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Review

Effect of respiratory muscle training in asthma: A systematic review and meta-analysis

Ana Lista-Paz[a,b,*], Lucía Bouza Cousillas[a], Cristina Jácome[c], Guilherme Fregonezi[d,e], Noé Labata-Lezaun[f,g], Luis Llurda-Almuzara[f,g], Albert Pérez-Bellmunt[f,g]

[a] University of A Coruña, Faculty of Physiotherapy, A Coruña, Spain
[b] Psychosocial and Functional Rehabilitation Intervention Research Group, The University of A Coruña, A Coruña, Spain
[c] Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto (FMUP), Porto, Portugal
[d] PneumoCardioVascular Lab/HUOL, Hospital Universitário Onofre Lopes, Empresa Brasileira de Serviços Hospitalares and Departamento de Fisioterapia Universidade Federal do Rio Grande do Norte, Natal, Brazil
[e] Laboratório de Inovação Tecnológica em Reabilitação, Departamento de Fisioterapia, Universidade Federal do Rio Grande do Norte, Natal, Brazil
[f] Faculty of Medicine and Health Sciences. Universitat Internacional de Catalunya (UIC-Barcelona), Spain
[g] ACTIUM Functional Anatomy Group. Barcelona, Spain

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ABSTRACT

Background: The last systematic review about respiratory muscle training (RMT) in people with asthma was published almost 10 years ago. Since then, several works have been published.
Objective: To review the effect of RMT in people with asthma.
Methods: We conducted a systematic review of research included up to September 2021 in PubMed/MEDLINE, PEDro, Scopus, Web of Science, CINAHL, LILACS, Cochrane Central Register of Controlled Trials and ClinicalTrials.gov. We included randomized controlled trials and quasi-experimental studies assessing the effect of RMT on respiratory muscle function, rescue medication, asthma-related symptoms, lung function, exercise capacity, healthcare use, health-related quality of life (HRQoL) and adverse effects in people with asthma. Risk of bias and methodological quality were assessed with the Cochrane Risk of Bias assessment tool and the PEDro scale. Meta-analysis was performed whenever possible; otherwise a qualitative approach was followed.
Results: Eleven studies (270 participants) were included, 10 with only adults and were included in the meta-analysis. Inspiratory muscle training (IMT) had beneficial effects on maximal inspiratory pressure (PImax: mean difference [MD] 21.95 cmH_2O [95% confidence interval [CI] 15.05; 28.85]), with no changes in maximal expiratory pressure (MD 14.97 cmH_2O [95%CI -5.65; 35.59]), lung function (forced expiratory volume in 1 sec: MD 0.06 [95%CI -0.14; 0.26] L; force vital capacity: MD 0.39 [95%CI -0.24; 1.02] L) and exercise capacity (standard mean difference [SMD] 1.73 [95%CI -0.61; 4.08]). Subgroup analysis revealed that IMT load >50% PImax and duration >6 weeks were beneficial for exercise capacity. The qualitative analysis suggested that IMT may have benefits on respiratory muscle endurance, rescue medication and exertional dyspnoea, with no adverse effects.
Conclusions: This systematic review and meta-analysis showed a significant increase in PImax after IMT in adults with asthma and reinforced the relevance of the dose–response principle of training. More evidence is needed to clarify the effect of IMT in respiratory muscle endurance, rescue medication, exercise capacity, healthcare use and HRQoL.
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Introduction

Asthma is one of the most prevalent chronic respiratory diseases worldwide [1,2]. It is considered a major social and health concern, being associated with a high economic burden, estimated at about 1% to 2% of the total sanitary costs in industrialized countries [3]. Asthma is characterized by chronic airway inflammation, defined by a history of respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough that vary over time and intensity, together with variable expiratory airflow limitation, which may later become persistent [4]. Along with these symptoms, some individuals with

* Corresponding author at: Faculty of Physiotherapy, The University of A Coruña, Campus Universitario de Oza, n°1, 15006, A Coruña, Spain.
E-mail address: ana.lista@udc.es (A. Lista-Paz).

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asthma can present respiratory muscle dysfunction [5,6]. The respiratory muscle dysfunction can be present both in the stable phase [7] and during exacerbations [8]. Increased airway resistance and hyperinflation may be responsible for the respiratory muscle disfunction because they help flatten the diaphragm, driving it to work in a disadvantageous force–length relation [9]. This diaphragm mechanical disadvantage can lead to increased work of inspiratory muscles, especially during exercise, when dynamic hyperinflation may occur, and to increased dyspnoea [5,10]. Also, some studies have shown that high doses of systemic corticosteroids used in people with asthma can cause muscle weakness or steroid-induced myopathy [11,12]. In addition, thoracoabdominal asynchrony during moderate exercise has been observed in individuals with mild stable asthma [13]. To identify respiratory muscle weakness, the assessment of maximal respiratory pressures is common in clinical practice because it is volitional and non-invasive [14]. Maximal inspiratory and expiratory pressures (PImax, PEmax) are considered reduced when the values are below 65% to 80% predicted [15].

Respiratory muscle disfunction needs to be considered in long-term management of asthma. According to the chronic care model and interdisciplinary perspective, comprehensive programs integrating education, breathing exercises and exercise training have been highlighted as adjuvant therapies to asthma pharmacological treatment [10,16-18]. However, respiratory muscle training (RMT) has not been routinely included in these programs. RMT has found effective in people with chronic obstructive pulmonary disease (COPD) [19,20] and in different populations with respiratory impairments [21,22]. However, in people with asthma, the effectiveness of RMT is still uncertain.

The last systematic review and meta-analysis on this topic was published in 2013. It included 5 randomized controlled trials (RCTs) that assessed the effect of inspiratory muscle training (IMT) in people with asthma, showing a significant increase in PImax [23]. However, even with this positive finding, the authors concluded not enough evidence to support the use of IMT in asthma. This conclusion was mainly related to the low methodologic quality of the individual studies. Furthermore, none of the studies reported results related to other relevant clinical outcomes, such as hospital admissions, exacerbations and inspiratory muscle endurance, and results were restricted to adults.

Given the growth in clinical interest of RMT in asthma and that recent works have been published, we considered that a new systematic review with a broader scope in terms of interventions and clinical outcomes was needed. Thus, this systematic review aimed primarily to analyse the effect of RMT in people with asthma regarding respiratory muscle strength and/or endurance and use of rescue medication. Secondary aims were the effect of RMT in 1) asthma-related symptoms and asthma control, 2) adherence to treatment, 3) lung function, 4) exercise capacity, 5) number of emergency department visits and number of hospital admissions, 6) health-related quality of life (HRQoL), and 7) adverse effects in people with asthma.

Methods

This systematic review and meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [24]. The protocol of this systematic review was published in the International Prospective Register of Systematic Reviews (PROSPERO-CRD42020221939).

Systematic literature search

We conducted a systematic literature search for studies included up to September 2021 in the electronic databases PubMed/MEDLINE, Physiotherapy Evidence Database (PEDro), Scopus, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Latin American and Caribbean Health Science Information Database (LILACS), Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov. Additional explorations were performed from weekly automatic updates retrieved from these databases. The electronic inspection was supplemented by a hand search of the reference lists of the included studies, key articles and previous systematic reviews on the topic.

Four domains (participants, intervention, outcomes and study design) were used for the search strategy. The main terms selected were 1) participants: asthma*OR bronchial spasm OR bronchoconstriction; 2) intervention: breathing exercises OR respiratory muscle training OR inspiratory muscle training OR expiratory muscle training; 3) outcomes: maximal respiratory pressures OR maximal voluntary ventilation OR dry powder inhalers OR metered dose inhalers OR rescue medication OR respiratory function test* OR exercise tolerance OR dyspnoea OR quality of life OR adverse effects; and 4) study design: the search strategy proposed by Cochrane [25] was used to include RCT and quasi-experimental studies. The general search strategy was then adapted to each specific database (Appendix A).

