Evidence for pulmonary rehabilitation in chronic respiratory diseases in sub-Saharan Africa: a systematic review

Fanuel Meckson Bickton1, Cashon Fombe2, Enock Chisati3, Jamie Rylance1,4

1. Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, Malawi
2. Physiotherapy Department, Queen Elizabeth Central Hospital, Blantyre, Malawi
3. Physiotherapy Department, College of Medicine, Blantyre, Malawi
4. Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, United Kingdom

Corresponding author:

Fanuel Meckson Bickton, BSc. PT (Hons), Pre-MSc Research Intern, Lung Health Research Group, Malawi-Liverpool-Wellcome Trust Clinical Research Programme, P.O. Box 30096, Chichiri, Blantyre 3, Malawi, Cell: +265 882 63 06 94, E-mails: [fbickton@mlw.mw](mailto:fbickton@mlw.mw) / [fmbickton@stud.medcol.mw](mailto:fmbickton@stud.medcol.mw)

Short-running head:Pulmonary rehab in sub-Saharan Africa

Abstract word count: 197

Main text word count: 2, 601

Number of tables (main body): 1

Number of tables (supplementary): 2

Number of figures (main body): 1

Number of figures (supplementary): 0

Number of references: 62

# Abstract

**Background:** Pulmonary rehabilitation is a highly effective non-pharmacological treatment for patients with chronic respiratory diseases.

**Objectives:** We aimed to synthesize the evidence for practice and efficacy of pulmonary rehabilitation in sub-Saharan Africa.

**Methods:** We searched in PubMed and Scopus for relevant studies as well as scanned reference lists of relevant studies from these databases for additional studies. Articles meeting the inclusion criteria were included. Pre-determined data were extracted independently by two reviewers. A narrative synthesis approach was used in the interpretation of findings.

**Results:** Six studies were included, totalling 275 participants. Indications for pulmonary rehabilitation were chronic obstructive pulmonary disease, asthma, pulmonary tuberculosis and post-tuberculosis lung disease. Programmes ran for 6-12 weeks, universally incorporated exercise, and variously used home-based and hospital-based delivery models. All were interventional studies, of which two were randomized controlled trials, and primarily reported pulmonary function and exercise tolerance endpoints. Evidence for individualising the exercise regimen was available in three studies.

**Conclusions:** There is limited evidence on the design and efficacy of pulmonary rehabilitation in sub-Saharan Africa, but available data support its use in a variety of chronic respiratory conditions. Future studies should report core outcome sets and their individualised exercise and education regimens.

**Keywords:** pulmonary rehabilitation, chronic respiratory diseases, sub-Saharan Africa, systematic review

**PROSPERO registration number:** CRD42019128929

# Introduction

Chronic respiratory diseases (CRDs) are a major and increasing global health issue, of which COPD and asthma are the most common1 with combined annual death rates of approximately 3·15 million2,3.COPD is increasing in incidence, with age-standardised mortality being highest in Low and Middle Income Countries (LMICs), particularly South Asia and sub-Saharan Africa (SSA) 4,5. Known risk factors for CRDs include smoking, outdoor air pollution, household smoke exposure, occupational dust exposure, ozone and second-hand smoke6. Pulmonary tuberculosis (PTB) can also lead to irreversible lung damage which is most frequently radiologically apparent as bronchiectasis, fibrosis and cavitation 6,7. Progressive loss of lung function is associated with long-term respiratory symptoms and clinical presentation as CRDs, including COPD, bronchiectasis and aspergillosis6. These conditions can jointly be referred to as post-TB chronic lung disorders (p-TBLD) 8. As TB remains one of the top 10 causes of mortality worldwide, with an estimated 10.4 million new cases and 1.3 million deaths in 2016, the problem of p-TBLD is likely to be substantial but is poorly measured6.

CRDs can lead to significant chronic morbidity and loss of economic productivity, which burden patients, families and health systems alike. For conditions such as COPD, pharmacotherapy such as bronchodilators is currently the mainstay of the treatment. However, none of the drugs currently available for COPD can reduce the progressive decline in lung function which is the hallmark of this disease9. In addition, drugs for CRDs can be less available and affordable, especially in low-income settings including SSA where the availability and affordability of medicines and diagnostics recommended for the management of asthma and COPD is a big challenge10.

