Title: Responsiveness and minimal clinically important difference of the Brief-BESTest in people with COPD after pulmonary rehabilitation

Running head: Brief-BESTest in COPD: responsiveness and MCID

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ABSTRACT (295/300 words)

Objective: The Brief-Balance Evaluation Systems Test (Brief-BESTest) is a comprehensive, reliable and valid balance test, which provides valuable information to guide balance training in people with COPD. Its clinical interpretability is, however, currently limited, as cutoff points to identify clinical relevant changes **in people with COPD,** after pulmonary rehabilitation (PR), are still lacking. This study aimed to establish the responsiveness and minimal clinically important difference (MCID) for the Brief-BESTest **in people with COPD, after PR.**

Methods: A secondary analysis of data from two previous studies was conducted. The modified British Medical Research Council (mMRC) dyspnea scale, the six-minute walk test (6MWT) and the Brief-BESTest (0-24 points) were collected in people with COPD pre/post a 12-week PR program including balance training. The MCID was computed using anchor- and distribution-based methods. Changes in the 6MWT and the mMRC were assessed and used as anchors. The pooled MCID was computed using the arithmetic weighted mean (2/3 anchor- and 1/3 distribution-based methods).

Results: Seventy-one people with COPD (**69±8 years**; 76% male; FEV_1 49.8±18% predicted) were included. There was a significant improvement in the Brief-BESTest after PR (mean difference **3±3** points; $p<0.001$). Significant correlations were found between the Brief-BESTest and the mMRC ($r=-0.31$; $p=0.008$), and the 6MWT ($r=0.37$; $p=0.002$). The pooled MCID was 3.3 points.

Conclusion: An improvement of at least 3 points in the Brief-BESTest **in people with COPD** will enhance the interpretability of PR effects on balance performance **of this population** and guide tailored interventions.

Impact: This study reports on the responsiveness and the MCID of the Brief-BESTest, in people with COPD following PR. This outcome measure is comprehensive, **easily administered** and simple to interpret in clinical practice. This study represents a significant contribution for the clinical interpretation of changes in balance **in people with COPD,** following PR.

KEYWORDS: Responsiveness; minimal clinically important difference; balance; pulmonary rehabilitation; Brief-BESTest; COPD

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) has a progressive deterioration not limited to pulmonary function, but including several other systemic effects, such as impairments in skeletal muscle function, which are closely related to reduced mobility, exercise intolerance and balance impairment.[1-4]

Balance control is a complex skill[5,6] and the ability to maintain balance is essential to preserve one's mobility, functional independence in activities of daily living[7] and to avoid falls.[8] Impaired balance has been associated with the age-related process,[5] however, in people with COPD this decline is further marked by other mechanisms, e.g., peripheral muscle weakness,[9] somatosensory deficits,[10] exercise intolerance and dyspnea.[11,12]

Impaired balance leads to an increased risk of falls in people with COPD,[9] resulting in harmful consequences on mobility[13] and increased injury-related mortality[14] in this population. Given the relevance of balance in chronic respiratory diseases, the American Thoracic Society/European Respiratory Society statement recommended its assessment in people referred to pulmonary rehabilitation (PR).[15]

Several outcome measures exist to assess balance **in people with COPD**, however, most do not identify the different balance systems, present ceiling effects and/or are time-consuming.[5] The Brief-Balance Evaluation Systems Test (Brief-BESTest), a comprehensive and **easy to administer** measure, was developed to overcome these limitations and provides valuable information to tailor balance training.[16] **The validity and reliability of** the Brief-BESTest are well-established **in people with COPD**,[1] nevertheless, its responsiveness and clinical interpretability are currently unknown. Determining the responsiveness and minimal clinically important difference (MCID) of

the Brief-BESTest is important to define its utility as an outcome measure of balance **in people with COPD,** following PR[17] and to clinically interpret the changes achieved.[18,19,20] This information will be further useful to guide and inform balance tailored interventions, establish expected endpoints in clinical trials,[19,21] define sample sizes[19] and develop guidelines.[20]

Thus, this study aimed to determine the responsiveness and MCID of the Brief-BESTest in people with COPD after PR. **Furthermore,** we hypothesised that changes in Brief-BESTest, **used to determine both responsiveness and MCID,** would correlate moderately (0.3-0.5)[11,12,17] and: i) positively with changes in **exercise tolerance**; and ii) negatively with changes in **dyspnea**.

