ORIGINAL RESEARCH

# Balance impairment in individuals with COPD: a systematic review with meta-analysis

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## ABSTRACT

**Background** People with chronic obstructive pulmonary disease (COPD) are four times more likely to fall than healthy peers, leading to increased morbidity and mortality. Poor balance is a major risk factor for falls. This review aims to quantify the extent of balance impairment in COPD, and establish contributing clinical factors, which at present are sparse.

**Methods** Five electronic databases were searched, in July 2017 and updated searches were performed in March 2019, for studies comparing balance in COPD with healthy controls. Meta-analyses were conducted on sample mean differences (MD) and reported correlations between balance and clinical factors. Meta-regression was used to quantify the association between mean difference in percentage predicted forced expiratory volume in 1 s ($FEV_1$) and mean balance impairment. Narrative summaries were provided where data were insufficient for meta-analysis.

**Results** Twenty-three studies were included (n=2751). Meta-analysis indicated COPD patients performed worse than healthy controls on timed up and go (MD=2.77 s, 95% CI 1.46 s to 4.089 s, p=<0.005), single leg stance (MD=−11.75 s, 95% CI −15.12 s to −8.38 s, p=<0.005) and berg balance scale (MD=−6.66, 95% CI −8.95 to −4.37, p=<0.005). The pooled correlation coefficient between balance and reduced quadriceps strength was weak-moderate (r=0.37, 95% CI 0.23 to 0.45, p=<0.005). The relationship between differences in percentage predicted $FEV_1$ and balance were negligible ($r^2$ =<0.04).

**Conclusions** Compared with healthy controls, people with COPD have a clinically meaningful balance reduction, which may be related to reduced muscle strength, physical activity and exercise capacity. Our findings support a need to expand the focus of pulmonary rehabilitation to include balance assessment and training, and further exploration of balance impairment in COPD.

**PROSPERO registration number**
CRD4201769041

## Key messages

### What is the key question?

- What is the extent of balance impairment in COPD and what are the mechanisms underlying it?

### What is the bottom line?

- Balance is impaired in people with COPD and this impairment is moderately associated with reduced strength and may be also be associated with reduced physical activity and exercise capacity.

### Why read on?

- This is the first systematic review with meta-analyses to synthesise and quantify balance impairment and clinical associations in people with COPD highlighting important directions for future research.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is associated with breathlessness resulting in reduced exercise tolerance and poor health-related quality of life.[1] However, people with COPD are also four times more likely to fall than healthy peers, leading to increased morbidity, mortality and healthcare costs.[2–5]

Balance impairment is a key risk factor for falls and people who fall have worse balance.[6] However, individual studies have shown varying degrees of balance impairment in COPD.[7–11] Reports also indicate more marked balance impairment following an acute exacerbation of COPD (AECOPD).[10 12] However, studies investigating balance impairment in COPD are often underpowered and feature small samples sizes, and vary widely in outcomes used, and associated factors investigated, making it difficult to draw firm conclusions. It is unclear why balance is impaired in COPD; proposed contributing factors include reductions in proprioceptive control, trunk and respiratory muscle coordination, skeletal muscle dysfunction, reduced exercise capacity and physical activity levels, dyspnoea and systemic inflammation.[8 10 12–17]

Despite increasing awareness of balance impairment, routine assessment is not part of international guidelines for COPD.[1] Nevertheless, the use of balance outcomes was briefly commented on by the American Thoracic Society/European Respiratory Society ‘Key concepts in pulmonary rehabilitation’ (PR)[18] and treatment of balance impairment is becoming more frequent within PR with the emergence of effective balance training.[19]

The objectives of this systematic review are to; (1) Quantify the extent of balance impairment in COPD compared with healthy controls, when data are synthesised across studies, and (2) Explore which clinical factors contribute to balance impairment in

| | |
|---|---|
| S1 | (copd or chronic obstructive pulmonary disease) (54,471) |
| S2 | (MH "Pulmonary Disease, Chronic Obstructive+") OR "copd" (59,309) |
| S3 | (MH "Bronchitis Chronic") (1,619) |
| S4 | emphysema (31,427) |
| S5 | (MH "Emphysema+" OR (MH "Pulmonary Emphysema") (25,822) |
| S6 | "Balance" OR (MH "Postural Balance") (211,628) |
| S7 | (MH "Gait+) OR (MM "Walking Speed") (22,099) |
| S8 | walking (65,330) |
| S9 | "gait impairment" (478) |
| S10 | (MH "Postural Balance" OR (MH "Posture" (73,685) |
| S11 | postural control (5,276) |
| S12 | S1 OR S2 OR S3 OR S4 OR S5 (84,921) |
| S13 | S6 OR S10 OR S11 (266,426) |
| S14 | S7 OR S8 OR S8 OR S9 (78,098) |
| S15 | S12 AND S13 (943) |
| S16 | S12 AND S14 (1,617) |
| S17 | S15 OR S16 (2,519) |
| S18 | 17 OR 18 Limiters – English Language (2,246) |

