



SYSTEMATIC REVIEW

Effects of physical therapy on lung function in children with asthma: a systematic review and meta-analysis

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BACKGROUND: Asthma is a common chronic respiratory disease in children. In addition to medications, physical therapy is considered as a treatment strategy for asthma. We conducted this study to investigate the effects of physical therapy on lung function in children with asthma.

METHODS: Three databases were searched. We conducted the meta-analysis for the forced expiratory volume in the first second in percent predicted values [FEV1(%pred)], the forced vital capacity in percent predicted values [FVC(%pred)], and the peak expiratory flow in percent predicted values [PEF(%pred)] by using a random effect model.

RESULTS: Of the 6474 identified studies, 18 studies (16 in physical training, 2 in breathing exercise or inspiratory muscle training) were included in the systematic review and 11 studies (all in physical training) were included in the meta-analysis. The meta-analysis showed a significantly improved FVC(%pred) in the experimental group.

CONCLUSIONS: Physical training improved FVC(%pred) significantly in children with asthma. Further study is needed, especially on the effects of breathing exercise and inspiratory muscle training in children with asthma.

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IMPACT:

- Our study reviewed the physical therapies for children with asthma and clarified whether and how these therapies affect them.
- Our study found that physical training improved the forced vital capacity in percent predicted values [FVC(%pred)] significantly in asthmatic children.
- Our study provided evidence that physical training could improve lung function in children with asthma, which is not identical to the Global Initiative for Asthma (GINA) guidelines.

INTRODUCTION

Asthma is a common chronic respiratory disease seriously affecting patients' life quality and quantity.¹ As estimated by the Global Initiative for Asthma (GINA), there are 300 million people affected by asthma worldwide, leading to a great burden on the healthcare system and a huge economic loss.² However, the etiology of asthma is not totally clear although some environmental risk factors, including allergen exposure, smoking exposure as well as air pollution exposure, and genetic risk factors, such as GATA binding protein 3 and Fc fragment of IgE receptor 1b, have been reported.³ Patients with asthma present symptoms with wheezing, cough, shortness of breath, and chest tightness resulting from airway hyperresponsiveness and airway remodeling.⁴ Acute exacerbation may pose a threat to the patient's life, and they may need to be hospitalized as soon as possible.⁵

Asthma care is comprehensive, involving patient's assessment, strategies' adjustment, and treatments' review.⁶ Pharmacologic therapy has been widely regarded as an important component of asthma treatment.⁷ Medications include control agents and relief

agents, aiming to prevent or relieve asthma exacerbations, respectively.⁸ Besides, different types of physical therapy are considered as a part of asthma treatment due to the general health benefits.⁹ Physical training, breathing exercise, and inspiratory muscle training (IMT) are the three most relevant physical therapies for asthma.¹⁰

As reported, physical training is beneficial to physical and psychosocial health in healthy people.¹¹ In asthmatic patients, it may improve their lung function by strengthening respiratory muscles, reducing airway inflammation, and increasing bronchioles' patency.¹² Breathing exercise can be performed in various forms such as the Papworth method and the Buteyko breathing technique,¹³ aiming to adapt asthmatic patients to an appropriate breathing pattern with a longer expiration and a lower respiratory rate, and thereby reduce hyperventilation and hyperinflation.¹⁴ There are three types of IMT, including normocapnic hyperpnea, flow-resistive loading, and pressure threshold loading.¹⁵ IMT is performed with a technique that can improve the strength and endurance of the diaphragm and the accessory inspiratory muscles.¹⁶

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Although there are some published system review and meta-analysis evaluating the effects of physical therapy on patients with asthma, they did not exclude adults.^{10,17,18} Although some excluded adults, they involved only one type of physical therapy.^{19,20} Thus we performed this systematic review and meta-analysis focusing on children only and involving at least one of the three most relevant physical therapies, namely, physical training, breathing exercise, and IMT. Our aims were to demonstrate the effects of physical therapy on lung function in children with asthma and provide evidence-based information for doctors on the choice of physical therapy for asthmatic children.

METHODS

This system review and meta-analysis was registered at the international prospective register of systematic reviews, and the registration number is CRD42019121627. The study protocol has been published previously,²¹ and we reported this systematic review and meta-analysis in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.²² No ethical approval was required for this study because there was no direct involvement of humans.

Search strategy

We searched three main databases from their inception to 30 November, 2018: PubMed, Embase, and the Cochrane Library. The search strategy in PubMed is described in Table 1. The same search strategy was used in Embase and the Cochrane Library based on different specific requirements. We also scanned the reference lists of studies and relevant systematic reviews for additional trials.

Selection criteria

We regarded studies as eligible for inclusion if they met the following criteria:

1. Randomized controlled trials (RCTs) published in English.
2. The study population included had to meet the age <18 years and the diagnosis as asthma by clearly defined or internationally recognized criteria.

3. Apart from the treatment for the control group, at least one of the three most relevant physical therapies, which are physical training, breathing exercise, and IMT, should be applied to the experimental group with a minimum duration of 2 weeks.
4. The study had to report lung function at the end of the intervention period: peak expiratory flow (PEF), forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC, and forced expiratory flow (FEF) in percent predicted values or absolute values.