METHODS

Study design and participants

A secondary analysis of data from a real-world non-randomised controlled study (**NCT03799666**) to assess the cost-effectiveness of community-based PR[22] and a prospective cohort study (NCT03701945), was conducted according to the guidelines for measurement properties studies proposed by the COnsensus-based Standards for the selection of health status Measurement Instruments (COSMIN) initiative[23]. This work is described according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[24] Ethical approval **for the above mentioned studies** was obtained from the Ethics Committee for Health of the *Administração Regional de Saúde do Centro* (Ref. 73/2016; 85/2018) and from the National Committee for Data Protection (no. 7295/2016). Informed consent was obtained from all participants prior to data collection.

People with COPD were recruited via clinicians at *Centro Hospitalar do Baixo Vouga* and at primary healthcare centres of the center region of Portugal from January 2019 to March 2020 and enrolled in a 12-week community-based PR program. Individuals were included if diagnosed with COPD[3] and clinically stable for 1 month prior to the study (no hospital admissions or exacerbations, nor changes in medication, according to Global Initiative for Chronic Obstructive Lung Disease – GOLD report).[3] Individuals were excluded if they presented other respiratory diseases or any clinical condition that precluded them from being involved in community-based PR (i.e., signs of cognitive impairment or presence of neoplastic disease or a significant cardiovascular, neurological, musculoskeletal or infectious disease).

Data collection

Sociodemographic (age, gender), anthropometric (height and weight to compute body mass index [BMI]) and general clinical (smoking habits, medication or number of exacerbations in the past year) data were first collected. Lung function values were obtained from participants' medical records. Participants were classified according the severity of airway limitation (GOLD grades 1-4) and ABCD assessment tool (GOLD groups A-D), as recommended by GOLD report.[3] The severity of comorbid diseases was recorded and scored according to the Charlson Comorbidity Index.[25] The remaining measures were collected before (T0) and after the PR program (T1), by two physiotherapists experienced in administering performance-based tests.

The mMRC was used to assess functional dyspnea[26] and to classify participants according to the ABCD assessment tool.[3] This questionnaire is a 5-point scale, where 0 represents the lowest and 4 the greatest dyspnea level of dyspnea impairment

perceived.[27] The mMRC has been shown to be valid and reliable, **presenting a MCID of -1 point, in people with COPD, after PR**.[28,29]

Exercise tolerance was measured with the 6MWT, according to the international guidelines.[30] The 6MWT has been shown to be valid and reliable, **with a MCID of 25 meters in people with COPD, following PR.**[31,32]

The Brief-BESTest was used to assess balance.[16] This is a 6-item balance test containing 1 item of each of the 6 subsections of the full BESTest: biomechanical constraints, stability limits/verticality, transitions/anticipatory postural adjustments, reactive postural control, sensory orientation and stability in gait.[16] Each task is scored on a 4-point scale (0-3), with a maximum score of 24 points, where higher scores indicate better balance performance.[16] The Brief-BESTest has shown to be a valid and reliable instrument, able to differentiate between people with COPD with and without a history of falls (cutoff for fall risk: 16.5 points).[1]

Intervention

All participants completed a 12-week community-based PR program, consisting of two weekly sessions of exercise training and one session of education and psychosocial support every two weeks.[15] Exercise training sessions included aerobic and resistance exercises plus a balance training component. All participants received balance training, as the World Health Organization recommends that people aged 65 years old or over must perform balance training 2-3 times/week.[33] Balance exercises consisted of 15 minutes of performing tasks targeting the six subsystems of balance control of the Brief-BESTest (Appendix 1). When participants performed a task independently and with little instability, the difficulty level of that subsystem task was increased by introducing more

158 challenging tasks (e.g., eyes closed, adjustments of the centre of gravity in static and
159 dynamic postures, increased speed/repetitions, perturbations, and dual cognitive and
160 motor tasks). Further information regarding the intervention has been published
161 elsewhere.[22]

162 **Data analysis**

163 Statistical analysis was performed using IBM SPSS Statistics version 24 and plots created
164 using GraphPad Prism 8 and MetaXL 5.3. The analysis included only participants that
165 adhered to at least 65% of PR, according to the international recommendations which
166 refer that 8 weeks of PR are needed to achieve substancial benefits.[15] The level of
167 significance was set at 0.05.