**Figure 1** Example search strategy performed in MEDLINE.

COPD. Results will inform development of targeted assessment and treatment strategies to improve balance and reduce fall risk in COPD.[3 4 20]

## MATERIALS AND METHODS

The review was registered on PROSPERO in June 2017 and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[21]

### Search strategy

Figure 1 shows the search strategy. Searches of MEDLINE, CINAHL, AMED, Scopus and EThOS were undertaken by KL, after health librarian consultation, in July 2017 and updated in March 2019. The review initially included both balance and gait as falls occur during static and dynamic activities. However, due to the large volume of articles found, this review focus is balance only. The results of studies reporting gait outcomes were excluded and will be presented in a separate systematic review on gait impairment. This systematic review will provide an update, and meta-analysis in addition to that presented in a previous systematic review on gait analysis in COPD.[22]

### Selection of articles, data extraction, risk of bias and quality assessment

Inclusion criteria was informed by PICO; population – adults with a primary diagnosis of COPD by GOLD criteria,[1] comparison – healthy controls, outcomes – static (eg, posturography) or dynamic balance measures (eg, berg balance scale (BBS), single leg stance (SLS) and timed up and go (TUG)), that is, functional balance measures in a single activity or a standardised scoring system. Grey literature, case study reports, commentary, conference abstracts, reviews and study protocols were included and reference lists were handsearched. Measures where balance is one aspect of a global functioning instrument, and non-English language articles were excluded. Falls outcomes were also excluded as they detect the risk or quantity of falls and do not indicate the extent or nature of balance problems that may result in a fall. All screening and full text reviews were undertaken by two pairs (KL, SLH and MKB, SR). Data were extracted by KL and verified by SLH using a standardised template. Any discrepancies were resolved by consensus. A quality assessment including questions on risk of bias, was undertaken (by KL, SLH) using the Downs and Black tool.[23] As studies were not testing interventions no intervention questions were included, thus the maximum score was 18. An analysis of small study effects (publication bias) was performed on studies included in the meta-analyses.

### Data analysis

Outcomes reported in five or more studies[24] were included in meta-analyses and meta-regressions using Comprehensive Meta-Analysis Software (CMA V3). Reported conversion equations[25 26] were used to calculate means (SD) from medians (IRQ) in three studies, assuming that departures from Gaussian distributions were not severe. When data were reported solely for subgroups, pooled study effect sizes and SDs were estimated using reported equations.[27] Authors were contacted when data were unusually different from other studies data and when there were extreme outliers or concerns of data reporting errors. One author reported that data were not available, and no response was received from other contacted authors, thus sensitivity analyses were undertaken with and without these studies data. Mean differences (MD) were compared with previously published minimal clinically important difference (MCID) values for COPD.[28–30]

Random effects meta-analyses were undertaken using differences in sample means as outcomes. Second, a meta-regression was performed on all studies that were in the meta-analyses to quantify the extent that study mean disease severity (using the mean difference in percentage predicted forced expiratory volume in 1 s ($FEV^1$) between COPD and healthy controls in each study) was associated with study mean balance impairment. Finally, a meta-analysis of reported Pearson's correlation coefficients reported in each study for the association between balance impairment and strength in each study sample was performed. Low study numbers prevented the analysis of other factors. Ninety-five per cent CIs and prediction intervals were reported,[31] and heterogeneity was quantified using the $I^2$ and Tau statistics.[32 33] Posturography studies, featuring heterogeneity in measurement units and test conditions, rendered meta-analysis inappropriate. The remainder of clinical balance outcomes are reported as narrative summaries along with AECOPD results. The presence of small study effects were explored for using a Funnel plot and Egger's regression analysis.

## RESULTS

### Electronic literature search results

Of 11 506 search results, 3904 titles were screened, 75 full texts were assessed for eligibility (including one identified by handsearching reference lists and two identified during the updated searches) and 23 studies were included (see figure 2).

### Description of studies, risk of bias and quality assessment

Study characteristics are reported in online supplementary table 1. Seventeen studies featured clinical balance outcome measures; BBS, (n=8), BESTest (n=1), Mini BESTest (n=1), Tinetti (n=2), TUG, (n=9), SLS (n=6), Functional Reach Test (n=2) and Community Balance and Mobility Scale (CBMS) (n=1), six of these studies used more than one clinical balance outcome. Posturography featured in 13 studies, 7 of those combining posturography with clinical balance outcome measure.

