Received: 14 September 2022 | Accepted: 31 January 2023

DOI: 10.1111/ene.15743

european journal of neurology
the official journal of the european academy of neurology

REVIEW ARTICLE

# A systematic review and meta-analysis of respiratory dysfunction in Parkinson's disease

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## Abstract

**Introduction:** Respiratory dysfunction in Parkinson's disease (PD) is common and associated with increased hospital admission and mortality rates. Central and peripheral mechanisms have been proposed in PD. To date no systematic review identifies the extent and type of respiratory impairments in PD compared with healthy controls.

**Methods:** PubMed, EMBASE, CINAHL, Web of Science, Pedro, MEDLINE, Cochrane Library and OpenGrey were searched from inception to December 2021 to identify case–control studies reporting respiratory measures in PD and matched controls.

**Results:** Thirty-nine studies met inclusion criteria, the majority with low risk of bias across Risk of Bias Assessment tool for Non-randomized Studies (RoBANS) domains. Data permitted pooled analysis for 26 distinct respiratory measures. High-to-moderate certainty evidence of impairment in PD was identified for vital capacity (standardised mean difference [SMD] 0.75; 95% CI 0.45–1.05; $p < 0.00001$; $I^2 = 10\%$), total chest wall volume (SMD 0.38; 95% CI 0.09–0.68; p = 0.01; $I^2 = 0\%$), maximum inspiratory pressure (SMD 0.91; 95% CI 0.64–1.19; $p < 0.00001$; $I^2 = 43\%$) and sniff nasal inspiratory pressure (SMD 0.58; 95% CI 0.30–0.87; $p < 0.00001$; $I^2 = 0\%$). Sensitivity analysis provided high-moderate certainty evidence of impairment for forced vital capacity and forced expiratory volume in 1 s during medication ON phases and increased respiratory rate during OFF phases. Lower certainty evidence identified impairments in PD for maximum expiratory pressure, tidal volume, maximum voluntary ventilation and peak cough flow.

**Conclusions:** Strong evidence supports a restrictive pattern with inspiratory muscle weakness in PD compared with healthy controls. Limited data for central impairment were identified with inconclusive findings.

KEYWORDS
meta-analysis, Parkinson's disease, respiratory, systematic review

## INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder that manifests as a consequence of dopamine loss in the substantia nigra,[1–4] and results in cardinal motor symptoms of bradykinesia, rigidity, resting tremor and postural instability and non-motor symptoms of autonomic dysfunction, sleep disturbances, cognitive and psychological disorders, and respiratory deficits.[1–4] Respiratory dysfunction has been associated with PD since the condition was first documented and is a recognised predictor of mortality and

morbidity in PD.[5–8] Pneumonia is frequently cited as the most common cause of death in PD, [9–12] and a review of hospital admissions for individuals with PD[13] reported 33% of admissions resulted from respiratory system diseases. Increased hospital mortality, length of stay and healthcare costs are further associated with respiratory system diseases in PD.[14–16]

Despite James Parkinson noting in 1817 "…he fetched his breath rather hard…", indicating easily observed clinical features of respiratory dysfunction in PD,[17] the aetiology of this dysfunction remains unclear to this day.[18–21] Mechanisms for respiratory deficits in PD have been proposed in recent narrative reviews and include both peripheral and central systems.[18–20] Peripheral mechanisms include restrictive dysfunction, obstructive dysfunction and adverse effects of PD medications. Restrictive dysfunction may result from motor impairments of bradykinesia and rigidity,[22] muscle weakness[20] and/or postural changes of camptocormia and kyphoscoliosis,[23] side effects of PD medications[24, 25] and autonomic dysfunction.[23, 26] Obstructive disorders may affect the upper or lower airways, with upper airways obstruction often presenting as stridor and postulated to be caused by basal ganglia dysfunction, with lower airway obstruction considered to be induced by rigidity.[19] Medications are proposed to have positive and negative effects on respiratory function, by improving muscle co-ordination and maintaining inspiratory muscle strength, but also causing side effects including stridor and diaphragmatic dyskinesia.[22, 24, 25, 27, 28] Central mechanisms focus on brain and brain stem respiratory control centre changes, with clinical signs including dyspnoea, sleep apnoea and pneumonia.[18–21] Impaired chemosensitivity has been proposed as another mechanism warranting consideration.[29, 30] Changes in central ventilatory control, presenting as abnormal perception of dyspnoea, link to the recognition of brainstem involvement in early, premotor impairment stages of PD.[29–31] The Braak hypothesis suggests early central mechanisms affect respiratory control structures functioning to co-ordinate ventilation and detect peripheral oxygen and carbon dioxide levels.[19, 31]

A consistent finding across the narrative reviews conducted to date is the presence of multiple, conflicting reports of respiratory dysfunction in PD.[18–21] To date, no study has summarised what is currently known and has been measured in respiratory function in individuals with PD. This systematic review aims to identify and quantify the body of knowledge relating to respiratory impairments in PD in comparison with healthy controls and highlight remaining knowledge gaps in this field. Planned sensitivity analysis will explore the influences of medication, examining the ON phase, where medications to treat the symptoms of PD are working and reducing symptoms, compared with the OFF phase, where PD symptoms deteriorate despite medication, and disease progression stage as per the Hoehn and Yahr (H&Y) scale on respiratory impairments.

## METHODOLOGY

Guided by PRISMA,[32] a systematic search to identify relevant articles in the following sources was completed from database inception to December 2021: PubMed, EMBASE, CINAHL, Web of Science, Pedro, MEDLINE, Cochrane Library and OpenGrey. No language, publication status or publication year restrictions were imposed. Authors were contacted directly for information and data where conference abstracts were returned or data were missing. Studies were excluded from meta-analysis if no response was received or data requested were unavailable. PROSPERO reference number: CRD42018111782.

Inclusion criteria: studies comparing outcomes of respiratory function in PD participants to age- and gender-matched controls. Exclusion criteria: studies with outcomes related to sleep, swallow, speech, mortality and morbidity where no respiratory measures are reported.

Independent review of identified studies was conducted by two reviewers in a standardised manner to screen against inclusion and exclusion criteria at title, abstract and full manuscript stages. If unclear whether inclusion criteria were met, the study progressed to the next review stage for in-depth appraisal. Disagreements between reviewers were resolved through discussion.

Following screening stages, both reviewers independently extracted data from studies under the headings: Study Population, Comparison Population, Outcome Measures and Results using a proforma.

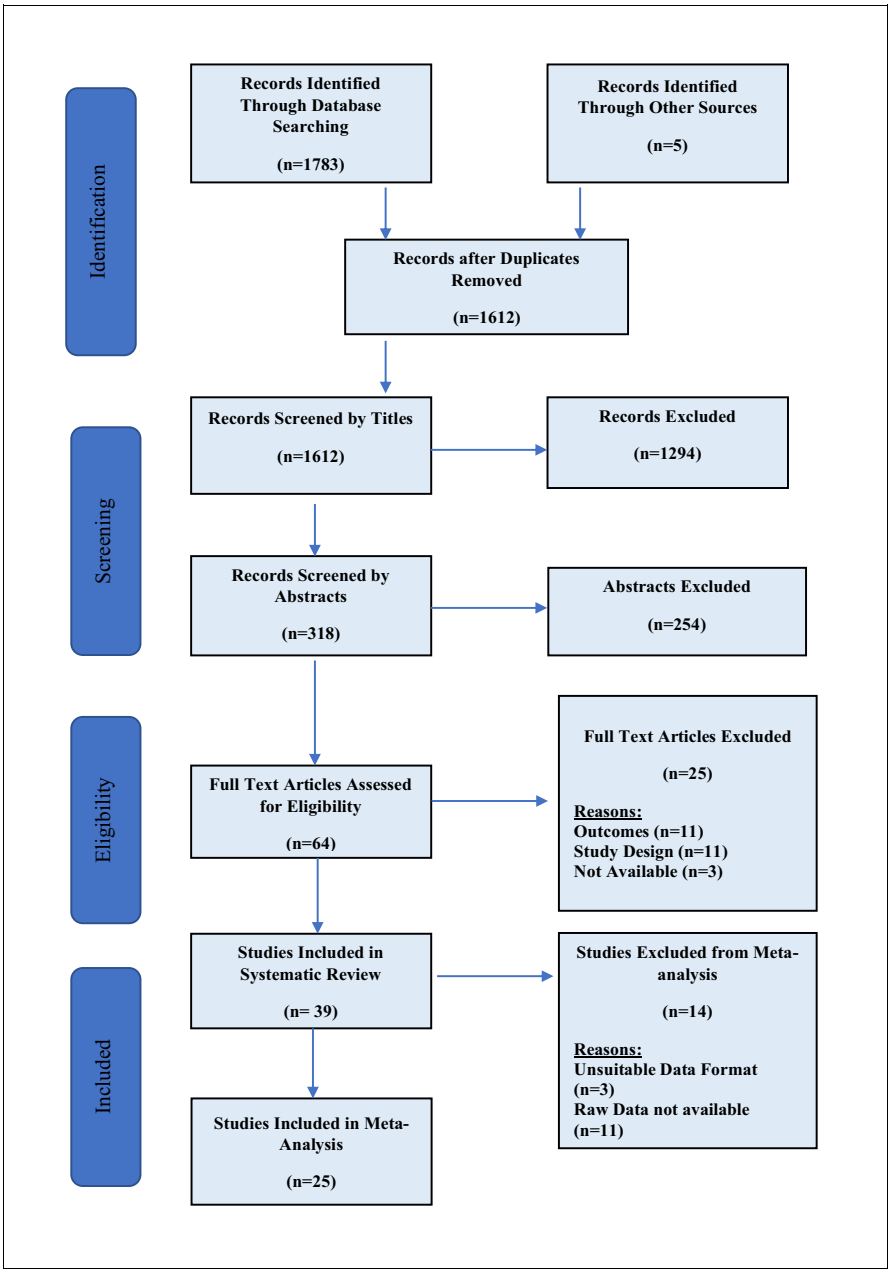
The Risk of Bias Assessment tool for Non-randomized Studies (RoBANS)[33] was used by two reviewers to independently assess quality of studies.

A dual approach was adopted for data synthesis. A meta-analysis was conducted where two or more studies reported the same respiratory measure in PD and controls. Mean and standard deviation of each measure were extracted to establish pooled mean differences data using Review Manager.[34] Measures expressed as median and interquartile ranges were converted to mean and standard deviation using the method published by Wan et al.[35] When the same control or PD group was included more than once in the same meta-analysis, the group was halved to avoid double counting.[36] Data were analysed using a random-effects model. The $I^2$ statistic assessed heterogeneity. Forest plots were developed to illustrate the pooled mean differences with 95% confidence intervals (CIs) for each measure. Values of $p < 0.05$ were considered statistically significant. Where data allowed, sensitivity analysis was planned to examine the effect of H&Y stages, disease duration, medication phase, sex and ethnicity. A narrative overview summarised additional outcomes where data did not permit meta-analysis.

## RESULTS

The PRISMA flowchart in Figure 1 depicts the study selection process. From a total of 1612 studies identified, 39 were included in the systematic review, of which 25 contributed to meta-analyses conducted. Table 1 provides a detailed summary of included studies. Overall, the risk of bias across studies was low using the RoBANS tool, [33] with Table 2 providing an overview of the Risk of Bias assessment for each study.