168 Regarding the sample size, we aimed to recruit at least 50 participants, as it has been
169 established as adequate to compute the MCID.[34] Differences between participants and
170 dropouts, and T0-T1, were explored with independent t-test/Mann-Whitney U test and
171 paired t-test/Wilcoxon signed-rank tests, according to the normality of data distribution.
172 Floor and ceiling effects of the Brief-BESTest were verified and considered inexistent if
173 less than 15% of participants scored at the bottom or top, respectively.[35] Effect sizes (ES)
174 were calculated through Cohen's d or with nonparametric tests, when data was not
175 normally distributed;[36] and interpreted as small (≥0.2 or ≥0.1), medium (≥0.5 or ≥0.3)
176 and large (≥0.8 or ≥0.5), if calculated from Cohen's or with nonparametric tests,
177 respectively.[37,38] ES were considered as minimally clinically/subjectively important when
178 ≥0.2.[37]

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Responsiveness

Responsiveness of the Brief-BESTest to PR in people with COPD was determined using the Pearson's correlation coefficient as recommended by the COSMIN guidelines.[39] These correlations were explored between the mean change of the Brief-BESTest and the mean changes of the mMRC and six-minute walk distance (6MWD).[20] Significant correlations ≥0.3 were considered adequate.[17,40]

Minimal clinically important difference

MCID was established using a combination of both anchor- and distribution-based methods,[40,41] which were weighted on a ratio of 2/3 and 1/3, respectively, according to the authors' best judgement and previous work.[19] The final MCID was calculated through the arithmetic weighted mean. The MCIDs generated from the different methods were entered into the MetaXL 5.3 to create the MCID plots.

<u>Anchor-based methods</u>

For anchor-based methods, the mMRC and the 6MWD, outcome measures with previously established MCIDs (-1 point[29] and 25m[32], respectively) **in people with COPD,** after a PR program were selected as possible anchors.[40] The suitability of the mMRC and 6MWD to be used as anchors were confirmed if the Pearson correlation coefficients, previously explored in the responsiveness analysis, were ≥0.3.[40]

The MCID of the Brief-BESTest was calculated with three different methods: i) the mean change (i.e., the absolute difference between the mean scores of the Brief-BESTest at T1 and T0), of those individuals who achieved the MCID established for the anchors;[41,42] ii) the receiver operating characteristic (ROC) curves (the area under the curve [AUC] of

a ROC>0.7 was considered adequate); and iii) the linear regression analysis (the estimated change was considered the MCID for the Brief-BESTest).[41]

Distribution-based methods

Five distribution-based methods were calculated: i) 0.5*standard deviation (SD);[43] ii) standard error of measurement (SEM);[44] iii) 1.96*SEM;[43] iv) minimal detectable change (MDC), **i.e., the absolute measure of reliability**;[43] and, v) ES[36,45] (Table 1). The intraclass correlation coefficient (ICC) used for the SEM calculation was based on test-retest reliability previously published for the Brief-BESTest **in people with COPD** ($ICC_{2,1}$=0.82).[1]

(please insert Table 1 here)

After combining both anchor- and distribution-based methods, the pooled MCID value was used to compute the matching ES[41] according to the formula: $MCID_{ES} = MCID_{pooled}/\sqrt{(SD_{T1}^2 + SD_{T0}^2)/2}$. A $MCID_{ES}$ between 0.3-0.5 has been recommended.[41]

Role of the funding source

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RESULTS

Sample characterization

A total of 71 patients were analyzed. A flow diagram of the participants is provided in Figure 1.

(Please insert Figure 1 here)

At baseline, no differences were observed between the included patients and drop-outs **(p>0.05)** (Table 2). Most participants were male (n=54; **76**%) with a **mean age of 69±8** years old, had severe airway obstruction (n=30; **42**%) and were at GOLD grades 2 and 3 (n=58; **81**%) and GOLD group B (n=40; **56**%).