Quality scores ranged from 10 to 14 (see online supplementary table 2). Frequent issues included low external validity and confounding internal validity, due to poor reporting of sample selection and characteristics, and lack of a power calculation. Due to the narrow range of quality scores adjustment for study quality was not made. Seven studies featured adjustments for confounders (see table 1 for details). The results for small study effects (an indicator of publication bias) were; TUG=Egger's regression intercept 2.65 (95% CI −7.35 to 12.66), p=0.28; SLS=Egger's regression intercept −1.11, (95% CI −4.26 to

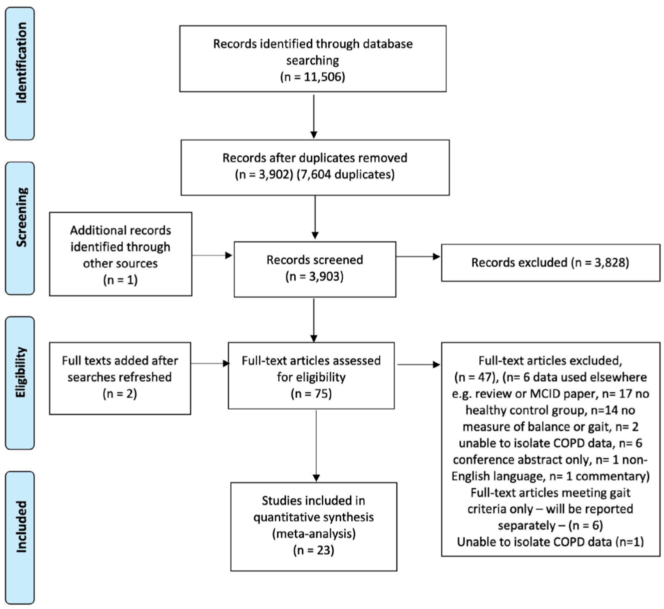


**Figure 2** Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram.

2.02), p=0.19; BBS=Eggers regression intercept −3.50, (95% CI −9.62 to 2.62), p=0.10 (see figure 3).

### Balance impairment in stable COPD

A meta-analysis comparing balance in COPD versus healthy controls was performed for the TUG (n=9), SLS (n=6) and BBS (n=8) (including stable and control groups from studies investigating AECOPD, stable COPD and healthy controls). People with COPD had poorer performance on the TUG, (MD=2.77 s, 95% CI 1.46 s to 4.089 s, Tau=1.93, Q value =181.87, $I^2$ = 95.60, p≤0.005, n=582) (figure 4), SLS, (MD=−11.75 s, 95% CI −15.12 s to −8.38 s, Tau=3.22, Q value=17.00, $I^2$= 70.59, p=<0.005, n=288) (figure 5) and BBS, (MD=−6.66, 95% CI −8.95 to −4.37, Tau 3.03, Q value= 64.62, $I^2$=89.17, p=<0.005, n=512) (figure 6). MCIDs in COPD for the TUG, SLS and BBS are 2.68 s, −4.03 s and −3.5, respectively,[28–30] and all were exceeded. Table 1 summarises the sensitivity analyses which had little effect on outcomes. The 95% prediction intervals for the TUG, SLS and BBS MDs were −1.92 to 7.46, −21.13 to −2.37 and −14.31 to 0.98, respectively.

Balance deficits were reported to be greater in COPD in seven out of eight studies using clinical balance measures not included in the meta-analyses. The seven studies (n=1899) used; BESTest (MD 21.3, 95% CI 17.1 to 25.4, p=<0.001),[11] Mini BESTest (p=<0.005) and TUG with dual task (p=0.0005),[34] CBMS Scale (p=0.001),[35] Tinetti test (p=<0.001 and p=<0.05)[36 37] and Functional Reach Test (p=≤0.001, and 3.0 cm, p<0.0001, 95% CI −4.2 to −1.8).[14 38] One study using the standing balance test (n=35 participants) reported no difference (p value unavailable).[9]

People with COPD performed worse on posturography in 8 out of 11 studies. Three studies reported slower postural responses in COPD; responses to perturbations were slower (MD 49 ms, 95% CI 6 to 91, p=0.027),[11] return to baseline of COPD after arm movements were slower (p=0.023)[17] and standing phase of sit-to-stand-to-sit (STSTS) (p=0.028) and stand-to-sit phase of STSTS was slower (p=0.001).[13] One study demonstrated a reliance on ankle over back proprioceptive strategy (p=0.047).[8] Four studies reported worse postural control in COPD; SLS on a balance platform (p=0.01),[39] quiet standing with and without vision (p=0.005 and p=0.005),[34] static balance standing on foam (p=<0.05)[15] and static balance over various conditions before (p=<0.042) and after (p=0.040) upper limb exercise[40]