**FIGURE 1** PRISMA flow diagram.




## Participant demographics

Studies included $N = 1070$ participants with idiopathic PD. Gender was unreported in 3 studies. The remaining 36 studies identified $N = 554$ (52%) participants with PD as male and $N = 375$ (48%) as female. The minimum number of subjects with PD in any study was $N = 7$ and the maximum was $N = 107$. A total of 31 studies (97%) used the H&Y classification to measure disease severity, with scores reported in a variety of ways: H&Y stage ($N = 8$), number of participants in each H&Y stage ($N = 17$), average H&Y score ($N = 5$) and median H&Y score ($N = 1$). A total of $N = 928$ healthy controls were identified, $N = 596$ (64%) male and $N = 332$ (36%) female in the 32 studies documenting gender. Meta-analyses conducted did not distinguish by sex or H&Y stage as data presented did not facilitate sensitivity analysis. The minimum number of control subjects in any study was 5; the maximum was 107. A known respiratory disease diagnosis was an exclusion criterion in all but five studies; these were subsequently excluded from meta-analyses conducted.

Different ethnic populations were represented across the studies; $N = 7$ studies comprised Asian participants, $N = 1$ Black participants, $N = 13$ Hispanic participants and $N = 18$ White participants. Meta-analyses conducted did not distinguish by ethnicity but, where feasible, additional sensitivity analyses were performed.

## Respiratory measures

Eligible studies covered a wide range of respiratory metrics that included spirometry measures: forced vital capacity (FVC), forced expiratory volume in 1 min (FEV1), ratio of forced expiratory volume in

**TABLE 1** Characteristics of included studies.

| Authors, year, country | Study population | Comparison population | Outcome measures | Results |
|---|---|---|---|---|
| 1. Apps et al.[37]<br>1985<br>England | *N* = 12 PD<br>Mean age: 57.9 ± 8.99<br>9M:3F<br>H&Y: 1 (*N* = 1), 2 (*N* = 5), 3 (*N* = 5), 4 (*N* = 1)<br>Disease duration recorded: 1–12 years<br>Medication phase: ON | *N* = 12 HC<br>Mean age: 57.9 ± 8.99 | RR | • Patients with PD had a significantly faster RR when awake vs. controls, $p < 0.006$ |
| 2. Baille et al.[27]<br>2018<br>England | *N* = 41 PD<br>Mean age: 61.7 ± 7.7<br>25M:16F<br>H&Y: <3<br>Disease duration recorded: 1.9 ± 1.7 years<br>Tremor dominant: 15<br>Akinetic rigid: 26<br>Medication phase: OFF | *N* = 36 HC<br>Mean age: 61 ± 5.2<br>24M:12F | Dyspnoea: MRC Scale, TLC, FVC, FEV1, MIP, SNIP | • The following outcomes were significantly higher in PD vs. control group: TLC ($p = 0.004$), FEV1 ($p = 0.002$) and FVC ($p = 0.002$)<br>• Inspiratory muscle weakness was significantly reduced in the PD group ($p = 0.011$) with both MIP ($p = 0.035$) and SNIP ($p = 0.004$) significantly lower vs. controls |
| 3. Barbic et al.[38]<br>2007<br>Italy | *N* = 19 PD<br>• Mean age: 66 ± 2<br>• M:F: 13:6<br>• H&Y: 2.67 ± 0.17<br>• Disease duration recorded: 7.5 ± 1 years<br>*N* = 21 PD with OH<br>• Mean age: 69 ± 1<br>• M:F: 15:6<br>• H&Y: 2.75 ± 0.08<br>• Disease duration recorded: 10.5 ± 2 years<br>Medication phase: ON | *N* = 20 HC<br>Mean age: 64 ± 2<br>M:F = 12:8 | RR | • RR was significantly increased in PD + PD OH groups vs. control ($p < 0.05$) |
| 4. Bonjorni et al.[39]<br>2012<br>Brazil | *N* = 10 PD<br>Mean age: 72.7 ± 10<br>8M:2F<br>H&Y: 1–4<br>Disease duration: not recorded<br>Medication phase: not documented | *N* = 15 HC<br>Mean age: 64.8 ± 6.7<br>12M:3F | FEV1, FVC, FEV1/FVC, MVV, MIP, MEP | • No difference in FEV or FVC for PD vs. control<br>• The following were significantly lower for PD group vs. control: FEV1/FVC ($p = 0.0001$), MVV ($p = 0.004$), MIP ($p = 0.04$) and MEP ($p = 0.03$) |
| 5. Borders et al.[40]<br>2021<br>USA | *N* = 16 PD<br>Mean age: 73.31 ± 5.91<br>M:F: 9:7<br>H&Y: 2 (median)<br>Disease duration recorded: 8.93 ± 5.28 years.<br>Medication phase: ON | *N* = 26 HC<br>Mean age: 70.42 ± 6.84<br>M:F: 14:12<br>*N* = 25 healthy controls<br>Mean age: 23.32 ± 3.51<br>M:F: 11:14 | PEFR | • No statistically different differences in PEFR across all groups ($p = 0.108$)<br>• An increased PEFR variability in PD group compared with healthy older adults was not significant ($p = 0.529$) |

**TABLE 1** (Continued)

| Authors, year, country | Study population | Comparison population | Outcome measures | Results |
|---|---|---|---|---|
| 6. Brandimore et al.[41]<br>2017<br>USA | *N* = 16 PD<br>Mean age: M: 74.22 ± 7.1<br>F: 72.14 ± 4.2<br>M:F: 9:7<br>H&Y: 1(3), 2(6), 2.5 (4), 3(1), 4(2)<br>Disease duration:8.93 years<br>Medication phase: ON | *N* = 28 HC<br>Age range: 55–85<br>M:F 14:14 | PEFR | • PEFR was significantly lower in PD vs. control group ($p = 0.031$) |
| 7. Cardoso & Pereira[42]<br>2002<br>Brazil | *N* = 40 PD<br>Mean age: 65.5 ± 9.3<br>M:F: 21:19<br>H&Y: stages 1–3<br>Disease duration: not documented<br>Medication phase: ON | *N* = 40 HC<br>Mean age: 65.5 ± 9.3<br>21M:19F | Thoracic amplitude, VC, FVC, FEV1, FEV1/FVC, MIP, MEP | • Significant decrease in Tx. amplitude in PD vs. non-PD ($p = 0.00001$)<br>• No difference in MIP + MEP in PD vs. non-PD<br>• VC significantly lower in PD group ($p = 0.00001\%$) FVC was significantly lower in PD ($p = 0.0023\%$) FEV1/FVC no significant difference between groups |
| 8. Ebihara et al.[43]<br>2003<br>Japan | *N* = 25 female PD<br>*N* = 15 early stage<br>• Mean age: 67.1 ± 5.4<br>• H&Y: 2.6 ± 0.7<br>• Disease duration recorded: 5.8 ± 5.2 years<br>*N* = 10 advanced stage<br>• Mean age: 70.9 ± 88<br>• H&Y: 4 ± 0<br>• Disease duration recorded: 9.7 ± 6.3 years<br>Medication phase: ON | *N* = 15 HC<br>Mean age: 69.8 ± 10.3 | FEV1, FVC<br>Voluntary cough peak flow - cough intensity (L/min), cough reflex sensitivity (g/L) | • No significant difference in early vs. advanced PD vs. control for FEV1 or FVC<br>• Peak cough flow was significantly weaker in both early ($p < 0.005$) and advanced PD ($p < 0.0001$) vs. control<br>• Cough reflex sensitivity in advanced PD was lower than both early PD ($p < 0.005$) and control groups ($p < 0.01$) |
| 9. Florêncio et al.[44]<br>2019<br>Brazil | *N* = 27 PD<br>Median age: 61.5<br>M:F: not documented<br>H&Y: 2 & 3<br>Disease duration: not recorded<br>Medication phase: ON | *N* = 29 HC<br>M:F: not documented<br>Median age = 57<br>*N* = 20 post-stroke<br>Median age = 57 | FVC, FEV1, FEV1/FVC, MIP MEP, RR, I:E time<br>Chest wall kinematics; pulmonary ribcage, abdominal ribcage, abdominal | • Significantly lower FVC + FEV1 in PD vs. healthy control ($p < 0.05$)<br>• Significantly lower MIP + MEP in PD vs. healthy control ($p < 0.05$)<br>• PD participants >3 years since dx had lower MP + MEP ($p < 0.05$)<br>• In PD participants with restrictive respiratory disease, pulmonary ribcage volume was reduced vs. control<br>• PD participants with inspiratory paradoxical movement had reduced pulmonary ribcage volume |
| 10. Fontana et al.[45]<br>1998<br>Italy | *N* = 23 PD<br>Age range: 55–79, mean: 64<br>Median age: 64<br>M:F: 16:7<br>H&Y: 1 (5), 1.5 (3), 2 (7), 2.5(4), 3 (2), 4 (2)<br>Disease duration: 5.3 ± 3.6 years<br>Medication phase: ON | *N* = 23 HC<br>Mean age: 65.7<br>Age range: 44–78<br>M:F: 17:6 | PEmax, EMG activity of abdominal muscles (during MVC), EMG activity of abdominal muscles RC, FEV1, FEV1/FVC<br>FRC, $Vmax_{50}$ | • No significant difference between PD and control group for FEV1, FEV1/FVC, FRC and $Vmax_{50}$<br>• PD group had statistically significantly lower PEmax, vs. control ($p < 0.01$)<br>• IEMG of abdominal muscles was lower during MVC, RC and PEmax in the PD group vs. control group ($p < 0.01$) |

(Continues)

**TABLE 1** (Continued)

| Authors, year, country | Study population | Comparison population | Outcome measures | Results |
|---|---|---|---|---|
| 11. Frazao et al.[46]<br>2014<br>Brazil | *N* = 15 PD<br>Mean age: 59.07 ± 9.34<br>M:F: 12:3<br>H&Y: 2 & 3<br>Disease duration: not documented<br>Medication phase: ON | *N* = 15 HC<br>Mean age: 58.8 ± 9.02<br>M:F: 12:3 | FEV1, FVC, PEF, FEF25%–75%, FEV1/FVC, MIP, MEP, SNIP<br>Total chest wall volume, PulRC volume, AbRC volume, abdominal volume, chest wall volumes using PEP, RR, I:E ratio, respiratory cycle time, TV | • PD group had significantly lower spirometry + respiratory muscle strength vs. control ($p < 0.01$)<br>• MV was similar in both groups<br>• TV was significant lower in PD vs. control ($p < 0.01$) secondary to reduced TV of ribcage<br>• RR was higher in PD vs. control however it was not significant<br>• PEP: increased chest wall volume + TV significantly ($p < 0.001$) |
| 12. Gama Vieira et al.[47]<br>2013<br>Brazil | *N* = 107 PD<br>Mean age: 65.43 ± 9.46<br>M:F: 60:47<br>H&Y: 1(63), 1.5(19), 2(15), 2.5(4), 3(4)<br>Disease duration: 6.3 ± 3 years<br>Medication phase: ON | *N* = 107 HC<br>Mean age: 65.32 ± 9.33<br>M:F: 63:44 | MIP, MEP, PCF | • The following were all statistically significantly decreased in PD group vs. control: MIP ($p < 0.01$), MEP ($p < 0.01$) and PCF ($p < 0.01$) |
| 13. Gonçlaves et al.[48]<br>2016<br>Brazil | *N* = 41 PD<br>Median age: 70<br>M:F 58.5%:41.5%<br>H&Y: 0–3<br>Disease duration: not documented<br>Medication phase: OFF | *N* = 41 HC<br>Median age: 66<br>M:F: 24.4%:75.6% | FVC, FEV1, PEF, FEF25%–75%, MIP | • Significantly lower FVC ($p = 0.046$) and FEV1 ($p = 0.22$) in PD vs. control<br>• MIP values were lower in PD group but not significantly ($p = 0.07$)<br>• No significant difference in PEF or FEF25%–75% between PD and control |
| 14. Guedes et al.[49]<br>2009<br>Brazil | *N* = 10 PD<br>Mean age: 64.6 ± 6.2<br>M:F: 6:4<br>H&Y: 2(2), 2.5(7), 3(1)<br>Disease duration recorded: 10.6 ± 3.43 years<br>Medication phase: ON & OFF | *N* = 9 HC<br>Mean age: 61.4 ± 5.9<br>M:F: 5:4 | MIP, EMG of SCM during MIP, EMG of SCM at rest | EMG SCM at rest and during MIP<br>• PD ON vs. OFF: no significant changes ($p = 0.13$)<br>• PD ON vs. control: no significant changes ($p = 0.06$)<br>• PD OFF vs. control: increased EMG activity of SCM in PD patients ($p = 0.03$) |
| 15. Guedes et al.[50]<br>2012<br>Brazil | *N* = 26 PD<br>Mean age: 63 ± 7<br>M:F: 16:10<br>H&Y: 2&3<br>Disease duration recorded: 9.1 ± 0.3 years<br>Medication phase: ON & OFF | *N* = 26 HC<br>Mean age: 64 ± 7<br>M:F: 16:10 | MIP, MEP | • Women had a significantly lower MIP in the OFF phase vs. controls ($p = 0.04$), with no significant difference between ON phase and controls<br>• Women had a significantly lower MEP in both ON ($p = 0.00$) and OFF ($p = 0.00$) phases compared with controls<br>• Men had a significantly lower MIP and MEP in both ON and OFF phases compared with controls ($p = 0.00$) |
| 16. Haas et al.[51]<br>2004<br>England | *N* = 66 PD<br>Mean age: 62.95 ± 9.7<br>M:F: 47:19<br>Disease duration recorded: 6.26 ± 4.1 years<br>H&Y: median = 2.09<br>Medication phase: ON | *N* = 32 HC<br>Mean age: 63.84 ± 5.95<br>M:F: 19:13 | MIP, MEP | • MIP and MEP were significantly lower in PD vs. controls ($p < 0.05$) |