Selection criteria

This systematic review included RCTs and quasi-experimental studies with a sample of children and/or adults with asthma, regardless of the severity. Studies had to use an IMT and/or expiratory muscle training (IMT/EMT) program as a single intervention, defined as any intervention that applies an external load (inspiratory and/or expiratory) to the airways through an external device to improve respiratory muscle strength and/or endurance. The external load had to be based on PImax and/or PEmax [26]. Acceptable comparators were sham or simulated IMT/EMT, usual care (medication and/or education programs) or no intervention.

At least one of the following outcomes had to be reported in the primary articles to be included: respiratory muscle strength, respiratory muscle endurance, use of rescue medication, asthma-related symptoms and asthma control, adherence to treatment, lung function, exercise capacity, number of emergency department visits, number of hospital admissions, HRQoL and adverse effects.

We excluded articles with the following: 1) had participants with other chronic respiratory diseases and/or other comorbidities that could compromise the respiratory muscle strength (i.e., neuromuscular diseases, infection with severe acute respiratory syndrome coronavirus 2, among others); 2) had interventions combining RMT with other interventions (i.e., exercise training, yoga, Tai Chi, pulmonary rehabilitation, etc.); and 3) were written in other languages than English, Spanish, French, Portuguese or Italian. We also excluded book chapters, review articles, commentaries to articles, unpublished work, and study protocols.

Screening, selection process and data extraction

After removing duplicate studies, the articles were independently screened by 2 reviewers (ALP and LBC) to identify relevant works by the title and abstract, by using the Rayyan software (https://rayyan.qcri.org) [27]. In case of any disagreement, a third researcher (CJ) was consulted. The Cohen kappa coefficient (k) was calculated to assess inter-rater agreement [28]. The 2 reviewers (ALP and LBC) used a standardized form to independently extract data from each article, including the author's last name and year of publication, study design, sample size, participants and severity of asthma, interventions, outcomes, and results. The third author (CJ) was consulted in case of discrepancies.

Assessment of methodological quality and risk of bias

Risk of bias and methodological quality of the included trials were independently assessed by 2 authors (LLA and NLL) using the

Cochrane Risk of Bias (RoB2) assessment tool [29] and the Physiotherapy Evidence Database (PEDro) scale [30], respectively. We considered that the combination of these 2 tools would enrich the assessment of the methodological quality of the included studies. Any disagreements were resolved by discussion or with a third reviewer (APB). Inter-rater reliability was calculated with the Cohen kappa coefficient.

RoB2 is a widely accepted tool to evaluate the quality of an RCT in the biomedical field, proposed by the Cochrane Collaboration [29]. It divides quality assessment into 6 domains involving 8 items: 1) randomization sequence generation, 2) allocation concealment, 3) blinding participants, 4) blinding therapists, 5) blinding outcome assessors, 6) incomplete outcome data, 7) source of funding bias/selecting outcome reporting and 8) other bias. Each item is classified as low (green), unclear (yellow) or high (red) risk of bias [29].

The PEDro scale was especially designed to assess the quality of physiotherapy trials based on random allocation; concealed allocation; baseline between-group similarity; blinding of participants, therapists, and assessors; dropouts; intention-to-treat statistical analysis; between-group statistical comparison; point measures; and variability data. A PEDro score <4 is considered "poor"; 4 to 5 "fair"; 6 to 8 "good" and 9 to 10 "excellent" [30].

Finally, publication bias was assessed by visual inspection of funnel plots [25].

Data synthesis and analysis

Review Manager 5 (Cochrane Collaboration, Oxford, UK) was used for all statistical analyses. For all continuous outcomes, sample size, post-intervention means, and standard deviations (SDs) were extracted. For dichotomous outcomes, the number of events and sample size were extracted. If data were not reported in the paper, the authors were contacted by e-mail to obtain the necessary data to be included in the quantitative analysis.

The mean difference (MD) was used as the effect size if studies used the same tool to measure the outcome. The standard mean difference (SMD) was used as the effect size if studies used different tools to measure the outcome. All effect sizes are expressed with their 95% confidence interval (CI). The inverse of the variance (IV) statistical test was used for the quantitative analysis. A random-effects model was used in all analyses to determine the overall effect size because the number of included studies was small [31]. $p < 0.05$ was considered statistically significant.

Heterogeneity was evaluated by the I^2 statistic, classified as low, moderate, or high with I^2 <25%, 25–50%, and >50%, respectively [32,33]. With high heterogeneity (I^2 >50%), we performed a heterogeneity analysis using subgroups [34]. Subgroups were considered by age of the sample, publication year, region, intensity of the intervention (load ≤50% and >50% PImax) and total duration of the IMT program (≤6 and > 6 weeks). Next, a sensitivity analysis was performed to evaluate the consistency of the results. For this purpose, articles that were not RCTs, that were conference abstracts, or that had at least a "high risk" score in the RoB2 were not included.

Results

Study selection

The database search retrieved 1002 studies. After removing duplicate results, 329 articles were screened for relevant content. During title and abstract reading, 308 articles were excluded. Finally, 21 articles were selected for full-text screening. Two additional papers were included by a manual search and screening the reference lists of full-text articles. We excluded 12 articles for ineligibility and finally selected 11 studies for the qualitative analysis (Fig. 1). Because only one article included children [35], it was excluded from the meta-analysis. The Cohen k coefficient between the 2 reviewers showed almost perfect agreement (k =0.91, 95%CI 0.80; 1.00) [28].

Study characteristics

Details of the included studies are in Table 1. Any missing data is due to the absence of response from authors. The 11 works were published between 1992 and 2021, and 4 were conducted by the same research group in Israel, with different objectives [9,36-38]. Nine were RCTs [35–43] and 2 were quasi-experimental studies [9,44]. Nine were published as articles and 2 as conference abstracts [41,42].

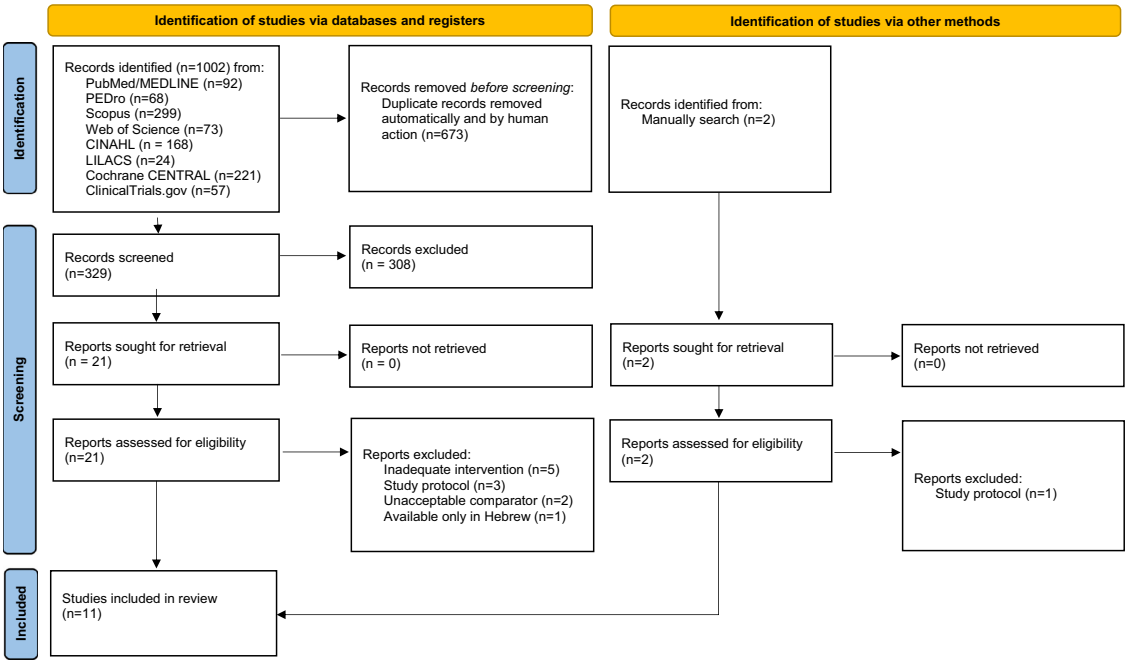

Fig. 1. Flow diagram of the literature search.