(please insert Table 2 here)

The Brief-BESTest did not present a ceiling effect at T0, with only 8 (11%) participants scoring at the top of the scale. A ceiling effect was however observed at T1, with 18 (25%) individuals scoring at the top of the scale. After PR, there was a significant decrease in mMRC **(mean difference of -1±1)** and increase in the performance of both 6MWD (mean difference of **38±67** meters) and Brief-BESTest (mean difference of **3±3** points) (Table 3). Thirty-two **(45%)** participants improved beyond the MCID of -1 point established for the mMRC and 41 **(58%)** above the 25m in the 6MWD.

(please insert Table 3 here)

Responsiveness

Changes in the Brief-BESTest correlated moderately with changes in the mMRC (r=-0.314; p=0.008) and in the 6MWD (r=0.366; p=0.002).

Minimal clinically important difference

The MCIDs resulting from the mean change of responsive participants to the mMRC and 6MWT were 3.6 and 3.4, respectively (Supplementary Table 1).

Using ROC statistics, no significant results or AUCs over 0.7 were found for the discrimination ability of the Brief-BESTest using the mMRC (AUC= 0.64 [0.51-0.77] 95%CI; p=0.047) or the 6MWD (AUC=0.63 [0.5-0.76] 95%CI; p=0.068) as anchors. Thus, ROC statistics could not be used to compute the MCID.

Using linear regression, the estimated MCID for the Brief-BESTest was 3.3 [3.328-3.338] 95%CI (p=0.008) and 2.6 [1.637-3.583] 95%CI (p=0.002), using the mMRC and the 6MWT, respectively (Supplementary Figure 1).

(Please insert Figure 2 here)

The distribution-based methods and the overall MCID pooled values are presented in Table 4 and plots of pooled MCID in Figure 2. Pooled MCID for the Brief-BESTest was 3.3 points.

(Please insert Table 4 here)

(Please insert Figure 2 here)

DISCUSSION

This work showed that the Brief-BESTest is a responsive measure and established a pooled MCID of 3 points **in people with COPD, after PR. Furthermore, improvements in balance were moderately associated with improvements in exercise tolerance and dyspnea. These results confirm our hypothesis that changes in Brief-BESTest would correlate moderately (0.3-0.5)[11,12,17] and: i) positively with changes in exercise tolerance; ii) negatively with changes in dyspnea; in agreement with previous literature.[11,12]**

Similarly to the Berg Balance Scale,[5] the Brief-BESTest was able to detect changes after balance training, however, the Brief-BESTest has the additional advantage of enabling clinicians to identify impairments in specific balance systems and tailor the treatment accordingly. Additionally, the Brief-BESTest has shown excellent validity and reliability.[1] Thus, Brief-BESTest can be advocated as a worthwhile, adequate and psychometrically sound outcome measure **to assess effects of PR on balance in people with COPD**.

The MCID found in our study (i.e., 3.3 points) is similar to the one computed for individuals after total knee arthroplasty (i.e., 2-3 points),[46] but smaller than the MCID estimated for people with subacute stroke (i.e. 4.5-5.5 points).[47] These differences might be explained by the discrepancies among populations, due to the different pathophysiology of the diseases, but also different baseline values, i.e., those with subacte stroke presented lower Brief-BESTest baseline values than participants from our study (8.8 vs 17.5 points, respectively), having a greater room for improvement. Additionally, the differences might also be explained by the different interventions and methodologies used to compute MCIDs. Although there are no other studies focusing

on the MCID of the Brief-BESTest **in people with COPD,** the MDC previously found for the Brief-BESTest (4.9 points)[1] was similar to ours (5.6 points). It is known that MDC computation leads to larger estimates[48,49] and does not take into account the clinical meaning provided by anchor-based methods.[40,48] In our study, the MDC also displayed the highest value among all methods used. When computing MCID, it is therefore important to use different approaches and integrate a wide range of anchor- and distribution-based methods, as performed in this study.[40,48]

Important strengths of our study include the robust methodology used to establish responsiveness, following the international recognised COSMIN guidelines,[23] and the estimate of the Brief-BESTest MCID using both anchor- (provide clinical meaning) and distribution- (add statistical difference) based methods, as previously recommended.[40,48] Moreover, our study is in accordance with the recommendation of having anchor- prevailing over distribution-based methods.[40,41] Finally, our work adds value to the body of literature by enhancing the interpretability of balance **in people with COPD**, with a measure that can be easily implemented in clinical practice. Treatment can now be guided and personalised to improve one of the main contributors, balance impairment, to the morbidity and risk of falls **in people with COPD**, and increased burden for the society.[13,50]