Fortunately, the rational use of pharmacotherapy for CRDs could be complemented by non-pharmacologic treatments. For COPD, pulmonary rehabilitation (PR) is well established as a highly effective intervention which improves symptoms, quality of life and survival11. It is more effective in these domains over periods up to 6 months than long-acting inhaled bronchodilators and combination inhaled long-acting bronchodilators and corticosteroids, and a recent trial has shown a substantial reduction in the risk of readmission in patients who undertake PR immediately after admissions for COPD 12. Recent evidence also supports PR for other CRDs, including p-TBLD, asthma, and interstitial (fibrotic) lung disease (ILD) 13. In addition, while there is still a cost in providing it, PR is relatively more cost-effective than the pharmacotherapy for CRDs, as it may be delivered using existing local staff with minimal equipment. Hence it would require little investment, be sustainable and scalable in resource-limited settings such as SSA14.

PR is a comprehensive package of interventions which can include exercise training, education and behaviour management 15. Exercise training is a core component which should be prioritised 16,but may require modification of traditional training paradigms, and taking into consideration patient strength and endurance 17. It has been suggested that PR is now sufficiently understood to obviate further randomized trials in High Income Countries (HICs) 18. However, given the design and delivery of programmes should be individualised to patient groups and context 19, high-quality data are needed outside HICs.

While the need for PR in SSA is clear, there is currently no systematic review that has investigated the research evidence for its practice and effectiveness in the region. We aimed to close this research gap. With reference to the PICOS approach (participants, interventions, comparisons, outcomes, and study design), we systemically reviewed randomized controlled trials (RCTs) and non-RCTs to answer the following questions: (a) In which CRDs has PR been tested in SSA? (b) What designs and modes of delivery have been used in PR programs tested in people with CRDs in SSA? (c) What is the evidence for individualising the exercise regimens of the PR programmes tested in people with CRDs in SSA? (d) What is the effectiveness of PR in people with CRDs in SSA?

# Methods

A protocol for this review was registered in the International Prospective Register of Ongoing Systematic Reviews (PROSPERO) 20 on July 1, 2019 (registration number: CRD42019128929). The conduct and reporting of the review were guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) 21,22. Ethics approval was not required as we used only publicly available data.

**Study eligibility criteria and identification**

JR and FB determined eligibility independently, and discrepancies were resolved by consensus. With reference to the same PICOS approach that informed our review questions, our eligibility criteria were studies with the following characteristics: participants with CRDs, attending a PR programme. The comparison or control domain was not necessary since additional RCTs comparing PR and conventional care in CRDs are not warranted as there is now enough evidence on the superiority of PR18. Hence, we included both RCTs and non-RCTs. In the absence of standardized PR core outcomes, we captured the broadest range of outcomes possible, including symptoms, functional limitation, spirometry and quality of life.

We selected peer-reviewed articles of studies conducted within SSA between 1997 and 2019. The start year (1997) was chosen to coincide with the publication of the first Pulmonary Rehabilitation Evidence-Based Guidelines23. Articles must have been accessible in full text in English (or available translation) and describe a study of pulmonary rehabilitation for a defined respiratory disease or syndrome. The searches were performed in April 2019, using keywords and MeSH terms in PubMed and Scopus (see supplementary table 1 (Table S1) for search terms used in PubMed), with scanning of reference lists for relevant secondary references.

Data extraction, synthesis and analysis

Data were independently extracted by two reviewers (FB and CF) using a data extraction form which was based on our pre-review of identified manuscripts, with consensus-resolution of disagreement. The following data were sought and either coded or maintained in narrative form: study characteristics (country, year of publication and design), participant characteristics (sample size, condition and mean age), intervention characteristics (setting of delivery, duration of session and programme, frequency, components, team composition, and evidence for individualizing the exercise regimen), endpoints (primary and secondary), and summary measures of effect. We extracted all reported outcomes and synthesized and analyzed the extracted data by a narrative description and tabular summary of key characteristics of the studies.