**TABLE 1** (Continued)

| Authors, year, country | Study population | Comparison population | Outcome measures | Results |
|---|---|---|---|---|
| 17. Köseoğlu et al.[52]<br>1997<br>Turkey | *N* = 9 PD<br>Mean age: 54.6 ± 16.5<br>4M:5F<br>H&Y: 0(1), 1(2), 1.5(3), 2(3)<br>Disease duration recorded: 5.7 ± 4.1 years<br>Medication phase: not documented | *N* = 9 HC<br>4M:5F | FVC, FEV1, FEV1/FVC, FEF25%–75%, FEF50%, PEF, MVV, VC, TV, ERV, IC, Ve, RR, FEF50%/FIF50%, PIF, 6MWT | • No difference between PD + control in TV, MV, ERV or RR<br>• Statistically significant decreases noted for FVC, FEV, FEF50%, FEF25%–50%, MVV, PEF, FIF, IC, VC, FEF50%/FIF50% and 6MWT in PD group vs. control<br>• *P* values not documented |
| 18. Leite et al.[53]<br>2012<br>Brazil | *N* = 14 PD<br>Mean age: 66.35 ± 4.65<br>M:F: 10:4<br>H&Y: 2–3<br>Disease duration: not documented<br>Medication phase: ON | *N* = 14 HC<br>Mean age: 71.14 ± 4.16<br>M:F: 4:10 | MIP ($cmH_20$), MEP ($cmH_20$), FVC (L), FEV1 (L), PEF (L/min), volume of chest wall, % PulRC, %AbRC and Ab, inspiratory time, expiratory time | • MIP ($p < 0.01$), MEP ($p < 0.01$), PEF ($p = 0.003$) and inspiratory time ($p = 0.04$) were significantly lower in PD patients vs. controls<br>• No difference in the pattern of compartmental distribution of lung volumes between the groups<br>• The volume in the abdominal compartment was higher than the PulRC and AbRC in both groups ($p < 0.001$) |
| 19. Marinelli et al.[54]<br>2013<br>Italy | *N* = 11 PD and camptocormia<br>Mean age: 74 ± 4<br>M:F: 8:3<br>H&Y: 3.2 ± 1.3<br>Disease duration recorded: 14 ± 7 years<br>Medication phase: ON | *N* = 10 HC<br>Mean age: 70 ± 7<br>M:F: 4:6 | Spirometry in sitting and standing at 45°: FEV1, FVC, SVC, IC | • Statistically significantly lower lung volumes noted in PD vs. controls in both 45° and supine ($p < 0.05$)<br>• Supine to 45° significant: improvement noted in FEV, FVC, SVC, ERV in healthy subjects whereas for PD only significant improvement seen in SVC and ERV ($p < 0.05$)<br>• Camptocormia is not associated with significant alterations in lung volumes |
| 20. Mikaelee et al.[34]<br>2007<br>Iran | *N* = 25 PD<br>Mean age: 63.8 ± 11.1<br>M:F: 19:6<br>H&Y: 1(9), 2&3(8), 4(8)<br>Disease duration: not documented<br>Medication phase: ON | *N* = 20 HC<br>Mean age: 61.6 ± 7.51<br>M:F: not documented | RV, TLC, FVC, MMEF, FRC, TCAW, ECAW, FEV1, FEV1/FVC | • Significant difference noted for RV, FVC, MMEF and FEV1/FVC in PD vs. control ($p < 0.05$) |
| 21. Monteiro et al.[55]<br>2014<br>Brazil | *N* = 30 PD (18 without swallowing complications, 12 with swallowing complications)<br>Mean age: 61.6 ± 10.7<br>M:F: 17:13<br>H&Y: 2.1 ± 0.8<br>Disease duration recorded: 7.2 ± 3.6 years<br>Medication phase: ON | *N* = 35 HC<br>Mean age: 60.7 ± 63<br>M:F: 9:26 | FVC, FEV1, PEF, FEF25%–75%, FEV1/FVC | • FVC ($p = 0.006$), FEV1 ($p = 0.005$), PEF ($p = 0.006$) and FEV1/FVC ($p = 0.04$) were all significantly lower in PD groups vs. controls<br>• PD participants with a swallowing complaint had significant lower FVC + PEF than the PD group without swallowing complaint |
| 22. Moreau et al.[56]<br>2016<br>France | *N* = 66 PD<br>Mean age: 62.5 ± 7.9<br>M:F: 42:24<br>H&Y: not documented<br>Disease duration recorded: 1.26 ± 1.0 years<br>Medication phase: OFF | *N* = 36 HC<br>Mean age: 61.1 ± 4.1<br>M:F: 24:12 | FVC, VC, PEFR, FEV1, MIP, MEP, SNIP, MRC breathlessness scale | • Approximately 24% of patients reported mild dyspnoea<br>• No significant difference for spirometry values between PD and controls<br>• Significant decrease in MIP and SNIP in both male ($p = 0.01$, $p = 0.0005$) and female ($p = 0.05$, $p = 0.05$) PD groups vs. controls |

(Continues)

**TABLE 1** (Continued)

| Authors, year, country | Study population | Comparison population | Outcome measures | Results |
|---|---|---|---|---|
| 23. Onodera et al.[30]<br>2000<br>Japan | *N* = 25 PD<br>Mean age: 60.1 ± 8<br>M:F: 11:14<br>H&Y: 2&3<br>Disease duration: not documented<br>Medication phase: ON | *N* = 11 HC<br>Mean age: 53.8 ± 9.5<br>M:F: 7:4 | VC, FEV1, arterial $O_2$ tension, carbon-dioxide tension, chemosensitivity to hypoxia and hypercapnia Borg under hypoxic conditions and under hypercapnic conditions | • PD patients had normal pulmonary function at baseline<br>• Both chemosensitivity to hypoxia ($p = 0.012$) and Borg under hypoxic conditions ($p = 0.0015$) were significantly lower in PD vs. controls<br>• There was no significant difference in chemosensitivity to hypercapnia or Borg under hypercapnic conditions in PD vs. controls |
| 24. Owolabi et al.[57]<br>2016<br>Nigeria | *N* = 78 PD<br>Mean age: 62.32 ± 8.67<br>M:F: 60:18<br>H&Y: 1(14), 2(30), 3(8), 4(24), 5(2)<br>Disease duration recorded: 0.25–16 years; Median = 2 years<br>Medication phase: ON/medication naive | *N* = 78 HC<br>Mean age: 62.31 ± 8.66<br>M:F: 60:18 | FVC, FEV1, FEV1/FVC, PEFR | • FVC, FEV1, FEV1/FVC and PEFR were all significantly lower in PD vs. control ($p < 0.0001$) |
| 25. Pal et al.[22]<br>2007<br>India | *N* = 53 PD<br>Mean age: 53.3 ± 9.5<br>M:F: 38:15<br>H&Y (OFF): 2(34), 3(17), 4(2)<br>Disease duration recorded: 3.1 ± 3.3 years<br>Medication phase: ON and OFF | *N* = 53 HC<br>Mean age: 52.6 ± 7.7<br>M:F: 38:15 | MIP, MEP, FVC, FEV1, PEFR MVV, FEV1/FVC, FEV1/PEFR | • FVC, PEFR, MVV, MEP and MIP were all significantly lower in PD vs. control in ON + OFF states ($p < 0.0001$)<br>• FEV1 was significantly lower in PD vs. control in ON ($p < 0.005$) + OFF ($p < 0.0001$) states |
| 26. Parreira et al.[58]<br>2003<br>Brazil | *N* = 10 PD<br>Mean age: 66±4<br>M:F: 5:5<br>H&Y: 3(8), 4(2)<br>Medication phase: OFF | *N* = 10 HC<br>Mean age: 69 ± 6<br>M:F: 5:5 | TV, RR, MV, % inspiratory time, mean peak inspiratory flow, rib cage contribution to TV, abdominal contribution to TV | • Significantly lower TV ($p = 0.01$), MV ($p = 0.02$) and mean inspiratory flow ($p = 0.03$) in PD patients vs. control<br>• Significantly higher RR in PD patients vs. control ($p = 0.02$)<br>• No significant differences in rib cage or abdominal contribution to TV |
| 27. Polatli et al.[59]<br>2001<br>Turkey | *N* = 21 PD (6 smokers, 15 non-smokers)<br>Mean age: 64.67 ± 10.76<br>M:F: 10:11<br>H&Y: 1(6), 2(9), 3(6)<br>Disease duration recorded:<br>• Smokers:5.17 ± 3.06<br>• Non-smokers:5.17 ± 3.06<br>Medication phase: ON | *N* = 16 HC<br>Mean age: 59.16 ± 10.43<br>M:F: 7:9<br>All non-smokers | FVC, FEV, FEV/FVC, VC, MVV, PEF, MEF75%, MEF50%, MEF25%, FEF25%–75% | • PD smoker vs. PD non-smoker: significantly lower FEV and MEF25% in PD smoker group ($p < 0.05$)<br>• PD non-smoker vs. control: significant decrease in PEF ($p < 0.05$), MEF75% ($p < 0.05$) and MVV ($p < 0.0001$) in PD non-smoker vs. control<br>• All PFTs reduced as H&Y increased<br>• MVV was most affected by disease severity |
| 28. Sanches et al.[60]<br>2014<br>Brazil | *N* = 20 PD<br>Mean age: 71.0 ± 7.72<br>M:F: 11:9<br>H&Y: 2–4<br>Disease duration: not documented<br>Medication phase: ON | *N* = 25 HC<br>Mean age: 69.4 ± 8.21<br>M:F: 10:15 | PImax, PEmax, Tx mobility (cirtometry) | • MIP and MEP were significantly lower in PD vs. control ($p = 0.01$)<br>• No significant difference in Tx cirtometry in PD vs. control |