Studies were excluded if it did not meet the inclusion criteria. Study selection was performed by two authors independently. We first reviewed the titles and abstracts of the papers, and the studies that were considered eligible were retrieved for full-text assessment. Any difference of opinion between the two authors was consulted with a third author.

Data extraction

Data were extracted from each selected study by two authors independently, including general information of the study (author, year, country), population information (number completed, age range (mean)), intervention (the type of physical therapy, duration), and outcomes reported (lung function). When extraction was finished, data were checked with each other by the two authors and the disputes were solved with the help of a third author.

Risk of bias assessment

The methodological quality of each included study was measured independently by two authors according to the Cochrane Collaboration’s tool.²³ The following contents were evaluated: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.²³ Each domain was judged to a high level, low level, or an unclear level.²³ Any disagreements were solved by discussion or with the help of a third author.

Statistical analysis

Based on the selection criteria, the experimental group was treated with the therapies for the control group plus physical

Table 1. Search strategy in PubMed.

Search	Query
1	"Asthma"[Mesh] OR asthma*[Title/Abstract]
2	"Child"[Mesh] OR children[Title/Abstract] OR school age[Title/Abstract] OR "Adolescent"[Mesh] OR adolescen*[Title/Abstract] OR teen*[Title/Abstract] OR youth*[Title/Abstract]
3	#1 AND #2
4	physiotherapy[Title/Abstract] OR physical therapy[Title/Abstract] OR physical intervention[Title/Abstract] OR physical rehabilitation[Title/Abstract] OR pulmonary therapy[Title/Abstract] OR pulmonary intervention[Title/Abstract] OR pulmonary rehabilitation[Title/Abstract] OR respiratory therapy[Title/Abstract] OR respiratory intervention[Title/Abstract] OR respiratory rehabilitation[Title/Abstract]
5	(breath*[Title/Abstract]) AND (exercise*[Title/Abstract] OR train*[Title/Abstract] OR retrain*[Title/Abstract] OR educat*[Title/Abstract] OR reeducat*[Title/Abstract] OR physiotherap*[Title/Abstract] OR physical therap*[Title/Abstract] OR respiratory therap*[Title/Abstract] OR buteyko[Title/Abstract])
6	IMT[Title/Abstract] OR inspiratory muscle train*[Title/Abstract] OR inspiratory muscle strength[Title/Abstract] OR inspiratory muscle endurance[Title/Abstract] OR respiratory muscle train*[Title/Abstract] OR respiratory muscle strength[Title/Abstract] OR respiratory muscle endurance[Title/Abstract]
7	physical training[Title/Abstract] OR physical activity[Title/Abstract] OR rehabilitat*[Title/Abstract] OR exercis*[Title/Abstract] OR fitness*[Title/Abstract] OR train*[Title/Abstract] OR aerobic[Title/Abstract] OR swim*[Title/Abstract] OR bik*[Title/Abstract] OR joy*[Title/Abstract] OR walk*[Title/Abstract] OR run*[Title/Abstract] OR sport*[Title/Abstract] OR danc*[Title/Abstract] OR motor[Title/Abstract]
8	#4 OR #5 OR #6 OR #7
9	(((((randomized controlled trial [pt]) OR controlled clinical trial [pt]) OR randomized [tiab]) OR placebo [tiab]) OR groups [tiab]) OR randomly [tiab]) OR trial [tiab])
10	#3 AND #8 AND #9

therapy in all included studies, meaning that the physical therapy was compared with no physical therapy. Studies reporting one of the following outcomes were included in the meta-analysis: the peak expiratory flow in percent predicted values [PEF(%pred)], the forced expiratory volume in the first second in percent predicted values [FEV1(%pred)], or the forced vital capacity in percent predicted values [FVC(%pred)]. Studies with a statistically significant difference at baseline between groups were excluded in the meta-analysis. We used the Revman Manager 5.3 to manage and analyze data. Mean \pm standard deviation (SD) of post-intervention from groups were used to calculate the mean difference (MD) and the 95% confidence interval (CI) and weight between groups by using a random-effect model due to the large diversity of intervention. $P < 0.05$ was considered to be statistically significant. If studies reported pre mean \pm SD and change mean \pm SD, values were used to calculate post mean \pm SD according to the Cochrane handbook.²⁴ If studies reported the standard error of mean or the 95% CI, values were converted into SD. If two or more experimental groups were reported, values were combined. Subgroup analyses were not conducted because studies with breathing exercise or IMT did not satisfy the included criteria for meta-analysis.

We also assessed heterogeneity by χ^2 test with $P < 0.10$ indicating statistical significance, and I^2 test with $I^2 > 50\%$ indicating moderate-to-high heterogeneity.²⁵ Sensitivity analysis

was performed by excluding one study each time sequentially and comparing the results by using a random-effect model and a fixed-effect model. We constructed a funnel plot and used Egger's tests to assess publication bias in Stata 14.0, with $P < 0.1$ indicating significant bias. Quality of evidence was assessed based on the grading of recommendations assessment, development, and evaluation (GRADE) system.²⁶

RESULTS

There were 6463 records identified through 3 databases by searching and 11 additional records by scanning the reference lists of studies and relevant systematic reviews. After duplicates were removed, there were 4656 records, of which 4571 records were excluded by screening the titles or/and abstracts. The full texts of the remaining 85 articles were assessed, of which 67 articles were excluded owing to inappropriate population, intervention, outcome, study design, or other reasons (on-going research, system review, publication language, etc.). Finally, 18 articles fulfilled the inclusion criteria, of which 11 articles reporting PEF(%pred), FEV1(%pred), or FVC(%pred) were included for meta-analysis. The results of study selection are summarized in a PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram (Fig. 1).