## Assessment of reporting and methodological quality

We employed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist24 and assessed potential for bias using the Newcastle–Ottawa Scale (NOS) 25 for cohort studies (non-RCTs). For RCTs, we employed a 2017 Consolidated Standards of Reporting Trials (CONSORT) checklist of information to include when reporting a randomized trial assessing nonpharmacologic treatments (NPTs) 26 (for 2-arm parallel-group trials) and a CONSORT checklist for reporting of multi-arm parallel-group randomized trials 27. For methodological quality, we incorporated a revised Cochrane Risk-of-Bias Tool for randomized trials (RoB 2)28,29 in tandem with the CONSORT checklist.

# Results

## Study selection

Literature search terms identified 86 articles, of which six met criteria for inclusion (see Figure 1). We excluded 72 non-relevant articles during title and abstract review. Of the remaining 14 articles, we further excluded one duplicate30, one with abstract only and no author contact details 31, one non-research guideline32, and five not meeting inclusion criteria 33-37.

## Study characteristics

Of the six finally included, three studies were conducted in South Africa38-40, two in Uganda41,42 and one in Nigeria43, and all were published between 2010 and 2018. The studies were focused on the feasibility and acceptability of the PR programmes. All the six were experimental or intervention studies, with two being RCTs and 4 being pre-post (before-and-after) non-RCTs (see Table 1).

## Participant characteristics

A total of 275 participants were represented, all aged 18 years or older. Of these, COPD was the indication for inclusion in 59 participants across three studies 38,42,43. A further 88 participants had asthma within a single study40, 61 participants had p-TBLD in the two Uganda studies 41,42 and 67 participants were included in a separate study of pulmonary tuberculosis (PTB) during anti-tuberculous treatment39 (see Table 1).

## Interventions

The PR programmes used were based either in referral-level hospitals (n=3) or at participants’ homes (n=3). Their durations ranged from 6 to 12 weeks, with variations in composition as follows: exercise, education, nutrition, self-management activities and psycho-social support. The staff who delivered and supervised the programmes were variously composed across the studies, with at least a physiotherapist being found in all programmes, to deliver and supervise the exercise training component. The other components of the programmes such as education were delivered and supervised by various professionals including medical doctors, nurses, physiotherapists, counsellor, home-based caregiver, students (medical, physiotherapy, and nutrition), assistant researcher (with unspecified expertise or profession), or a qualified practitioner in exercise therapy and rehabilitation. More specific information for each study is shown in Table 1.

## Methodological quality

A standard NOS criterion for what constitutes a high-quality study has not yet been universally established, but we considered scores ≥7 to reflect high-quality44. Based on this, all four non-RCTs were found to be at high risk of bias (score ≤5). The issues included inadequate and/or lack of information on the three domains (selection, comparability and outcome) on which quality assessment was based. Inadequate and/or lack of information on important areas were also an issue in the RCTs. Detailed results from the methodological quality assessment of all studies are shown in supplementary table 2 (Table S2).

## Exercise individualisation and education

Evidence for individualising the exercise regimens of the PR programmes was available in three studies 40-42, including the evidence for progression of exercise training loads. For example: “The exercise regime was individually prescribed, monitored, and increased as the program progressed…”41, “The intervention was performed in groups, but the exercise training was individually prescribed and intensified as the program progressed”42, and “Individual age predicted maximum heart rate (HRmax) was utilized… to develop a suitable program for all subjects without the need for expensive equipment…”40. The remaining three studies had no explicit evidence for individualisation of their exercise regimens. Details for other components of the programmes, including education and self-management aspects, were very limited (either completely missing or inadequate).