Table 1
Characteristics of included studies.

Author (y)	Design	Participants	Intervention	Outcomes measures	Findings
Weiner et al., 1992 [9]	Quasi experimental	Moderate to severe asthma IG n 15 M/F 9/6 Age 42.3 (7.6) y CG n 15 M/F 98/6 Age 38.7 (6.2) y	IG IMT Device: Threshold IMT® Load: 15% of PImax Progression: 15%-80% of PImax (measured every 2 months) Frequency: 30 min/day x 5/w Duration: 6 months CG Sham Same program with no resistance	Inspiratory muscle strength PImax Respiratory muscle endurance (P_mPeak/PImax) β_2-agonist consumption Severity of asthma symptoms: -Nighttime (scale 0-4) -Daytime (scale 0-4) -Cough (scale 0-4) Pulmonary function (FEV_1, FVC) Number of hospital/ emergency visits	IG PImax (cmH_2O): Pre 84 (4.3); Post 107 (4.8); $p <$ 0.0001 P_m Peak/PImax (%): Pre 68 (3); Post 93 (1); $p <$ 0.0001 Decrease in the β_2-agonist consumption ($p <$ 0.05) Improvement in nighttime asthma ($p <$ 0.05); morning tightness ($p <$ 0.05); daytime asthma ($p <$ 0.01); cough ($p <$ 0.005) FEV_1(%): Pre 57 (3); Post 65 (3); $p <$ 0.005 FVC (%): Pre 77 (3); Post 87 (3); $p <$ 0.005 Decrease the number of hospital/emergency visits ($p <$ 0.05) Decrease in sick-leave ($p <$ 0.05) CG No significant changes
McConnell et al., 1998 [5]	RCT	Mild to moderate asthma n 18 M/F 10/8 IG n 9 M/F 5/4 CG n 9 M/F 5/4	IG IMT Device: POWERBreathe® Load: 50% of PImax Repetitions and frequency: 30 rep x 2/day x 7/w Duration: 3 w CG Device: POWERBreathe® Load: 20% of PImax Repetitions and frequency: 60 rep x 2/day x 7/w Duration: 3 w	Respiratory muscle strength (PImax, PEmax) Exertional dyspnoea: modified Borg scale Pulmonary function (FEV_1, FVC, PEF)	IG PImax (cmH_2O): Pre 109; Post 121.7 (30.1); $p <$ 0.004 PEmax (cmH_2O): Post 152.8 (53.6) No changes in FEV_1 and FVC: FEV_1(L): Post 3.79 (0.63) FVC (L): Post 5.13 (0.91) PEF (L/min): Pre 510; Post 551 (84); $p <$ 0.05 Dyspnoea: 12% reduction; Post 2.12 (0.93) ($p <$ 0.006) CG No significant changes
Weiner et al., 2000 [36]	RCT	Mild, stable asthma (FEV_1 >80%) High β_2-agonist consumers (>1puff/day) n 23 M/F 15/8 Age 34 (2.8) y IG n 11 CG n 11	IG IMT Device: Threshold IMT® Load: 15% of PImax Progression: 15%-60% of PImax until 1 month (increases of 5-10% each session). 60% of PImax at 2-3 months (measured every week). Frequency: 30 min/day x 6/w Duration: 3 months CG Sham Same program with no resistance	Inspiratory muscle strength (PImax) β_2-agonist consumption during the last 4 w Dyspnoea: modified Borg scale (after a respiratory muscle endurance test) Pulmonary function (FEV_1, FVC)	IG PImax (cmH_2O): Pre 94.1 (5.1); Post 109.7 (5.2); $p <$ 0.005 β_2-agonist consumption (puffs/day): Pre 2.6 (0.4); Post 1.6 (0.4); $p <$ 0.001 Individual changes in Borg scores during breathing with resistance to create a P_m of 20 cmH_2O decreased significantly CG PImax (cmH_2O): Pre 97.6 (5.1); Post 98.1 (5.3); no significant differences β_2-agonist consumption (puffs/day): Pre 2.8 (0.3); Post 2.9 (0.4); p 0.17 No significant changes in Borg scores
Weiner et al., 2002 [38]	RCT	Mild to moderate asthma (FEV_1 >60%) Age 36.2 (3.1) y IG n 11 M/F 0/11 CG n 11 M/F 0/11	IG IMT Device: Threshold IMT® Load: 15% of PImax Progression: 15%-60% of PImax until 1 month (increases of 5-10% each session). 60% of PImax at 2-3 months (measured every week). Frequency: 30 min/day x 6/w Duration: until women reached a mean of PImax equal to male subjects (20 w)	Inspiratory muscle strength (PImax) β_2-agonist consumption Dyspnoea: modified Borg scale (after a respiratory muscle endurance test) Pulmonary function (FEV_1, FVC)	IG PImax (cmH_2O): Pre 73.1 (5.1); Post 103.9 (5.9); $p <$ 0.005 β_2-agonist consumption during the last 4 w (puffs/day): Pre 3.4 (0.6); Post 2.1 (0.5); $p <$ 0.001 Dyspnoea: decreased ($p <$ 0.05) No changes in FEV_1 CG PImax (cmH_2O): no significant differences No changes in FEV_1

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Table 1 (*Continued*)