**TABLE 1** (Continued)

| Authors, year, country | Study population | Comparison population | Outcome measures | Results |
|---|---|---|---|---|
| 29. Santos et al.[61]<br>2019<br>Brazil | *N* = 49 PD<br>Mean age: H&Y1: 57 ± 9, H&Y2: 63 ± 8, H&Y3/4: 67 ± 9<br>M:F: not documented<br>H&Y: 1(17), 2(19), 3/4(13)<br>Disease duration: not documented<br>Medication phase: ON | *N* = 17 HC<br>Mean age: 66 + 6<br>M:F: not documented | MIP, MEP, FVC, FEV1, FEV1/FVC, FEF25%–75%, PEF | • MIP ($p < 0.0001$) and MEP ($p = 0.0005$) were significantly lower in PD vs. controls<br>• FVC ($p = 0.0006$), FEV1 ($p = 0.0002$), FEF25%–75% ($p = 0.01$) and PEF ($p = 0.0001$) were all significantly lower in PD vs. controls |
| 30. Sathyaprabha et al.[24]<br>2005<br>India | *N* = 35 PD<br>Mean age: 53 ± 10<br>M:F: not documented<br>H&Y: 1(3), 2(32)<br>Disease duration recorded: 1-5 years<br>Medication phase: ON & OFF | *N* = 35 HC<br>Mean age: 51.3 ± 6.7<br>M:F: not documented | FVC, MVV, MEP, MIP, FEV, PEFR, IRV | • A significant improvement in FEV1, FVC, MVV, MIP and MEP ($p < 0.001$), IRV ($p = 0.003$) and PEFR ($p = 0.004$) was noted in ON state compared to OFF state<br>• A significant reduction in the following measures was noted in PD group vs. control group: MVV, MEP, MIP, FEV, PEFR ($p < 0.001$) and IRV ($p = 0.002$) |
| 31. Serebrovskaya et al.[62]<br>1998<br>Ukraine | *N* = 7 PD<br>Mean age: 58.9 ± 1.8<br>7M<br>H&Y: 2–2.5<br>Disease duration recorded: 7.1 ± 3.9 years<br>Medication phase: ON | *N* = 17 HC<br>12 with mean age: 24.6 ± 1.9<br>5 with mean age: 61.8 ± 2.4<br>17M | MV, respiratory frequency (bpm), $O_2$ uptake ($VO_2$ STPD), $CO_2$ production ($VCO_2$ STPD), $PET0_2$, $PETCO_2$, HVR | • A significant difference was noted for MV in PD group vs. control ($p < 0.01$)<br>• Hypoxic ventilatory drive was increased in PD group vs. control for severe hypoxia, but no difference noted for minor hypoxia |
| 32. Shaheen et al.[63]<br>2009<br>Egypt | *N* = 30 PD<br>Mean age: 67.7 ± 8.4<br>M:F: 28:2<br>H&Y: 1.5(6), 2.5(7), 3(15), 4(2)<br>Disease duration recorded: 3 ± 2.3 years<br>Medication phase: ON and OFF | *N* = 15 HC<br>M:F: 14:1 | FVC, FEV1, FEV1/FVC | • PD participants had a statistically significantly lower FVC and FEV1 vs. controls ($p = 0.000$)<br>• No significant difference in FEV1/FVC in PD vs. controls ($p = 0.80$)<br>• Improvement in parameters noted in ON compared with OFF phase; however they were not statistically significant |
| 33. Solomon & Hixon[64]<br>1993<br>USA | *N* = 14 PD<br>Mean age: 66.3±9.22<br>14 M<br>H&Y: 3+<br>Disease duration: not documented<br>Medication phase: ON and OFF | *N* = 14 HC<br>Mean age: 66 ± 7.53 | VC (l), VC (% predicted), RR, MV, chest wall volume, ribcage volume, abdominal volume | • At rest, participants with PD had a significantly increased RR ($p = 0.03$) and MV ($p = 0.02$)<br>• Ribcage contribution to lung volume was lower in PD vs. controls ($p = 0.047$)<br>• No significant difference was noted for VC (% predicted) |
| 34. Strano et al.[65]<br>2016<br>Italy | *N* = 18 PD newly diagnosed<br>Mean age: 59.3 ± 10.5<br>M:F: 6:12<br>H&Y: 1&2<br>Disease duration recorded: 15 ± 8.8 years<br>Medication phase: drug naïve | *N* = 18 HC | FEV1, FVC | • No significant difference in FEV1 or FVC in PD group vs. control |

(Continues)

**TABLE 1** (Continued)

| Authors, year, country | Study population | Comparison population | Outcome measures | Results |
|---|---|---|---|---|
| 35. Tamaki et al.[66]<br>2000<br>Japan | *N* = 7 PD<br>Mean age: 57.3 ± 14.5<br>M:F: 6:1<br>H&Y: not documented<br>Disease duration: not documented<br>Medication phase: ON | *N* = 14 HC<br>Mean age: 27.7 ± 5.8<br>14M | VC, FVC, chest volume, abdominal volume, chest wall movement, abdominal wall movement | Compared with controls, patients with PD had significantly decreased:<br>• %VC ($p < 0.05$)<br>• Chest volume ($p < 0.05$)<br>• % FVC ($p < 0.05$)<br>• Chest movement during forced maximum inspiration ($p < 0.05$)<br>• Abdominal movement during forced maximum inspiration ($p < 0.05$) |
| 36. Tzelepis et al.[67]<br>1988<br>USA | *N* = 9 PD<br>Mean age: 64 ± 7.13<br>6M:3F<br>H&Y: 1(3), 2(2), 3(4)<br>Disease duration recorded: 4.56 ± 5.19 years<br>Medication phase: ON | *N* = 5 HC<br>Mean age: 67.2 ± 9.15<br>2M:3F | TV, VC, TLC, FEV1/FVC<br>MVV, PImax, MV, rate of work during repetitive tasks | • No evidence of obstructive or restrictive disease<br>• No statistically significant difference in PImax<br>• During repetitive respiratory tasks, rate of work was significantly lower in PD group vs. controls ($p < 0.01$) |
| 37. Wang et al.[68]<br>2014<br>China | *N* = 30 PD<br>Mean age: 61.80 ± 4.2<br>M:F: 16:14<br>H&Y: 2(5), 2.5(13), 3(10), 4(1), 5(1)<br>Disease duration recorded: 4.9 ± 3.10 years<br>Medication phase: ON | *N* = 20 HC<br>M:F: 10:10<br>Mean age: 60.85 ± 4.87 | VC, TLC, RV, RV:TLC, FEV1<br>FVC, FEV1/FVC, PEF, MVV<br>MEF50%, MIP, MEP, DLCO, P0.1 | • VC, FEV1 and FVC were decreased in PD vs. controls ($p < 0.05$)<br>• RV and RV:TLC were increased in PD vs. control ($p < 0.05$)<br>• MIP ($p < 0.05$), MEP ($p < 0.001$) and DLCO ($p < 0.001$) were decreased in PD vs. control |
| 38. Weiner et al.[28]<br>2002<br>Israel | *N* = 20 PD<br>Mean age: 66.2 ± 2.2<br>10M:10F<br>H&Y: 2(8), 3(12)<br>Disease duration recorded: 7.5 ± 1.1 years<br>Medication phase: ON and OFF | *N* = 20 HC<br>10M:10F | FVC, FEV1, PImax, PEmax, PmPeak, perception of dyspnoea (modified Borg Scale) | • Mild restrictive patterns were seen in most PD participants<br>• No significant different in FVC and FEV1 in ON or and OFF phases<br>• MIP, MEP and PmPeak were all significantly lower in PD group vs. control (*p* values not reported)<br>• POD was increased in PD vs. control ($p < 0.01$) |
| 39. Zhang et al.[69]<br>2019<br>China | *N* = 43 PD<br>Mean age: 62.6 ± 6.6<br>M:F: 19:24<br>H&Y: 1(43)<br>Disease duration recorded: 1.67 ± 1.14 years<br>Medication phase: ON | *N* = 41 HC<br>Mean age: 61.39 ± 5.87<br>M:F: 21:20 | FVC, FEV1, FEV1/FVC, PEF<br>RV, TLC, PImax, PEmax, P0.1, DLCO | • FVC, FEV1, FEV1/FVC, PEF, RV, TLC and DLCO were not statistically different in PD vs. control, indicating no ventilation dysfunction<br>• There was a statistically significant decrease in PImax ($p = 0.002$) and PEmax ($p = 0.001$) in PD vs. control<br>• PD group had a significant increase in respiratory muscle drive as demonstrated with increased P0.1 ($p < 0.001$) |

Abbreviations: Ab, abdominal; AbRC, abdominal ribcage; DLCO, carbon monoxide diffusion capacity; Dx, diagnosis; ECAW, effective conductance of airways; EMG, electromyography; ERV, expiratory reserve volume; F, female; FEF25%–75%, forced expiratory flow at 25% and 75% of the lung volume; FEF50%, forced expiratory flow at 50% of lung volume; FEV1, forced expiratory volume in 1 second; FEV1/FVC ratio of forced expiratory volume in 1 second to forced vital capacity; FRC, functional residual capacity; FVC, forced vital capacity; HC, healthy control; H&Y, Hoehn & Yahr; HVR, hypoxic ventilatory response; I:E, inspiratory to expiratory; IC, inspiratory capacity; IEMG, integrated electromyography; IRV, inspiratory reserve volume; M, male; MEF25%, maximal expiratory flow at 25% of FVC; MEF50%, maximal expiratory flow at 50% of FVC; MEF75%, maximal expiratory flow at 75% of FVC; MEP/PEmax, maximum expiratory pressure; MIP/PImax, maximum inspiratory pressure; MMEF, maximal mid-expiratory flow; MRC, Medical Research Council; MV, minute ventilation; MVC, maximal voluntary cough; MVV, maximum voluntary ventilation; 6MWT, six minute walk test; n, number; OH, orthostatic hypotension; P0.1, airway occlusion pressure; PCF, peak cough flow; PD, Parkinson's disease; PEF(R), peak expiratory flow (rate); PFT, pulmonary function tests; PEP, positive expiratory pressure; PIF, peak inspiratory flow; PmPeak, inspiratory muscle endurance; PIR, Peak Inspiratory Flow; POD, perception of dyspnoea; PulRC, pulmonary ribcage; RC, reflex cough; RR, respiratory rate; SCM, sternocleidomastoid; SNIP, sniff nasal inspiratory pressure; STPD, standard temperature and pressure of dry gas; SVC, slow vital capacity; TCAW, total conductance of airways; TLC, total lung capacity; TV, tidal volume; Tx, Thoracic; VC, vital capacity; Ve, minute ventilation.