**Table 1** Summary of sensitivity analysis results

| Outcome | Study removed | Reason for removal | Difference in means | SE | CI lower limit | CI upper limit | P value | Heterogeneity |
|---|---|---|---|---|---|---|---|---|
| TUG | None | N/A | 2.773 | 0.671 | 1.457 | 4.089 | <0.005 | $I^2$=95.601, Tau=1.929, Q value=181.868, p=<0.005 |
| TUG | Butcher *et al* 2004[35] | SE converted to SD | 2.985 | 0.743 | 1.529 | 4.441 | <0.005 | $I^2$=95.972, Tau=2.001, Q value=173.763, p=<0.005 |
| TUG | Crişan *et al* 2015, Voica *et al* 2016[63] and Tudorache *et al* 2015[10 12] | IQR and medians converted to mean and SD | 1.742 | 0.517 | 0.729 | 2.755 | 0.001 | $I^2$=90.748, Tau=1.185, Q value=54.045, p=<0.005 |
| SLS | None | N/A | −11.754 | 1.720 | −15.124 | −8.384 | <0.005 | $I^2$=70.583, Tau=3.222, Q value=16.997, p=0.005 |
| SLS | Butcher *et al* 2004[35] | SE converted to SD | −12.809 | 1.793 | −16.324 | −9.295 | <0.005 | $I^2$=71.539, Tau=3.117, Q value=14.054, p=0.007 |
| SLS | Crişan *et al* 2015, Voica *et al* 2016 and Tudorache *et al* 2015[10 12] | IQR and medians converted | −9.236 | 2.747 | −14.620 | −3.853 | 0.001 | $I^2$=42.297, Tau=3.157, Q value=3.466, p=0.177 |
| BBS | None | N/A | −6.659 | 1.168 | −8.947 | −4.371 | <0.005 | $I^2$=89.168, Tau=3.028, Q value=64.622, p=<0.005 |
| BBS | Crişan *et al* 2015, Voica *et al* 2016 and Tudorache *et al* 2015[10 12] | IQR and medians converted | −7.110 | 1.617 | −10.279 | −3.941 | <0.005 | $I^2$=92.110, Tau=3.397, Q value=50.697, p=<0.005 |
| BBS | Porto *et al* 2017[42] | SE converted to SD | −7.110 | 1.332 | −9.720 | −4.499 | <0.005 | $I^2$=90.453, Tau=3.254, Q value=62.847, p=<0.005 |
| BBS | Ozalevli *et al* 2011[16] | Outlier | −5.101 | 0.703 | −6.479 | −3.724 | <0.005 | $I^2$=68.575, Tau=1.477, Q value=19.093, p=0.004 |

BBS, berg balance scale; SLS, single leg stance; TUG, timed up and go.