Author (y)	Design	Participants	Intervention	Outcomes measures	Findings
			CG Sham Same program with no resistance		
Weiner et al., 2002 [37]	RCT	Mild to moderate asthma (FEV_1 >60%) IG n 15 M/F 9/6 Age 39.7 (5) y CG n 15 M/F 8/7 Age 37.1 (4.8) y	IG IMT Device: Threshold IMT® Load: 15% of PImax Progression: 15%-60% of PImax until 1 month (increases of 5-10% each session). 60% of PImax at 2-3 months (measured every week). Frequency: 30 min/day x 6/w Duration: until they reached and increased by greater than 20 cmH_2O over the baseline (16-26 w) CG Sham Same program with no resistance during 12 w	Inspiratory muscle strength (PImax) β_2-agonist consumption Dyspnoea: modified Borg scale (after a respiratory muscle endurance test) Pulmonary function (FEV_1, FVC)	IG PImax (cmH_2O): Pre 92.1 (5.6); Post 111.5 (6.2); $p < 0.005$ No changes in FEV_1 and FCV The increased in PImax was associated with a gradual decreased in the Borg score ($p < 0.001$) and in the β_2-agonist consumption ($p < 0.001$) CG PImax (cmH_2O): Pre 86.4 (5.31); Post 85.1 (5.4); no significant differences No changes in FEV_1 and FCV
Sampaio et al., 2002 [43]	RCT	Clinical diagnostic of asthma IG n 10 M/F 2/8 Age 21.4 (7) y CG n 10 M/F 2/8 Age 23.2 (4.8) y	IG 3 sessions of re-education breathing pattern + IMT Device: Threshold IMT® Load: 40% of PImax (adjusted every session) Frequency: 10 min x 3/w Duration: 6 w CG no intervention unless bronchial hygienic techniques were needed	Respiratory muscle strength (PImax, PEmax)	IC PImax (cmH_2O): Pre 58.5 (19.5); Post 78.7 (22.2); $p < 0.05$ PEmax (cmH_2O): Pre 51.2 (21.9); Post 72.8 (26.8); $p < 0.05$ GC No significant changes in PImax, PEmax PImax: Post 66.9 (21.5) PEmax: Post 59.3 (13.6)
RCT	Children from 8 to 12 years with uncontrolled asthma IG n 25 M/F 9/16 Age 9.6 (1.2) y CG n 25 M/F 7/18 Age 9.8 (1.2) y	IG IMT, breathing exercises, medical visits and educational program Device: Threshold IMT® Load: 40% of PImax Sets: 10 sets x 60 s (with 60 s of rest in between) during 20 min. Following by 5 min of uninterrupted training Frequency: 25 min/day x 2/w Duration: 7 w CG medical visits and educational program	Respiratory muscle strength (PImax, PEmax) Rescue medications Asthma related symptoms (frequent asthma attacks, diurnal and nocturnal symptoms and impaired ability to perform ADL) PEF Number of emergency department visits Number of hospital admissions	IG PImax (cmH_2O): Pre 48.32 (5.7); Post 109.92 (18); $p < 0.0001$ PEmax (cmH_2O): Pre 50.6 (6.5); Post 82.9 (17); $p < 0.0001$ Number of uses of rescue bronchodilator: Pre 25 Post 21 ($p < 0.0001$) PEF (L/min): Pre 173 (50.8); Post 312 (54.8); $p < 0.0001$ Emergency department visits (n): Pre 25; Post 3 Hospital admissions (n): Pre 25 Post 3 (p 0.17) CG PImax (cmH_2O): Pre 46.9 (4.7); Post 46.7 (4.1) PEmax (cmH_2O): Pre 49.2 (5.5); Post 49.6 (5.5) Rescue bronchodilator use: Pre 25 Post 4 PEF (L/min): Pre 188 (43.9); Post 208.8 (44.2) Emergency department visits (n): Pre 25; Post 8 Hospital admissions (n): Pre 25 Post 3	
Turner et al., 2011 [44]	Quasi experimental	Mild to moderate asthma (FEV_1 >70%) M/F 7/8 Age 24 (1) y IG n 7 CG n 8	IG IMT Device: POWERBreathe® Load: 50% of PImax Repetitions and frequency: 30 rep x 2/day x 7/w Duration: 6 w CG Device: POWERBreath® Load: 15% of PImax Repetitions and frequency: 30 rep x 1/day x 7/w	Inspiratory muscle strength (PImax) Exertional dyspnoea: modified Borg scale Adherence to treatment Maximal cardiopulmonary test (PPO, VO_{2peak}) Endurance cardiopulmonary test performed at 70% of PPO (Tlim) Pulmonary function (FEV_1, FVC, PEF)	IG PImax pre-exercise (cmH_2O): Pre 114.6 (10.1); Post 145.4 (11.7); $p < 0.05$ Borg score at the end of the Tlim: Pre 5.9 (0,8); Post 5.1 (0.9); $p < 0.05$ Compliance: 94% VO_2 (L/min): Pre 2.9 (0.3); Post 2.58 (0.24); $p < 0.05$ VCO_2 (L/min): Pre 3.04 (0.4); Post 2.7 (0.28); $p < 0.05$ Tlim (min): Pre 8.5 (0.9); Post 10.6 (1.5); $p < 0.05$ No changes in pulmonary function FEV_1(L): Pre 3.61 (0.22); Post 3.63 (0.21)

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Table 1 (*Continued*)

Author (y)	Design	Participants	Intervention	Outcomes measures	Findings
			Duration: 6 w		FVC(L): Pre 4.33 (0.26); Post 4.34 (0.25) PEF(L/min): Post 435 (25.3) CG PImax pre-exercise (cmH_2O): Pre 114.3 (10.3); Post 120.6 (9.2) Compliance: 92% No changes in Borg scale, VO_2, VCO_2, Tlim and pulmonary function
Delgado et al., 2014 [42]	RCT	Controlled asthma IG n 5 M/F Age CG n 5 M/F Age	IG IMT Device: POWERBreathe® Load: 50% of PImax Repetitions and frequency: 30 rep x 2/day x 5/w Duration: 6 w CG Device: POWERBreathe® Load: 15% of PImax Repetitions and frequency: 30 rep x 1/day x 5/w Duration: 6 w	Inspiratory muscle strength (PImax) Pulmonary function (FEV_1, FVC, PEF) Exercise capacity: 6MWT	IG PImax (cmH_2O): Pre 89.8 (24.2); Post 136.4 (22.5); $p < 0.05$ 6MWT (m): Pre 648.2 (96.1); Post 693.4 (77); $p < 0.05$ No changes in pulmonary function: FEV_1(L): Pre 3.5 (1); Post 3.4 (0.9) FVC(L): Pre 4.4 (1.4); Post 4.5 (1.5) PEF(L/min): Post 408 (72) CG PImax (cmH_2O): Pre 82.6 (28.6); Post 112.6 (15.5) 6MWT (m): Pre 599.8 (63.1); Post 626.3 (59); $p < 0.05$ FEV_1(L): Pre 2.8 (0.3); Post 2.6 (0.5) FVC(L): Pre 3.2 (0.5); Post 3.3 (0.8) PEF(L/min): Post 348 (78)
RCT	Mild to moderate asthma (FEV_1 >70%) IG n 20 M/F 6/14 Age 46.5 (13.4) y CG n 18 M/F 1/17 Age 42.7 (18.9) y	IG IMT, breathing exercises, and educational session Device: POWERBreateh® Load: 50% of PImax Repetitions and frequency: 30 rep x 2/day x 3/w Duration: 6 w CG Educational session	Respiratory muscle strength (PImax, PEmax) Dyspnoea: mMRC Perceived fatigue: Turkish version of FSS Adherence to treatment Pulmonary function (FEV_1, FVC) Exercise capacity: 6MWT HRQoL: SGRQ ADL: LCADL	IG PImax (cmH_2O): Pre 52 (32.6); Post 88.7 (42.8); $p < 0.001$ PEmax (cmH_2O): Pre 69 (42.1); Post 83.3 (41.5); p 0.149 mMRC: Pre 2.1 (0.9); Post 1.5 (0.5); $p < 0.001$ FSS: Pre 39 (12.9); Post31 (10.4); p 0.028 Compliance: 89% No changes in pulmonary function: FEV_1(L): Pre 2.89 (1.29); Post 2.65 (0.84) FVC(L): Pre 3.82 (1.82); Post 3.78 (1.2) 6MWT (m): Pre 445.7 (130.07) Post 503.5 (92.5); p 0.001 No changes in SGRQ: significant changes in symptoms score (p 0.34) LCADL: significant changes in physical activity score (p 0.045) and leisure score ($p < 0.001$) CG No significant changes Pre and Post in any outcomes: PImax (cmH_2O): Pre 43.84 (18.96); Post 40.17 (7.95) PEmax(cmH_2O): Pre 58.22 (30.89); Post 53.02 (24.67)
Lage et al., 2021 [40]	RCT	Non-smokers, controlled asthma IG n 20 M/F 6/14 Age 40.3 (13.4) y CG n 19	IG IMT and educational program Device: POWERBreathe K3® Load: ≥50% of PImax (adjusted weekly to a Borg score 4-6) Repetitions and frequency: 3 sets of 30 rep x 2/day x 5/w	Inspiratory muscle strength (PImax) Inspiratory muscle endurance test duration Adherence to treatment Pulmonary function (FEV_1, FVC, PEF) Number of hospital admissions after 6 months Number of episodes of exacerbation after 6 months	IG PImax (cmH_2O): Pre 76.5 (28.2); Post 118.05 (32.38); $p < 0.001$ Inspiratory endurance test (s): Pre 226.9 (31.4); Post 434.8 (40.2); $p < 0.001$ Compliance: 82% No changes in pulmonary function

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Table 1 (*Continued*)

Author (y)	Design	Participants	Intervention	Outcomes measures	Findings
		M/F 4/15 Age 42.3 (12.6) y	Duration: 8 w CG Educational program	Exercise capacity: ISWT HRQoL: AQLQ (S)	Hospital admissions (n): 0 Number of episodes of exacerbation (n): 5 ISWT (m): Pre 393.2 (26.7); Post 424 (25.9) AQLQ (S): Pre 5.2 (0.2); Post 5.9 (0.2); $p < 0.05$ CG PImax (cmH_2O): Pre 83.5 (32.5); Post 91.45 (35.16) Inspiratory endurance test (s): Pre 225.1 (33.2); Post 222.4 (41) No changes in pulmonary function Hospital admissions (n): 2 Number of episodes of exacerbation (n): 9 ISWT (m): Pre 320.6 (27.5); Post 312.5 (25.4) AQLQ (S): Pre 4.9 (0.2); Post 5.3 (0.2); $p < 0.05$

6MWT, 6-min walk test; ADL, activities of daily living; AQLQ (S), Standardized Asthma Quality of Life Questionnaire; CG, control group; cmH_2O, centimetres of water; F, female; FCV, forced vital capacity; FEV_1, forced expiratory volume in one second; FSS, fatigue severity scale; HRQoL, health-related quality of life; IG, intervention group; ISWT, incremental shuttle walking test; LCADL, London Chest Activity of Daily Living; M, male; mMRC, modified Medical Research Council; PEF, peak expiratory flow; PEmax, maximal expiratory pressure; PImax, maximal inspiratory pressure; Post, postintervention; Pre, preintervention; PPO, peak power output measured in watts; RCT, randomized controlled trial; rep, repetition; SGRQ, St George's Respiratory Questionnaire; Tlim, time to the limit to exercise tolerance; VO_{2peak}, w, week; y, years.