**TABLE 2** Risk of bias in included studies: Risk of Bias Assessment tool for Non-randomised Studies (RoBANS).

| Authors | Participant selection | Confounding variable | Exposure measurement | Blinding outcome assessment | Incomplete outcome data | Selective outcome reporting |
|---|---|---|---|---|---|---|
| 1. Apps et al.[37] | Low | Low | Low | Low | Low | Low |
| 2. Baille et al.[27] | Low | Low | Low | Low | Low | Low |
| 3. Barbic et al[38] | Unclear | Low | Low | Low | Low | Low |
| 4. Bonjorni et al.[39] | Low | Low | Low | Low | Low | Low |
| 5. Borders et al.[40] | Low | Low | Low | Low | Unclear | Low |
| 6. Brandimore et al.[41] | Low | Low | Low | Low | Low | Low |
| 7. Cardoso & Pereira[42] | Low | Low | Low | Low | Low | Low |
| 8. Ebihara et al.[43] | Low | Low | Low | Low | Low | Low |
| 9. Florêncio et al.[44] | Low | Low | Low | Low | Low | Low |
| 10. Fontana et al.[45] | Low | Low | Low | Low | Low | Low |
| 11. Frazao et al.[46] | Low | Low | Low | Low | Low | High |
| 12. Gama Vieira et al.[47] | Low | Low | Low | Low | Low | Low |
| 13. Gonçlaves et al.[48] | Low | Low | Low | Low | Low | Low |
| 14. Guedes et al.[49] | Low | Low | Low | Low | Low | Low |
| 15. Guedes et al.[50] | Low | Low | Low | Low | Low | Low |
| 16. Haas et al.[51] | Low | Unclear | Low | Low | Low | High |
| 17. Köseoğlu et al.[52] | Low | Low | Low | Low | Low | Low |
| 18. Leite et al.[53] | Low | Low | Low | Low | Low | Low |
| 19. Marinelli et al.[54] | Low | High | Low | Low | Low | Low |
| 20. Mikaelee et al.[34] | Low | Low | Low | Low | Low | Low |
| 21. Monteiro et al.[55] | High | High | Low | Low | Low | Low |
| 22. Moreau et al.[56] | Low | Low | Low | Low | Unclear | Low |
| 23. Onodera et al.[30] | Low | Unclear | Low | Low | Low | Low |
| 24. Owolabi et al.[57] | Low | Low | Low | Low | Low | Low |
| 25. Pal et al.[22] | Low | Low | Low | Low | Low | Unclear |
| 26. Parreira et al.[58] | Low | Low | Low | Low | Low | Low |
| 27. Polatli et al.[59] | Low | Low | Low | Low | Low | Low |
| 28. Sanches et al.[60] | Low | Unclear | Low | Low | Low | Low |
| 29. Santos et al.[61] | Unclear | Unclear | Low | Low | Low | Low |
| 30. Sathyaprabha et al.[24] | Low | Low | Low | Low | Low | Low |
| 31. Serebrovskaya et al.[62] | Low | Low | Low | Low | Low | High |
| 32. Shaheen et al.[63] | Low | Low | Low | Low | Low | Low |
| 33. Solomon & Hixon[64] | Low | Low | Low | Low | Low | Low |
| 34. Strano et al.[65] | High | Low | Low | Low | Low | Low |
| 35. Tamaki et al.[66] | Unclear | High | Low | Low | Low | Low |
| 36. Tzelepis et al.[67] | Low | Unclear | Low | Low | Unclear | Low |
| 37. Wang et al.[68] | Low | Unclear | Low | Low | Low | Low |
| 38. Weiner et al.[28] | Low | Unclear | Low | Low | High | High |
| 39. Zhang et al.[69] | Low | Low | Low | Low | Low | Low |

1 min to forced expiratory capacity (FEV1/FVC), peak expiratory flow rate (PEFR); lung volume measures: total lung capacity (TLC), residual volume (RV), tidal volume (TV), minute ventilation (MV), maximum voluntary ventilation (MVV); cough function measures: peak cough flow (PCF), cough reflex sensitivity; respiratory muscle strength measures: maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), sniff nasal inspiratory pressure (SNIP); and other measures: respiratory rate (RR), inspiratory to expiratory (I:E) ratio, carbon monoxide diffusion capacity (DLCO) and chest wall volumes.

Measures reported as percentage of predicted values were pooled where possible in preference to the raw data to control for confounding factors including sex, height, age and ethnicity. Reference sources

**TABLE 3** Summary of meta-analysis findings.

| Outcome measure | Studies (*N*) | PD (*N*) | Controls (*N*) | *Z* | *p* | $I^2$ | 95% CI | Effect size |
|---|---|---|---|---|---|---|---|---|
| Spirometry | | | | | | | | |
| 1. FVC (%) | 15 | 467 | 400 | 4.81 | <0.00001* | 76% | [0.44, 1.06] | SMD: 0.75 |
| 2. FEV1 (%) | 16 | 506 | 420 | 4.11 | <0.0001* | 69% | [0.28, 0.79] | SMD: 0.54 |
| 3. FEV1/FVC (%) | 15 | 526 | 416 | 0.44 | 0.66 | 66% | [−0.3, 0.19] | SMD: −0.05 |
| 4. PEF (%) | 7 | 251 | 200 | 3.9 | <0.0001* | 78% | [0.46, 1.38] | SMD: 0.92 |
| 5. FEF25%–75% (% predicted) | 5 | 138 | 124 | 2.43 | 0.02* | 0% | [0.06, 0.57] | SMD: 0.32 |
| Lung volumes | | | | | | | | |
| 6. TLC (%) | 3 | 93 | 82 | 0.84 | 0.28 | 75% | [−0.77, 0.58] | SMD: −0.1 |
| 7. RV (%) | 2 | 73 | 61 | 0.54 | 0.59 | 85% | [−1.20, 0.68] | SMD: −0.26 |
| 8. TV (ml) | 3 | 34 | 30 | 4.12 | <0.00001* | 0% | [81.16, 184.34] | MD: 132.75 |
| 9. MV (L/min) | 5 | 75 | 73 | 1.9 | 0.06 | 16% | [−0.02, 1.45] | SMD: 0.71 |
| 10. MVV (%) | 3 | 59 | 56 | 9.64 | <0.00001* | 0% | [26.75, 40.40] | MD: 33.58 |
| 11. VC (%) | 6 | 115 | 109 | 4.9 | <0.00001* | 10% | [0.45, 1.05] | SMD: 0.75 |
| Respiratory muscle strength | | | | | | | | |
| 12. MIP (%) | 7 | 271 | 195 | 6.46 | <0.00001* | 43% | [0.64, 1.19] | SMD: 0.91 |
| 13. SNIP (%) | 3 | 122 | 87 | 4.01 | <0.0001* | 0% | [0.30, 0.87] | SMD: 0.58 |
| 14. MEP (%) | 7 | 253 | 181 | 4.28 | <0.0001* | 78% | [0.56, 1.5] | SMD: 1.03 |
| Cough function | | | | | | | | |
| 15. Peak cough flow (L/min) | 2 | 132 | 123 | 3.93 | <0.0001* | 48% | [43.27, 129.34] | MD: 86.31 |
| 16. Cough reflex sensitivity (g/L) | 2 | 48 | 39 | 0.45 | 0.65 | 23% | [−0.62, 0.39] | SMD: −0.12 |
| Chest wall volumes | | | | | | | | |
| 17. Total chest wall volume (L) | 6 | 87 | 93 | 2.53 | 0.01* | 0% | [0.09, 0.68] | SMD: 0.38 |
| 18. Pulmonary ribcage volume (L) | 3 | 56 | 58 | 2.25 | 0.01* | 35% | [0.15, 1.11] | SMD: 0.63 |
| 19. Abdominal ribcage volume (L) | 3 | 56 | 58 | 1.16 | 0.25 | 0% | [−0.15, 0.59] | SMD: 0.22 |
| 20. Abdominal volume (L) | 6 | 87 | 93 | 3.07 | 0.01* | 22% | [−0.89, −0.2] | SMD: −0.54 |
| 'Other' | | | | | | | | |
| 21. Respiratory rate (bpm) | 6 | 111 | 100 | 2.99 | 0.003* | 90% | [0.56, 2.72] | SMD: 1.64 |
| 22. Respiratory cycle time (s) | 2 | 42 | 44 | 1.34 | 0.18 | 0% | [−0.14, 0.72] | SMD: 0.29 |
| 23. Inspiratory time (s) | 4 | 66 | 68 | 1.10 | 0.31 | 30% | [−0.21, 0.64] | SMD: 0.22 |
| 24. Expiratory time (s) | 3 | 56 | 58 | 1.79 | 0.07 | 0% | [−0.03, 0.71] | SMD: 0.34 |
| 25. DLCO (%) | 2 | 73 | 61 | 2.55 | 0.01* | 0% | [1.32, 10.12] | SMD: 5.72 |
| 26. Mean peak inspiratory flow rate (%) | 2 | 25 | 25 | 2.65 | 0.008* | 0% | [14.42, 95.89] | MD: 55.16 |

Abbreviations: %, % predicted; *, statistically significant; CI, confidence interval; DLCO, carbon monoxide diffusion capacity; FEF25%–75%, forced expiratory flow at 25% and 75% of the lung volume; FEV1, forced expiratory volume in 1 second; FEV1/FVC, ratio of the forced expiratory volume in the first one second to the forced vital capacity; FVC; forced vital capacity; MD, mean difference; MEP, maximum expiratory muscle strength; MIP, maximum inspiratory muscle strength; MV, minute ventilation; MVV, maximum voluntary ventilation; n, number; PD, Parkinson's disease; PEF, peak expiratory flow; RV, residual volume; SMD, standardised mean difference; SNIP, sniff nasal inspiratory pressure; TLC, total lung capacity, TV, tidal volume; VC, vital capacity.

used in studies to determine the percentage of the predicted value differed across studies. In meta-analyses conducted where different reference sources were pooled, standardised mean differences were calculated otherwise mean differences were reported. Similarly, where measures were gathered using different techniques (e.g., spirometry vs plethysmography), standardised mean differences were calculated.

## Data synthesis

Data extracted from 25 studies permitted meta-analyses for 27 respiratory outcomes. Table 3 summarises these results, detailing the number of studies, number of participants (PD and controls), test for overall effect (Z), significance (*p*), heterogeneity ($I^2$), effect size and 95% CI. The remaining outcomes were summarised narratively.

## Spirometry

### Meta-analysis of pooled spirometry data

Significant differences in pooled percentage predicted values FVC, FEV1, PEF (and L/min) and FEF25%–75% were observed in individuals with PD compared with controls. High heterogeneity was observed in all results except FEF25%–75% where heterogeneity was low (Figure 2).

FVC and FEV1 were in the impairment range for participants with PD across several studies; 10 of 13 studies demonstrated a FVC <80% in PD indicating a restrictive disorder, and 7 of 13 studies demonstrated a FEV1 of <80%. FEV1/FVC remained in the normal range of >70% in PD participants in all studies, indicating an absence of airways obstruction.

Sensitivity analysis, evaluating the effect size for spirometry data collected during the ON phase, improved heterogeneity of results, identifying impairments in PD compared with controls in FVC and FEV1. FVC (13 studies; standardised mean difference [SMD] 0.76; 95% confidence interval [95% CI] 0.59, 0.93; $z = 8.83$; $p < 0.00001$; $I^2 = 0\%$) and FEV1 (13 studies; SMD 0.59; 95% CI 0.42, 0.77; $z = 6.66$; $p < 0.00001$; $I^2 = 10\%$). No improvement in heterogeneity values was observed in PEF (% predicted and L/min), FEV1/FEV, FVC (L/min) or FEV1 (L/min) or FEF25%–75% (L/min) during sensitivity analysis.

A second sensitivity analysis evaluated the effect size for data collected on different ethnic groups in the ON phase. Both FVC (8 studies; mean difference [MD]: 10.32; 95% CI 6.98, 13.65; $z = 5.66$; $p < 0.00001$; $I^2 = 0\%$) and FEV1 (7 studies: 7, MD: 9.88; 95% CI 5.87, 13.90; $z = 4.82$; $p < 0.00001$; $I^2 = 0\%$) were significantly reduced with low heterogeneity in Hispanic and FVC in Asian groups: (4 studies; MD: 13.17, 95% CI 7.79, 18.55; $z = 4.80$; $p < 0.00001$; $I^2 = 31\%$).

### Narrative synthesis of spirometry data

In individual studies, measures of airway obstruction, FEF50%, FEF50%/FIF50%, PIF, FEV1/PEFR and MEF 75%, were reported as significantly reduced in people with PD compared with controls,[52] while PEFR,[40] MEF 25% or MEF 50%[52] were not. Slow vital capacity (SVC), a relaxed measure of VC from a position of maximal inspiration to maximal expiration, [70] was significantly reduced in PD compared with controls.[54]

## Lung volume and capacities

### Meta-analysis of lung volume and capacity measures

The number of studies and participants were relatively low for measures of lung volume. Meta-analyses of pooled data (Figure 3) identified statistically significant lower measures in individuals with PD compared with controls for TV (ml), VC (% predicted) and MMV (% predicted) with low heterogeneity observed. A pooled mean difference in TV of 133 ml (95% CI 81–183) was observed between PD and controls, with two of the three included studies demonstrating lower than anticipated volumes given the sex distribution[71] in groups. While VC was also significantly reduced compared with controls, two-thirds of studies included registered mean percentage predicted scores >90%. Two studies, registering volumes of 67%[50] and 75%,[60] had older participants and H&Y ranges of 1–5. Pooled data did not identify statistically significant differences in PD compared with controls for measures of TLC (% predicted), RV (% predicted) or MV (L/min).

