiratory Questionnaire.

Discussion

Multiple anchor- and distribution-based methods have been used, leading to high variability in MCIDs estimations. MCIDs estimations were larger for distribution-based than for anchor-based methods. This variability enhances the need to use and combine both methods to strengthen the results. Since no guidelines exist on how to weight these approaches, it has been recommended to use anchor-based prevailing distribution-based methods.[6,9] Authors of the included studies have arbitrarily attributed 2/3 to anchor and 1/3 to distribution-methods. Guidelines are needed to elucidate which are the best methods to compute MCIDs and how to weight them. Close collaboration between statisticians and health professionals is fundamental for agreeing on the appropriate statistical methods to establish MCIDs for PR.

Ethics committee and informed consent:

The current research was approved by independent ethics committees and subjects gave their informed consent before they were enrolled in the study.

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