Additional details of the Delgado et al. [42] conference abstract were extracted from the master's thesis [45].

Participants

A total of 295 participants with asthma were included. However, 25 dropped out, so results for 270 participants were reported. Only Lima et al. [35] included children from 8 to 12 years old, and the other works included adults; 9 studies reported mean ages of 21.4 to 46.5 years [9,36-40,43,44].

Regarding asthma severity, 6 trials included participants with mild to moderate asthma [36-39,41,44] and one trial, moderate to severe asthma [9]. Lima et al. [35] included children with uncontrolled asthma, whereas Delgado et al. [42] and Lage et al. [40] included adults with controlled asthma. The mean (SD) baseline PImax in adults was 43.84 (18.96) to 114.6 (10.1) cmH_2O [9,36-44] and in children, 47.6 (5.2) cmH_2O [35].

Interventions

None of the included studies used an EMT program. For IMT, 10 studies used mechanical threshold loading devices [9,35-39,41-44], whereas Lage et al. [40] used an electronic tapered flow resistive loading device. All studies used a supervised IMT program, apart from McConnell et al. [41], in which this is not clearly stated and from whom we did not obtain additional information. Loads training ranged from 15% to 80% PImax in the studies conducted by Weiner et al., [9,36-38]. The remaining studies set the resistance from 40% to 50% PImax, with the progression based on the periodic re-assessment of the PImax. Only Lage et al. [40], added the modified Borg scale for that purpose. Some authors prescribed a fixed duration for the training (10 to 30 min per session) [9,35-38,43], whereas others prescribed based on the number of repetitions per session and number of daily sessions (from 60 to 90 repetitions, twice a day) [39-42,44]. The frequency of the sessions varied from 2 to 7 days per week and the length of the programs from 3 weeks to 6 months. Regarding the comparators, 7 studies conducted a sham intervention using the same device as for the training group, without resistance [9,36-38] or with a minimum load set at 15% [42,44] to 20% [41] PImax. The remaining control groups received an educational program [35,39,40] or bronchial hygienic techniques whenever needed [43]. Only Lima et al. [35] combined the respiratory muscle strengthening program with an inspiratory muscle endurance period of 5 min without rest.

Risk of bias

Results of the RoB2 tool summary and graph are shown in Appendix B and Fig. 2. Nine of the 11 reports had at least one "unclear risk" domain, and 5 reports had at least one "high risk" domain. Seven reports had issues with the reporting data and 8 with the allocation procedure. For the inter-rater reliability, the Cohen k coefficient was 0.81 [95% CI 0.69; 0.93]. No publication bias was identified by visual inspection of the funnel plots (Appendix C).

Methodological quality

The average score for the PEDro scale was 6.8/10, considered "good" methodological quality across the studies included in the systematic review (Table 2) [30]. The Cohen k coefficient was 0.86 [95%CI 0.76; 0.96].

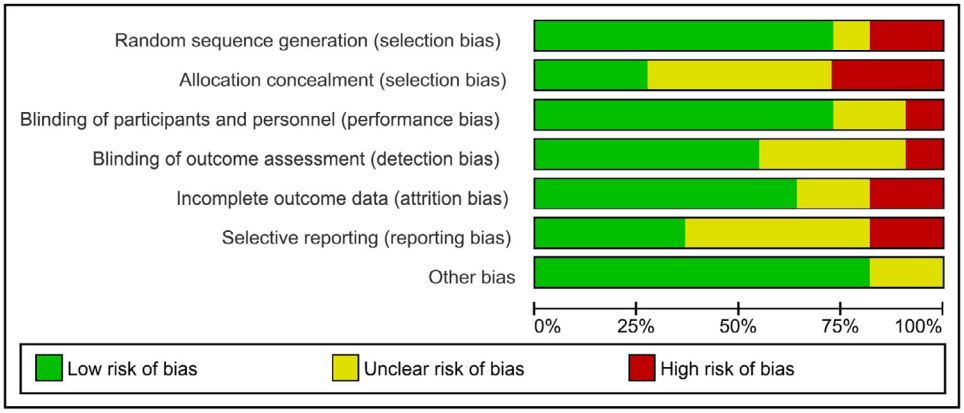

Fig. 2. Risk of bias graph.

Effect of interventions

Respiratory muscle strength and endurance

The PImax was reported for 9 studies [9,36,37,39-44]. Only Turner et al. [44] measured the PImax pre- and post-exercise, before and after IMT, so the results of pre-exercise measurements were selected for the meta-analysis to be comparable with the other studies. Fig. 3 shows the comparison between the IMT and control groups. The overall MD was 21.95 cmH_2O [95%CI 15.05; 28.85] and overall effect Z=6.23 ($p < 0.01$). Heterogeneity was considered high (I^2=85%). Subgroup analysis could not explain the heterogeneity (Appendix D, Table D.1). Moreover, when the quasi-experimental studies were removed [9,44], the MD was 20.10 cmH_2O [95%CI 10.13; 30.07] (Appendix E, Table E.1). The complete sensitivity analysis gave no relevant differences when excluding conference abstracts and articles with a "high risk" of bias (Appendix E, Table E.1).

The PEmax was assessed in 3 studies [39,41,43]. Fig. 4 shows the comparison between the IMT and control groups related to PEmax. The overall MD was 14.97 cmH_2O [95%CI -5.65; 35.59] and overall effect Z=1.42 (p = 0.15). The heterogeneity was moderate (I^2=43%). Sensitivity analysis gave no relevant differences when excluding the articles with "high risk" of bias (Appendix E, Table E.2).

The endurance of respiratory muscles was assessed in only 2 studies [9,40] using different approaches, so a meta-analysis was not possible. Weiner et al. [9] reported a significant increase in peak pressure (from mean [SD] 68% [3] to 93% [1]; $p < 0.0001$), defined as the pressure achieved with the heaviest load for at least 60 sec. Lage et al. [40] found a significant increase in endurance of respiratory muscles at a constant load of 50% to 60% of baseline PImax (from mean 226.9 [31.4] to 434.8 [40.2] sec; $p < 0.001$).

Use of rescue medication

Four studies from the same research group presented data on the effect of IMT on the use of rescue medication (puffs/day) in adults with asthma [9,36-38], but a meta-analysis was not possible because of missing data. Three studies found a significant decrease in β2-agonist consumption in the IMT group and no significant changes in the control groups [9,36,38]. The same pattern was observed in children [35].

Asthma-related symptoms and asthma control

Nine studies evaluated at least one asthma-related symptom [9,35-41,44]. Given the high variability in the reported outcomes, a meta-analysis was not possible. Weiner et al. [9] observed a significant improvement in asthma symptoms after IMT, and Lima et al. [35] observed significant differences between groups regarding the severity of asthma symptoms in children. Lage et al. [40] counted the number of exacerbations after 6 months of IMT, but no correlation was found.