Sensitivity analysis by sex was not feasible with the data presented. When data collected during the ON phase was examined, meta-analysis continued to identify statistically significant differences for TV, with low heterogeneity (2 studies; MD: 135.62, (95% CI 70.79, 200.45; $z = 4.10$; $p < 0.0001$; $I^2 = 0\%$). One study[58] reporting in the OFF phase identified TV values of 212 ml, well below that expected for either sex (300–500 ml).[72] Sensitivity analysis in OFF phases for metrics of VC, TLC, RV or MV was not possible due to insufficient data. Sensitivity analysis for VC data collected on different ethnic groups was feasible where results continued to demonstrate a significantly decreased VC in Asian participants with PD (2 studies; SMD: 1.09, 95% CI 0.58, 1.61; $z = 4.15$; $p < 0.0001$; $I^2 = 0\%$) and White participants with PD (4 studies; SMD: 0.61, 95% CI 0.26, 0.95; $z = 3.46$; $p < 0.0005$; $I^2 = 6\%$) compared with controls.

### Narrative synthesis of lung volume and capacity measures

Conflicting results were reported for several measures. For IC, no significant difference was reported in one study between PD and controls,[52] yet a significant decrease in IC was reported in another study in PD with camptocormia.[54] In expiratory reserve volume (ERV), one study reported no differences in PD compared with controls, [52] with a second reporting a significant decrease for PD with camptocormia compared with controls.[54] A final study reported RV was significantly increased in PD versus controls, but no differences in TLC or functional residual capacity (FRC) were observed.[34]

## Respiratory muscle strength

### Meta-analysis of respiratory muscle strength

Significantly lower respiratory muscle strength was observed in PD compared with controls for all measures; however, only SNIP exhibited low heterogeneity, with moderate heterogeneity observed for MIP and MEP (Figure 4).

Sensitivity analysis, exploring effects of ON/OFF phases on heterogeneity, identified low heterogeneity for MIP (% predicted) (4

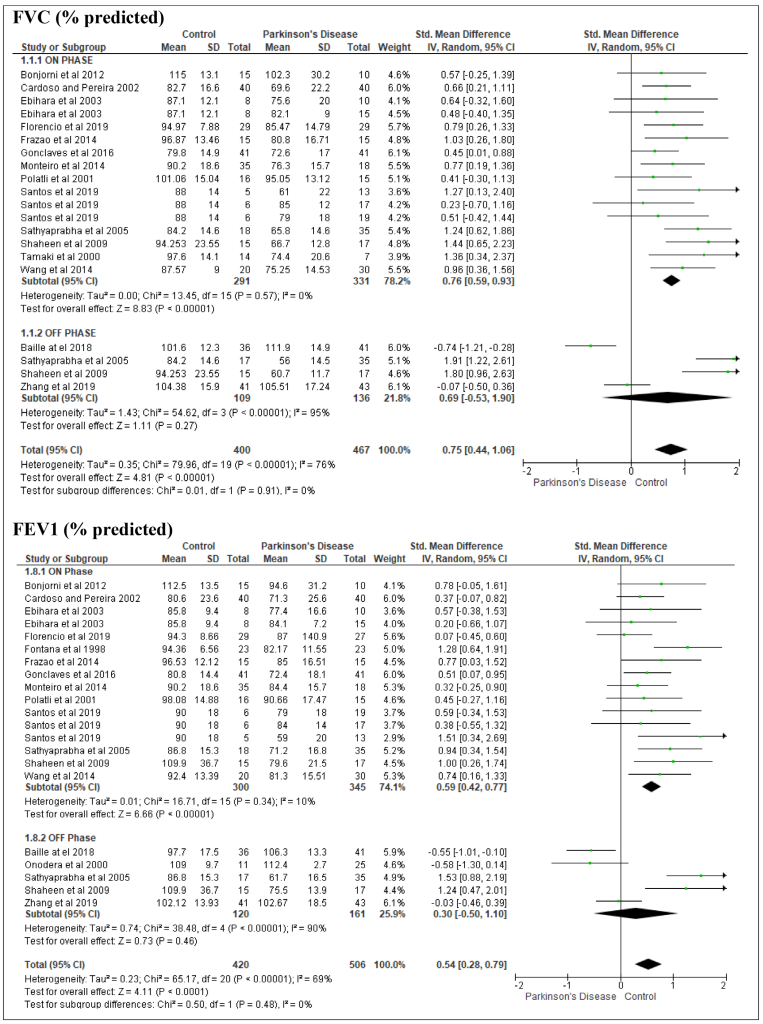



**FIGURE 2** Pooled analyses of spirometry data in Parkinson's disease versus healthy controls. FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

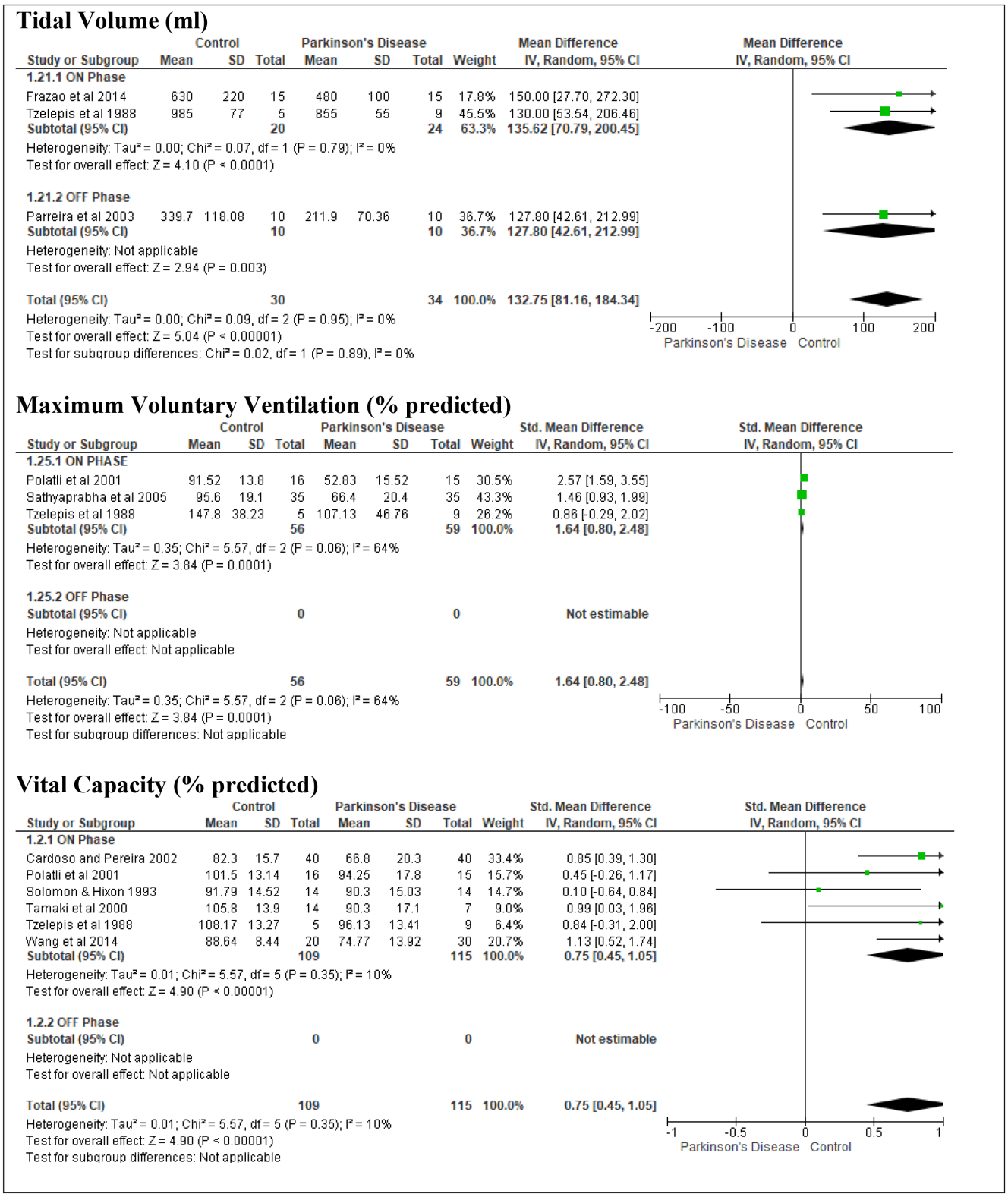



**FIGURE 3** Pooled analyses of lung volumes and capacity measures in Parkinson's disease versus healthy controls. FEF, forced expiratory flow; PEF, peak expiratory flow.

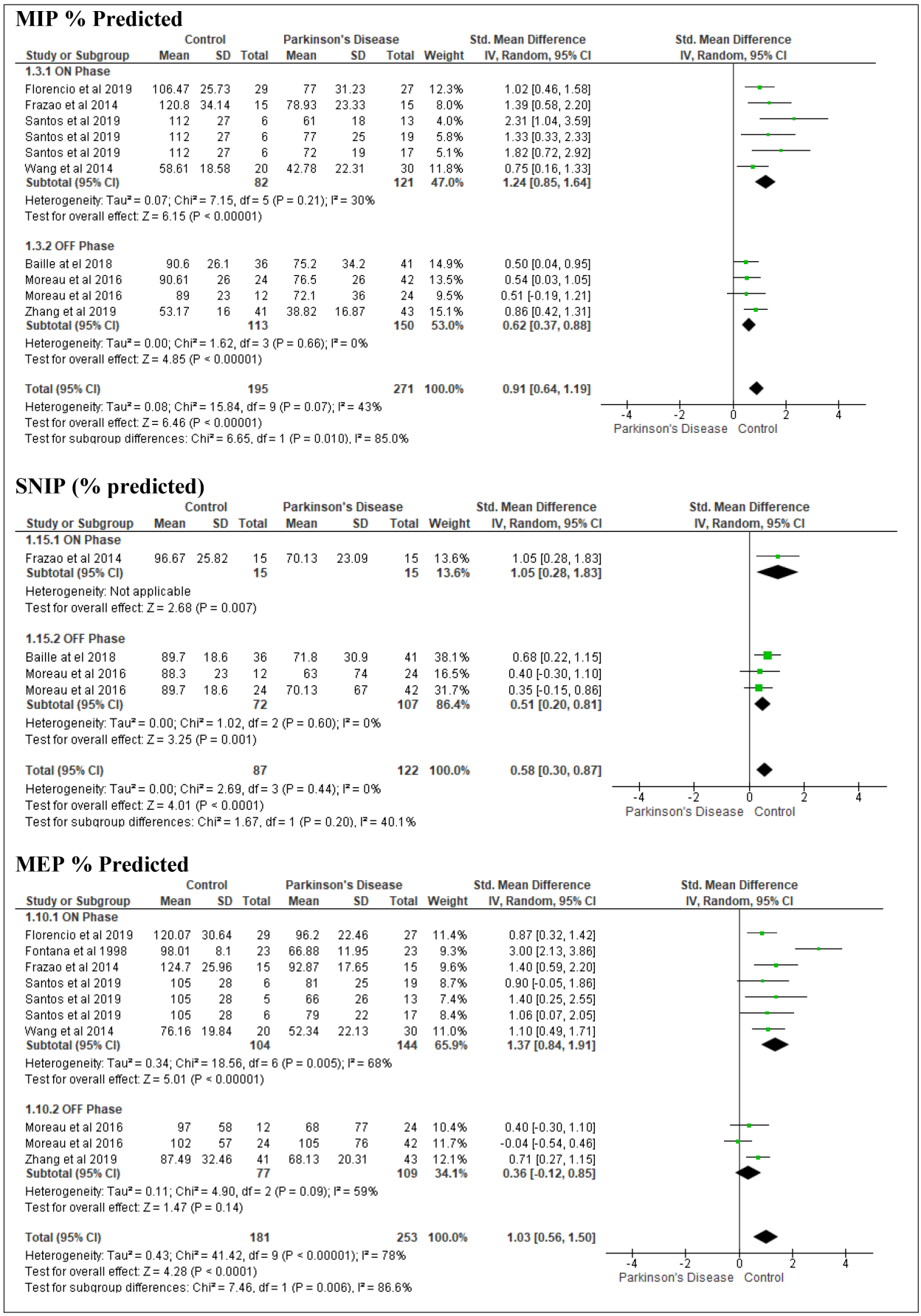



**FIGURE 4** Pooled analyses of respiratory muscle strength in Parkinson's disease versus healthy controls. MEP, maximum expiratory muscle strength; MIP, maximum inspiratory muscle strength; SNIP, sniff nasal inspiratory pressure.

studies; SMD 1.24; 95% CI 0.85, 1.64; $z = 6.15$; $p < 0.00001$; $I^2 = 30\%$) during the ON phase. Heterogeneity remained high for MEP (% predicted), MEP ($cmH_20$) and MIP ($cmH_20$) during the ON phase.