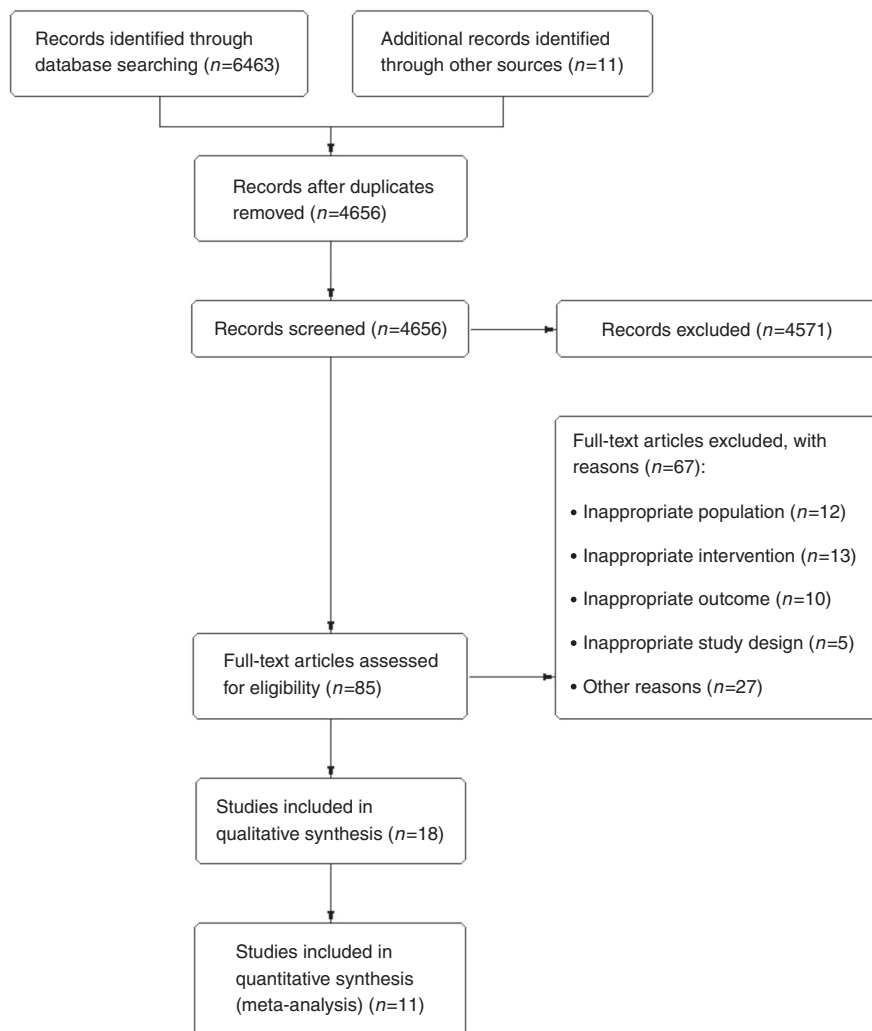


Fig. 1 Results of study selection summarized in a PRISMA flow diagram. PRISMA preferred reporting items for systematic reviews and meta-analyses.

Study characteristics of the included studies

The characteristics of the included studies are summarized in Table 2. There were 18 studies involving 711 participants that completed the trials, of which 16 studies involving 631 participants performed physical training,^{27–42} 1 study involving 30 participants performed breathing exercise,⁴³ and 1 study involving 50 participants performed breathing exercise plus IMT.⁴⁴ Studies were published between 1990 and 2018, of which 9 studies were between 2000 and 2009,^{28,30,31,34,37,38,40,41,44} and 6 studies were between 2010 and 2018,^{27,29,33,36,42,43} and the remaining 3 studies were before 2000.^{32,35,39} The studies were conducted in 12 countries, and most of them were in Europe and America. The age range (mean) of participants overall was 7–18 (11.71) years, in studies with breathing exercise or IMT it was 8–17 (12.59) years, and in studies with physical training it was 7–18 (10.83) years according to the existing data.

Risk of bias in the included studies

Risk of bias for each included study is summarized in Fig. 2, and each item presented as percentages across all included studies is presented in Fig. 3.

Allocation. All included studies were randomly allocated, but only five studies had described a well-randomized method and were judged as low risk of bias.^{27,29,34,41,43} Two studies reported a non-random component in the sequence generation process and were judged as high risk.^{35,44} Only one study supplied details regarding allocation concealment and was judged as low risk.²⁷ Two studies were allocated based on alternation or a random number and were judged as high risk.^{35,41} The remaining studies were classified as unclear risk of bias for allocation concealment.

Blinding. The studies were all judged as high risk because it was impossible to avoid performance bias involving physical therapy. One study specified blinding of outcome assessment and was judged as low risk.²⁷ The other studies were judged as an unclear risk of detection bias.