Five studies evaluated the exertional dyspnoea using the modified Borg scale [36-38,41,44]. Two studies observed a significant reduction in exertional dyspnoea after IMT [41,44]. Three works showed a significant association between increased PImax and decreased dyspnoea [36–38]. Duruturk et al. [39] measured the perception of dyspnoea using the modified Medical Research Council scale, describing a significant decrease after IMT. Furthermore, the authors assessed perceived fatigue using the Fatigue Severity Scale, showing a significant decrease only in the IMT group, with significant differences between groups. No scales or other tools were used in the included articles to assess asthma control.

Adherence to treatment

Adherence to treatment was not objectively measured in any of the studies. Yet, 3 studies reported compliance with IMT as an indirect indicator of the adherence, which ranged from 82% to 94% [39,40,44].

Lung function

Five studies assessed lung function [39-42,44]. Fig. 5 shows the comparison between IMT and the control groups related to forced expiratory volume in 1 sec (FEV_1), forced vital capacity (FVC) and peak expiratory flow (PEF). No significant differences were found in any of the parameters. Sensitivity analysis revealed no relevant differences for FEV_1 and PEF (Appendix E, Tables E.3 and E.4). Regarding FVC, heterogeneity was high (I^2=68%). Subgroup analysis dividing the studies by region and age of publication reduced the heterogeneity (Appendix D, Table D.2). For FVC, we found significant differences in favour of IMT when eliminating quasi-experimental articles (MD 0.69 L [95%CI 0.21; 1.16]; I^2=0%) or those with a "high risk" of bias (MD 0.75 L [95%CI 0.18; 1.32]; I^2=0%) (Appendix E, Table E.5).

Exercise capacity

Exercise capacity was reported in 2 studies as meters walked during the 6-min walk test (6MWT) [39,42] and in one study as meters walked during the incremental shuttle walk test (ISWT) [40] (Fig. 6). The analysis showed no significant differences between groups in walking tests. The heterogeneity was high (I^2=93%). Subgroup analysis dividing the studies by the intensity and duration of the IMT program reduced the heterogeneity and showed statistical differences in studies with load > 50% PImax and duration > 6 weeks (Appendix D, Table D.3). Sensitivity analysis showed no relevant differences (Appendix E, Table E.6).

Table 2
PEDro scale.

Study	Eligibility criteria	Random allocation	Concealed allocation	Baseline similarity	Blind subjects	Blind therapists	Blind assessors	Less than 15 % dropouts	Intention-to-treat analysis	Between- group comparisons	Point measures and variability	Total*
Weiner, 1992 [9]	0	0	0	1	1	1	0	1	0	1	1	6
McConnell, 1998 [5]	1	1	0	1	1	0	0	0	0	1	1	5
Weiner, 2000 [36]	1	1	0	1	1	1	1	1	0	1	1	8
Weiner, 2002 [38]	1	1	0	1	1	1	1	1	0	1	1	8
Weiner, 2002 [37]	1	1	0	1	1	1	0	1	0	1	1	7
Sampaio, 2002 [43]	1	1	0	1	0	0	0	1	0	1	1	5
Lima, 2008 [35]	1	1	0	1	0	0	0	1	0	1	1	5
Turner, 2011 [44]	0	0	0	1	1	1	0	1	0	1	1	6
Delgado, 2014 [42]	1	1	1	1	1	1	1	1	0	1	1	9
Dururturk, 2018 [39]	1	1	1	1	1	0	1	1	0	1	1	8
Lage, 2021 [40]	1	1	1	1	0	1	0	1	1	1	1	8
Average												6.8

* Item 1 is not used to calculate the PEDro score

Number of emergency department visits and hospital admissions

Only 3 studies reported these outcomes [9,35,40], showing a significant decrease in number of hospital admissions after IMT in one study [9].

Health-related quality of life

Only 2 studies reported HRQoL outcomes using 2 distinct instruments [39,40]. In Duruturk et al. [39], only the symptom score of the St George's Respiratory Questionnaire was significantly lower than in the control group after the intervention. Lage et al. [40] found significant differences pre- and post-intervention in the Standardised Asthma Quality of Life Questionnaire in both groups but not between groups.

Adverse effects

Only 2 studies reported no adverse effects after IMT [39,40].

Discussion

This systematic review and meta-analysis showed that an IMT program is an effective intervention to improve inspiratory muscle strength in people with asthma and suggests that it may have a positive effect on respiratory muscle endurance, the use of rescue medication and exertional dyspnoea, with no adverse effects. IMT did not improve expiratory muscle strength or lung function, and the results are inconclusive regarding the benefits for exercise capacity, hospital admissions and HRQoL.

As compared with the review published in 2013 [23], the current systematic review included more than double the number of participants analysed (n=270 vs n=103), added 6 studies, incorporated different subgroup analysis (e.g., IMT intensity, duration of the IMT program, study design, etc.) and also included more outcomes, such as respiratory muscle endurance, exercise capacity and HRQoL. Although the present systematic review sought to evaluate the effectiveness of both IMT and EMT, none of the included studies used EMT alone or combined with IMT. A systematic review of people with COPD found higher PImax and PEmax in the EMT than control group, and these differences were larger with IMT and EMT combined. Furthermore, weakness in expiratory muscles was correlated with more exacerbations, hospital admissions and mortality [46]. In that sense, we believe that future studies are needed to explore the possible benefits of EMT combined with IMT in asthma.

Clearly, IMT can lead to a significant increase in PImax in adults with asthma (21.95 cmH_2O [95%CI 15.05; 28.85]) as compared with no intervention, sham or educational programs. Data from Lima et al. [35] was not introduced in the meta-analysis given that it was the only study involving children. Only one study did not find differences between the intervention and control groups [41]. In that study, the control group followed the same protocol as the intervention group but with a load of 20% PImax, whereas the remaining studies selected a sham protocol with lower loads [9,36-38], either without load or load set at 15% PImax [42,44]. Most of the studies implemented sham-IMT in chronic respiratory diseases using a training load ≤15% PImax, which does not generate changes in strength [10]. Thus, we believe that a load of 20% PImax was probably enough to increase the inspiratory muscle strength in the control group [41].

Although the minimal clinical important difference (MCID) for PImax in asthma is still unknown, the results of this meta-analysis may be clinically meaningful considering the recently stablished MCID for PImax in people with COPD, set at 17.2 cmH_2O [47]. We found a change above the MCID for COPD in the meta-analysis of people with asthma (21.95 cmH_2O [95%CI 15.05; 28.85]). As expected, results of the meta-analysis did not show significant changes in the PEmax, which agrees with the specificity principle of IMT [48].

Respiratory muscle endurance was assessed in only 2 studies, with positive results but using 2 different assessment methods

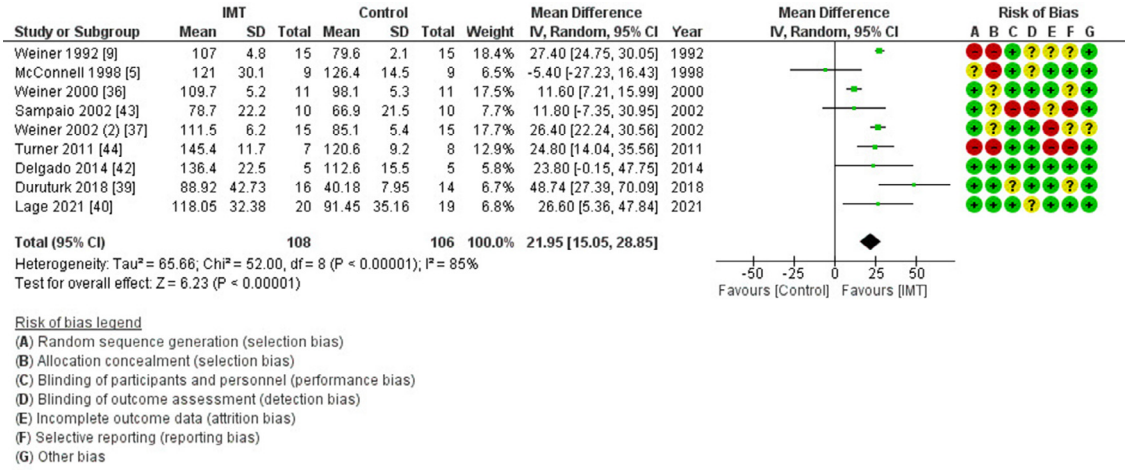

Fig. 3. Comparison of maximal inspiratory pressure (PImax) (cmH_2O) between inspiratory muscle training (IMT) and control groups. CI: confidence interval; I^2: heterogeneity statistic; IV: inverse variance

[9,40]. The results were in line with findings observed in COPD after IMT [49]. Even with respiratory muscle pressures being the most common measurements in clinical practise for assessing respiratory muscle function, the importance of their endurance component is remarkable, given their role in enabling ventilation and gas exchange during physical activities and its implications during activities of daily living [50]. An additional measurement of respiratory muscle endurance can be valuable to further understand the effectiveness of RMT. People with asthma would be more able to deal with the ventilatory demands of the daily life if they can breathe longer through a threshold. Thus, we believe that future studies should also include the assessment of respiratory muscle endurance.