Sensitivity analysis examining the impact of different ethnic groups where population-specific normative values were employed demonstrated lower heterogeneity in pooled results for MIP and MEP; MIP (% predicted) Hispanic normative values (3 studies; MD 37.41; 95% CI 28.27, 46.54; $z = 8.03$; $p < 0.00001$; $I^2 = 0\%$), MIP (% predicted) Asian normative values (2 studies; MD 14.76; 95% CI 8.77, 14.76; $z = 4.83$; $p < 0.00001$; $I^2 = 0\%$), MIP (% predicted) European normative values (2 studies; MD 15.14; 95% CI 6.7, 23.59; $z = 3.51$; $p = 0.0004$; $I^2 = 0\%$); MEP (% predicted) Hispanic normative values (3 studies; MD 27.87; 95% CI 29.27, 26.46; $z = 6.35$; $p < 0.00001$; $I^2 = 0\%$), MEP (% predicted) Asian normative values (2 studies; MD 21.57; 95% CI 13.29, 29.84; $z = 5.11$; $p < 0.00001$; $I^2 = 0\%$).

### Narrative synthesis of respiratory muscle strength

Impairment of inspiratory muscle strength for males and females in the ON and OFF phases were identified. Two studies reported mean MIP values below the normal cut-off for males and females of $>70 cmH_20$[71] in the ON phase[50, 60] and one study reported MIP values in the OFF phase.[50]

A MEP of $>60 cmH_20$ and $>80 cmH_20$ is considered normal for females and males, respectively.[71] Conflicting evidence of impairment in males and females with PD in the ON phase was identified in two studies reporting mean MEP values above and below normal range.[50, 60] One study evaluating MEP in the OFF demonstrated impairment in males and females.[50]

Two studies evaluated muscle activity using electromyography (EMG) in the abdominal muscles[45] and the sternocleidomastoid (SCM) muscle.[49] Compared with controls, lower EMG activity of abdominal muscles was noted in PD versus controls during a voluntary cough[45] and increased SCM activity was identified while performing a MIP during OFF phase.[49]

## Cough function

### Meta-analysis of cough function outcomes

Pooled studies (all in the ON phase) show poor PCF in PD participants versus health controls, with moderate heterogeneity observed (Table 3). One study of female participants[43] reported mean values below the cut-off level of cough impairment level (360 L/min) in early PD. In the advanced stage, mean and standard deviation scores bordered 180 L/min level, [43] suggesting participants could not cough effectively for secretion removal.[73, 74] A second study with participants in H&Y stages 1–3 reported higher scores with data spread suggesting several PD participants fall into the cough impairment range.[47] No significant difference between PD and controls was identified in pooled data for cough reflex sensitivity.

### Narrative synthesis of cough function outcomes

One study reported an outcome of cough variability by evaluating changes to cough motor performance during voluntary cough. Variability was increased in PD compared with controls but the results were not statistically significant.[40]

## Chest wall volumes

### Meta-analysis of chest wall volumes

Chest wall volumes (in litres) were measured by plethysmography or a magnetometer. Pooled data identified significantly lower overall total chest wall volumes in PD compared with controls with low heterogeneity observed (Figure 5). When chest wall volumes were broken down into component parts, a significant difference remained for pulmonary ribcage volume, no differences for abdominal ribcage volume and, interestingly, a higher abdominal volume in PD was identified. Sensitivity analysis in ON/OFF phases was not feasible due to insufficient data.

### Narrative synthesis of chest wall volumes

Three studies examined thoracic dynamics in people with PD during the ON phase compared with controls. The first evaluated thoracic mobility at maximum inspiration and maximum expiration,[60] the second evaluated thoracic mobility during a normal breath and at maximum inspiration and maximum expiration[42] and the third evaluated thoracic mobility during forced maximum inspiration.[66] Conflicting reports of impairment in maximum inspiratory and expiratory effort were evident,[42, 60] whereas thoracic mobility during normal breathing and forced maximum inspiration were reported as reduced in PD.[42, 66] Abdominal wall movement was reported in one study as significantly reduced during forced maximum inspiration in PD[55].

## Other outcomes

### Meta-analysis of other outcomes

*Respiratory rate*

Pooled RR data identified significantly higher rates/minute in people with PD compared with controls with high heterogeneity observed (6 studies; SMD 1.64; 95% CI 1.64, 2.72; $z = 2.99$; $p = 0.003$; $I^2 = 90\%$). In five of six pooled studies, RR recorded in PD was outside normal adult values (12–16 bpm) but within reported rates in older adults.[75, 76]

Sensitivity analysis, exploring the effect of ON/OFF phases on heterogeneity, identified that high heterogeneity remained during the ON phase in PD participants (4 studies; SMD 1.95; 95% CI 0.42, 3.49; $z = 2.49$; $p = 0.01$; $I^2 = 93\%$) but not during the OFF phase, (2 studies; SMD 0.99; 95% CI 0.32, 1.67; $z = 2.88$; $p = 0.004$; $I^2 = 0\%$).

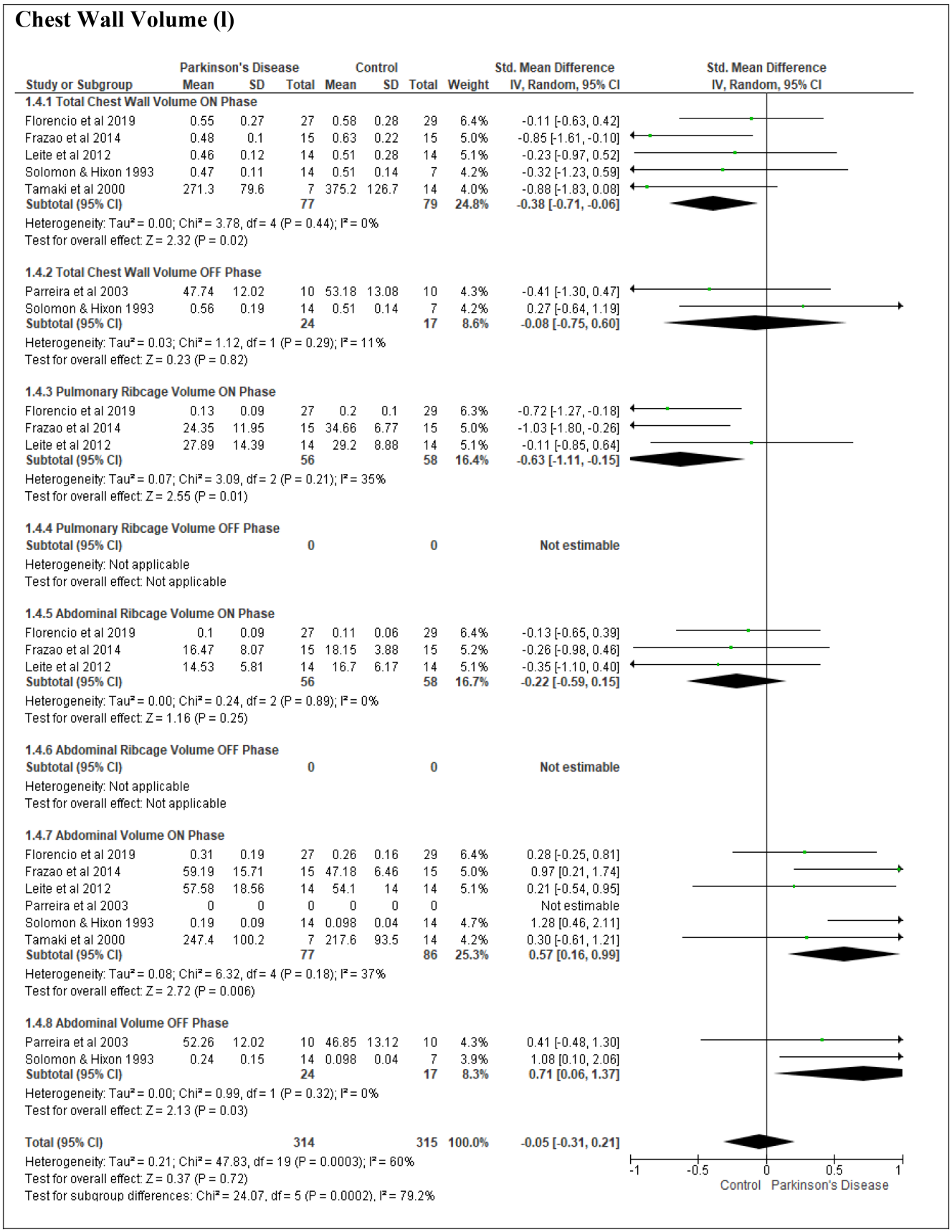



**FIGURE 5** Pooled analyses of chest wall volumes in Parkinson's disease versus healthy controls.

*Carbon monoxide diffusion capacity*

Pooled DLCO measures were significantly lower in PD compared with controls with low heterogeneity (Table 3). In one study,[77] mean values were below the normal threshold of 80% applied by the authors.

*Mean peak inspiratory flow rate*

Pooled peak inspiratory flow, the average highest inspiratory flow rate, was significantly impaired in PD compared with controls with low heterogeneity observed (Table 3).

*Respiratory cycle times*

Pooled data identified no significant differences between PD and controls for respiratory cycle time, expiratory time or inspiratory time.

## Narrative synthesis of 'other' outcomes

*Dyspnoea*

Two studies reported perceived breathlessness at rest in PD compared with controls. The first investigated self-reported dyspnoea using the Medical Research Council scale.[56] Dyspnoea was not identified in controls, whereas 24% of people with PD reported perceived dyspnoea. The second study evaluated dyspnoea using the modified Borg Dyspnoea Scale with perception of dyspnoea increased in PD (raw data were not presented).[28] A final study using the modified Borg Dyspnoea Scale examined reported dyspnoea under hypoxic and hypercapnic conditions with lower scores in PD, reaching significance in the hypoxic condition only.[30]

*Chemosensitivity*

Two studies addressed ventilatory chemosensitivity impairment in PD compared with controls using the rebreathing method. One study identified that chemosensitivity was significantly lower in people with PD to hypoxia but not to hypercapnia.[30] A second study identified a significant increase in hypoxic ventilatory drive at severe levels of hypoxia in PD but not at minor levels.[62]

*Arterial tension*

One study reported arterial blood gases and concluded arterial $O_2$ tension and $C0_2$ tension were normal in PD and comparable to healthy controls.[30]

# DISCUSSION

Meta-analyses of evidence of respiratory impairment in PD compared to healthy controls confirm restrictive dysfunction in PD manifesting primarily as significantly decreased lung volumes, respiratory muscle strength and ineffective cough, with little evidence of airways obstruction.