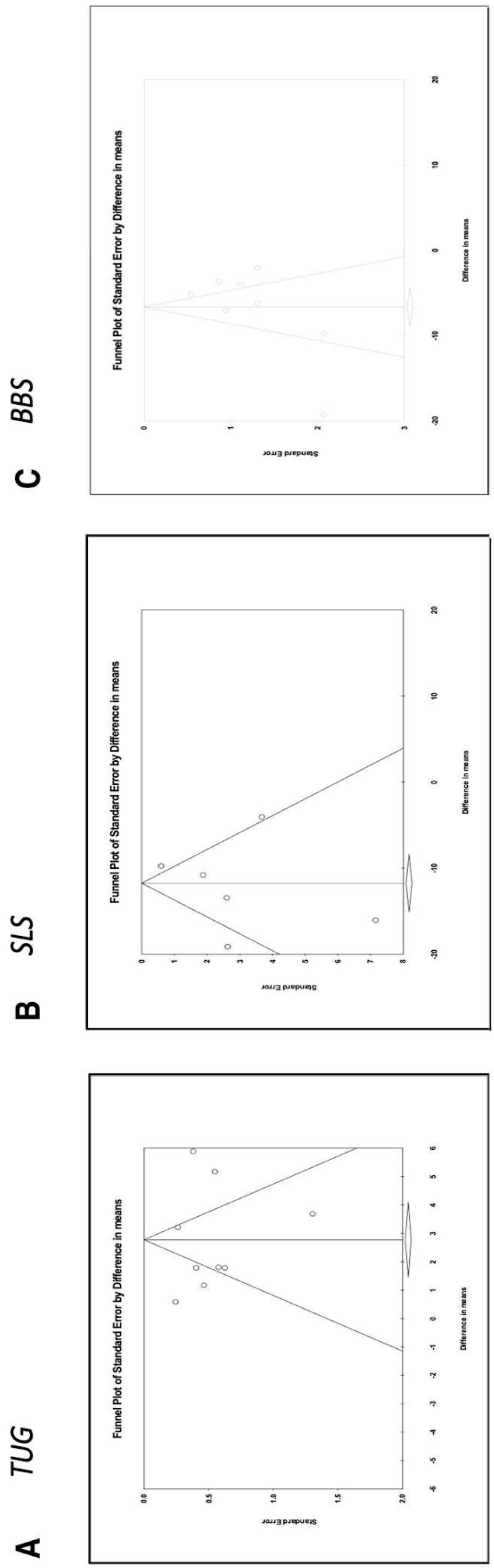


**Figure 3** Funnel plot of assessments of small study effects (publication bias) for (A) TUG, (B) SLS, and (C) BBS. BBS, berg balance scale; SLS, single leg stance; TUG, timed up and go.

(n=432 across all eight studies). Three studies reported no difference between COPD and control groups (p values unavailable)[37 41 42] (n=223).

The Sensory Organisation Test (SOT) for balance using posturography showed greater overall balance impairment in COPD in one study (p=0.016)[43] and on only one test condition (eyes open moving platform) in another (p=<0.05 and unavailable)[35] (n=91). However, no one sensory system was able to explain variability in balance control.[35 43]

## Balance impairment in AECOPD

Three studies compared BBS, TUG, SLS and posturography in three groups; people with COPD who were experiencing an AECOPD, people with stable COPD and in healthy controls. All three studies reported worse balance impairment during AECOPD compared with healthy controls (n=175) when using both dynamic (p=<0.001)[10 12] and static balance measures (p=≤0.05).[15] Balance was reported to be further impaired during AECOPD when compared with stable COPD, in two of the three studies, using dynamic balance measures (p=<0.001 in both[10 12]) (n=124). The third study reported no difference in balance impairment between stable COPD and AECOPD measured with BBS (p value unavailable). Postural sway, measured by posturography in this study,[15] was impaired in all four standing conditions examined (normal standing, eyes closed, feet together and foam base) in AECOPD and only in foam base standing in stable COPD, additionally 30% (n=8) of the AECOPD group and 7% (n=2) of the stable COPD group were unable to perform the foam standing condition or refused to attempt it due to poor balance confidence (p value unavailable between AECOPD and stable COPD results were not reported, n=51).[15]

## Factors associated with balance impairment

Meta-analysis was performed on reported correlations of balance measures (TUG, BBS, SLS, and BESTest) with quadriceps strength (peak torque Nm/kg, kg of force, Newton metres, and 0 to 5 manual scale testing). A weak-to-moderate pooled association was detected between increased balance impairment and reduced quadriceps strength (r=0.37, 95% CI 0.23 to 0.50, Tau= 0.00, Q value 3.98, $I^2$=0.00, p=<0.005, n=271) (figure 7). One study investigating balance during AECOPD found reduced BBS scores (r=0.51, p=0.01)[15] and worse sway on an unstable surface were associated with reduced quadriceps strength (r=0.53 and 0.53, p=<0.05, n=51).[15]

Two out of three studies investigating balance impairment and reduced physical activity (PA) levels reported an independent association with SLS and daily steps (r=0.821, p=0.001) and moderate-to-vigorous PA (r=0.645, p=0.014).[9] Physical Activity Scale for Elderly (PASE) scores were positively associated with BBS scores (r=0.41, p=0.007) and BESTest scores (r=0.40, p=0.008)[11] (n=86). A third study reported no association with postural control deficits on SOTs in COPD (n=40) and PA, but there was no significant difference in PASE scores (p>0.05) between COPD and control groups (r and p values unavailable).[43] Three studies investigated balance impairment and exercise capacity and all reported that shorter 6MWDs were correlated with poorer performance on clinical balance outcomes; BBS (r=0.61, p=<0.01),[16] TUG (r=0.43, p=0.002)[39] and SLS (r=0.504, p=0.017)[9] (n=163). Two studies reported worse balance outcomes with fatigue; after upper limb exercise,[40] and with leg fatigue severity (r=0.38, p=<0.05)[16] (n=88 participants).