Limitations

This study presents some limitations that should be acknowledged. **A ceiling effect (25%) of the Brief-BESTest was observed at T1. At T0, there was no ceiling effect (only 11% of the participants scored at the top of the scale), which emphasizes that a real improvement on balance after PR was observed. Nevertheless, it should be noticed**

that the presence of balance impairments was not an inclusion criteria of our study. In fact, at T0, most of our sample scored above the cutoff for risk of fall (54% of participants>16.5 points[1]). After PR, balance improved in most of our participants, explaining why we had a relatively large proportion of participants (25%) scoring at the top of the scale at T1. It is however possible that the observed ceiling effect at T1 biased the results and led to an overestimation of the MCID. This is consistent with the fact that the Brief-BESTest $MCID_{ES}$ found in our study corresponded to 0.81, instead of the desirable ES between 0.3-0.5.[41] However, having significant improvements in balance (ES=0.68) even with a population with lower balance impairment shows that PR is an effective intervention improving balance and that the Brief-BESTest is a responsive measure to PR. Thus, the Brief-BESTest is a good measure to be applied before and after PR, and in real-world settings, where human resources, time and equipment are scarce, urges as an excellent, simple and easy to administer measure to screen balance impairment. However, special attention is needed to those people scoring at the top of the scale at the baseline, where the use of the BESTest is recommended.[18] Moreover, our sample was mainly composed of GOLD B and male participants, with high functional capacity (6MWD>300m),[32] therefore the external validity of our results might have been affected and the established MCID might not be generalisable to all people with COPD. Future studies involving participants with different disease severity and presenting risk of falls should be conducted to further validate these results. It is also important to notice that our study provides the MCID of Brief-BESTest **for people with COPD enrolling a community-based PR.** Further studies, in this population integrating a hospital-based PR program are needed to confirm this estimation in all PR-settings. Lastly, in our study, it was not possible to compute the

anchor-based methods through the ROC curves. Consequently, Brief-BESTest may not be a good measure to discriminate between people with COPD who improved in dyspnea and exercise tolerance.

CONCLUSION

The present study suggests that Brief-BESTest is a responsive measure and an improvement greater than 3 points in this outcome measure is clinically relevant for people with COPD after PR. These results can now inform future studies regarding sample calculation and will aid health professionals to understand the effects of PR on balance performance and develop tailored interventions **for people with COPD.**

AUTHORS' CONTRIBUTIONS

AM obtained the funding, had full access to all data in the study and takes responsibility for the data and the accuracy of data analysis, including and especially any adverse effects. AM and AO conceived the idea. All authors contributed to the design and interpretation of data. CP, PR, AO, VM and PS contributed to data acquisition. CP performed the analysis and drafted the paper. All authors critically revised the manuscript and approved the final version.

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TABLES

Table 1 Distribution-based methods to estimate the minimal clinically important difference.

Method	MCID calculation
0.5SD	$0.5*SD_{T0}$
SEM	$SD_{T0}\sqrt{(1-r)}$
1.96SEM	$1.96*(SD_{T0}\sqrt{(1-r)})$
MDC	$1.96 \times SEM \times \sqrt{2}$
ES	$(mean_{T1} - mean_{T0})/\sqrt{(SD_{T1}^2 + SD_{T0}^2)/2}$
ES_{NP}	$\lvert z \rvert/(\sqrt{n})$

Legend: ES – effect size; ES_{NP} – Nonparametric effect size; MCID - minimal clinically important difference; MDC – minimal detectable change; n – number of total matched pairs; r - test-retest reliability coefficient; SD – standard deviation; SEM – standard error measurement; T0 – baseline; T1 – after the pulmonary rehabilitation program; z-statistic test.

518 **Table 2** – Sample characterization.