Looking at how individuals with PD breathe at rest, meta-analyses confirm people with PD in comparison to controls have a higher RR, a significantly reduced TV and abnormal breathing pattern. In all studies, except one, RRs observed were above the normal adult range and between 1 and 6 bpm higher than controls; however, they remained within rates reported in older adults without respiratory complications.[75, 76] High heterogeneity and relatively small numbers observed may limit meaningful interpretation of RR findings which differ from animal studies in PD where basal RR during daytime is reduced.[18, 21, 78–81] One explanation may be the prevalence of levodopa-induced dyskinesia during the ON phase of medication causing an increased and irregular RR.[82] A growing number of case reports demonstrate peak-dose levodopa-induced respiratory symptoms and a dose-related response in symptoms presenting as irregular tachypnoea alternating with brief periods of apnoea and self-reported dyspnoea in a pattern consistent with a central origin.[83, 84] Data did not allow evaluation of inspiration and expiration ratio in detail nor determination of the presence of respiratory muscle dyssynergia. Further research is required.

While TV decreases during basal breathing were apparent in PD, the number of studies and participants were small[42, 77] and the majority reported percentage predicted scores within expected values.[85] TV decreases are contradictory to those observed in PD in preclinical murine studies, where an augmented TV is reported and explained by deficient dopaminergic neurotransmitters, known to inhibit ventilation during breathing.[86] Most pooled studies measured TV during the ON phase which may account for this discrepancy between animal and human studies, but data from one study during the OFF phase also reported significantly lower TV in PD compared with controls.[58] Minute ventilation (MV), the product of RR and TV, was not significantly different between PD and controls, suggesting the increased RR offsets reduced TV, ensuring normal MV. Evidence from other neurological populations such as Duchenne's muscular dystrophy identify this phenomenon as a strategy to compensate for neuromuscular weakness.[87] Total chest wall volume was reduced in PD, and when the breathing pattern at rest was broken down, rib cage volumes were reduced in PD, while abdominal volumes increased. This result differs from other neurological conditions presenting with neuromuscular weakness, where a decrease in the contribution of the abdomen to chest wall volume and an increase in the contribution of the ribcage compartment has been established.[87] In healthy subjects, chest wall movements investigated using plethysmography and ultrasound imaging appear highly and positively correlated with diaphragmatic excursion during inspiration in tidal and deep breathing, with the abdominal compartment identified as the main predictor of diaphragmatic movement.[88] Given this and the finding of increased abdominal volume in people with PD during tidal breathing, diaphragmatic displacement in people with PD may be optimised to compensate for thoracic wall rigidity. However, diaphragmatic impairment cannot be excluded given the high RRs observed and the influence of phasic diaphragmatic dyssynergia due to PD medications.[89, 90]

Meta-analyses of spirometry data demonstrate a pattern more suggestive of a restrictive respiratory disorder, as reported in the literature,[91] than obstructive. This is supported by low heterogeneity and a significantly reduced FVC and FEV1 in the ON phase, a normal FEV1/FVC[92, 93] and DLCO within normal ranges (>75% predicted)[94] in people with PD. Longitudinal data in PD demonstrate FEV1 and FVC decline after 1 year compared with controls, with little change in FEV1/FVC, indicating lung volume decreases associated with respiratory muscle weakness.[95] Normal DLCO ranges with a pulmonary function test (PFT) restrictive pattern suggests a neuromuscular disease or chest wall disorder[94] with restrictive mechanisms in PD linked to rigidity, stiffness, camptocormia and bradykinesia resulting in reduced chest wall compliance and reduced respiratory volumes.[22, 23, 96] While no evidence of elevated TLC and RV indicative of obstructive lung disease[97–99] was identified, PEF was reduced in people with PD (values ranging from 36% to 76% in the ON phase). PEF measurement has high intrinsic variability,[100] and reduced PEF in the absence of FEV1/FVC changes indicates airway obstruction that more likely reflects poor participant effort and respiratory muscle strength.[100, 101] In the absence of early versus later data in PD it is difficult to distinguish whether the evident dysfunction is directly related to neurodegeneration of dopaminergic neurons of substantia nigra or to more indirect mechanisms including thoracic rigidity, although the presentence of inspiratory muscle weakness is clearly a secondary effect that compounds issues with vital capacity and chest wall volume. The evidence identifying an increased respiratory rate in PD during the OFF phase of medication, when considered in the context of normal blood gases/oxygen levels, is indicative of more central issues likely more directly related to dopamine loss. However, the exact mechanisms remain speculative.

Inspiratory muscle weakness has been identified in early-stage,[27] moderate-stage[77] and advanced-stage PD[77, 102] and is amenable to exercise-based interventions.[103] Meta-analyses of respiratory muscle strength now present robust evidence of inspiratory muscle weakness in PD with homogeneity in the data presented for MIP and SNIP data in ON and OFF phases. Although MEP scores appear reduced in PD compared with controls, high heterogeneity remains in ON and OFF phases, limiting interpretability of those findings. Reduced inspiratory strength in conjunction with inconclusive expiratory strength findings could be suggestive of isolated diaphragmatic weakness,[104] although this appears contradictory to the findings from the abdominal contribution to the total chest wall volumes identified. MVV (L/min) during repetitive maximal breaths[104] is a measure of respiratory muscle endurance[105] with reduced MVV strongly linked with diaphragmatic fatiguability.[106, 107] Factors reported to reduce MVV include altered co-ordination of respiratory muscles, musculoskeletal disease of the chest wall, deconditioning and ventilatory defects.[108] MVV was significantly reduced in PD during meta-analysis and may be a result of respiratory muscle dyskinesis, chest wall rigidity, respiratory muscle deconditioning and/or restrictive ventilatory deficits. It may also indicate reduced amplitude during repetitive movements associated with the condition.[109, 110] The potential contribution of diaphragmatic fatigue and decreased amplitude of diaphragm and/or chest wall excursion during repetitions to the lower MVV cannot be determined from the data presented.

To enhance our understanding of respiratory dysfunction in PD, results should be considered in combination rather than in isolation. On balance, results point toward a strong pattern of restrictive dysfunction potentially caused by the inspiratory muscle weakness. Inspiratory muscle strength plays an important role in TV[104, 111] and VC,[112] both of which were reduced, and weakness can cause decreased TLC and FRC, while FEV1/FVC and RV remain relatively normal once expiratory muscles are not weak[91]as also identified in this review. Reduced MIP is a known predictor of diaphragm muscle weakness well before evidence of change in VC[104] or FVC.[113] In terms of reduced inspiratory muscle strength, meta-analyses results in TV, VC and FVC that point to diaphragm weakness. Although early EMG studies in PD suggested no diaphragmatic impairment,[114, 115] murine models show diaphragmatic impairments in the resting state and hypercapnia-induced mobility[116, 117] that emerge at the same time as motor impairments and not as a consequence of them. While comparability of preclinical murine studies and human studies has been queried considering their disrepencies,[21] a study using ultrasound imaging determined significant differences in people with PD in H&Y stage 1–2 compared with H&Y stage 2.5–3 during quiet breathing for diaphragmatic contractile thickness, excursion and contractile velocity that was not influenced by motor subtype.[118] More studies examining the role of the diaphragm and its contribution to raised RR are required across the full ON and OFF phases.

Two studies considered differences in PCF between people with PD in ON phase and controls. Results indicate a weaker, less effective cough in PD. The mean results and standard deviations in certain studies suggest insufficient flow for secretion clearance. An effective cough consists of three stages: an inspiratory phase producing a fast and large TV, a compressive phase with a closed epiglottis developing increased intrathoracic pressure facilitating expectoration and an expiratory phase with epiglottal opening and high PEF removing mucus.[119] VC, shown to be reduced in this review, needs to be three times greater than TV to produce an effective cough.[120] While the volume and respiratory strength results identified explain in part the contribution of decreased lung volume and respiratory muscle strength to findings, the contribution of abdominal muscle activity and upper airway muscle weakness resulting in inadequate glottic closing/opening in the compressive and expiratory phases[119] cannot be accounted for in the findings presented. In other neuromuscular disorders, inspiratory muscle weakness is shown to cause impaired cough, atelectasis,[121] mucus retention[122] and predispose individuals to infections and higher mortality rates;[123] the same must now be considered in PD.

Clinically, findings highlight the need to assess and treat respiratory dysfunction in PD across the trajectory of the condition, beginning with routine respiratory assessment at the diagnostic

stage. Assessment and monitoring of respiratory dysfunction is important in both symptomatic and asymptomatic patients, as PD patients may remain asymptomatic even with abnormal PFTs.[124] There is reasonably strong evidence that longitudinal spirometry measurements of acceptable quality can be obtained in patients with PD, even when motor fluctuations are present.[125] Key items in the clinical assessment of respiratory function in PD include resting RR, spirometry, respiratory strength and PCF. Individualised, targeted interventions should be provided where impairment(s) is identified to reduce the respiratory morbidity and mortality associated with PD. A systematic review of non-pharmacological interventions for respiratory health in PD shows evidence supporting exercise-based interventions and inspiratory and expiratory muscle training to affect changes in MIP, MEP PCF and perceived dyspnoea.[103] Currently no evidence supports interventions to affect changes in lung volumes.

Results must be considered in the light of the following limitations. First, moderate to high heterogeneity is observed in several outcomes despite sensitivity analyses. Second, numbers in some pooled data sets were small and further data are required to support these findings. Third, data based on plethysmography can overestimate lung volume[126] and we did not distinguish between the methods used, opting instead to report standardised mean differences. Lastly, data reported did not permit a breakdown of respiratory measures by stages of disease progression or disease duration. While H&Y scale and disease duration were well documented in studies, inconsistencies in reporting methods did not allow sensitivity analysis by disease stage or duration. Studies with clear documentation of respiratory outcomes in each disease stage would allow for a more comprehensive evaluation and understanding of respiratory dysfunction in PD.

## CONCLUSIONS

Strong evidence of respiratory impairment in PD in comparison to healthy controls exists for FVC, VC, total chest wall volume, MIP and SNIP. Less conclusive evidence, due to smaller numbers and/or high heterogeneity, exists for TV, PCF and RR. Results point to a restrictive disorder with no conclusive evidence of airways obstruction. Studies identified did not allow examination of inspiratory (I) time, expiratory (E) time and I:E ratio and the contribution of the diaphragm to ventilatory impairments could not be elucidated in the results presented. Additional research is required, including data collection by stage of disease progression and across the entire ON and OFF phases, to identify potential phasic respiratory dysfunction and perceived dyspnoea as well as monitoring the effects of sleep and activities on respiratory metrics.

### AUTHOR CONTRIBUTIONS

Laura McMahon: study design; data collection; analysis of research; manuscript drafting; critical review of manuscript, review and acceptance of manuscript contents prior to submission.

Olive Lennon: study design; analysis of research; critical review of manuscript; review and acceptance of manuscript contents prior to submission.

Catherine Blake: study design; analysis of research; critical review of manuscript; review and acceptance of manuscript contents prior to submission.

### ACKNOWLEDGEMENTS

The authors would like to thank Professor Sean Gaine, Consultant Respiratory Physician and Ciaran Heatley, Chief Respiratory Physiologist (Mater Misericordiae University Hospital, Eccles Street, Dublin 7, Ireland) for their comments and discussion on the results. Open access funding provided by IReL.

### FUNDING INFORMATION

This research did not receive any specific grants from funding agencies in the public, commercial or not-for-profit sectors.

### CONFLICT OF INTEREST STATEMENT

None declared.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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**How to cite this article:** McMahon L, Blake C, Lennon O. A systematic review and meta-analysis of respiratory dysfunction in Parkinson's disease. *Eur J Neurol*. 2023;00:1-24. doi:10.1111/ene.15743