| Study name | Difference in means | Standard error | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|---|
| Butcher et al., 2004 | 1.185 | 0.468 | 0.267 | 2.103 | 0.011 |
| Crisan et al., 2015 | 3.700 | 1.309 | 1.135 | 6.265 | 0.005 |
| de Castro et al., 2016 | 1.800 | 0.407 | 1.002 | 2.598 | 0.000 |
| Mkacher et al., 2014 | 3.230 | 0.265 | 2.710 | 3.750 | 0.000 |
| Morlino et al., 2017 | 1.820 | 0.580 | 0.683 | 2.957 | 0.002 |
| Roig et al., 2010 | 1.800 | 0.630 | 0.566 | 3.034 | 0.004 |
| Tudorache et al., 2015 | 5.900 | 0.385 | 5.145 | 6.655 | 0.000 |
| Voica et al., 2016 | 5.185 | 0.553 | 4.101 | 6.269 | 0.000 |
| Yumrutepe et al., 2015 | 0.600 | 0.248 | 0.113 | 1.087 | 0.016 |
| | 2.773 | 0.671 | 1.457 | 4.089 | 0.000 |

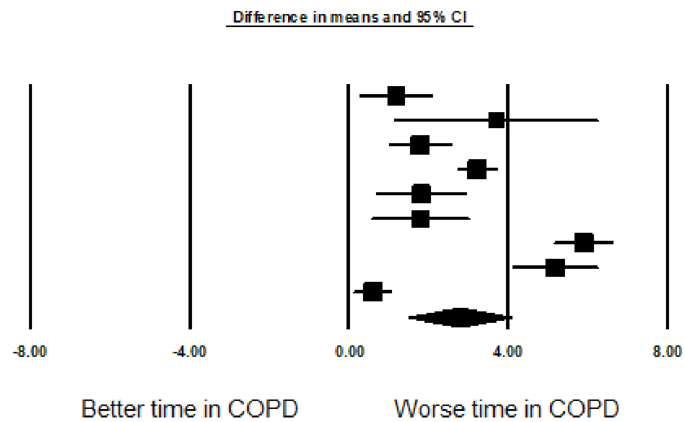


**Figure 4** Meta-analysis of timed up and go scores in people with COPD versus healthy controls.

A meta-regression identified no clear association between mean disease severity and clinical balance outcomes (TUG intercept −1.23, p=0.70, 95% CI −7.68 to 5.22, $I^2$=95.20%, n=582, SLS intercept −14.99, p=0.17, 95% CI −36.29 to 6.30, $I^2$=74.53%, n=288, BBS intercept −4.68, p=0.48, 95% CI −17.76 to 8.39, $I^2$=90.46%, n=512). $FEV^1$ and other measures of disease severity were associated with balance impairments in five studies (n=429) which used; $FEV^1$ with posturography (p=<0.005, r=0.416 and 0.479) and CBMS (p=0.586);[35] CAT score and BBS (p=0.03, y=0.24x+42.3);[10] severity of COPD with slower postural responses in an anteroposterior direction (p=0.031);[17] BODE Index with Tinetti (p<0.05, r=−0.78);[37] lower oxygen saturation after 6MWD (r=0.30, p=<0.05) and partial arterial oxygen pressure before exercise with BBS (r=0.28)[16] (n=238). However, four studies reported no associations between balance and disease severity ($FEV^1$) or hypoxia; with Mini BESTest (p>0.41)[34] ; GOLD stages or BODE index[39] with people unable to complete a SLS with or without supplementary oxygen (p value unavailable);[35] number of anteroposterior and mediolateral postural adjustments, and postural responses by disease severity (p>0.28)[17] (n=221).

Results of further clinical associations are limited by small study numbers and are presented in an e-supplement (online supplementary file 3), these are; inspiratory muscle strength, dyspnoea, anxiety, depression, inflammation, COPD phenotype, body mass index, vitamin D, sex and gait quality.

## DISCUSSION

Pooled analyses of the most frequently used clinical balance measures (TUG, SLS and BBS) showed both statistical and clinically important balance deficits in COPD compared with healthy controls.[44 45] Posturography measures were common but measurement and design varied widely limiting between-study comparisons. Fewer studies have examined balance impairment during AECOPD and no firm conclusions can be made. Balance impairment was associated with reduced strength, but not disease severity.

This review reports a high magnitude of balance impairment in people with COPD using robust and commonly used balance outcomes. There are however, known ceiling effects of the BBS and SLS[44 45] potentially underestimating the extent of balance impairment. Balance impairment is one of the strongest independent risk factors for falls which are a predictor of mortality in COPD,[46] however balance exercises are not routinely provided as part of PR. Balance training incorporated into PR is feasible and effective,[19 47–49] not only for improving balance but also general physical function, although there remain few studies in this area. Our findings support a need for expanding the focus of rehabilitation to include balance and further exploration of balance and falls in COPD.