Characteristics	**Participants included (n=71)**	**Drop-outs (n=39)**	**p-value**
Age, years	**69±8**	**66±10**	0.086
Gender, male n (%)	54 **(76)**	28 **(72)**	0.624
BMI, kg/m^2	**26±5**	**28±5**	0.192
Smoking status, n (%)			0.334
Current	9 **(13)**	6 **(15)**	
Former	48 **(68)**	21 **(54)**	
Never	14 **(19)**	12 **(31)**	
Packs/year	**53±40**	**42± 31**	0.949
Exacerbations/year[1]	**1±1**	**1±1**	0.156
Lung function (post-bronchodilator)			
FEV$_1$, L	1.3±0.5	1.3±0.5	0.832
FEV$_1$, %predicted	49.8±18	50.8±17.5	0.771
FEV$_1$/FVC, %	50.1±13.1	54.7±12.9	0.075
GOLD grade, n (%)			0.766
1	6 **(9)**	2 **(5)**	
2	28 **(39)**	19 **(49)**	
3	30 **(42)**	14 **(36)**	
4	7 **(10)**	4 **(10)**	
GOLD groups, n (%)			0.172

A	11 **(16)**	7 **(18)**	
B	40 **(56)**	14 **(36)**	
C	2 **(3)**	3 **(8)**	
D	18 **(25)**	15 **(38)**	
CCI, n (%)			0.785
1-2	8 **(11)**	6 **(15)**	
3-4	38 **(54)**	21 **(54)**	
≥5	25 **(35)**	12 **(31)**	
Medication, n (%)			
Bronchodilators			
SABA	8 (11)	6 (16)	0.519
SAMA	3 (4)	1 (3)	0.664
SABA/SAMA combination	3 (4)	1 (3)	0.656
LABA	7 (10)	5 (13)	0.618
LAMA	21 (30)	15 (40)	0.319
LAMA/LABA combination	21 (30)	15 (39)	0.342
ICS	13 (18)	4 (11)	0.286
ICS/LABA combination	35 (49)	18 (46)	0.752
LAMA/LABA/ICS	1 (1)	0 (0)	0.457
LTRA	5 (7)	6 (15)	0.163
Xanthines	6 (9)	8 (21)	0.069
Expectorants	5 (7)	4 (10)	0.556
Antibiotics	1 (1)	0 (0)	0.457

mMRC	**2±1**	**2± 1**	0.723
6MWD, meters	**402±121**	**388±104**	0.540
Brief-BESTest, points	**18±5**	**18±5**	0.438

519 **Notes:** Values are presented as mean±standard deviation or median [interquartile
520 range], unless otherwise stated. [1]past-year.

521 **Legend:** 6MWD – 6-minute walk test total distance; AECOPD – acute exacerbation of
522 chronic obstructive pulmonary disease; BMI – body mass index; Brief-BESTest – Brief-
523 Balance Evaluation Systems Test; CCI – Charlson comorbidity index; FEV_1 – forced
524 expiratory volume in one second; FVC – forced vital capacity; GOLD - Global Initiative for
525 Chronic Obstructive Lung Disease; ICS – inhaled corticosteroids; LABA – long-acting beta-
526 agonists; LAMA – long-acting muscarinic antagonists; LRTA – leukotriene receptor
527 antagonists; mMRC – modified British medical research council questionnaire; SABA –
528 short-acting beta-agonists; SAMA – short-acting muscarinic antagonists.

Table 3 - Outcome measures before and after the 12-week community-based pulmonary rehabilitation program in people with COPD (n=71)

Outcome measure	Baseline	Post-PR	Δ	95% CI	p-value	ES
mMRC	**2±1**	**1±1**	**-1± 1**	-0.7 to -0.3	<0.001*	0.48¥
6MWD	**402±121**	**440±123**	**38±67**	21.3 to 53.2	<0.001*	0.31
Brief-BESTest	**18±5**	**21±3**	**3±3**	2.1 to 3.5	<0.001*	0.68

Notes: Values are presented as mean±standard deviation or median [interquartile range], unless otherwise stated. *p<0.05; ¥Non-parametric ES.

Legend: Δ – mean/median change; 6MWD – 6-minute walk test total distance; Brief-BESTest – Brief-Balance Evaluation Systems Test; CI – Confidence Intervals; ES: Effect size; mMRC – modified British medical research council questionnaire; PR – pulmonary rehabilitation.