Incomplete outcome data. Six studies with a high rate of withdrawal were judged as high risk.^{27,31,33,34,41,42} Two studies specified withdrawals, but we judged them as low risk because missing outcome data were unlikely to be related to true outcomes.^{43,44} The other ten studies were judged as low risks.

Selective reporting. Although the study protocols of the included studies were not available, outcomes listed in the “Methods” section were all reported. Therefore, we judged them as low risk.

Other potential sources of bias. Three studies reported a statistically significant difference at baseline between groups and were judged as high risk.^{35,42,43} The remaining studies were judged as an unclear risk because there was no enough information provided.

Types of physical therapy

The summary of interventions is shown in Table 1. At least one of the three most relevant physical therapies was applied to the experimental group in 18 included studies. One study was conducted with breathing exercise for 12 weeks, with two 20-min sessions per week.⁴³ One study was conducted with breathing exercise plus IMT for 7 consecutive weeks, with two 50-min sessions per week.⁴⁴ The remaining 16 studies were conducted with physical training and variety modes were used, including walking, running, swimming, cycling, crawling, basketball, football, Tai Chi, and a combination of training.^{27–42} The duration ranged from 5 weeks to 1 year except during school holidays. Most of the studies had 2 sessions or 3 sessions per

week,^{27,28,30,31,33–42} except 2 studies that had 1 session per week.^{29,32} Each session lasted from 20 to 90 min, and most were 40–60 min per session.^{27–36,40–42}

Outcome measures and findings

In each included study, the effects of physical therapy in the experimental group were compared with no physical therapy in the control group. Across the 18 studies included in the qualitative synthesis, six outcomes related to lung functions were assessed in percent predicted values (%pred) or absolute values, including FEV1,^{27–32,34–44} FVC,^{27–30,36,38–42} PEF,^{28–30,33,38,40,41,43,44} FEV1/FVC,^{28,29,31,40,42} FEF 50%,⁴⁰ and FEF 25–75%.^{31,34,40–42} In this review, those reporting outcomes with FEV1(%pred), FVC(%pred), and PEF(%pred) were included in quantitative synthesis.

Forced expiratory volume in the first second. FEV1 was assessed in 16 studies, with 13 studies^{27–29,31,32,34,36–38,40–43} reporting in % pred and 7 studies^{30,35,37–39,41,42} reporting in absolute values. Six of those studies reported a significant improvement in FEV1.^{27,30,35,36,40,42}

Meta-analysis: Of those studies reporting with %pred, 11 studies were included in the meta-analysis.^{27–29,31,32,34,36–38,40,41} Two studies were excluded because there was a significant difference in lung function at baseline between groups.^{42,43} The included studies were all conducted with physical training.

The corresponding forest plot is shown in Fig. 4. There was no statistically significant difference in FEV1(%pred) of post-intervention between two groups (MD, 1.77; 95% CI, –0.76 to 4.30; $P = 0.17$). The heterogeneity was acceptable ($I^2 = 32\%$).

Forced vital capacity. FVC was the second most outcome measured in 10 studies, with 7 studies^{27–29,36,40–42} reporting in %pred and 5 studies^{30,38,39,41,42} reporting in absolute values. Five of those studies reported a significant improvement in FVC.^{27,29,30,36,42}

Meta-analysis: Of those studies reporting with %pred, six studies were included in the meta-analysis.^{27–29,36,40,41} One study was excluded because there was a significant difference in lung function at baseline between two groups.⁴² The included studies were all conducted with physical training.

The corresponding forest plot is shown in Fig. 4. There was a statistically significant difference in FVC(%pred) of post-intervention between two groups (MD, 4.56; 95% CI, 1.33–7.79; $P = 0.006$). The heterogeneity was not detected ($I^2 = 0\%$).

Peak expiratory flow. PEF was evaluated in 9 studies, with 4 studies^{28,29,41,43} reporting in %pred and 6 studies^{30,33,38,40,41,44} reporting in absolute values. Four of those studies reported a significant improvement in PEF.^{30,33,40,44}

Meta-analysis: Of those studies reporting with %pred, three studies were included in the meta-analysis.^{28,29,41} One study was excluded because there was a significant difference in lung function at baseline between two groups.⁴³ The included studies were all conducted with physical training.

The corresponding forest plot is shown in Fig. 4. There was no statistically significant difference in PEF(%pred) of post-intervention between two groups (MD, 0.78; 95% CI, –5.24 to 6.97; $P = 0.78$). The heterogeneity was not detected ($I^2 = 0\%$).

Sensitivity analysis

We performed the sensitivity analysis by excluding one study each time sequentially and found that the pooled results were not changed significantly under any circumstances in a random-effect model or in a fixed-effect model, suggesting the stability of our meta-analysis. In addition, we found the study written by

Table 2. Characteristic summary of the included studies.