Effectiveness

Table 1 shows the effects of PR programmes. Multiple primary outcomes were the norm in all the studies, some of which were inconsistently used, which resulted in reporting of various effects: physical, psychosocial, self-esteem, health literacy, economic, exercise tolerance, pulmonary function and quality of life. Pulmonary function and exercise tolerance effects were predominantly assessed and reported. Forced Expiratory Volume in one second (FEV1) and Forced Expiratory Volume (FVC) were common outcome measures for pulmonary function, while the 6 Minute Walk Test (6MWT) and Incremental Shuttle Walk Test (ISWT) were used as outcome measures for exercise tolerance. Pulmonary function was reported in five studies 38-41,43, of which three 38-40 (including the two RCTs37,38) demonstrated improvement after the programme, one 41 suggested a non-significant but potentially clinically important increase and one43 showed no significant change. Exercise tolerance was reported in four studies 38,39,41,43, of which one43 reported significant improvement, one 41 reported a non-significant but potentially clinically important increase, and two 38,39 showed no significant change (including an RCT39). Dyspnoea, as the most frequently reported symptom in chronic respiratory disease45, was assessed in four studies 38,39,41,43. Of these, two 38,39reported significant improvements (including an RCT39), one 41 reported a non-significant but potentially clinically important difference, and one 43 showed no significant change.

# Discussion

We found evidence of clinically significant improvements in symptoms and lung function in patients receiving pulmonary rehabilitation for various chronic respiratory diseases in sub-Saharan Africa. However, data were limited and only three countries were represented. Studies predominantly examined participants with COPD (three out of the six studies). While the evidence base for PR outside of Africa is dominated by this patient group, recent evidence suggests that similar benefits could be gained in other CRDs including interstitial lung disease, bronchiectasis, asthma, cystic fibrosis, lung transplantation, lung cancer, and pulmonary hypertension15,46,47. For example, a new study has shown that patients with bronchiectasis benefit from PR to broadly same extent as patients with COPD 48. PR is also clearly indicated in the management of patients with p-TBLD 15,49 which is infrequently found in high income countries, but extremely common in TB endemic regions 6, particularly LMICs 50. It is reported that, in these settings, TB increases the odds of p-TBLD by more than threefold on average 6.

PR can be home- or hospital-/centre-based11; each was equally represented in this systematic review. Although it is recognized that hospital-/centre-based programmes are a standard mode of delivery of PR51,both modes were effective in various study outcomes of interest in this systematic review. In a multicentre randomised trial52, home-based rehabilitation was found to be a useful, equivalent alternative to hospital-based rehabilitation in patients with COPD. In addition, another recent study, which aimed to compare the cost‐effectiveness and cost‐utility of home and centre‐based PR for adults with stable COPD, concluded that home‐based PR provided a cost‐effective alternative model for people with COPD who cannot access traditional centre‐based programmes53. However, to date, home-based PR has still not been widely adopted into clinical practice, possibly because a sound economic model has not been developed 17.

In line with recommendations54, each PR programme ran for at least 6 weeks and focussed on exercise training, which seems reasonable as exercise is a component with the strongest level of evidence for beneﬁt 16. However, the health gains attributable to a broader package are important and may be under-represented in the existing African literature. In addition, to optimize the physical and physiological benefits, it is necessary to individualise exercise training for each patient, including exercise intensity 55.In this systematic review, there was no record of evidence for individualising the exercise regimens of PR programmes in 3 studies, making it difficult to assess the quality of the programmes. Moreover, the issues of methodological quality may limit the validity of the studies’ results when using them as a basis for recommending, with absolute certainty, PR in the management of CRDs in SSA.

There was variable reporting of outcomes of interest, of which pulmonary function and exercise tolerance indices predominated. Studies in our review noted improvements in lung function which might not be typical of the broader literature. This raises the possibility that, perhaps due limited access to pharmacological therapy, patients in SSA may benefit differently to those in whom prior pharmacotherapy was optimal. We note that the choice of reported metrics was also variable, leading to heterogeneity which limits the potential for meta-analysis or broader assessment 56,57. Our review would support the suggestion of a consistently implemented “core outcome set” 58,59. This could reduce outcome reporting bias, and broaden the relevance to different stakeholders including patients, healthcare workers and those overseeing the wider healthcare system60. In this systematic review, both exercise tolerance and dyspnoea were outcomes in four of six studies 38,39,41,43; these are well-recognized and stakeholder-valued positive outcomes of PR in other settings61. Selection of core outcomes should include reaching a consensus on the key measures which best represent them.

Our systematic review used a broad search strategy to identify relevant evidence for pulmonary rehabilitation in sub-Saharan Africa and rigorous implementation of PRISMA guidelines. However, only studies published in English were included. This may have limited our sample, but we found no examples of this during article screening. The small number of studies, their heterogeneity, and the lack of consistent outcome variables did not allow meta-analysis.