Table 4 – Anchor- and distribution-based methods used to calculate the minimal clinically important difference of Brief-BESTest in people with COPD after the 12-week community-based PR program

			Brief-BESTest
Anchor-based methods	mMRC	Mean change	3.6 (2.5 to 4.7)
		Linear regression	3.3 (3.328 to 3.338)
	6MWT	Mean change	3.4 (2.4 to 4.5)
		Linear regression	2.6 (1.637 to 3.583)
Distribution-based methods	0.5SD		2.35
	SEM		1.99
	1.96SEM		3.91
	MDC		5.53
	ES		0.66
	Pooled MCID		**3.3**
	MCID ES		0.81

Legend: 6MWT – 6-minute walk test; Brief-BESTest – Brief-Best Evaluation System Test; ES – effect size; MDC – minimal detectable change; MCID - minimal clinically important

542 difference; mMRC – modified British medical research council questionnaire; SD –

543 standard deviation; SEM – standard error measurement.

FIGURE LEGEND

Figure 1: Flow diagram of participants recruited and included in the study. COPD – Chronic obstructive pulmonary disease; PR – pulmonary rehabilitation.

Figure 2: Plot of the pooled MCID for the Brief-BESTest in people with COPD after the 12-week community-based PR program. The horizontal plots represent the MCID estimates derived in this study. When appropriated, the estimates included the 95% confidence intervals (95% CI).

Legend: 6MWT – 6-minute walk test; Brief-BESTest – Brief-Best Evaluation System Test; CI, confidence intervals; ES – effect size; MDC – minimal detectable change; mMRC – modified British medical research council questionnaire; SD – standard deviation; SEM – standard error measurement.

APPENDIXES

Appendix 1

Balance training

Instructions: The balance training should be performed in all exercise training sessions during, at least, 15 minutes. Start with the 1st exercise of each component. The same exercise can be performed 3 times in the same session. Progress should be made when the final goal established for each exercise is achieved, by reducing the support base, the visual input or by adding a cognitive task.

1. BIOMECHANICAL CONSTRAINTS	**FINAL GOAL**
Hip extension, standing	Hold 20 sec
Hip abduction, standing	Hold 20 sec
Hip flexion, standing	Hold 20 sec
Step-up	5 reps
Lateral step-up	5 reps
Toe/heel raises	Hold 5 sec
2. STABILITY LIMITS	**FINAL GOAL**
Reach forward/lateral, sitting	Shortest time to reach an object
Reach forward/lateral, standing	Shortest time to reach an object
Reach diagonal, sitting/standing	Shortest time to reach an object
Standing, pick up an object	Shortest time to reach an object
Tandem stand, reach lateral	Shortest time to reach an object
One-legged stand, reach lateral	Shortest time to reach an object
3. TRANSITIONS- ANTICIPATORY POSTURAL ADJUSTMENT	**FINAL GOAL**

Transfer from one chair to another	1 rep
Sit on ball, extend the knees (one of each time)	Hold 20 sec
Stair tapping	5 reps
Side step with squat	1 rep
Kick a ball	5 reps
Throw/grab the ball	5 reps
4. REACTIVE POSTURAL RESPONSE	**FINAL GOAL**
Standing, disturbances (backward, forward, sideward), narrow stance	5 reps. Recover the stability without arms and hips movements.
Tandem, disturbances (backward, forward, sideward)	5 reps. Recover the stability without arms and hips movements.
One-legged stance, disturbances (backward, forward, sideward)	5 reps. Recover the stability without arms and hips movements.
Step forward	5 reps. Recover the stability without arms and hips movements.
Step sideward	5 reps. Recover the stability without arms and hips movements.
Step backward	5 reps. Recover the stability without arms and hips movements.
5. SENSORY ORIENTATION	**FINAL GOAL**
Eyes closed, narrow stance	Hold 1 min.

Eyes open, narrow stance in foam	Hold 1 min.
Eyes closed, narrow stance in foam	Hold 1 min.
Eyes closed, tandem stance	Hold 30 sec
Eyes open, one-legged stance in foam	Hold 30 sec
Eyes closed, ramp	Hold 30 sec
6. STABILITY IN GAIT	**FINAL GOAL**
Backwards walk	Shortest time possible
Walk and look at side	Shortest time possible
Walk and quick direction change ("change")	Shortest time possible
Walk with countdown	Shortest time possible
Obstacle course	Shortest time possible
Time Up and Go	Shortest time possible

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