Author	Year	Country	Number completed	Age range (mean, years)	Interventions	Durations	Outcomes
Breathing exercise or IMT							
Bignall et al. ⁴³	2015	USA	30	12–17 (15.47)	Breathing exercise	Two 20-min sessions per week for 12 weeks	FEV1(%pred), PEF(%pred)
Lima et al. ⁴⁴	2008	Brazil	50	8–12 (9.7)	Inspiratory muscle training and breathing exercise	Two 50-min sessions per week for 7 consecutive weeks	PEF
Physical training							
Abdelbasset et al. ²⁷	2018	Egypt	38	8–12 (9.94)	Physical training (walking, etc.)	Three 40-min sessions per week for 10 weeks	FEV1(%pred), FVC(%pred)
Basaran et al. ²⁸	2006	Turkey	15	7–15 (10.4)	Physical training (basketball, etc.)	Three sessions (55–60 min) per week for 8 weeks	FEV1(%pred), FVC(%pred), FEV1/FVC, PEF(%pred)
Carew and Cox ²⁹	2018	Ireland	41	9–16 (12.9)	Physical training (swimming, football, basketball)	One 40-min session per week for 6 weeks	FEV1(%pred), FVC(%pred), FEV1/FVC(%pred), PEF(%pred)
Chang et al. ³⁰	2008	China	30	— (9.9)	Physical training (Tai Chi Chuan)	Three 40-min sessions per week for 12 weeks	FEV1, FVC, PEF
Counil et al. ³¹	2003	France	16	10–16 (13)	Physical training (cycling)	Three 45-min sessions per week for 6 weeks	FEV1(%pred), FEV1/FVC, FEF 25–75% (%pred)
Edenbrandt et al. ³²	1990	Sweden	41	7–13 (—)	Physical training (relay racing, swimming, etc.)	One session (20–25 min) per week for 1 year except during school holidays	FEV1(%pred)
Latorre-Roman et al. ³³	2014	Spain	105	— (11.53)	Physical training (walking, running, etc.)	Three 60-min sessions per week for 12 weeks	PEF
Moreira et al. ³⁴	2008	Finland	34	— (12.7)	Physical training	Two 50-min sessions per week for 12 weeks	FEV1(%pred), FEF 25–75% (%pred)
Neder et al. ³⁵	1999	Brazil	42	8–16 (12.4)	Physical training (cycling)	Three sessions (45–55 min) a week for 8 weeks	FEV1
Onur et al. ³⁶	2011	Turkey	30	8–13 (9.8)	Physical training (cycling)	Two 60-min sessions per week for 8 weeks	FEV1(%pred), FVC(%pred)
Sliva et al. ³⁷	2006	Brazil	69	8–11 (9.4)	Physical training (running, swimming, etc.)	Two 90-min sessions per week for 16 weeks	FEV1, FEV1(%pred)
Van et al. ³⁸	2001	Netherlands	47	8–13 (10.6)	Physical training	Twice a week (1 h) in a gymnasium and once 20-min exercise session a week at home for 12 weeks	FEV1, FEV1(%pred), FVC, PEF
Varray et al. ³⁹	1991	France	14	9–13 (11.4)	Physical training (swimming, running, crawling, etc.)	Two sessions per week for 24 weeks	FEV1, FVC
Wang and Hung ⁴⁰	2009	China	30	7–12 (10)	Physical training (swimming)	Three 50-min sessions per week for 6 weeks	FEV1(%pred), FVC(%pred), FEV1/FVC, PEF, FEF 50% (%pred), FEF 25–75% (%pred)
Weisgerber et al. ⁴¹	2003	USA	18	7–14 (7.9)	Physical training (swimming)	Two 45-min sessions per week for 5 or 6 weeks	FEV1, FEV1(%pred), FVC, FVC(%pred), PEF, PEF(%pred), FEF 25–75% (%pred)
Wicher et al. ⁴²	2010	Brazil	61	7–18 (10.6)	Physical training (swimming)	Two 60-min sessions per week for 12 weeks	FEV1, FEV1(%pred), FVC, FVC(%pred), FEV1/FVC, FEV1/FVC(%pred), FEF 25–75% (%pred)

FEV1 forced expiratory volume in the first second, PEF peak expiratory flow, FVC forced vital capacity, FEF forced expiratory flow at 50% of forced vital capacity, FEF 25–75% forced expiratory flow between 25% and 75% of forced vital capacity, %pred in percent predicted values.

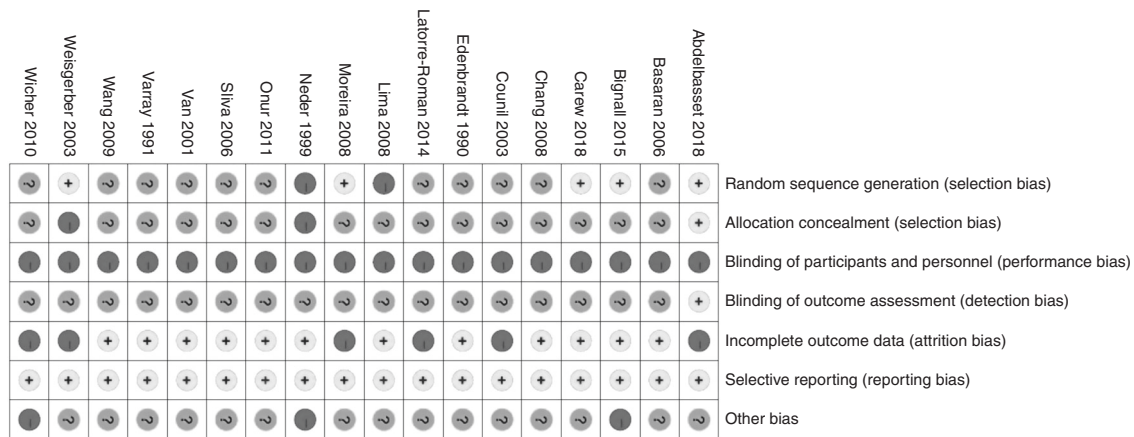


Fig. 2 Risk of bias summary. Review authors' judgments about each risk of bias item for each included study.