## **Conclusions**

Despite limitations, all the included studies in this review suggest that extending pulmonary rehabilitation programmes in sub-Saharan Africa could be beneficial to patients. Efforts should be made to individualise the exercise regimens of the pulmonary rehabilitation programmes in the region. Larger studies with high methodological quality and using consistent outcome variables are warranted, to allow careful meta-analysis of both effectiveness and cost-effectiveness.

# Authors’ contributions

FMB contributed to study conception and design (including search strategy), literature searches and screening, data extraction, quality assessment, data synthesis and analysis, manuscript drafting, and critical revision of the manuscript for important intellectual content. CF contributed to data extraction and manuscript preparation. EC contributed to study conception and critical revision of the manuscript for important intellectual content. JR contributed to study conception and design (including search strategy), data synthesis and analysis, manuscript preparation, and critical revision of the manuscript for important intellectual content. All authors approved of the final version of the manuscript and its submission for publication.

# Conflict of interest

The authors declare that they have no conflicts of interest.

# Funding

FMB receives research internship funding from the Malawi-Liverpool-Wellcome Trust Clinical Research Programme.

# Acknowledgements

We thank Dr. Diston Chiweza, the Librarian at the University of Malawi, College of Medicine, for training the corresponding author in systematic review methods.

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Additional records identified through reference scanning   
(n = 4)

Records identified through database searching   
(n = 86)

## Identification

Records after duplicates removed   
(n = 86)

## Screening

Records excluded   
(n = 72)

Title & abstract screening   
(n = 14)

Full-text articles excluded   
(n = 8)

Full-text review & inclusion criteria   
(n = 6)

## Eligibility

Studies included in synthesis & analysis   
(n = 6)