Another important finding of this systematic review is the association between IMT and reduced use of rescue medication, reported in 4 trials of adults [9,36-38] and one trial of children [35]. Clinically, this is relevant because the excessive short-acting β2-agonist consumption (≥3 inhalers/year) can be harmful, related to more severe asthma exacerbations and increased risk of asthma-related deaths [4]. The use of short-acting β2-agonists is directly related to the perceived dyspnoea, which was decreased (both during activities of daily living and exertional dyspnoea) after IMT in all studies that considered this outcome [36-39,41,44]. Given that one of the long-term goals of asthma therapeutic interventions is symptom control, this is an achievement to consider [4]. The stronger hypothesis behind the decrease in perceived dyspnoea after IMT in asthma is a possible positive effect in the dynamic hyperinflation, allowing the diaphragm to work in a more advantageous force–length relationship and allowing for the generation of a given pressure with less respiratory motor drive [10]. People with different levels of pulmonary obstruction have less dyspnoea when they have higher PImax [51]. Regarding the impact on asthma control, number of emergency department visits and number of hospital admissions, the evidence is scarce. Only 3 of the included articles took this outcome into account [9,35,40], showing a trend to a positive effect, decreasing the number of hospitalizations after IMT. Although Lima et al. [35] did not find significant differences between the intervention and the control group, the number of hospitalizations after 3 months of IMT decreased from 25 to 3. Variables other than the number of hospitalizations and emergency department visits could be considered in future studies for a deeper knowledge of the impact of IMT in the health system, such as the severity of exacerbations, number of unscheduled medical appointments and number of days hospitalized. Additionally, analysing adherence to an IMT program more objectively would be advisable, especially when it includes unsupervised sessions. In this regard, only 3 studies indirectly considered adherence to treatment, ranging from 82% to 94% [39,40,44].

Regarding the impact of all these results on HRQoL, the evidence is scarce, so conclusions cannot be drawn at this time.

Pulmonary function results were pooled in this meta-analysis, with no significant differences in FVC, FEV_1 and PEF found, which agrees with the previous systematic review [23]. Concerning FVC, when the Turner et al. [44] study was removed in the sensitivity

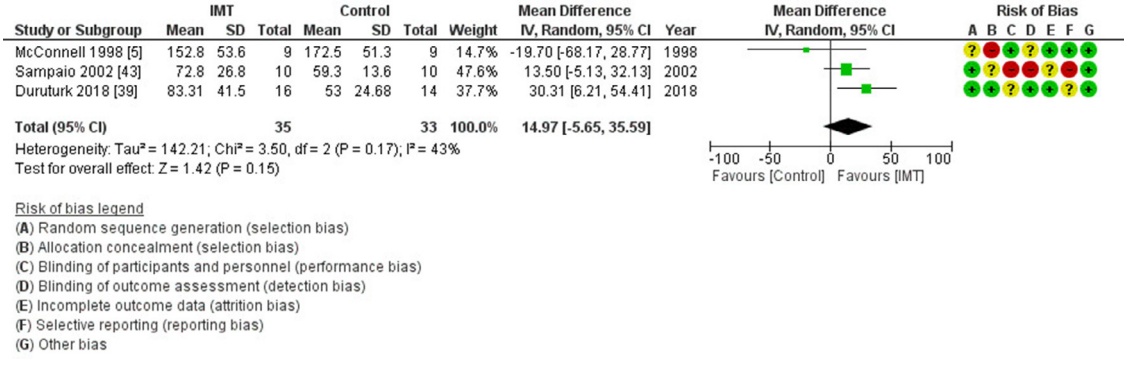

Fig. 4. Comparison of maximal inspiratory pressure (PEmax) (cmH_2O) between IMT and control groups. CI: confidence interval; I^2: heterogeneity statistic; IMT: inspiratory muscle training; IV: inverse variance

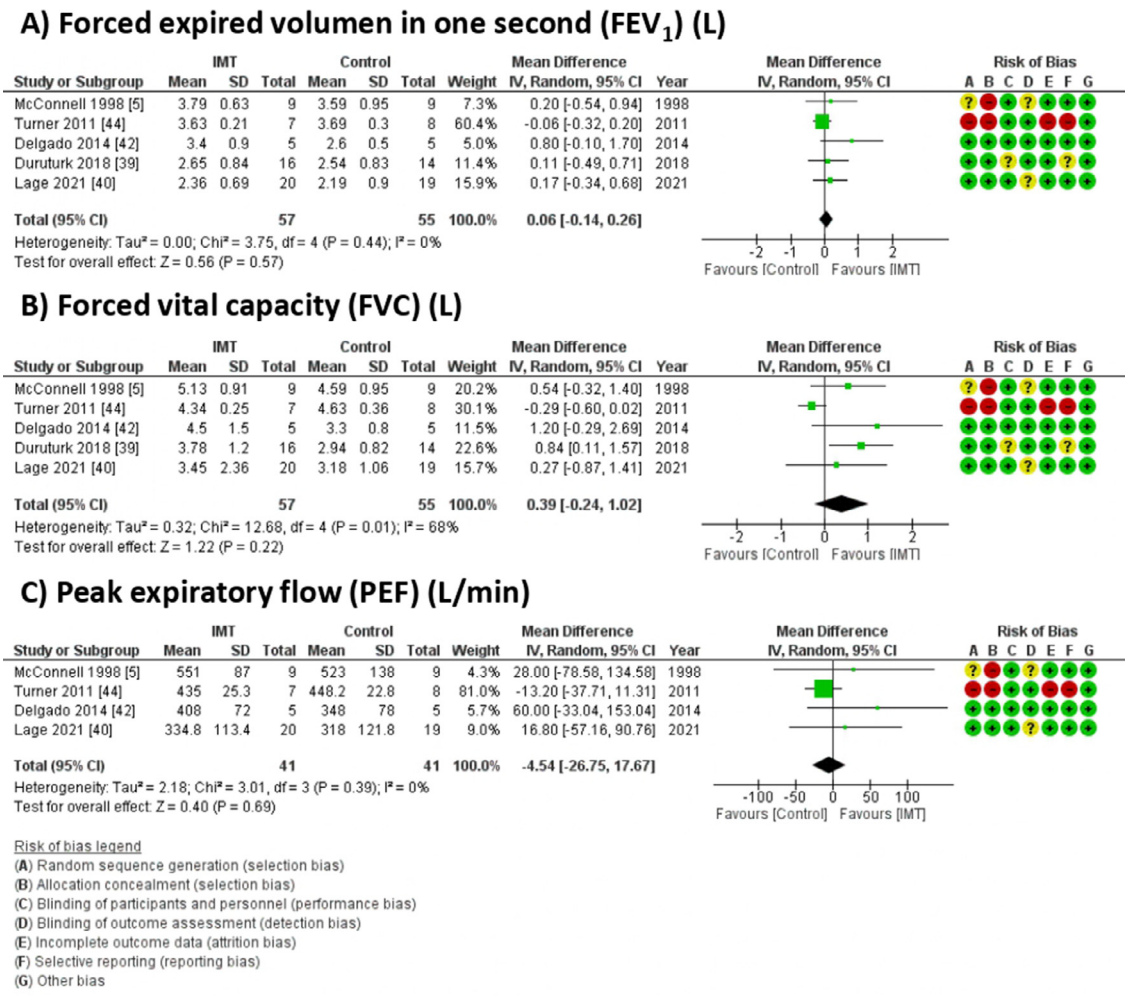

Fig. 5. Comparison of forced expiratory volume in 1 sec (FEV_1) (L), forced vital capacity (FVC) (L) and peak expiratory flow (PEF) (L/min) between IMT and control groups. CI: confidence interval; I^2: heterogeneity statistic; IMT: inspiratory muscle training; IV: inverse variance