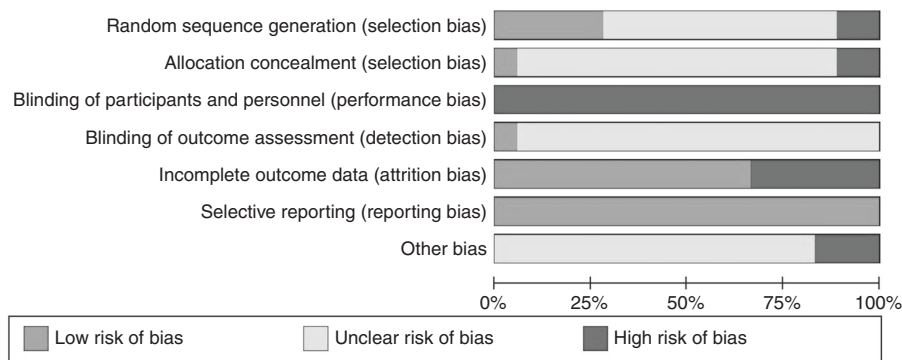


Fig. 3 Risk of bias graph. Review authors' judgments about each risk of bias item presented as percentages across all included studies.

Abdelbasset in 2018²⁷ was the only source of heterogeneity in Fig. 4a.

Reporting bias

We constructed a funnel plot to evaluate the reporting bias and the shape presented symmetry basically (Fig. 5). Egger's test was further conducted and the result indicated that there was no significant reporting bias ($P = 0.797$; Fig. 6, Table 3).

Quality of evidence

Quality of evidence based on the GRADE system is summarized in Table 4. Owing to the high risk of performance bias across all included studies, we downgraded one point on the risk of bias item. The result showed a moderate level of the evidence's quality in all outcomes.

DISCUSSION

The aim of this study was to investigate the effects of physical therapy on lung function in children with asthma. We included 18 studies in the systematic review, of which 16 were related to physical training and 2 were related to breathing exercise or IMT. In the meta-analysis, 11 of those related to physical training were included. No breathing exercise or IMT studies were included in the quantitative synthesis. Compared with the control groups, our results showed a significantly improved FVC(%pred) in groups with physical training (MD, 4.56; 95% CI, 1.33 to 7.79). No statistically significant difference was detected on FEV1(%pred) (MD, 1.77; 95% CI, -0.76 to 4.30) and PEF(%pred) (MD, 0.78; 95% CI, -5.24 to 6.97).

In the management of asthma, physical therapy is now considered as a treatment in addition to medications and is

recommended in the GINA guideline.² According to the guideline, physical training is encouraged for its general health benefits, and breathing exercise and IMT may be useful for asthma.² However, whether and how these physical therapies benefit patients with asthma are not totally certain, especially in children. Besides, the results reported in different reviews are controversial. For example, one previous systematic review reported that physical training did not improve lung function in children with asthma by using FEV1(%pred) for meta-analysis,⁴⁵ while another review found swimming improved FEV1(%pred).²⁰

Our study involved the three most relevant physical therapies for asthma and conducted the meta-analysis by using FEV1(%pred), FVC(%pred), and PEF(%pred), which are the most commonly used parameters to evaluate lung function in clinical work. More importantly, the %pred could significantly reduce the heterogeneity among different trials and the pooled results became more comparable because lung function is related to participant's characteristics such as region, race, age, and sex.

A key finding of this study is that physical training significantly improved FVC(%pred) in children with asthma. It provides statistical evidence to encourage children with asthma to take part in physical training. The possible reason why effects were found only for FVC(%pred) but not for FEV1(%pred) and PEF(%pred) is described below. The pathophysiology of asthma is complex and characterized by airway inflammation and bronchial hyperresponsiveness. It leads to not only the airway obstruction but also to the diminishing of the pulmonary elastic recoil. FVC(%pred) is a parameter that mainly reflects the pulmonary capacity, while FEV1(%pred) and PEF(%pred) are often used to evaluate the airway patency. Physical training can significantly improve pulmonary elastic recoil, resulting in an increase of pulmonary capacity. But the effects on reducing airway inflammation and