## Included

**Figure 1: Flow chart of the study selection, adapted from PRISMA group 2009 flow diagram**

**Table 1: Study characteristics and extracted data**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study** | **Design** | **Intervention** | **Endpoints** | **Results Summary[[1]](#footnote-1)** |
| Clarke et al, South Africa (2016)38 | Pre-post, single arm (non-RCT)  n=7 COPD; age range 31-71y (mean 57) | *Setting*: Home-based;  *Timing*: 12 weeks duration;  *Content*: exercise, nutrition & education;  *Staff*: supervised home-based caregiver, medical student, physiotherapy student & human nutrition student;  *Text evidence for individualization*: Absent | ***Primary***  Δ pulmonary function; Δ 6MWD; Δ QoL; Δ BODE index  ***Secondary***  Δ health literacy (Inhaler technique & disease-specific insight) | (1) No significant improvement in FEV1%, 6MWTD or BODE index @ wk 6  (2) Improved QoL score in symptom score component only @ wk 6 (p = 0.03)  (3) Improved FEV1% by mean 8% @ 12 wks\*  (4) Improved QoL score @ wk 12  (5) Non-significant increase in 6MWT @ wk 12  (6) Non-significant change in BODE index @ wk 12  (7) Inappropriate inhaler technique in 5/7 pts @ baseline, 3/7 at wk 6, and 2 at wk 12  (8) No knowledge of COPD in 5 pts @ baseline and inadequate knowledge in 2 pts  (9) Adequate COPD knowledge in 5 pts @ wk 12  (10) Inadequate COPD knowledge in 2pts @ wk 12 |
| Jones et al, Uganda (2017)41 | Pre-post single arm, mixed methods (non-RCT)  n=29 post-TBLD pts; mean age 45y | *Setting*: Hospital-based;  *Timing*: 6 weeks duration, ~2hrs/session;  *Content:* exercise & education;  *Staff*: physiotherapist, doctor, specialist nurse & counsellor;  *Text evidence for individualization*: available | ***Primary***  Δ health status (CCQ); Δ exercise tolerance  ***Secondary***  Δ pulmonary function; biometrics; Δ chest pain; Δ haemoptysis; Δ cough; participation & completion level | (1) 0.95 mean improvement in CCQ & health status (CCQ) scores exceeded MCID of -0.4 post PR  (2) 90 m (MCID 48 m) mean improvement in ISWT  (3) 2.5 second improvement in Sit-to-Stand test time, also beyond MCID (MCID 2.3 seconds)  (4) Individual-level improvements in ISWT level 59% of pts & 61% of pts in Sit-to-Stand test & 61% of pts above MCIDs.  (3) High level participation and completion @ 85% |
| de Grass et al,South Africa (2014)39 | Pre-post, RCT (2-arm)  n=67 PTB pts; 18-65 yrs;  IG (n=34), CG (n=33) | *Setting*: Home-based;  *Timing*: 6 weeks duration;  *Content*: exercise, self-management activities & education;  *Staff*: assistant researcher (expertise not specified) and physiotherapist;  *Text evidence for individualization*: Absent | ***Primary***  Δ pulmonary  Function; Δ exercise tolerance; Δ HRQoL  ***Secondary***  Δ Modified Borg Scale | (1) No significant differences in wk 6 in FEV1 (p=0.1; 95% CI: -0.07 to  0.51) and FVC (p=0.2; 95% CI: -0.9 to 0.51)  (2) Significant differences in both values for FVC (p=0.004; 95% CI: -0.36 to -0.07) and FEV1 (p=0.001; 95% CI: -0.33 to -0.08) following intragroup analysis of baseline versus wk 6  (3) Significant difference in distance in IG @ wk 6 (p=0.007; 95% CI: 15.37 to 92.7)  (4) Significant difference in Modified Borg Scale @ wk 6 (p=0.03)  (5) No significant differences in exercise tolerance at wk 6 after adjusted analysis (P>0.05)  (6) No significant difference over HRQoL over 6 wk period (p=0.789) |
| Jones et al, Uganda (2018)42 | Pre-post single arm, qualitative (non-RCT), n=32 p-TBLD, n=10 COPD pts | *Setting*: Hospital-based;  *Timing*: 6 weeks duration, x2/week, 2hours/session;  *Content*: exercise & education;  *Staff*: physio, doctor, specialist nurse & counsellor  *Text evidence for individualization*: available | ***Primary***  Δ experiences of CRD post-PR  ***Secondary***  Participant recommendations to improve PR | (1) experiences of a complex array of interacting problems (e.g. physical, social, psychological, economic) pre-PR  (2) positive Δ in experiences above post-PR |
| Ige et al, Nigeria (2010)43 | Pre-post single arm non-RCT,  n=42, COPD, Mean age: 66y | *Setting*: Hospital based;  *Timing*: 6 weeks duration, x2/week, 2hrs a session;  *Content*: exercise, education & psycho-social support;  *Staff*: nurse educator, physio, respiratory physician;  *Text evidence for individualization*: Absent | Δ pulmonary function; Δ exercise tolerance; Δ SaO2; Δ breathlessness; Δ resting cardiogram; Δ condition-specific measure; Δ psychological distress measure; Δ QoL measure; Δ HRQoL; Δ anxiety & depression; Δ SIP | (1) No significant Δ pulmonary function (mean ± SD for FEV1 (L) was 0.74 ± 0.34 @ 3 months and 0.70 ± 0.26 @ 6 months; mean ± SD for VC (L) was 1.99 ± 0.66 @ 3 months and 1.92±0.64 @ 6 months; mean ± SD for PEFR (L/min) was 142.6 ± 51.4 @ 3 months and 137.9 ± 40.2 @ 6 months)  (2) No Δ SaO2 & breathlessness (mean ± SD = 90.4 6± 5.4 @ 3 months and 90.29 ± 5.4 at 6 months)  (3) Significant Δ in ISWTD (95% CI: 11, 39) (mean ± SD = 182.6 ± 104 @ 3 months (p<0.001) and mean ± SD = 193.9 ± 103 @ 6 months)  (4) Significant improvement @ 3 months in HRQoL as measured on the CRDQ and, apart from breathlessness, the  improvements were maintained @ 6 months), i.e., mean difference (95%CI, =p<0.05) from baseline for dyspnoea was 1.9 (0.5, 3.5) @ 3 months and 1.7(-0.2, 3.5) @ 6 months; mean difference (95%CI, =p<0.05) from baseline from baseline for fatigue was 2.7 (1.5, 4.1) @ 3 months and 1.6(0.03, 3.2) @ 6 months; mean difference (95%CI, =p<0.05) from baseline for emotion was 3.2 (1.8, 4.6) @ 3 months and 2.5 (0.2, 4.8) @ 6 months; and mean difference (95%CI, =p<0.05) from baseline for mastery was 2.0 (0.7, 3.3) @ 3 months and 2.8 (1.3, 4.2) @ 6 months  (5) No significant Δ in SIP @ 3 months (mean difference (95%CI) from baseline = +0.5 (-1.9, 2.8)) but significant @ 6 months (mean difference (95%CI) from baseline = -1.5(-3.3, 0.3))  (6) Significant reduction in both the anxiety and depression sub-scale scores as measured on the HAD (mean difference (95%CI) from baseline for Anxiety was -0.7 (-0.04, -1.4) @ 3 months and -0.8(-0.2, 1.8) @ 6 months; mean difference (95%CI) from baseline for depression was -0.5 (-0.2, 1.2) @ 3 months and -0.69-0.1, 1.4 @ 6 months) |
| Shaw et al, South Africa (2011)40 | Pre-post 4-arms (NE, AE, DR, CR) comparison RCT  n=88 asthmatics (moderate-persistent); 18-34yrs | *Setting*: Home-based;  *Timing*: 8 weeks duration, x3/week;  *Content*: exercise;  *Staff*: qualified  practitioner in exercise therapy & rehabilitation;  *Text evidence for individualization:* available | ***Primary***  Δ pulmonary function; Δ abdominal and thoracic dimensions & kinematics  ***Secondary***  Level of compliance/adherence to exercise programs | Significant and superior improvements in pulmonary function & abdominal  & thoracic kinematics with CE @ 8 wks:  (1) FVC (p<0.001), FEV1 (p<0.001), FEV1/ FVC ratio (p = 0.031), PEF (p = 0.001), MVV (p = 0.001), and IVC (p<0.001) changed signiﬁcantly from baseline (mean ± SD for FVC was 2.87 ± 0.67 @ 0 weeks and 3.68 ± 0.82 @ 8 wks; mean ± SD for FEV1 was 2.70 ± 0.67 @ 0 wks and 3.30 ± 0.70 @ 8 wks; mean ± SD for FEV1/ FVC ratio was 93.82 ± 5.47 @ 0 wks and 91.23 ± 5.74 @ 8 wks; mean ± SD for PEF was 7.14 ± 2.22 @ 0 wks and 7.99 ± 2.22 @ 8 wks; mean ± SD for MVV was 99.90 ± 41.79 @ 0 wks and 119.01 ± 43.9 @ 8 wks; and mean ± SD for IVC was 3.26 ± 0.97 @ 0 wks and 3.78 ± 0.9 @ 8 wks)  (2) No signiﬁcant improvements in FEF25, FEF50, FEF75, FEF25-75, VE, Fb, and VT (mean ± SD for FEF25 was 2.46 ± 1.09 @ 0 wks and 2.29 ± 0.56 @ 8 wks; mean ± SD for FEF50 was 4.21 ± 1.50 @ 0 wks and 4.31 ± 1.0 @ 8 wks; mean ± SD for FEF75 was 6.24 ± 1.87 @ 0 wks and 6.61 ± 1.51 @ 8 wks; mean ± SD for FEF25-75 was 3.90 ± 1.44 @ 0 wks and 3.88 ± 0.85 @ 8 wks; mean ± SD for VE was 14.38 ± 9.76 @ 0 wks and 16.00 ± 11.82 @ 8 wks; mean ± SD for Fb was 23.57 ± 8.18 @ 0 wks and 26.08 ± 8.48 @ 8 wks; and mean ± SD for VT was 0.72 ± 0.48 @ 0 wks and 0.75 ± 0.59 @ 8 wks)  (3) Signiﬁcant (p ≤ 0.05) improvements were found in chest circumference (cm) during inspiration at the height of the second intercostal space following CE (p<0.001) (mean ± SD for inspiratory circumference was 92.18 ± 6.38 @ 0 wks and 94.76 ± 6.49 @ 8 wks)  (4) No signiﬁcant improvements in chest circumferences (cm) following CE during rest and expiration at the height of the second intercostal space (mean ± SD for resting circumference was 87.52 ± 6.36 @ 0 wks and 87.47 ± 6.3 @ 8 wks; mean ± SD for expiratory circumference was 86.21 ± 6.96 @ 0 wks and 86.04 ± 6.95 @ 8 wks)  (5) Signiﬁcant improvements, following CE, in chest circumferences (cm) during inspiration (p<0.001), expiration (p = 0.002) and rest (p = 0.023) at the height of the xiphoid process (mean ± SD for inspiratory circumference was 84.30 ± 6.66 @ 0 wks and 87.48 ± 6.88 @ 8 wks; mean ± SD for expiratory circumference was 79.06 ± 7.06 @ 0 wks and 77.82 ± 7.57 @ 8 wks; and mean ± SD for resting circumference was 80.18 ± 6.55 @ 0 wks and 79.07 ± 7.03 @ 8 wks)  (6) Signiﬁcant improvement in abdominal circumference (cm), following CE, during inspiration (p<0.001) and expiration (p<0.001) at the height of the midpoint between the xiphoid process and umbilicus (mean ± SD for Inspiratory circumference was 75.42 ± 8.49 @ 0 wks and 78.40 ± 8.90 @ 8 wks; mean ± SD for expiratory circumference was 72.54 ± 8.58 @ 0 wks and 69.65 ± 8.29 @ 8 wks)  (7) No signiﬁcant improvement, following CE, in the resting circumferences (cm) at the height of the midpoint between the xiphoid process and umbilicus (mean ± SD for resting circumference was 74.23 ± 7.95 @ 0 wks and 73.60 ± 8.56 @ 8 wks) |