analysis, the heterogeneity was 0% and the results showed significant differences between the IMT and control group, with MD 0.69 [95%CI 0.21; 1.16]. This was the only quasi-experimental study among the 5 assessing FVC [39-42,44]. Additionally, it was the study with the younger participants (mean age 24 [1] years) and higher baseline data for FVC, showing both groups, before and after the intervention, with > 95% predicted FVC. When subgroup sensitivity analysis was performed excluding one study with "high risk" of bias [41], the heterogeneity was 0% and the results also showed significant differences between the IMT and control group, with MD 0.75 L [95%CI 0.18; 1.32]. In that case, the age of the sample is unknown. Another factor that could influence the results of IMT in FVC is the lung volume used during the training program [52,53]. However, this information was missing in all the included studies. Only Turner et al. [44], mentioned that each breath was performed from residual lung volume. Therefore, from these results, we cannot conclude that IMT

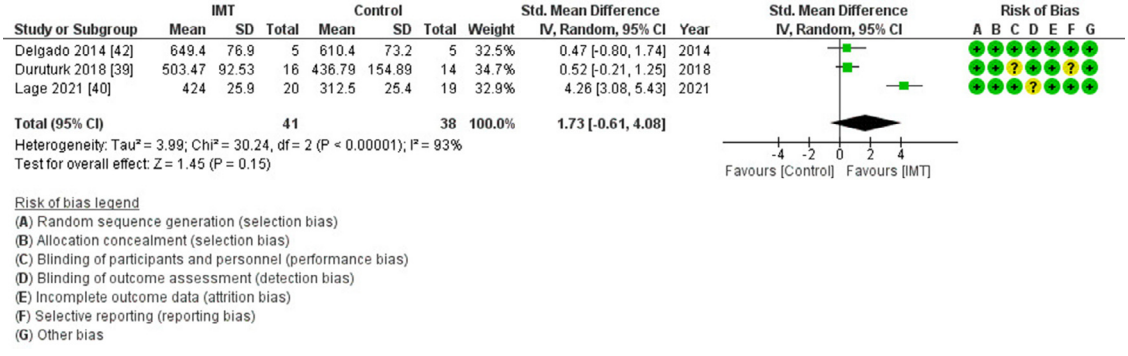

Fig. 6. Comparison of exercise capacity (meters) between IMT and control groups. CI: confidence interval; I^2: heterogeneity statistic; IMT: inspiratory muscle training; IV: inverse variance

can affect FVC in people with asthma, but future studies with a more defined IMT protocol, especially regarding the lung volume required, could help clarify this finding.

In terms of exercise capacity, results of the meta-analysis showed no significant differences between groups after IMT. In agreement with other studies, in people with COPD [49], no changes were found in 6MWT between IMT and the sham-control group. Nevertheless, the heterogeneity of this meta-analysis was high (I^2=93%). On subgroup analysis, taking into account the intensity and total duration of the IMT program, the group with higher load (>50% PImax) and longer duration (> 6 weeks), only in the Lage et al. [40] study, showed significant results in favor of IMT [54]. These results reinforce the relevance of the dose−response principle of training, found for IMT in other populations, such as people with stroke [55]. Lage et al. [40] used meters walked during the ISWT, whereas the remaining articles used the 6MWT [39,42]. Duruturk et al. [39] found significant differences between groups after IMT, with a difference between pre- and post-intervention in the IMT of 57.8 m, which is larger than the MCID known for COPD, set at 25 to 30 m [56]. However, Delgado et al. [42] did not offer an intergroup analysis, outlining also a significant difference of 26.5 m between pre- and post-intervention results in the IMT group. Of note, a more sensitive outcome should be used to assess the effects of IMT in exercise capacity, such as a cycling test [49]. In this regard, Turner et al. [44] found a significant increase of 22% in time to the limit of exercise tolerance after IMT but no significant changes in the sham group. Furthermore, the IMT group showed a significant decrease in oxygen consumption (VO_2), with no changes in the control group. This reduction in the whole-body oxygen consumption could be influenced by a reduction in metabolic respiratory muscles [10]. In healthy individuals, the oxygen consumption required by respiratory muscles during high intensity exercises is about 2% to 10% in people with respiratory diseases, but these requirements can increase to 35% to 40% of total oxygen consumption during a cycle test [57].

Strengths and limitations

More than 8 years has passed since the last systematic review and meta-analysis on the effectiveness of RMT in asthma [23], which revealed a need for a new evidence summary in this topic. This work was reported rigorously according to the PRISMA guidelines [24]. The scope of the previous systematic review was extended considering the effect of both IMT and EMT programs in asthma, looking at new outcomes, such as respiratory muscle endurance, exercise capacity or HRQoL. Moreover, we could perform subgroup analyses in terms of different characteristics of the studies, sample and interventions but not in the previous systematic review because of only 5 trials included [23]. Because of the broad range of outcomes considered in this review, it is more clinically applicable and at the same time highlights what should be addressed in further studies with improved methodological quality.

However, this study has some limitations. First, because of some missing data in the included studies, they could not be pooled in the meta-analysis because of lack of response from the authors [9,35-38,41,44]. Second, we found high variability regarding the protocols used for the IMT programs, especially in external load, ranging from 15% to 80% PImax. This was the main reason why a subgroup heterogeneity analysis was performed taking into account the threshold of 50 cmH_2O. Also, the variability of baseline PImax was wide in adults, ranging from a mean of 43.84 (18.96) to 114.6 (10.1) cmH_2O. This variability, together with differences in characteristics of the participants, the state of disease progression, time elapsed between the studies and the assessment protocols, contributed to high heterogeneity among studies, particularly for the variables PImax, FVC and exercise capacity. In addition, the strategy followed to explore heterogeneity by subgroup analysis may be limited by the low number of articles in each of the subgroups, so findings should be interpreted with caution. Moreover, although funnel plots did not reveal any publication bias, no meta-analysis exceeded 10 studies, so these results should be interpreted with caution [25]. Third, given the scarcity of primary data, we could not cover all of the objectives of this work, even when investigating EMT and IMT effectiveness in asthma: we found no trials using EMT or IMT and EMT combined. Only one work included children [35]. Consequently, the results could not be extrapolated to this population. Most of the included studies selected participants with mild to moderate asthma, so the effectiveness of this intervention in people with moderate to severe asthma is still unknown. Finally, some of the outcomes of interest were rarely examined in the primary studies, so conclusions based on a high level of evidence, for example, for respiratory muscle endurance, asthma control, adherence to treatment, number of emergency department visits, number of hospital admissions and HRQoL, could not be extracted.

Conclusions

This systematic review showed a significant increase in inspiratory muscle strength after an IMT program in adults with asthma, with no changes in expiratory muscle strength and lung function. Additionally, our review reinforces the relevance of the dose−response principle of training and that this intervention may decrease the use of rescue medication and the perceived dyspnea. In the short run, IMT effects in respiratory muscle endurance, exercise capacity, hospital admissions, and HRQoL could be clarified. Furthermore, future studies need to explore the effectiveness of EMT programs alone (or combined with IMT) as well as children/adolescents with different asthma severity.

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Declaration of Competing Interest

None declared.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.rehab.2022.101691.

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