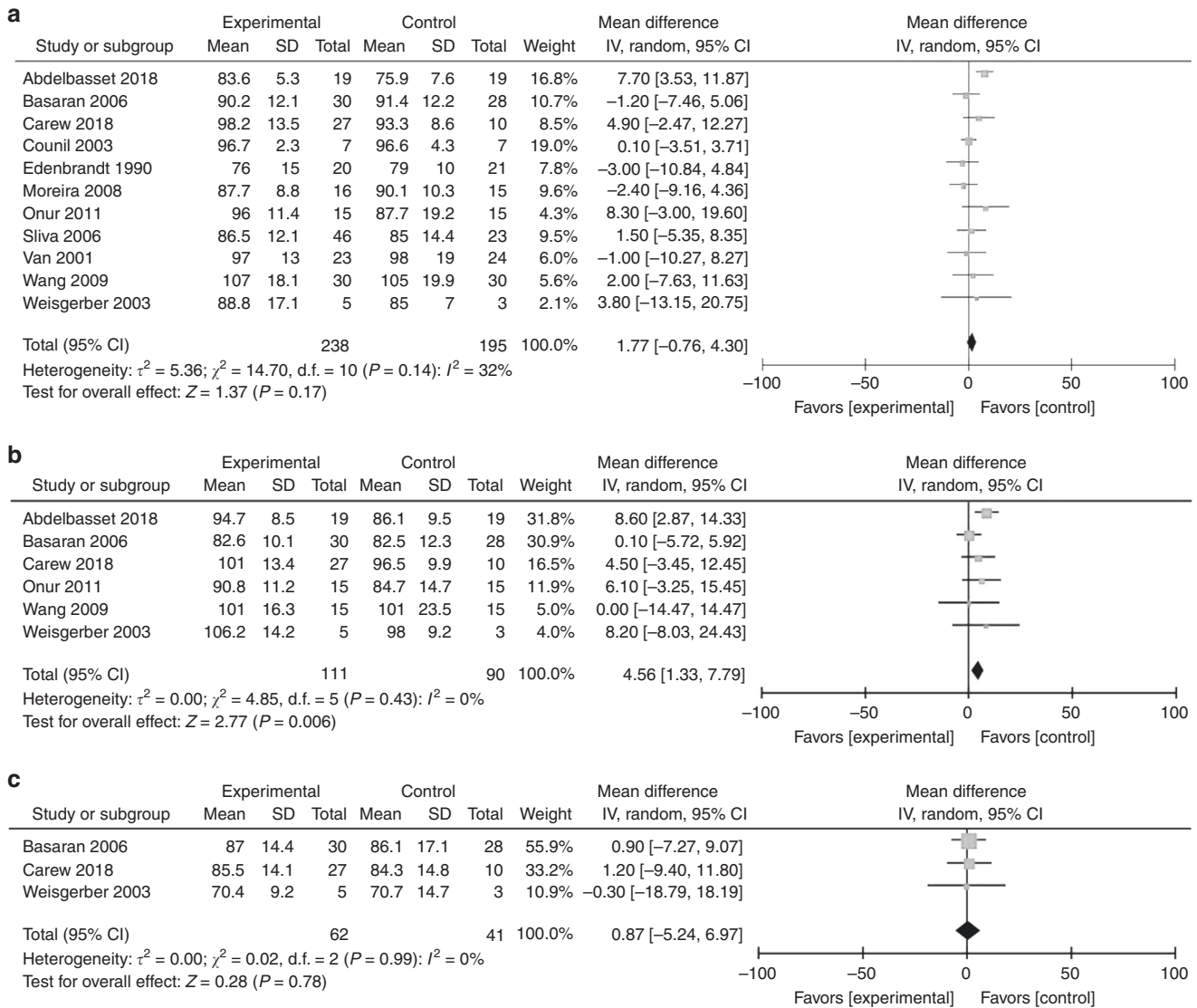


Fig. 4 Forest plot of comparison. Physical training versus control: **a** outcome: FEV1(%pred); **b** outcome: FVC(%pred); **c** outcome: PEF(%pred). FEV1(%pred) forced expiratory volume in the first second in percent predicted values, FVC(%pred) forced vital capacity in percent predicted values, PEF(%pred) peak expiratory flow in percent predicted values, SD standard deviation, CI confidence interval, IV inverse variance.

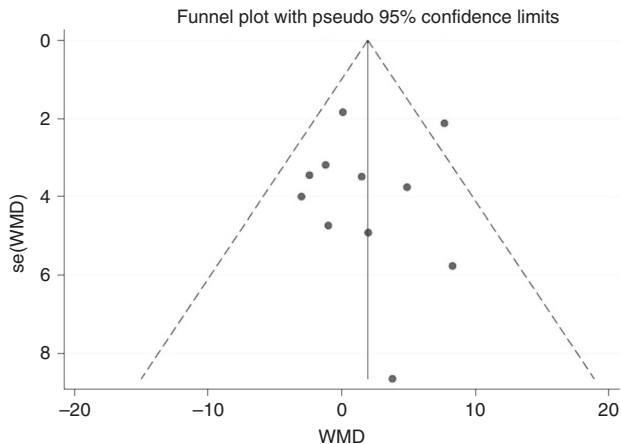


Fig. 5 Funnel plot with pseudo 95% confidence limits. WMD weighted mean difference, SE standard error.