| Study name | Difference in means | Standard error | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|---|
| Butcher et al., 2004 | -4.000 | 3.691 | -11.233 | 3.233 | 0.278 |
| Crisan et al., 2015 | -13.400 | 2.613 | -18.522 | -8.278 | 0.000 |
| Iwakura et al., 2016 | -16.000 | 7.169 | -30.051 | -1.949 | 0.026 |
| Mkacher et al., 2014 | -10.750 | 1.891 | -14.456 | -7.044 | 0.000 |
| Tudorache et al., 2015 | -9.700 | 0.610 | -10.895 | -8.505 | 0.000 |
| Voica et al., 2016 | -19.078 | 2.644 | -24.259 | -13.896 | 0.000 |
| | -11.754 | 1.720 | -15.124 | -8.384 | 0.000 |

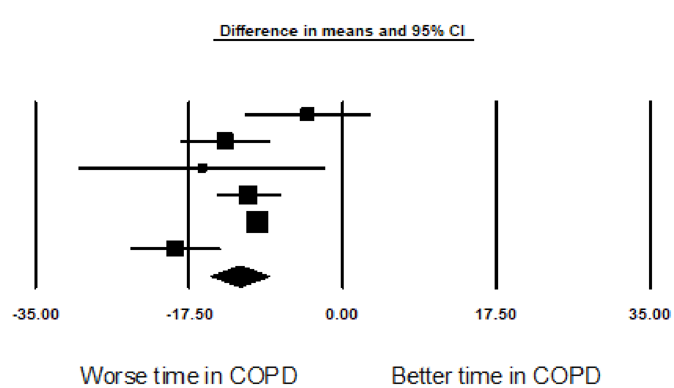


**Figure 5** Meta-analysis of single leg stance times in people with COPD versus healthy controls.

| Study name | Difference in means | Standard error | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|---|
| Beauchamp et al., 2012 | -6.200 | 1.313 | -8.774 | -3.626 | 0.000 |
| Crisan et al., 2015 | -2.000 | 1.316 | -4.580 | 0.580 | 0.129 |
| Mkacher et al., 2014 | -5.140 | 0.548 | -6.214 | -4.066 | 0.000 |
| Oliveira et al., 2015 | -3.600 | 0.871 | -5.307 | -1.893 | 0.000 |
| Ozalevil et al., 2011 | -19.200 | 2.073 | -23.262 | -15.138 | 0.000 |
| Porto et al., 2017 | -4.000 | 1.119 | -6.194 | -1.806 | 0.000 |
| Tudorache et al., 2015 | -7.000 | 0.948 | -8.859 | -5.141 | 0.000 |
| Voica et al., 2016 | -9.741 | 2.085 | -13.828 | -5.654 | 0.000 |
| | -6.659 | 1.168 | -8.947 | -4.371 | 0.000 |

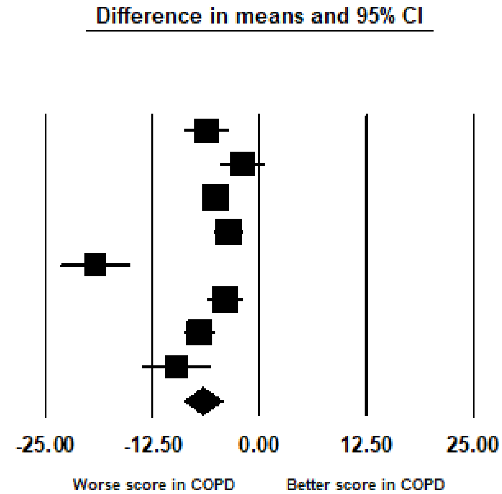


**Figure 6** Meta-analysis of berg balance scale scores in people with COPD versus healthy controls.

Although less conclusive, posturography studies also indicated balance impairment in COPD. Posturography is less functional than clinical balance measures and does not typically identify dynamic balance impairment, potentially explaining inconclusive results. However, posturography studies using SOTs were able to rule out sensory issues as a mechanism for balance impairment. Additionally, posturography studies looking at specific mechanisms like reaction times and joint motions at ankles and hips/back were more likely to highlight problems with neuromuscular control of balance.[11 17] This finding is consistent with literature indicating that ankle over back strategy, which becomes less efficient in older age as nerve conduction slows,[50] may be relied on by people with COPD due to musculoskeletal changes around the trunk.[17 51 52]

Reduced strength is a common systemic effect of COPD[53] which may partly explain why balance is impaired. The majority of studies have investigated quadriceps strength despite other muscle groups having a role in balance, for example, trunk, hip and ankle muscles.[8 17] There may be an association between balance and reduced PA and exercise capacity which could impair balance by contributing to disuse of balance systems, including postural control muscles. Conversely, balance impairments may impact on PA and exercise capacity by reducing functional ability or increasing fear of falling.[54] Considering the negative findings of disease severity, we suggest balance impairment is multifactorial, relating to secondary impairments of disease interplaying with the effects of normal ageing on balance such as neuropsychological changes,[55] and increasing chronic pain.[56 57] Mechanisms underlying the deficits observed in COPD require further investigation including research into other contributing factors given the underwhelming strength of these associations.