\*One patient developed claudication symptoms in the course of the three-month intervention and had deterioration in walking distance while respiratory parameters improved.

***Abbreviations:***

Δ(s) = change(s) in; 6MWTD = 6 Minute Walk Test Distance; QoL = Quality of Life; BODE = **B**ody-mass index, airflow **O**bstruction, **D**yspnea, and **E**xercise; y/yrs = years; RCT = Randomized Controlled Trial; COPD = Chronic Obstructive Pulmonary Disease; @ = at; pts = patients/participants; wk = week(s); HRQoL = Health Related Quality of Life; p-TBLD = post-Tuberculosis Lung Disease; PR = Pulmonary Rehabilitation; CCQ = Clinical COPD Questionnaire; MCID = Minimal Clinically Important Difference; ISWTD; Incremental Shuttle Walk Test Distance; CRD = Chronic Respiratory Disease; SIP = Sickness Impact Profile; AE = Aerobic Exercise; NE = No Exercise; DR = **D**iaphragmatic Inspiratory **R**esistive Breathing; CR = AE combined with DR; HAD = Hospital Anxiety and Depression scale; SD = Standard Deviation; PEFR = Peak Expiratory Flow Rate; CI=Confidence Interval; CRDQ=Chronic Respiratory Disease Questionnaire; FEV1 = Forced Expiratory Volume in one second; VC = Vital Capacity; FEV1/FVC = Forced Expiratory Volume in 1 second/Forced Vital Capacity ratio; FEF; Forced Expiratory Flow; FEF25 = Forced Expiratory Flow at 25% of FVC; FEF50 = Forced Expiratory Flow at 50% of FVC; FEF75 = Forced Expiratory Flow at 75% of FVC; FEF25-75 = Forced Expiratory Flow between 25-75% of FVC; PEF = Peak Expiratory Flow; IVC = Inspiratory Vital Capacity; MVV = Maximal Voluntary Ventilation; Fb = Breathing Frequency; VE = Minute Ventilation; VT = Tidal Volume

1. In de Grass et al paper, no data on measures of central tendency and variability were available for results summaries 1–6, while in Clarke et al paper, no data on measures of central tendency and variability were available for results summaries 1, 2, 5 and 6. Moreover, in Clarke et al, there were no explicit data on whether the improvements reported in results summaries 2, 3 and 4 were statistically significant or not. [↑](#footnote-ref-1)