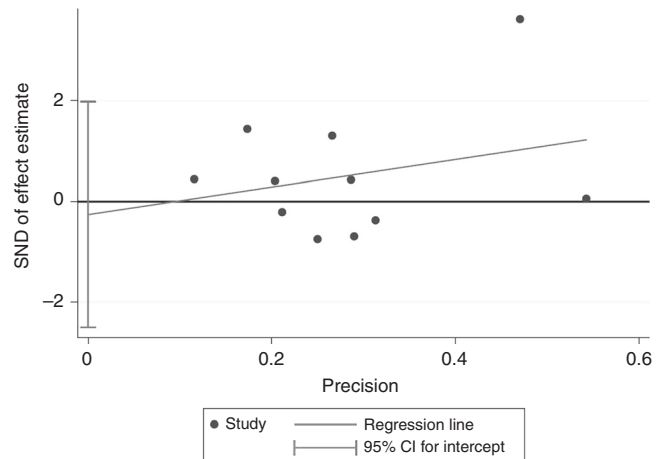


Fig. 6 Result of Egger's test. SND standard normal deviate, CI confidence interval.

Table 3. Result of Egger's test.

Standard efficiency	Coefficient	Standard error	t value	P value	95% confidence intervals
Slope	2.73759	3.219623	0.85	0.417	-4.545704, 10.02088
Bias	-0.2621734	0.9911181	-0.26	0.797	-2.504238, 1.979892

Table 4. Quality of evidence based on the GRADE system.

Physical training compared with no physical training for children with asthma

Patient or population: Children with asthma
Settings: Nine countries
Intervention: Physical training
Comparison: No physical training

Outcomes	Illustrative comparative risks ^a (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk No physical training	Corresponding risk Physical training				
FEV1(%pred)	The mean FEV1(%pred) ranged across control groups from 75.9 to 105	The mean FEV1(%pred) in the intervention groups was 1.77 higher (0.76 lower to 4.3 higher)	—	433 (11 studies)	⊕⊕⊕⊕ moderate ^b	I ² = 32%
FVC(%pred)	The mean FVC(%pred) ranged across control groups from 82.5 to 101	The mean FVC(%pred) in the intervention groups was 4.56 higher (1.33 to 7.79 higher)	—	201 (6 studies)	⊕⊕⊕⊕ moderate ^b	I ² = 0%
PEF(%pred)	The mean PEF(%pred) ranged across control groups from 70.7 to 86.1	The mean PEF(%pred) in the intervention groups was 0.87 higher (5.24 lower to 6.97 higher)	—	103 (3 studies)	⊕⊕⊕⊕ moderate ^b	I ² = 0%

FEV1(%pred) forced expiratory volume in the first second in percent predicted values, FVC(%pred) forced vital capacity in percent predicted values, PEF(%pred) peak expiratory flow in percent predicted values, CI confidence interval, GRADE grading of recommendations assessment, development, and evaluation.
^aThe basis for the assumed risk (e.g., the median control group risk across studies) is provided below. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
 GRADE Working Group grades of evidence.
 High quality: Further research is very unlikely to change our confidence in the estimate of effect.
 Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
 Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
 Very low quality: We are very uncertain about the estimate.
^bHigh risk of performance bias.

bronchial hyperresponsiveness are probably not obvious. Thus the effects for FEV1(%pred) and PEF(%pred) were not found. In this study, we could not compare the effects of the three types of physical therapy in quantity and determine which one was more helpful due to the limited studies involving breathing exercise or IMT. Further RCTs involving breathing exercise or IMT are needed.

Eleven studies involving physical training were included in the meta-analysis. Even though the statistical heterogeneity was acceptable or not detected, methodological diversity still existed because it was not possible to blind the participants involving physical training. Besides, there was clinical diversity with respect to the intervention designs. More specifically, the training modes ranged from a single mode such as swimming or cycling to a complex mode including a variety of training, the duration range from 5 weeks to 1 year except during school holidays, the length of each session range from 20 to 60 min, and the frequency range from 1 to 3 sessions per week.

Furthermore, we found the study written by Abdelbasset in 2018²⁷ was the only source of heterogeneity in Fig. 4a during the sensitivity analysis. We reassessed this study and found that the pulmonary functions in both the experimental and control groups reported significant changes. It was likely that all participants were instructed to receive asthma medications regularly and home breathing exercise was recommended when they were receiving aerobic exercise training.

In summary, our study demonstrates the effects of physical training on lung function in children with asthma. But more research on the mode, the duration, and the frequency of physical training is needed. Despite the physical health, the effects

of physical training on psychosocial health should not be neglected.

LIMITATIONS

There are some limitations to our study. First, all included studies have a high risk of performance bias because it was not possible to blind the participants involving physical training. Second, clinical heterogeneity exists due to the diversity of the intervention designs. Third, the outcome measures in this meta-analysis are too limited. It would be better if we could look at more outcome measures that could reflect the patient's respiratory condition more, such as respiratory muscle strength and dyspnea.

CONCLUSION

This meta-analysis demonstrates that physical training significantly improved FVC(%pred) in children with asthma. This finding may support the therapy of physical training in asthmatic children. But further research involving the physical training mode, the duration, and the frequency is needed. Besides, more trials on the effects of breathing exercise and IMT in children with asthma should be conducted in the future.

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AUTHOR CONTRIBUTIONS

Q.W. put forward the concept of this study. W.Z., W.Y., and L.L. were engaged in the study search, study selection, data extraction, risk of bias assessment, and data analysis. H.L. was responsible for project administration. W.Z. drafted the preliminary version of this manuscript. All authors critically reviewed, revised, and approved this final manuscript.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

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