Evidence for further balance impairment during AECOPD is scarce but supported by two of the three AECOPD studies included. An AECOPD may impair balance further as strength and PA are reduced post-AECOPD.[58] More studies are needed to fully elucidate the impact of AECOPD on balance including the

| Study name | Correlation | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|
| Ozalevli et al., 2011 | 0.230 | -0.107 | 0.519 | 0.179 |
| Beauchamp et al., 2012 | 0.240 | -0.091 | 0.523 | 0.154 |
| de Castro et al., 2016 | 0.370 | 0.093 | 0.594 | 0.010 |
| Iwakura et al., 2016 | 0.509 | 0.111 | 0.766 | 0.014 |
| Oliveira et al., 2017 | 0.590 | 0.263 | 0.796 | 0.001 |
| | 0.370 | 0.226 | 0.498 | 0.000 |

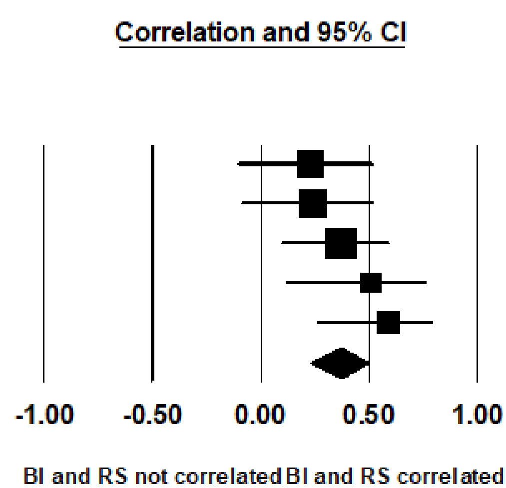


**Figure 7** Meta-analysis of reduced quadriceps strength and balance impairment correlations in people with COPD. BI= Balance Impairment; RI = Reduced Strength.


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feasibility, safety and role of early assessment and intervention of balance to ensure patients are not hindered by poor balance and falls when aiming to return to their pre-exacerbation strength and PA levels.

This review featured a wide-reaching search strategy and four reviewers; thus, missed studies are unlikely, and a strong inclusion consensus was reached. While meta-analysis revealed a large effect there was heterogeneity between studies as demonstrated by Tau and Prediction Intervals thus results should be interpreted with this in mind. COPD is a disease that features different phenotypes, subgroups and clusters of clinical characteristics, that vary in physiological, psychological and socioeconomical factors.[59–61] None of the studies included any measurement of, or adjustment for phenotypic differences. It is plausible that balance impairment affects different phenotypes to differing degrees. Additionally, other population variances were poorly reported and the majority of studies did not adjust for common confounders; with quality issues common again caution is advised regarding the results. However, a number of sensitivity analyses were performed which did not vary effect sizes or heterogeneity significantly. Meta-analysis of means, including regression analysis, was performed at study level which is a less robust approach. However, meta-analysis on correlations included individual level data, considered a 'deft' approach[62] and the use of five studies minimum for meta-analysis enhanced the robustness. A limited number of studies reporting data on sex and a narrow age range across studies prevented adjustments for both and the MCIDs used were developed based on within-subject change as none are available for between subject differences. The meta regressions were performed on a relatively low number of studies (n=9, n=6 and n=8 respectively) which were below the 10-study minimum recommended by the Cochrane Handbook for Systematic Reviews, therefore further investigation of the effect of disease severity is required, especially because we could not detect any clear meta-regression associations so these particular analyses may have been influenced by low statistical power. Meta-analysis was impossible for posturography. Strength measurements included less accurate measurements such as manual muscle strength testing, which was one of the weakest correlations perhaps underestimating the strength and balance association.

Researchers should improve quality by performing power calculations and reporting details of populations, participant selection and confounder adjustments. Agreement on outcomes is needed across studies to improve comparability. Studies should investigate links between balance and strength, PA, exercise capacity and other possible modifiable mechanistic factors, and, given that they are reduced after AECOPD, work is required to see if balance is worse after hospital discharge.

## CONCLUSIONS

People with COPD have extensive balance impairment which may be associated with reduced muscle strength, PA and exercise capacity. Balance may be worse during AECOPD, but evidence is scarce. More work is required to understand the mechanisms underlying balance deficits in COPD, including the investigation of novel clinical factors. Balance assessment and available interventions[19 47] should be incorporated into international guidelines for COPD care.[1]

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